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UMI
VERIFICATION OF RADIATION EXPOSURES IN A
CASE-CONTROL STUDY OF THYROID CANCER

by

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A thesis submitted in conformity with the requirements
for the degree of Master of Science
Graduate Department of Community Health
University of Toronto

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ABSTRACT

Self-reported medical radiation exposures of subjects in a case-control study of thyroid cancer were compared with medical records. Records were available for 52.4% of self-reports. Determinants of record availability included medical record source contacted, years elapsed since exposure, education and sex of respondent.

The proportion of agreement between self-reported exposures and available medical records was 83.9%. Record source was a determinant of agreement, with agreement increased if physicians' records were accessed.

The estimated odds of thyroid cancer associated with prior head and neck radiation, as determined by self-reports, medical records, and medically-verified data, were similar, suggesting that self-reports and their corresponding medical records produced comparable risk estimates.

Results suggest that self-reported exposures, even from long-ago, are quite accurate and have the advantage of being more readily available than medical records. However, this study could not adequately evaluate the extent of under-reporting and thus, the completeness of self-reported exposures.
ACKNOWLEDGEMENTS

The Holocaust taught my father many lessons, among them that an education is one of the few things of value that can never be taken away.

E.M. Roston, Ph.D.
1911 - 1994

With many thanks to:

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1. INTRODUCTION

1.1. MEDICAL RADIATION EXPOSURE AND THYROID CANCER

Ten years after Roentgen's discovery in 1895, indiscriminate use of X-rays was widespread as the treatment of choice for a variety of benign conditions of the head and neck, and only years later was a link made between prior irradiation and subsequent development of thyroid malignancies. Early follow-up studies of children exposed to therapeutic irradiation of the head and neck were limited by small numbers, short follow-up times, and poor response rates. Treatments were often administered in doctors' offices, where the variability in record keeping and the passage of time undoubtedly contributed to the early difficulty in ascertaining risk. Duffy and Fitzgerald (1) were the first to suggest a possible link between thyroid cancer and previous medical irradiation to the head and neck. Their report of a case series of 28 children with thyroid cancer published in 1950 led to the study of several medical cohorts exposed to therapeutic radiation in childhood for a variety of benign conditions of the head and neck.

Following the decline of radiotherapy treatment for benign conditions in the 1950’s, Mehta and colleagues (2) suggested that “radiation-induced thyroid neoplasms may be a vanishing problem, probably becoming statistically insignificant in the 1990’s”. However, increasing survival of cancer patients has refocused attention on thyroid cancer following therapeutic radiation for other malignancies. Problems inherent in the study of second cancers include a potential predisposition to cancer which may influence the development of subsequent tumours. Poor prognoses associated with certain cancers may result in a selection bias. Unravelling the effects of treatment age and radiation dose in young children may not be feasible. Exposure to chemotherapeutic agents may confound results. Finally, improvements in childhood cancer survival are recent and sufficient time for follow-up may not have elapsed.

The carcinogenic potential of I$^{131}$ on the thyroid has also been examined, but despite early animal studies demonstrating its effect and environmental studies of radiiodine exposure from nuclear fallout in Japan, the Marshall Islands, and Chernobyl confirming this potential in humans, no
increased risk of thyroid cancer has been observed in medically exposed cohorts. Negative findings may be due to lower doses than experienced with nuclear fallout, absence of contamination with the more volatile and radiogenic radioiodides found in environmental exposures, shorter follow-ups of medically exposed populations, selection bias in the cohort, or lack of suitable controls. Nevertheless, the potential carcinogenic effect of $^{131}$I remains a concern because of continuing medical and occupational exposures.

Findings from selected studies examining medical radiation exposure and thyroid cancer are summarized in Table 1. Despite some limitations, certain observations have been noted repeatedly. Cohort studies have indicated that the minimum induction time for radiation-induced thyroid cancer is at least 5 years following exposure. Age at exposure has been shown to be inversely proportional to risk, being highest among those exposed at youngest ages (< 10 years), and was particularly high in one study among parous women who had been exposed at young ages (3). The predominant pathologic types associated with radiation-induced thyroid cancer are papillary and mixed papillary-follicular carcinomas (4,5,6,7,8). Between adolescence and menopause, women are 3 times more likely than men to develop thyroid cancer, although pre-adolescent and post-menopausal ratios of females to males are lower (8). A family history of thyroid cancer has been frequently described by patients (3). Age > 25 years at first live birth and < 13 years of education, although the latter may have been confounded with other factors, were significant effect modifiers associated with increased thyroid cancer risk in an extensive cohort study (9).
<table>
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<tr>
<th>HISTOLOGY</th>
<th>PERIOD</th>
<th>MEAN VRS</th>
<th>EXP</th>
<th>SIZE</th>
<th>TYPE</th>
<th>STUDY</th>
<th>AUTHOR</th>
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<tr>
<td>mixed papillary</td>
<td>18.2</td>
<td>37 yrs</td>
<td>5 yrs</td>
<td>&gt; 1 year</td>
<td>cohort: 103</td>
<td>exp: 2.657</td>
<td>Hemphillman</td>
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<td>papillary</td>
<td>4.3</td>
<td>none</td>
<td>80 yrs</td>
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<td>control: 394</td>
<td>exp: 1.484</td>
<td>(5) Pfeifer</td>
</tr>
<tr>
<td>papillary</td>
<td>18.8</td>
<td>mixed papillary, 29 yrs, 1 year</td>
<td>24 yrs</td>
<td>&gt; 18 yrs</td>
<td>cohort: 1.199</td>
<td>exp: 1.590</td>
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<tr>
<td>papillary</td>
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<td>mixed papillary, 35 yrs, 2 yrs</td>
<td>exp: 1.875</td>
<td>&lt; 18 yrs</td>
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<td>exp: 1.50</td>
<td>(7) Tucker</td>
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<tr>
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<td>13</td>
<td>35 yrs, 2 yrs</td>
<td>1250 yrs</td>
<td>&gt; 18 yrs</td>
<td>cohort: 118</td>
<td>exp: 1.50</td>
<td>(3) Ron</td>
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<tr>
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<td>2.7</td>
<td>&lt; 18 yrs</td>
<td>exp: 1.50</td>
<td>&lt; 18 yrs</td>
<td>cohort: 118</td>
<td>exp: 1.50</td>
<td>(3) Ron</td>
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<td>exp: 1.50</td>
<td>&lt; 18 yrs</td>
<td>cohort: 118</td>
<td>exp: 1.50</td>
<td>(3) Ron</td>
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Table 1: Summary of Selected Thyroid Cancer Studies
1.2 CCRERG THYROID CANCER STUDY

Although thyroid cancer accounts for only 1 per cent of all new cases of cancer (excluding non-melanotic skin cancer) and only 0.2 per cent of cancer deaths in Canada (10), there is evidence that its incidence is increasing (11). The Canadian Cancer Registries Epidemiological Research Group (CCRERG) conducted a case-control study between January 1, 1986 and June 30, 1988, in Ontario and 8 other provinces (with the exception of Prince Edward Island) to assess possible risk factors for thyroid cancer, including exposure to diagnostic and therapeutic radiation. Self-administered questionnaires were used to record medical radiation exposures of both cases and controls. Verification of self-reported radiation exposures was undertaken by accessing medical records. Data obtained from the verification of exposures reported by Ontario subjects in the CCRERG study form the basis of this thesis.

The author did not participate in data collection, but developed a coding system that allowed for comparisons of self-reported exposures and exposures noted in medical records, reported procedure year and medical record procedure year, years elapsed between receipt of questionnaire and reported procedure year, and years elapsed between verification year and procedure year noted in medical records. Sociodemographic information required for analysis was coded from the subject questionnaire. All analyses were conducted by the author.

1.3 ASSURING DATA QUALITY

Collecting information retrospectively about medical events and procedures is problematic regardless of the data source or method followed. Case-control designs often rely on questionnaires to collect information on retrospective exposures. The accuracy of questionnaire-derived data is difficult to assess and confirmation is often dependent on a source external to the respondent, such as the medical record, as an imperfect "gold standard". The accuracy of medical records and subjects' self-reports are influenced by many factors, leaving both sources subject to variation from the actual events which they are intended to reflect.
In the 1963 Tristate Leukemia Survey, Graham et al (12) attempted to verify data on radiation exposure and illness experience provided by cases and controls during interviews, using hospitals', physicians', and dentists' records. They found that 80% of the x-rays noted in physicians' and dentists' records, and 67% of those noted in hospital records had not been mentioned during interviews. In many cases, respondents knew that they had been x-rayed, but not how many times. Their records revealed that they had received a large number of diagnostic x-rays. Furthermore, an even larger amount of irradiation was revealed in records where none was mentioned by the respondent. Conversely, a small number of x-rays was mentioned by subjects which could not be verified in medical records. Twenty-nine percent of fluoroscopies given in physicians' offices and 41% of those given in hospitals were not mentioned by the respondent, and a substantial proportion of those reported by respondents could not be found in records. Of particular significance in this study, was the finding that the number of x-rays discovered in medical records alone was such a large part of a respondent's whole radiation experience that reliance only on interview data could be completely invalid.

These findings emphasize the problems of recall in retrospective studies. However, a distinction must be made between recall which is not accurate and that which is biased. Accurate recall can be described as complete and correct reporting of both exposure and absence of exposure. Inaccurate recall, due to a memory lapse that is equally distributed in both case and control groups, can be considered a non-differential misclassification bias, whose effect will be to reduce the risk estimate towards the null (13). Recall accuracy may be influenced by demographic factors such as age, gender, education, or socioeconomic status, although no consistent relationship between recall accuracy and sociodemographic factors has been found (13). Accurate recall may also be compromised by the time since the event of interest, the complexity of the event to be recalled, and its significance to the respondent (14). Self-reported events also tend to be distorted in a socially desirable direction and behaviours which are associated with a social stigma or are perceived to be personally threatening are often under-reported (13).

Biased or differential recall suggests systematic reporting inaccuracy in one of the study groups. It has been described as an "embroidery" of the respondent's personal history (15). The effect of
biased recall will be to either magnify or reduce the risk estimate, depending on the direction of misclassification. Factors which have been shown to bias recall include case versus control status, current disease status, self-selection or motivation, and an awareness of, or belief in, certain etiologic hypotheses which can lead to an overzealous recall of exposure.

Unbiased records of exposure could rule out recall bias, and if available would be a less expensive and more accurate source of information than questioning respondents (15). Unfortunately such records rarely exist, and study participants continue to be prime data sources.

Apparent over-reporting by subjects may also be an indication of incomplete medical records rather than an incorrect self-reported medical history (14). Thus a positive self-report not substantiated in the medical record cannot necessarily be classified as incorrect because events may not always be recorded (16). Investigators cannot assume that the absence of positive information in the medical record can be treated as a negative response in the calculation of risk estimates in epidemiologic studies (17). Conclusions drawn from a comparison of a negative self-report and a positive medical record report are more conclusive. Some studies compare self-reported data with medical record information only if a respondent reports the exposure of interest. If a review of the medical records is restricted only to respondents who report being exposed, the measure of agreement will not assess false negatives. Similarly, when interviews are conducted only among subjects whose medical records contain documented evidence of exposure, the measure of agreement does not incorporate false positives (18).
2. REVIEW OF THE LITERATURE

2.1 FACTORS AFFECTING DATA QUALITY

Although the impact of sociodemographic (age, sex, education, race, marital status) and exposure-related characteristics (time of exposure, complexity/significance of event) on recall accuracy has been evaluated in several studies. Few have addressed the impact of these variables on the recall accuracy of medical radiation exposures. The ensuing review therefore encompasses a broader range of studies, confined to sociodemographic and exposure-related characteristics available in the CCERG study (age, sex, education, status, time of exposure).

2.2. SUBJECT AND EXPOSURE FACTORS

2.2.1. Sociodemographic Characteristics

When interviewing elderly persons regarding past events, recall may be adversely affected by age-linked declines in memory retrieval (19), and memory impairment may be almost inevitable among patients in poor health, particularly with diseases such as Alzheimer's (20).

A comparison of self-reported and physician reported medical history in a case-control study of cataract patients (14), found that age, sex, education and race had no major effect on the accuracy of self-reported medical history. However, age was described only as less than or more than 65 years, and in a group of cataract patients, the age variability may have been too small to observe possible differences.

When Paganini-Hill and Ross (21) examined the reliability of recall of reproductive history and other health-related information among white, affluent, health-conscious women living in a retirement community, they found excellent agreement between interview and medical record data. The women enrolled in this study had entered the retirement community and its associated comprehensive medical facilities after age 60. The study has been criticized because it may be only
a reflection of women's recall of their reproductive history recorded when entering the retirement community and their recall of the same information at entry into this study. Nevertheless, the study suggests that in a highly motivated group of elderly women, recall need not be compromised by age.

Linet et al (22) compared previous medical conditions and surgery reported in interviews of chronic lymphocytic leukemia patients with their medical records, and found that agreement between the two was generally higher for males than females and for whites than blacks. No consistent patterns were noted by age. Subjects from referral hospitals, which were generally university-affiliated institutions, consistently demonstrated good to excellent agreement between the two data sources compared with the poor to fair agreement for subjects from community hospitals. However, patients from referral hospitals were somewhat younger, better educated, and diagnosed with a more advanced stage of CLL than those from community hospitals, and were possibly more aware of, or interested in, their previous history, suggesting that current disease status may also play a role in recall ability.

In assessing the agreement between interview information and physician records on the history of menopausal estrogen use, Goodman (23) found that agreement between both sources was influenced by certain sociodemographic characteristics. The correlation between education and agreement was non-significant, but was significant for home-owners, suggesting that agreement was associated with socioeconomic status. The agreement was much lower for older women, since they had longer histories of estrogen use and thus more opportunity for inaccuracies in recall, although the agreement was better for those who were homeowners.

A recent study comparing self-reported hospital admissions with a computerized record of admissions (24) found that age, sex, and social class status did not significantly influence recall ability.

Findings from these studies are summarized in Table 2.
The lack of a consistent relationship between the accuracy of recall and sociodemographic factors may reflect differences in the study populations, the questions being asked, or the nature of the exposure. Different factors were considered in each study, and variability between these factors was often limited. Several studies were restricted to females. Further, small sample size in some studies may have lessened the power of the study to detect differences.

Table 2: Effect of Sociodemographic Factors on Recall

(+ = significant effect; - = no effect; n/a = not applicable)

<table>
<thead>
<tr>
<th>STUDY NO.</th>
<th>AGE</th>
<th>SEX</th>
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<td>14</td>
<td>-</td>
<td>M/F</td>
<td>-</td>
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<td>-</td>
<td>F</td>
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<tr>
<td>24</td>
<td>-</td>
<td>M/F</td>
<td>n/a</td>
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2.2.2. Case versus Control Status

Differential recall, as compared to non-differential recall, refers to reporting inaccuracies not evenly distributed among groups but involving one study group versus another. Cases may be more aware of, and sensitized to their previous medical history than controls. They may have been asked repeatedly about past exposures during medical examinations, in contrast to controls who may have had less frequent medical examinations and fewer opportunities to explore past exposures. Cases may also be more motivated to explore previous exposures than controls, particularly those which they perceive to be etiologic. For these reasons cases are suspected of providing more complete reports of their true exposure to hypothesized risk factors, thereby biasing upwards the estimate of effect (29).
Skegg (25) suggested that women with life-threatening diseases such as breast cancer may be more likely to answer questions with more care and attention than controls. They may also have been reflecting on possible etiologies of their disease. Interviewers may inadvertently introduce information bias if they are aware of the study hypothesis and question cases more thoroughly than controls. Reported family history has been shown to vary considerably depending upon whether the individual providing the information is a case or control, and the effect of this bias on estimates of risk may be significant (26).

Differential recall in case-control studies has been illustrated primarily with examples from obstetric and gynecologic epidemiology. The accuracy of self-reported exposures was assessed by Werler et al (27) by comparing interview data from new mothers with exposure information documented in obstetric records during their pregnancy. The authors expected that mothers of malformed infants would be more motivated in their search for prior exposures than mothers of unaffected infants. However, the presence and magnitude of recall bias was found to vary by exposure factor. For example, reporting accuracy of birth control after conception was much greater for mothers of malformed infants than for mothers of unaffected infants, possibly as a result of publicity surrounding the putative hazards of contraception in early pregnancy. While recall of over-the-counter drug use was reported with similar accuracy by both case and control mothers. The implication is that accuracy is affected by a complex mix of memory, emotion, and impressions of an exposure's hazards.

MacKenzie and Lippman (28) also investigated report bias in a case-control study of pregnancy outcome by comparing women's self-reports of exposures that might influence pregnancy outcome in early pregnancy and their self-reports following delivery. Their study design differed from that of Werler and colleagues who compared mothers reports to medical record data. When the two sets of responses were compared from control mothers of healthy infants, case mothers of malformed infants, and mothers of infants of intermediate health status, exposures noted in the pre-delivery questionnaire were reported less frequently in the post-delivery questionnaire. However, the changes observed in reporting were not associated with pregnancy outcome. The authors concluded that if biased reporting did occur in response to a very strong stimulus such as the birth
of a severely malformed infant, then this study design would require a very large number of pre-delivery respondents to demonstrate a case-control bias. Conversely, if the bias is so small that large sample sizes are required to demonstrate its impact, it is unlikely to interfere with the validity of most smaller-scale case-control studies.

In a study of hepatocellular adenoma, a disease associated with long and continuous oral contraceptive use, women's reported histories of oral contraceptive use were compared to physician records (29). Recall accuracy was very high despite the following two potential sources of bias: women who could not recall their physician's name and consequently may also have had difficulty recalling oral contraceptive use, were excluded from the study, which may have elevated the observed proportion of agreement. Secondly, physician's records used for comparison may have been a reflection of oral contraceptive use as recalled at an earlier date by a patient, rather than the prescribing physician's record, potentially increasing the observed proportion of agreement. Results indicated that agreement between self-reports and physician's records was better for cases than for controls. The authors suggest that better case verification may have been due in part to the nature of the disease under investigation which was associated with long and continuous oral contraceptive use. Such users may have had better recall than short term or occasional users.

In a comparison of physician and patient reports of Pap smear histories, Walter et al (30) found moderate agreement between patients' reports and physicians' records on the frequency and timing of Pap smears, as well as smear results. The poorest agreement concerned the timing of smears, but timing was reported somewhat more accurately for cancer cases than for controls, who tended to underestimate (telescope) the time since their most recent Pap smear.

When self-reports of the number of ovaries following gynecologic surgery were compared with the medical records of breast cancer cases and controls, Irwin et al (31) found very high levels of agreement among cases and controls for presence or absence of ovaries. Agreement on the exact ovarian number was also high, but was slightly higher for women who had been diagnosed with breast cancer. Methodologic biases in this study may have artificially elevated the observed levels
of agreement, although it is not clear whether these biases compromised the observed case-control difference in agreement.

As part of a case-control study of replacement estrogen use and breast cancer risk, agreement between interview information of replacement estrogen use and physician records was assessed (23). Significant differences were found in the level of agreement for age at initial estrogen use. The highest level of agreement was observed among hospital controls, followed by cases and neighbourhood controls. By way of explanation, the authors suggest that both hospital controls and cases were under the recent care of a physician, while some time may have elapsed between the time of the interview of neighbourhood controls and their last physician visit.

As part of a case-control study of menopausal estrogen therapy and breast cancer, Paganini-Hill and Ross (21) compared reported drug histories of women in a retirement community to physicians' records available in a centralized medical file within the community. The overall correspondence between reports and records was high, with no evidence of recall bias by cases on interview, indicating that cases did not preferentially recall more drug usage or past diseases than controls. However, as previously mentioned, this study has been criticized for being more a comparison of women's recall of their reproductive history when entering the retirement community and recall of that same information at entry into the breast cancer study. Further, as the women were all highly health conscious and motivated, it is not clear whether the observed proportion of seemingly accurate and unbiased recall is generalizable to other populations.

Although several studies exploring reproductive histories have included an exposure verification component, few studies examining prior medical radiation exposure have attempted to verify self-reports. Thus, it is not clear if reporting of radiation exposures differs for cases and controls. When McTiernan et al (32) studied medical and reproductive histories and past exposure to radiation treatments in a case-control study of thyroid cancer in Washington state, no attempt was made to verify any of the reported exposures. Similarly, Ron et al (3) in a case-control study of thyroid cancer in Connecticut, made no attempt to verify self-reported radiation exposures. In the 1963 Tristate Leukemia survey (12), data on radiation exposure and illness experience was gathered.
from hospital, physician, dentist, and chiropractic records to verify the interview responses of cases and controls. Discrepancies between self-reports and medical records were overwhelming in both groups. More recently Preston-Martin et al (33) compared dental X-ray information from interviews of a subset of participants in a case-control study of parotid gland tumours with information in patients' dental records. Because rates of agreement between interview and dental chart data were similar for cases and controls, the overall recall appeared to be unbiased. However, the authors did not confirm individual X-ray procedures, but rather the number of X-ray visits. and they suggest that had verification been based on the precise number of dental radiographic examinations, interview information would have misclassified a high proportion of cases and controls.

2.2.3. Significance of Event

Studies have suggested that recall ability is related to the significance of a past event to the subject. and that such factors as frequency, duration, vividness, and meaningfulness of an event all contribute to recall accuracy (13). Test-retest scenarios that have gathered data relating to the same time period, and studies comparing self-reports to documentation external to the respondent, have consistently found substantial and progressive under-reporting for longer periods of recall. This is particularly prominent for those events not involving major crises (34).

In a comparison of self-reported surgical histories and medical records, the hypothesis (35) that surgical operations and hospitalizations are major events in most peoples’ lives which might be expected to be remembered with greater accuracy than other details of medical histories, was substantiated. Dates of operations and hospitalizations were less clearly recalled.

In a study comparing self-reported hospital admissions with a national computerized record of all hospital admissions (24), a greater proportion of "first" admissions (68%) was recalled than of "readmissions" (45%). Generally the recalled admissions involved longer hospital stays. The time since admission did not appear to adversely affect recall, which appeared to be influenced more by the event's significance to the respondent, as well as its frequency.
In an interview study of women's drug exposure during the previous year (36), there was some suggestion that recall may vary according to the perceived nature of a drug. Recall of drugs which may have been considered by the respondent to be innocuous or unimportant, such as Darvon, a pain-killer and Valium, a tranquillizer, appeared to require more prompting than did recall of more "potent" or "important" drugs, such as Clomid, used in the treatment of infertility.

As part of a study of the effects of diethylstilbestrol (DES) exposure during fetal life, pregnancy history recall was compared to medical records (16). Mothers' questionnaires had fairly complete information on variables relating to their personal experiences such as previous pregnancies, previous miscarriages, and threatened miscarriages. However, significant gaps were noted in reported information regarding treatment and diagnostic procedures such as drugs taken and X-rays of the trunk.

The DES study (16) also underlined patients' lack of awareness of important, but non-invasive diagnostic procedures such as X-rays. This lack of awareness was also evident in the abysmally poor recall of diagnostic X-rays reported in the Tristate Leukaemia Study (12). Recall accuracy was much higher in Preston-Martin's dental X-ray validation study (33) which relied on personal interviews with specific probes to determine the number of X-ray visits, not the actual number of X-rays. However, in the absence of personal interviews and specific probes, the perceived lack of significance associated with prior X-ray exposure may significantly compromise the accuracy of recall of self-reported radiation exposures.

2.2.4. Response Rates, Self-selection, and Motivation

The relationship between response rates, self-selection, and motivation to participate in a study can influence estimates of association, artificially increasing or decreasing their observed strength. Non-response and self-selection are forms of sampling bias which can be reduced, if not prevented, and measured. Response rates of at least 80% (25) will limit non-response bias. Characteristics of non-responders need to be identified to determine whether they differ substantially from study respondents.
The impact of motivation and self-selection is well documented in the study of DES exposure during fetal life (16). Prenatal records were used to identify one case group of DES-exposed mothers and non-exposed control mothers. DES-exposed mothers who initiated their own enrolment in the study comprised a second DES-exposed case group. The verification component of this study compared data from questionnaires completed by mothers in all three groups to information in their medical records. Agreement between questionnaires and medical records was significantly better for mothers who had initiated their own enrolment as compared to control mothers, the two groups most different in their motivation to participate in the study, and slightly better than DES-exposed mothers identified through review of prenatal records.

2.2.5. Time Factors

Studies have consistently demonstrated that recall accuracy decreases for more distant events. Memory failures relating to time generally fall into two categories - errors of omission, as in forgetting the use of certain drugs, and time compression, or telescoping, of events that are recalled as having occurred more recently than they actually have (13).

Patients' accuracy in reporting their past medical history was explored in a study of 90 patients with peptic ulcer (37). Accuracy in reporting of all items covered in the interview showed a significant positive correlation with recentness of hospitalization. Accuracy in recalled admission weight was positively correlated with recentness of hospitalization, but declined for recall of admission weights during hospitalizations more than 5 years in the past. Thus the more recent the experience, the more likely it was to be accurately recalled.

Walter et al (30) looked at physician-patient agreement on dates of Pap smears during the previous five years. Both cervical cancer cases and age-matched controls were found to report more smears in the previous five years than was indicated in their charts, although the cancer cases were inclined to be more accurate with respect to the timing and frequency of smears. The tendency for the latest Pap smear to be reported at a more recent date than recorded in physicians' files, as well as the
tendency of both cases and controls to report significantly more smears than their physicians, was suggestive of memory telescoping, a tendency to collapse the time since an event.

In order to assess measures of mammography use, Degnan et al (38) compared self-reported data on mammography use with documented mammograms. Women were asked if they had ever had a mammogram and when they had their last mammogram. Respondents reported higher mammography usage within the previous year than noted in institutional records. Over-reporting in self-reports was attributed not to unconfirmed usage, but primarily to underestimation of time since the last mammogram. "telescoping" as was also noted by Walter et al (30).

When Glass et al (39) examined the recall accuracy of histories of oral contraceptive use, they found a high level of agreement between self-reports and medical records of ever/never use, current use, and duration of OC use. However, their study was limited to 75 healthy, motivated, and generally upper class women, attending family planning clinics where records were readily available. Further only four oral contraceptive preparations were dispensed at the clinics and some agreement may have been due to chance alone. Also, although the duration of recall ranged from three to seventeen years, the median duration of recall was just under 5 years.

Rosenberg et al (29) found a 90% agreement rate between recall of reported month-specific oral contraceptive use and physician records in a much larger sample of women than Glass et al (39). In two thirds of the sample with confirmed agreement, OC use had occurred between four and sixteen years previously. However, if women could not recall the name of the prescribing physician, they were excluded from the study. This may have left a higher proportion of better "rememberers", and artificially increased the level of agreement. Further, as in the Paganini-Hill study (21), participants who reported the same history which they had previously reported to their physicians, would elevate the observed proportion of agreement.

Little attention has been given to the recall accuracy of medical radiation exposures, particularly those occurring many years previously, and recent studies (3,32) have continued to rely on self-reported radiation exposures. Preston-Martin and colleagues (33) did verify information on dental
X-ray history obtained in patient interviews with information in their medical charts. The availability of complete dental records was clearly related to the time period of care. Few complete charts (12% of case dentists, 9% of control dentists) were available from dentists who were first visited more than 20 years prior to the reference year (45% of all dentists). Problems associated with verifying dental radiograph exposures may be intensified in verification of medical radiation exposures because of the diversity of settings and the large number and variety of practitioners involved.

2.2.6. Complexity

The complexity as well as the frequency of the events to be recalled may have a significant impact on the accuracy of subjects' recall. This was clearly demonstrated in the Tristate Leukemia Survey (12) where up to 80% of X-rays noted in medical records were not recalled by respondents. Often, if respondents recalled being X-rayed, they could not remember how many times.

Brody and colleagues (40) undertook an analysis of patients' recall of their therapeutic regimens in order to determine the factors which might discriminate between patients who accurately recalled their regimens and those who did not. The patients, predominantly black, female, and elderly, were interviewed immediately after seeing their physician. Errors were reported by 53% of the 104 patients interviewed. Patients who lived alone, had complex therapeutic regimens, and reported dissatisfaction with their physicians were at high risk of making errors, suggesting that inaccurate recall, possibly from poor understanding of a complicated treatment, can occur independently of time factors.

Kehoe et al (14) proposed a similar explanation for their finding in a case-control study of cataract patient, that clearly defined conditions, such as diabetes and hypertension, were more accurately recalled, than chronic illnesses with broader definitions, such as coronary heart disease and arthritis. This was echoed by Paganini-Hill and Chao (41) in a study comparing recall of hip fracture, heart attack and cancer reported in postal survey data, with medical records. They found that the accuracy of questionnaire responses varied by disease, with greatest correlation between clearly
defined conditions, such as hip fracture and cancer, and poorer correlation for less well-defined illness such as heart attack.

A study comparing physician diagnosis of lower respiratory illness and maternal recall of the occurrence of such illness (42) in a cohort of children under 1 year of age, revealed a poor relationship between diagnosis and recall. Because the questionnaire was administered to the mother at a child's first birthday, the passage of time is unlikely to wholly account for poor recall. Rather, the authors note that disagreement between mothers' recall and medical records occurred in one of two ways - either the mother failed to recall an illness that had been diagnosed and recorded by the physician, recalling instead a less alarming explanation that had been offered, or a mother recollected illnesses which were not diagnosed by the physician. This tended to happen in families where the adults themselves suffered more self-reported upper-respiratory illnesses. Although the frequency of reported upper respiratory illness in infants was positively correlated with development of some degree of future respiratory impairment, the study also demonstrated that inaccurate reporting can sometimes be the result of oversimplified or misleading information provided by the physician.

The Nurses' Health Study was established in 1976 as a prospective investigation of cancer, heart disease, and other serious illnesses in women. Substudies were conducted to validate self-reports of several medical conditions by study participants (43). For carcinomas, such as breast, large bowel and thyroid, with clear diagnostic features and definite histologic diagnosis made and reported to the patient, agreement approached 100% between self-report and histopathology records. However, when the treatment of malignant and premalignant conditions was similar, as in hysterectomy, or when detection of metastases led to diagnosis, the reliability of the reports decreased. Similarly self-reports of cardiovascular disease with less clearly defined endpoints were less reliable.

These studies indicate that the accuracy of self-reports may be compromised not only by the complexity and frequency of events to be recalled, but also by poor understanding of a complex medical event on the part of the patient or an oversimplified explanation offered by a physician.
2.2.7. Summary

In summary, recall accuracy can be influenced by several factors. Although sociodemographic variables such as age, sex, and education, had limited or no impact on recall accuracy among the studies cited (14, 19, 20, 21, 22, 23, 24, 38), time elapsed since exposure had a significant impact - either because events were forgotten or time since the event was collapsed (13, 21, 29, 30, 33, 34, 37, 38, 39). Events of a complex nature or with ill-defined parameters were also more poorly recalled (12, 16, 40-43). Events of particular significance to the respondent were more accurately recalled than those of less personal relevance (13, 16, 24, 34, 36). Finally, cases provided more complete and accurate histories than controls. In part this was due to motivation, although response rates and self-selection played a role (16, 20, 21, 23, 25-31, 33). These findings suggest that while sociodemographic factors are unlikely to affect the recall accuracy of past radiation exposures, the passage of time will be a significant factor. Additionally, medical radiation exposures may be considered to be so benign as to be completely forgotten, unless exposure was linked to an event of particular significance to the respondent (such as a car accident). Cases may also be more rigorous than controls in reporting certain types of exposures (head and neck X-rays).

2.3. QUESTIONNAIRE DESIGN

Questionnaires should provide both a valid and reliable measure of the information requested. However, both the design and administration of a questionnaire can have a significant impact on response quality.

Self-administered questionnaires have the advantage of being less expensive, and thus more easily accessible to a large number of subjects than those administered by an interviewer. Subjects may also be less reticent about reporting sensitive information. While there is no opportunity for an interviewer to introduce bias through questioning subjects or recording their information, there is also limited opportunity for the use of memory prompts to improve recall. Interviewer-administered studies using such prompts have found better agreement between questionnaire data and external data sources (33) than verification studies not employing such prompts (12). There are
several other disadvantages to self-administered questionnaires. Response rates are often notoriously low, compromising the power of the study, and respondents tend to differ systematically from non-respondents, being better educated and more motivated, thus introducing a self-selection bias. Even among returned questionnaires, individual questions are often left unanswered. Questions and instructions must be very clear, as there is no interviewer present for clarification. This is of particular concern where language is a barrier, or where either health, or reading and writing skills are impaired. There is also no control over whether the intended subject or a proxy completes the questionnaire. In Martin's study comparing self-reported child-bearing experiences with obstetric records (44), immigrant mothers who spoke little English often did not appear to know or understand the technical details of their pregnancy or delivery. Their limited English skills hindered understanding of the questionnaire and it was discovered that in some cases the questionnaire had been completed by the women's husbands.

Regardless of the route of administration, questions must be clear and not ambiguous. This can be achieved by providing a list of possible answer choices where feasible, and avoiding open-ended questions. A study examining the effect of questionnaire design on recall of drug exposure during pregnancy (36) questioned women in one of three ways. The first question was open-ended, the second asked about drug use for selected indications, and the third asked about use of specifically named drugs. Findings indicated that the amount of information obtained on antenatal drug exposure varied considerably according to how the mother is questioned and is directly related to the specificity of the questions asked. Questioning about drug use according to the specific drug name produced the greatest enhancement of maternal recall of antenatal drug use. If multiple choices are provided, a category for "other" should be included to cover any unforeseen possibilities, with instructions to explain the reason for this choice. In a study comparing the accuracy of recall of surgical histories obtained by postal survey with medical records (35), investigators found 10 surgical procedures recorded in subjects' medical records, but not recorded on questionnaires. The procedures were all minor and most had probably been performed in outpatient departments; however, respondents had been asked to give details of operations carried out specifically "in hospital" with no other location choice option. When choices include specified intervals, care must be taken to avoid overlapping intervals. Two part questions should be avoided,
As answers may relate to one or the other part and may be misleading. Instead, two separate questions should be asked. A comparison of postal survey data and medical records on hip fracture, heart attack, and cancer (41) asked respondents a specific question about hospitalizations and a second question about hip fractures and cancer. A number of patients indicated that they had had a hip fracture, but did not indicate hospitalization. Without the specific question on fracture, 5% of the true positive self-reports of hip fracture would have been missed. Technical language should also be avoided. Martin's study (44) comparing the congruity between mothers' self-reported child-bearing experiences and their obstetric records noted several reasons for discrepancies including mothers' limited knowledge or understanding of certain procedures and problems of interpretation and definition. For some questions it was better to use the technical terms for a procedure rather than a purely descriptive term, while for other questions the converse was true. Problems of definition and interpretation were most often related to events with broad definitions.

Of particular concern to the CCERG thyroid cancer study are questions asking for information about long ago events which may have more significance to investigators than study subjects. Answers to such questions may be arbitrary or influenced by some of the aforementioned biases. Questions asking for detailed answers may be similarly influenced (types of X-rays, when, where, by whom, for what reason), although asking for insufficient detail can produce equally unsatisfactory results (45).

Often overlooked in a discussion of questionnaires, are those sent to medical sources asking for verification of patients' questionnaire responses. They may be completed by a trained study abstractor, or more commonly by a variety of abstractors with varying training, interest, and time. In the experience of the Tristate Leukemia study (12), trained nurse-interviewers spent longer waiting to see physicians than they did interviewing, and often physicians declined to let interviewers review the record themselves. Even among trained abstractors, Horowitz (17) documented excerpting errors around classification of incomplete and ambiguous recorded information.
There is no indication in the literature that questionnaires sent to medical sources were part of any pre-testing, yet the same caveats apply. Posing open-ended questions may yield ambiguous responses. Multiple check boxes may be similarly misleading. The CCRERG verification form asked for confirmation of self-reported exposures recorded in the medical record within 5 years of the self-report. Answering "no" or "don't know" without further explanation could indicate that either the same procedure was performed at another time or not at all, or not by that physician. Further the often non-technical description of a procedure given by the respondent may be either unrecognizable to the physician, or sufficiently inaccurate for medical confirmation. References in the literature to questionnaires sent to medical sources are described, if at all, as "simple". Although brief confirmation questionnaires may increase compliance, they may compromise a study's verification potential.

2.4. MEDICAL RECORDS

Data sources external to the respondent are often considered to provide more accurate and unbiased information than the respondent. Medical records are often regarded as the "gold standard" despite some limitations which could restrict the evaluation of sensitivity and specificity, both of which depend on a true "gold standard". Horowitz et al (46) reported that odds ratios can differ considerably depending on how discrepancies in data from different sources are handled. Three factors determine the efficacy of the medical record as an objective source of data verification - availability, accessibility, and accuracy of the record.

2.4.1. Availability

A preliminary determinant of successful verification is the availability of the medical record. A dental X-ray verification study (33) found that the availability of complete dental records was clearly related to the time period of care. Forty-five percent of dentists named by study participants were visited more than 20 years earlier, and of these only 12% of case dentists and 9% of control dentists had complete charts. Legislation governing record retention requirements often determines the availability of the medical record. Record retention guidelines are of particular concern where
medical record verification of more distant events is being sought. In Canada, physicians and hospitals follow different provincially-mandated regulations. Minimum record-keeping requirements range from a minimum of 6 years to more than 20 years in some provinces (47.48).

Locating the medical record is frequently dependent on the respondent's recollection of where and when treatment was administered. However, subjects' recall of the exact time and location of treatment is subject to the same biases and inaccuracies as recall of the actual treatments. In their study comparing women's histories of oral contraceptive use with physician records, Rosenberg et al (29), excluded women who could not remember the names of their physicians. If these women were also less likely to recall their contraceptive history, their exclusion would elevate the observed proportion of agreement. The excluded women were grouped together with those whose medical records were unobtainable, and together represented 57% of the total sample. Although the sociodemographic characteristics of this group may have been "similar" according to the authors, the potential for bias was strong.

Often considerable effort and persistence are needed to obtain high physician response rates. Contacting multiple sources is a frequent requirement to access the appropriate data source. In their study, Goodman et al (23) found that multiple physician contacts were required for 84% of their study subjects.

2.4.2. Accessibility

Although medical records may be available, issues of consent, compliance, and confidentiality determine access to medical information. Consent is often sought at two levels, from a physician whose consent is asked to contact a patient, and from a study participant whose consent is required to access his/her medical record. If consent is denied, either because of physician concerns over the physical or mental well-being of the patient, or because a study subject is unable or unwilling to give consent, the medical records, although available, are rendered inaccessible. In Preston-Martin's dental X-ray validation study (33) the major reason given by study subjects for refusing permission to contact dentists was unpaid dental bills. Generally the proportion of cases granting consent to
access their files is greater than the proportion of controls, presumably because cases have more of a vested interest in the study results. Walter et al (30) found that 94% of cases compared to 82% of controls gave permission to contact their physicians regarding their Pap smear history.

In some cases physicians may be reluctant to provide information from their medical records, either because of the cost and inconvenience, or because of concern over legal action (43). This was the experience of Tilley et al (16) who suggested that physicians' reluctance during the data collection phase of their DES study, may have been due in part to the publicity around the many DES-related lawsuits filed against drug companies, and resultant apprehension among physicians regarding their own liabilities. Preston-Martin et al (33) similarly concluded that concern about malpractice implications may have led to caution on the part of some dentists in reporting radiographic exams on dental record abstraction forms. Some forms were returned with irrelevant and unsolicited comments regarding X-raying children or only vague information about the number of films used in a particular exam.

Concerns about confidentiality can also limit access of an abstractor to the medical record, with varying details of exposure information supplied by the medical practitioner either by letter or abstraction form.

2.4.3. Accuracy

Typically, the medical record is considered to be an accurate and objective source of information by which to verify a subject's self-reported history. Though in general the medical record is the most reliable source available, it is by no means the "gold standard" and several breaches in accuracy have been documented. Hewson and Bennett (49) found little support for the assumption that medical records are always more accurate and acceptable, at least insofar as childbirth research data, a finding echoed by other investigators (17,30,46). Preston-Martin (33) found that dental charts did not always contain a complete record of radiographs which, according to some dentists, were recorded primarily for billing purposes.
Information in the medical record may come from several sources. It may be a direct observation recorded by the patient's physician, referral letters between physicians, operative notes, nurses notes, or lab results. Sometimes conflicting reports are found in medical records particularly when multiple histories have been collected by different physicians (50). Often information recorded in the medical record is reported by the patient at entry into a new practice. This history is very much dependent on the patient's recall (51). Using this recorded history would serve only as a comparison between current and earlier self-reports as in Paganini-Hill's study (21), and not a verification of actual events. Linet et al (22) have suggested that mention of a medical condition or prior surgery in the medical record cannot be considered as confirmatory without the substantiation of laboratory test results or histopathologic diagnosis. Considering a previously dictated history as agreement with a current self-report would tend to elevate the observed proportion of agreement (29).

Misunderstandings by patients have been documented but misinterpretation by physicians may also contribute to errors and omissions in the medical chart. The absence of an exposure or event is usually not documented. Thus, in reviewing records it is unclear whether no mention of an exposure should be interpreted as "unexposed" or "unknown" (27). Further, the time and detail devoted to note-taking varies between physicians, affecting the quality of the medical record (30). Medical students, instructed to take extensive histories, have been shown to record the most complete notes (52). Widespread inconsistencies in the structure and content of general practice records have been documented (53). In researching childbirth data, Hewson and Bennett (49) also found that different criteria were used by different hospitals to record several common variables of childbirth such as Apgar scores.

Tilley et al (16) documented more missing information in physician's office charts than in records from clinics or hospitals. Incomplete patient histories in medical records may be more prevalent when patients are under the care of several physicians (14). Indiscriminate "pruning" of the medical record by the practitioner has also been suggested as one source of missing data (53). Referral letters included as part of the medical record have been shown to be incomplete with respect to drug use and adverse reactions to therapy (54). If medical history has been documented in multiple
volumes, a variable of interest may be recorded in an unavailable volume of a hospital chart (50). Purposeful omissions from the medical record have been uncovered as well, usually because of legal implications. Coulter et al (35) found suggestive evidence that deficiencies were in the medical notes and not in patients' self-reports. More than two thirds of the operations reported by patients but not recorded in their medical charts were D&Cs, although in over half of these cases references to the conditions which the patient reported as necessitating the procedure were found in the notes. In her study of maternity services, Martin (44) found evidence suggesting that mothers' reports of ultrasound in utero were correct, despite the lack of documentation in the medical record, possibly because of controversy over the use of ultrasound in pregnancy and the calls for follow-up studies.

An exposure suspicion bias may cause clinicians to search more enthusiastically among cases for suspected exposures, particularly if the cause is "known" or "suspected" or has received widespread attention. The magnitude of this bias was demonstrated in two studies of thyroid cancer in children (55,56) which found markedly different levels of exposure to prior irradiation depending on the intensity of the search. Werler et al (27) postulated that obstetric records could be biased if prenatal diagnosis of a malformed infant prompted obstetricians to document exposures more carefully. Further, women at high risk of producing a malformed infant would seek earlier obstetric care than women without an elevated risk, increasing the opportunity to document suspect exposures. Finally women with higher risk pregnancies would likely obtain care from a select group of obstetricians whose note-taking practices would be similarly complete or incomplete. Knowledge of a subject's prior exposure to a putative cause might also influence the intensity and outcome of the diagnostic process (26). Additional biases could be introduced if a prescribed drug noted in the medical record was never taken by the patient, or was taken during a different period than that for which it was prescribed (23).

Errors in abstracting information from medical records may also occur, particularly if abstracters are untrained, inexperienced or rushed. A 3% abstraction error rate was found in researching childbirth data, despite care in training and monitoring the abstraction staff (49). When each contacted medical source is responsible for abstracting its own records, there is no quality control
of the abstraction process. Horwitz and Yu (50) have documented several sources of transcription errors. Information available in the record has been missed by the abstractor, usually when it is in an unexpected part of the record such as nurses' notes or paramedical consultations. Occasionally data were incorrectly transcribed from the medical record. Where specific information was not noted but inferences could be made from recorded information, abstractors differed on the interpretation. Finally even when data were similarly interpreted and recorded by different abstractors, errors occurred if coding criteria were applied inconsistently.

2.5. SELF-REPORTS VERSUS MEDICAL RECORDS

One of the challenges of epidemiologic studies is to ensure that data collected for analysis is accurate. No amount of subsequent data manipulation can compensate for data of poor quality which can severely limit the validity of a study's conclusions. Several factors were identified in the preceding review that can compromise the quality of data collected from both self-reports and medical records. However, despite the limitations of each information source, a comparison of self-reported data with data obtained from the medical record can increase confidence in the accuracy of self-reports. Although the medical record may not be a 'gold standard', particularly in situations where the medical record source is dependent on subjects' recall, available medical records provide an opportunity to verify exposure measurements based on questionnaire data. To provide a comprehensive assessment of the overall accuracy of self-reports, both positive and negative self-reports should be evaluated against the medical record. In this way both the accuracy of self-reported events, as well as 'over-' and 'under-reporting' can be determined.
3. OBJECTIVES

The CCRERG thyroid cancer study relied on a self-administered questionnaire to collect information on medical radiation exposures. As part of the main study, verification of positive self-reports as well as a sample of reported non-exposure to radionuclides was undertaken using medical records. The overall objective of the verification component of the study was to assess the accuracy of self-reported exposure and non-exposure, thus providing a measure of the quality of the collected data. Ensuring the accuracy of self-reports increases the validity of the CCRERG study conclusions based on these data. The following specific objectives were addressed to achieve this goal:

1) To ascertain medical record availability and the determinants of record availability.

2) Where medical records were available, to evaluate the agreement between self-reported exposures and exposures noted in medical records, and to ascertain the determinants of agreement between self-reports and medical records.

3) To compare the effect of exposure measurements from different data sources on estimates of the relative risk of thyroid cancer.

4) To determine the accuracy of reported non-exposure to radionuclides in a sample of Ontario subjects.
4. METHODOLOGY

4.1. OVERVIEW OF CCERG CASE CONTROL STUDY OF THYROID CANCER

Cases of thyroid cancer for the Ontario portion of the national study were identified through the Ontario Cancer Registry (OCR), maintained by the Ontario Cancer Treatment and Research Foundation (OCTRF). Pathology reports, generally received by the OCR within 6 months of cancer diagnosis, were the source of case ascertainment. Only cases newly diagnosed with histologically-confirmed primary thyroid cancer (ICD9: 193) between January 1, 1986 and December 31, 1987 were eligible for the national study. Eligible cases were at least 16 years of age, resident of Ontario at the time of diagnosis, and alive and well enough to participate in the study. No proxy respondents were sought for the small anticipated number of ill or deceased patients. Subject to their physicians' consent, questionnaires were sent to eligible cases. Recruitment was not entirely prospective as the study did not begin until 1987, but given the high survival rate for most types of thyroid cancer, the risk of prevalence-incidence bias due to prior death was considered negligible.

Control subjects from the Ontario population were selected at random from the "Enumeration Composite Records (ECR)" of the Ontario Ministry of Revenue. This file consists of all residents of Ontario, including property owners, tenants, and non-paying residents, including children. Members of specific groups which do not come under provincial jurisdiction, such as native Indians, those in correctional institutions, and a small number of residents in unincorporated municipalities, are not included. The file is computerized and includes year of birth and mailing address for each resident. Individuals are eligible for selection only at their place of residence. The ECR has been used as source of controls in other studies in Ontario (57). Controls were selected by frequency matching according to the expected age (in 5 year age groups), sex, and region distribution of the case subjects, and with a control: case ratio of 2:1. Selected controls were checked against the Ontario Cancer Registry to exclude any individuals previously diagnosed with thyroid cancer; controls with cancer at other sites were not excluded.
All eligible cases and controls were sent an explanatory letter and a self-report questionnaire with stamped reply envelope. Subjects were telephoned one week later to check that the mailing had been received and to answer any queries about the study. Returned questionnaires were reviewed immediately upon receipt, and where necessary the subjects were interviewed by telephone to complete any missing information.

A consent form was included as part of the questionnaire package, asking respondents for their signed permission to allow researchers to approach hospitals and physicians for the purposes of the study. Wherever possible, and if the subject consented, reports of radiotherapy, use of radionuclides and x-rays (with the exception of dental, chest, leg, and lower arm x-rays) were checked by writing to the hospitals, clinics, or physicians concerned. Verification of a 10 percent sample of negative radionuclide reports was also undertaken.

4.2 VERIFICATION OF SELF-REPORTED EXPOSURE AND NON-EXPOSURE

4.2.1. Positive Self-Reports

4.2.1.1. Contact Of Medical Record Source

With subjects' consent, the medical facilities or attending physicians indicated on questionnaires were contacted for confirmation of reported exposures. Province-specific procedures were developed for verifying self-reported medical radiation exposures. Verification requests were first sent to physicians, and if unavailable, other medical avenues were pursued.

Verification with medical records was sought for self-reported exposures noted in Question 5 (X-ray examination), Question 6 (radiation treatment), and Question 7 (radioactive drugs for diagnosis or treatment) (Appendix 1). In Ontario, verification attempts were undertaken for all diagnostic X-rays noted in Question 5. Exposures not eligible for verification included chest, dental, leg, or lower arm X-rays, or X-rays taken within 2 years of the diagnosis date for cases or prior to January 1, 1986 for controls. Verification efforts were deemed too difficult to pursue for X-ray exposures that had occurred outside Canada. Ultrasound examinations were not verified.
Verification was attempted for all radiotherapy exposures noted in Question 6. For cases, this included exposures noted up to the date of diagnosis of thyroid cancer, unless the thyroid cancer was noted on the questionnaire as the condition treated in the year of diagnosis. In such cases, no verification was attempted. For controls, this included verification of all exposures regardless of the exposure date.

Verification of all exposures noted in Question 7 was carried out, unless either the exposure had occurred after the date of diagnosis of thyroid cancer, or radionuclides had been administered for diagnosis or treatment of a condition discovered to be thyroid cancer within a year of thyroid cancer diagnosis. For controls, verification was undertaken for all noted exposures to radionuclides regardless of exposure date.

Separate verification forms (Appendix 2) for each type of exposure (X-rays, radiotherapy, and radionuclides) listing the self-reported exposure and year of exposure, were sent to the reported medical source. A cover letter explaining the purpose of the inquiry and a copy of the subject's signed consent were included. Verification response options included “correct” if the same exposure was noted in the medical record within 5 years of the reported date, “incorrect” and “don’t know”. If medical record information differed from self-reported information, corrections were requested. Information on radiation dose was also solicited.

From the list of hospital, clinic, physician, or chiropractor names supplied on the questionnaire for each exposure, physician or chiropractor names were selected as the initial contact. Names and addresses were confirmed with either the Canadian Medical Directory or the Chiropractic Directory. If the physician's/chiropractor’s name was omitted by the respondent or unlisted in the directory, the verification form was directed to the Head of Medical Records at the hospital noted by the subject. If neither physician's or hospital’s names were given, clinics were contacted if their addresses could be located. Three to four weeks after mailing verification forms, non respondents were contacted by telephone.
4.2.1.2. Coding Of Variables

For all subjects, the following information was recorded from the subject questionnaire and medical record search, then coded and subsequently entered into a thyroid verification study database: age (at time of questionnaire mailing), sex, case-control status, education, self-reported exposure, self-reported year of exposure, medical record exposure (coded as missing if not available), year of procedure recorded in medical record (coded as missing if not available), and medical record source (coded as missing if not available).

Because of limited response opportunities on the questionnaire, and subjects' limited knowledge of medical terminology or poor understanding of anatomy, coding of self-reported exposures was "field"-specific (head, neck, heart, arm and shoulder, barium swallow/enema, abdomen including lumbar spine and pelvis, CT scan) rather than procedure-specific (see Appendix 5). Single fields were combined for analysis based loosely on the distance of the exposure field from the thyroid. In the absence of questionnaire elaboration, computerized tomography (CT) was grouped with X-rays of the head and neck, as estimates suggest that a large proportion of CT's are of the head. The following chart lists grouped exposure fields.

<table>
<thead>
<tr>
<th>Exposure Fields</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>QUESTION 5: X-RAYS</strong></td>
</tr>
<tr>
<td>Arm, Shoulder</td>
</tr>
<tr>
<td>Heart, Ribs, Mammography</td>
</tr>
<tr>
<td>Barium Swallow, Barium Enema</td>
</tr>
<tr>
<td>Abdomen, Spine, Hip</td>
</tr>
<tr>
<td><strong>QUESTION 6: RADIOTHERAPY</strong></td>
</tr>
<tr>
<td><strong>QUESTION 7: RADIONUCLIDES</strong></td>
</tr>
</tbody>
</table>

* Personal Communication: Dr. J. Glay, Radiologist
The following information was also calculated for all subjects: years elapsed between questionnaire mail date and self-reported year of exposure, years elapsed between medical verification form mail date and procedure year reported in medical record (coded as missing if not available), and difference in years between self-reported year of exposure and year reported in medical record (coded as missing if not available).

4.2.1.3. Definitions

AGREEMENT: The self-reported exposure was the same, or in the same field (see Appendix 5), as the exposure noted in the medical record. Because the medical verification form allowed for ± 5 year time interval from the self-reported year of exposure, and preliminary analysis indicated that virtually all verified procedures fell within this 5 year window, the definition of agreement does not include a time element.

INCORRECT: Either medical record source reported “incorrect” without any additional information, or the self-reported exposure was not in the same field as the exposure noted in the medical record.

NO SUBJECT RECORD: The medical record source reported “don’t know” without providing additional information, or reported no record of the self-reported exposure, no record of the subject, or no records from long ago.

NO FOLLOW-UP / NO REPLY: Either no medical record source was provided by the patient; or the source was provided, but could not be pursued (physician had died or retired, clinic could not be identified, source was outside of Canada, source would not accept photocopied consent); or no reply was received from the medical source; or the verification form requested the wrong patient report; or no attempt was made to verify an exposure.
4.2.1.4. Power

For the availability (Objective 1) and agreement (Objective 2) analyses, the power of the study to detect selected odds ratios was calculated, based on the number of 'cases' and the prevalence of selected 'exposure' variables. The power of detecting specified minimum excess odds ratios of thyroid cancer (Objective 3) given the prevalence of head and/or neck X-rays or CT scans in the sample was calculated for the original data set using self-reported exposures.

'Cases' were defined as those having the outcome of interest (available records - Objective 1; record agreement - Objective 2; and thyroid cancer - Objective 3). 'Exposure' categories were dichotomized for convenience in the power analyses, and the combined category that included the 'exposure' used as a referent level in multivariate analyses, was considered to be the 'unexposed' group (hospital/clinic records; ≤ 10 years since exposure; technical, trade, vocational or university education- Objective 1; hospital/clinic records - Objective 2; and no head or neck X-rays or CT scans - Objective 3). The ratio of controls to cases was calculated for each objective based on the definitions of cases and controls. Power calculations for a significance level (α) of 0.05 (2-tailed) were based on the following formula (45):

\[ z_\beta = \left[ \frac{(n)(d^*)^2(r)}{(r + 1)(\bar{p})(1 - \bar{p})} \right]^{1/2} - 1.96 \]

where:
- \( 1 - \beta \) = power
- \( n \) = number of cases
- \( d^* \) = \( p_1 - p_0 \)
- \( p_1 = \frac{p_0(OR)}{1 + p_0(OR - 1)} \)
- \( p_0 \) = proportion of exposed controls
- \( OR \) = minimum detectable excess odds ratio desired
- \( r \) = control-to-case ratio
- \( \bar{p} = \frac{[p_1 + (r)(p_0)]}{1 + r} \)
The power calculated for specified odds ratios given the prevalence of selected variables in the sample are shown in the charts below.

**Objective 1: Record Availability**

<table>
<thead>
<tr>
<th>Variable</th>
<th>$p_0$</th>
<th>$n$</th>
<th>$r$</th>
<th>Minimum Excess Detectable OR</th>
<th>Power (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician/Chiropractic</td>
<td>.42</td>
<td>982</td>
<td>1</td>
<td>1.5</td>
<td>99.3</td>
</tr>
<tr>
<td>Records</td>
<td></td>
<td></td>
<td></td>
<td>1.3</td>
<td>76.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2</td>
<td>43.3</td>
</tr>
<tr>
<td>$\leq$ High School Education</td>
<td>.48</td>
<td>982</td>
<td>1</td>
<td>1.5</td>
<td>99.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.3</td>
<td>82.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2</td>
<td>51.2</td>
</tr>
<tr>
<td>$&gt;10$ Years Elapsed since Exposure</td>
<td>.63</td>
<td>917*</td>
<td>1</td>
<td>1.5</td>
<td>97.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.3</td>
<td>77.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2</td>
<td>21.2</td>
</tr>
</tbody>
</table>

* Years elapsed not available for 65 cases who did not report an exposure year.

Based on the prevalence of 'exposure' and the number of available 'cases', the probability of detecting a statistically significant odds ratio for record availability (the power of the study) of 1.3 is relatively high, but the power drops for detection of a minimum excess odds ratio of 1.2.

**Objective 2: Record Agreement**

<table>
<thead>
<tr>
<th>Variable</th>
<th>$p_0$</th>
<th>$n$</th>
<th>$r$</th>
<th>Minimum Excess Detectable OR</th>
<th>Power (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician/Chiropractic</td>
<td>.41</td>
<td>824</td>
<td>.19</td>
<td>1.5</td>
<td>62.9</td>
</tr>
<tr>
<td>Records</td>
<td></td>
<td></td>
<td></td>
<td>1.3</td>
<td>32.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2</td>
<td>17.9</td>
</tr>
</tbody>
</table>
Based on the prevalence of 'exposure' and the number of available 'cases', the probability of detecting a statistically significant odds ratio for record agreement (power) of 1.5 is moderate, but the power declines for detection of a minimum excess odds ratio of 1.3 and 1.2.

**Objective 3: Exposure Measurements using Self-Reports**

<table>
<thead>
<tr>
<th>Variable</th>
<th>( p_0 )</th>
<th>( n )</th>
<th>( r )</th>
<th>Minimum Excess Detectable OR</th>
<th>Power (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head/Neck Xray</td>
<td>.26</td>
<td>447</td>
<td>2.5</td>
<td>1.5</td>
<td>92.1</td>
</tr>
<tr>
<td>CT scan</td>
<td></td>
<td></td>
<td></td>
<td>1.3</td>
<td>52.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2</td>
<td>31.9</td>
</tr>
</tbody>
</table>

Based on the prevalence of 'head and/or neck X-rays, or CT scans' in self-reports, and the number of available thyroid cancer cases, the probability of detecting a minimum excess detectable odds ratio of thyroid cancer (power) of 1.5 is high, but declines for detection of a minimum excess odds ratio of 1.3 and 1.2. Estimation based on medical record exposures would have less power.

4.3.1. Negative Self-Reports

Verification procedures for non-exposure were province-specific. In Ontario, the following criteria were used in the selection of the negative verification group:

1) Subjects who had either answered "NO" to Question 7 regarding radionuclide exposure, or whose radionuclide exposure had been within 2 years of thyroid cancer diagnosis for cases, or after January 1, 1986 for controls.
2) Subjects who were residents of Ontario either from 1945 or from the time of their birth (if later than 1945). Exposure to radionuclides prior to 1945 would be negligible, and out-of-province verification would be difficult.

3) Subjects who had indicated consent to verification.

Information recorded for subjects in the negative verification group included age, sex, case-control status, number of hospital contacts, results of medical record radionuclide search, and if positive, the year of radionuclide administration.

A random sample of 10% of cases and 5% of controls was selected from subjects satisfying criterion 1) above, using a random digit table. Nine cases and sixteen controls were subsequently excluded for out-of-province residence history. A further two cases and two controls were excluded for not providing consent. The final sample included 36 cases and 52 controls.

A list of licensed laboratories in Ontario with nuclear medicine facilities was obtained from the Toronto Institute of Medical Technology. In total, 66 hospitals in Ontario had labs with nuclear medicine facilities (see Appendix 3). A negative verification form was sent to each hospital. To determine which hospitals the verification forms should be sent to, the subjects' residence history was examined and the following chart was used:

<table>
<thead>
<tr>
<th>Location</th>
<th>Hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metro Toronto Area</td>
<td>All Toronto hospitals (21)</td>
</tr>
<tr>
<td>if residence included Scarborough</td>
<td>All Toronto hospitals (21) + Scarborough referral centres (2)</td>
</tr>
<tr>
<td>Areas surrounding Metro</td>
<td>Toronto referral hospitals (10) + nearest local hospital</td>
</tr>
<tr>
<td>Outside Metro and surroundings</td>
<td>Local hospitals and nearest university hospital</td>
</tr>
</tbody>
</table>
Respondents’ residence history was noted and all hospitals with nuclear medicine facilities in the area serving communities noted in the residence history were contacted. For subjects living in the Metro Toronto area, forms were sent to all Toronto hospitals with nuclear medicine facilities (21 hospitals). The larger teaching hospitals in Toronto were considered to be referral hospitals (10), as were 2 hospitals in the Scarborough area. Where subjects lived in areas surrounding Metro Toronto, verification forms were sent to the 10 Metro hospitals designated as referral centres.

The negative verification form (Appendix 4) included the subject’s name, date of birth, and current address. A “Yes/No/No Record” of radionuclide exposure prior to January 1, 1986 was requested for each subject and if “Yes”, the date of exposure. Hospitals were also asked to indicate which records were checked (inpatient and outpatient) and how far back their records went. Verification forms were directed to Medical Record departments rather than to Nuclear Medicine, because the latter only had current records (from 1980) available.

A covering letter was sent along with the verification form. Letter 1 was used for hospitals with fewer than 8 patients, which allowed for photocopies of the signed consent forms to be included with the mailed package. Letter 2 was used for hospitals with more than 8 patients. Photocopies of the consent were not included with this letter, but were sent out if requested by the hospital. In Letter 2, an offer to have a research assistant review the charts in the Metro area hospitals only was provided (Appendix 4). If the forms were not returned in 2 weeks, there was a telephone follow-up. Data were abstracted by a study research assistant for three hospitals.

This approach was based on the satisfactory results of a pilot study wherein a cover letter and form with the names of 6 patients were sent to the Medical Records Department of Mount Sinai Hospital in Toronto where the patients had all received radioactive drugs. Radioactive treatment was confirmed for 5 patients. The sixth patient may have been an outpatient.
4.4. STATISTICAL METHODS

Response rates to the mailed subject questionnaire were calculated separately for cases and controls. Univariate statistics were then used to describe respondents who reported verification eligible exposures. The variables examined included: case-control status, sex, age, education, type and year of self-reported exposure, years elapsed between questionnaire mail date and self-reported exposure year, source of medical record (physician, hospital, clinic, or chiropractor), type of exposure and year noted in the medical record, and the years elapsed between the verification form mail out and the year of exposure noted in the medical record. Graphs were used for illustration purposes where appropriate (e.g. self-reported year of exposure, distribution of differences between self-reported year of exposure and medical record year, distribution of medical record responses by exposure type and exposure year). Continuous explanatory variables (see list below) were categorized, for ease of analysis and interpretation. Categories were chosen to be both meaningful (e.g. approximate 15 year age intervals, decade of exposure, 5 year elapsed year intervals) and to distribute frequencies within each category as evenly as possible. To address Objectives 1 and 2, analysis was exposure-, not subject-specific, with each self-reported exposure listed as a unique observation.

<table>
<thead>
<tr>
<th>Categories used for Continuous Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: ≤ 34 Years</td>
</tr>
<tr>
<td>35-49 Years</td>
</tr>
<tr>
<td>50-64 Years</td>
</tr>
<tr>
<td>≥ 65 Years</td>
</tr>
</tbody>
</table>

Self-reported year of exposure / Medical record year of exposure:

1980 or later
1970-1979
1960-1969
1959 or earlier
Years elapsed between questionnaire mailout and self-reported exposure year:

- \( \leq 5 \) Years
- 6-10 Years
- 11-14 Years
- \( \geq 15 \) Years

Years elapsed between verification form mailout and medical record year:

- \( \leq 5 \) Years
- 6-10 Years
- 11-14 Years
- \( \geq 15 \) Years

Difference in years between self-reported and medical record year:

- \( >(-10) \) Year Difference
- \( -(6 - 10) \) Year Difference
- \( -(1 - 5) \) Year Difference
- Same Year
- \( +(1 - 5) \) Year Difference
- \( +(6 - 10) \) Year Difference

Objective 1:

To provide a suitable outcome variable by which to ascertain medical record availability, record availability was dichotomized to “No Record / Missing” (no record of subject, no follow-up of medical source possible, or no reply from medical source) and “Medical Record Available” (agreement between self-report and medical record, or verification response noted ‘Incorrect’ with or without additional exposure information). This was considered as the ‘broad’ definition of record availability and was used in bivariate and multivariate analysis.

The association of each categorical variable (see list above) with the outcome variable, record availability, was examined using a Pearson chi-square test for association (65). These analyses were carried out using SAS® software. To evaluate the determinants of record availability, variables
which were found to be significant in bivariate analyses were subsequently included in a multiple logistic regression model for medical record availability using EGRET software. A backward stepwise elimination of variables with p-values > .05 based on the Likelihood Ratio Statistic (LRS) was used to arrive at the final model. As an informal test of the goodness-of-fit of the model, the residual deviance was divided by the degrees of freedom. Values close to '1' suggest that the model is a good fit to the data.

To rule out the possibility that 'Incorrect' verification responses without any exposure information referred to subject records and not exposure records, 'Incorrect' responses without exposure information were excluded to form a second 'narrow' definition of record availability used in multivariate analysis. The estimate of the odds ratio of record availability using the 'narrow' definition was compared, fitting the same variables in a multiple logistic regression model.

In addition, to ensure that multiple observations from one individual did not bias the results, logistic regression analysis using a generalized estimating equation approach was carried out. This allowed for a comparison of standard error estimates using clustered (by subject identification number) and unclustered data (58).

Objective 2
When medical records were available, the accuracy of self-reported medical radiation exposures was evaluated by comparing self-reported exposures to exposures noted in medical records. The outcome variable, "Accuracy", was dichotomized into "Agreement", that is, whether self-reported exposures were the same, or in the same field, as exposures reported in the medical record, and "Incorrect", when either the medical record source reported 'Incorrect' or the self-reported exposure was not in the same field as the exposure noted in the medical record. Because preliminary analysis indicated that virtually all verified procedures fell within the 5 year time interval allowed on the verification form, time was not included in the definition of agreement / incorrect. Outcomes which included 'No Record' or 'No Follow-up / No Reply' were deleted from these analyses.
The proportion of agreement was used as a measure of agreement between self-reports and medical records. This method has been used in other verification studies. Other measures of agreement such as the kappa statistic, sensitivity and specificity, are inappropriate in this study. Although Kappa has the advantage of correcting for chance agreement, it operates under the assumption that errors between two data sources are independent (45). Since contact with the appropriate medical record source is dependent on subjects' recall of the source, this assumption is violated. Further, the completeness of both the available records and the record search are unknown and cannot be considered a 'gold standard' against which to evaluate self-reports in terms of either sensitivity, defined as the proportion of true positives, or specificity, the proportion of true negatives.

Bivariate analyses examined the association between each explanatory variable, categorized for continuous variables as before, and the outcome variable, "Accuracy", using a Pearson chi-square test for association (65). Variables which were found to be significantly associated with outcome, were subsequently included in a multiple logistic regression model (EGRET®) for agreement between self-reports and medical records. A backward stepwise elimination of variables with \( p \)-values > .05 based on the Likelihood Ratio Statistic (LRS) was used to arrive at the final model. The goodness-of-fit of the model was informally evaluated by dividing the residual deviance by the degrees of freedom. In addition, logistic regression analysis using a generalized estimating equation approach was fitted, allowing for a comparison of standard error estimates using clustered (by subject identification number) and unclustered data (58).

Objective 3
In order to compare the effect of exposure measurements from different data sources on estimates of the relative risk of thyroid cancer, exposure data were summarized for each subject. The resultant data set recorded the total frequency of each type of exposure for each subject. The year of each self-/medical report was no longer part of the record because exposures were now in aggregate form. A new exposure variable was created for use in subsequent analyses. 'Exposed' subjects were defined as those with any exposure to 'head X-rays and/or neck X-rays and/or CT scans'. 'Unexposed' subjects included those reporting no exposure of any kind as well as subjects
reporting exposures other than ‘head or neck X-rays, or CT scans’. Bivariate analyses (SAS*) examined associations between case-control status and exposure, age group, and sex. Analyses were carried out separately using exposure measurements from 4 data subsets: 1) Self-Reports, 2) Self-Reports with Available Medical Records, 3) Medical Record Reports, and 4) Self-Reports verified in Medical Records. If no medical record was available, observations were deleted from analyses relying on medical records. Logistic regression modelling (EGRET©) was carried out to estimate the odds ratios of thyroid cancer using exposure measurements from each data subset. Age and sex were also included in the model to check for residual confounding, because they were the basis of frequency matching in the original study population.

Objective 4
To determine the accuracy of reported non-exposure (negative self-reports) to radionuclides in the study population, univariate analysis using SAS* software was carried out to describe the data set. Bivariate analyses, using a Pearson $\chi^2$ test of association (65), examined associations between categorical variables (age, sex, case-control status, and number of hospital contacts) and the record search outcome (no record of subject, no radionuclide record, or positive radionuclide record).
5. RESULTS

1) STUDY POPULATION: DISTRIBUTION OF VARIABLES AMONG SUBJECTS REPORTING EXPOSURE

5.1. STUDY PARTICIPANTS

At the conclusion of the recruitment period, 678 cases and 2,000 controls were identified in Ontario. Physician consent was denied for 81 cases. Questionnaires were sent to the remaining 597 cases and 2,000 controls. Of these, 447 cases and 1,117 controls completed questionnaires (total = 1,564). Subjects reporting only chest, dental, leg or lower arm exposures, or exposures which had occurred outside Canada, or within 2 years of the diagnosis date were not eligible for the verification study, leaving 814 subjects (248 cases and 566 controls) with 1,873 reported verification-eligible exposures (Table 3). Cases reported 628 exposures (2.5 exposures per case). Controls reported 1,245 (2.2 exposures per control).

5.1.1. Sociodemographic Characteristics Of Participants

Controls were chosen to approximate the expected 3:1 female to male distribution of thyroid cancer cases. The sex distribution among respondents reporting exposure was similar (Table 4). The mean age of the study population (n=814) at the time of the questionnaire mailing was 47.8 years. Ages ranged from 16 to 86 years, with a median age of 47.5 years. Age was grouped into four intervals for subsequent analyses (Table 4). Education was categorized into 4 groups determined by years of schooling completed. Endpoints were selected to distribute the frequency of reported educational attainment within meaningful groups. The following 4 groups were used for analysis: subjects whose schooling had ended in Grade 9 or earlier (18.3%), subjects completing Grade 10 or higher in high school (32.8%), subjects completing some technical, trade or vocational school in addition to high school (25.0%), and subjects with some university education (24.0%) (Table 4).
<table>
<thead>
<tr>
<th>Table 3: Summary of Study Population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>A) Number of subjects identified (May 1989)</td>
</tr>
<tr>
<td>B) Number of MD case contact refusals</td>
</tr>
<tr>
<td>C) Number of questionnaires (Q) sent out</td>
</tr>
<tr>
<td>D) Q sent but undeliverable, lost to f/u. or subject ineligible</td>
</tr>
<tr>
<td>E) Number of non-respondents</td>
</tr>
<tr>
<td>F) Number of Refusals</td>
</tr>
<tr>
<td>G) Number of questionnaires returned</td>
</tr>
<tr>
<td>H) Response rate (%) (G/(C-D))</td>
</tr>
<tr>
<td>I) Consent rate (%) for verification</td>
</tr>
<tr>
<td>J) Respondents reporting medical radiation exposures</td>
</tr>
<tr>
<td>K) Respondents with verification eligible exposures*</td>
</tr>
<tr>
<td>L) % Respondents with verification eligible exposures (K/G)</td>
</tr>
<tr>
<td>M) Number of procedures eligible for verification</td>
</tr>
</tbody>
</table>

* excluding chest, dental, leg, arm exposures; exposures outside Canada; <2 yrs. prior to diagnosis date
Table 4: Summary of Sociodemographic Variables

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>FREQUENCY (PERCENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>604 (74.2)</td>
</tr>
<tr>
<td>Male</td>
<td>210 (25.8)</td>
</tr>
<tr>
<td>Age:</td>
<td></td>
</tr>
<tr>
<td>≤ 34 Years</td>
<td>198 (24.3)</td>
</tr>
<tr>
<td>35 - 49 Years</td>
<td>251 (30.8)</td>
</tr>
<tr>
<td>50 - 64 Years</td>
<td>222 (27.3)</td>
</tr>
<tr>
<td>≥ 65 Years</td>
<td>143 (17.6)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Grade 9 or less</td>
<td>149 (18.3)</td>
</tr>
<tr>
<td>Grade 10 - 13</td>
<td>266 (32.8)</td>
</tr>
<tr>
<td>Technical/Trade/Vocational</td>
<td>203 (25.0)</td>
</tr>
<tr>
<td>University ± Technical</td>
<td>195 (24.0)</td>
</tr>
</tbody>
</table>

1 n = 814
2 1 observation not reported
3 Includes 38 respondents with ≤ Grade 9 - some technical, trade, or vocational school
4 Includes 9 respondents with ≤ Grade 10 - some university, ± tech, trade, or vocational school

5.2. SOURCES OF MEDICAL RECORD INFORMATION

Sources noted were the final contacted sources of medical record information and may have been preceded by other unsuccessful attempts at record retrieval. Not all of the final contacted sources replied, but further avenues of medical record pursuit were exhausted. Physicians were the final record source contacted for 821 self-reported exposures, hospitals for 806 exposures, clinics for 46 exposures, and chiropractors for 31 exposures. No medical record source was available for 169 exposures, either because subjects failed to identify a record source, provided a source that could not be pursued because a practitioner had died or retired, or a clinic could not be located, or a photocopied consent was unacceptable to the source. Table 5 shows the distribution of final contacted medical record sources.
Table 5: Final Medical Record Source for 1,704 Self-Reports
with Medical Record Information*

<table>
<thead>
<tr>
<th>RECORD SOURCE</th>
<th>FREQUENCY (PERCENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician</td>
<td>821 (48.2)</td>
</tr>
<tr>
<td>Hospital</td>
<td>806 (47.3)</td>
</tr>
<tr>
<td>Clinic</td>
<td>46 (2.7)</td>
</tr>
<tr>
<td>Chiropractor</td>
<td>31 (1.8)</td>
</tr>
</tbody>
</table>

* A medical record source was not available for an additional 169 self-reports.

5.2.1. Response From Medical Record Sources

Medical record responses were grouped into 4 categories: ‘No Follow-up / No Reply’, ‘No Subject Record’, ‘Incorrect’, and ‘Self-Report = Medical Record’ (Exposure Agreement).

‘No Follow-Up / No Reply’ to requests for medical record information was the outcome of verification attempts for 360 self-reported exposures (19.2%). No source was given or available for 169 exposures, and no reply was received from a medical source for 187 exposures. Four requests for verification listed the wrong self-reported exposure on the form and were considered to have no follow-up.

‘No Subject Record’ was the reply for 531 self-reports (28.4%), with medical record source responses indicating either ‘Don’t Know’ without supplying additional information (245) or ‘No Subject Record’ (286).

A response of ‘Incorrect’ was received for 158 self-reported exposures (8.4%), with no additional information supplied by the medical record source for 120 of these exposures. The remaining 38 self-reported exposures were not in the same field as the exposure noted in the medical record. Self-reports were the same as medical records (Exposure Agreement) for 824 self-reported exposures (44%). Medical record outcomes are shown in Tables 6.
Table 6: Medical Record Responses*

<table>
<thead>
<tr>
<th>VERIFICATION OUTCOME</th>
<th>FREQUENCY (PERCENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Follow-Up /No Reply</td>
<td>360 (19.2)</td>
</tr>
<tr>
<td>No Subject Record</td>
<td>531 (28.4)</td>
</tr>
<tr>
<td>Incorrect</td>
<td>158 (8.4)</td>
</tr>
<tr>
<td>Exposure Agreement</td>
<td>824 (44.0)</td>
</tr>
</tbody>
</table>

* n = 1,873 self-reports

A response was received from a medical record source for over 80% of self-reported exposures (agreement + incorrect + no subject record). However, 28% of the responses indicated that there was no record of the subject, and hence, no medical record information. When information was available, the proportion of agreement between self-reported exposures and medical record exposures was 83.9% (agreement / (agreement + incorrect)).

5.3. EXPOSURE

5.3.1. Self-Reports

Self-reported exposure types were tallied individually, then classified into groups for subsequent analyses based on their distance from the thyroid. Multiple exposures of the same or different type may have been reported by a single respondent. The most commonly reported exposure field, accounting for 32% of all reported exposures, included 'head and neck X-rays and computerized tomography (CT) scans'. Because CT scans are commonly of the head, reported CT's (81) were grouped with head and neck X-rays. The second most commonly reported exposure (29.3%) included X-rays involving barium swallows or enemas (see Table 7).
5.3.2. Medical Records

Although medical record sources responded to requests for information for 982 self-reported exposures, a medical record of exposure was available for only 862 self-reports. The remaining 120 medical record responses noted ‘Incorrect’ on the verification form without providing any exposure information (see 5.2.2. ‘Incorrect’). Table 7 shows the frequency of exposure types in medical records (based on 862 exposures with medical record information) and self-reports (based on 1,873 self-reported exposures). ‘Head and neck X-rays and CT scans’ were most frequently reported, followed by X-rays involving barium swallows or enemas. These two exposure categories accounted for more than 60% of self-reports and medical record reports.

Table 7: Distribution of Radiation Exposures noted in Self-Reports and Medical Records

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Self-Reports* Frequency (Percent)</th>
<th>Medical Records** Frequency (Percent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head. Neck X-Ray: CT Scan</td>
<td>600 (32.0)</td>
<td>265 (30.7)</td>
</tr>
<tr>
<td>Upper Arm. Shoulder X-Ray</td>
<td>151 (8.1)</td>
<td>54 (6.3)</td>
</tr>
<tr>
<td>Heart. Rib X-Ray: Mammography</td>
<td>99 (5.3)</td>
<td>65 (7.5)</td>
</tr>
<tr>
<td>Barium Swallow / Enema</td>
<td>549 (29.3)</td>
<td>258 (30.0)</td>
</tr>
<tr>
<td>Abdomen. Spine. Hip X-Ray</td>
<td>336 (17.9)</td>
<td>156 (18.1)</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>50 (2.7)</td>
<td>15 (1.7)</td>
</tr>
<tr>
<td>Radionuclides</td>
<td>88 (4.7)</td>
<td>49 (5.7)</td>
</tr>
</tbody>
</table>

* n = 1,873 self-reported exposures

** n = 862 exposures noted in medical record (excludes 120 ‘Incorrect’ medical record responses without exposure information)
5.4. YEAR OF EXPOSURE

5.4.1. Self-Reported Year of Exposure

The majority of reported exposures occurred in more recent years, with fewer exposures in earlier time periods. A preference for reporting years ending in ‘0’ and ‘5’ is indicated by the observed peaks for these years (Figure 1). In subsequent analyses, reported years were grouped by decade. No year was provided for 89 (4.8%) self-reports (see Table 8).

Table 8: Self-Reported Decade of Exposure

<table>
<thead>
<tr>
<th>SELF-REPORTED EXPOSURE YEAR</th>
<th>FREQUENCY* (PERCENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1980</td>
<td>702 (37.5)</td>
</tr>
<tr>
<td>1970 - 1979</td>
<td>659 (35.2)</td>
</tr>
<tr>
<td>1960 - 1969</td>
<td>285 (15.2)</td>
</tr>
<tr>
<td>≤ 1959</td>
<td>138 (7.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>89 (4.8)</td>
</tr>
</tbody>
</table>

* n = 1,873 exposures
Figure 1: Self-Reported Year of Exposure
5.4.2. Years Elapsed between Questionnaire Mail Date and Self-Reported Exposure Year

The number of years between the questionnaire mail date and the self-reported year of exposure ranged from a minimum of 2 years (more recent exposures were not verified) up to 58 years. The mean number of years elapsed was 13.3 and the median, 11. Of the 1,784 exposures for which a year of exposure was reported, 65% were within 15 years of the questionnaire mail date. The number of years elapsed since exposure may provide information which is more generalizable to other studies than the reported year of exposure. In subsequent analyses, ‘Years elapsed’ was grouped by 5-year intervals, but exposures reported 15 or more years before the questionnaire mail out were grouped together. Table 9 shows the number of self-reports in each elapsed year group.

Table 9: Frequency of Exposures in each Elapsed Year Group
(Questionnaire Mail Date - Self-Reported Exposure Year)*

<table>
<thead>
<tr>
<th>YEARS ELAPSED</th>
<th>FREQUENCY (PERCENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 5 Years</td>
<td>401 (22.5)</td>
</tr>
<tr>
<td>6 - 10 Years</td>
<td>473 (26.5)</td>
</tr>
<tr>
<td>11 - 14 Years</td>
<td>287 (16.1)</td>
</tr>
<tr>
<td>≥ 15 Years</td>
<td>623 (34.9)</td>
</tr>
</tbody>
</table>

* n = 1,784 (1,873 - 89 exposures reported without a year of exposure)

5.4.3. Medical Record Year Of Exposure

Over half the documented exposures in medical records (51%) occurred after 1980, within 8 years of the verification form mailout, and 86% were reported after 1970. This may be related to record retention requirements, which obligate hospitals and practitioners to maintain records for prescribed periods, usually 7 - 10 years. In contrast, only 72% of self-reports were reported after
1970, while almost 23% of self-reports exposures were reported earlier. Table 10 compares the frequency of exposures in self-reported and medical record year groups.

Table 10: Distribution of Exposures in Self-Reported and Medical Record Year Groups

<table>
<thead>
<tr>
<th>REPORTED YEAR GROUP</th>
<th>SELF-REPORTS(^1) (%)</th>
<th>MEDICAL RECORDS(^2) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980 or later</td>
<td>702 (37.5)</td>
<td>440 (51.0)</td>
</tr>
<tr>
<td>1970 - 1979</td>
<td>659 (35.2)</td>
<td>309 (35.8)</td>
</tr>
<tr>
<td>1960 - 1969</td>
<td>285 (15.2)</td>
<td>90 (10.4)</td>
</tr>
<tr>
<td>1959 or earlier</td>
<td>138 (7.4)</td>
<td>14 (1.6)</td>
</tr>
<tr>
<td>not reported</td>
<td>89 (4.8)</td>
<td>9 (1.0)(^3)</td>
</tr>
</tbody>
</table>

\(^1\) \(n = 1,873\) self-reported exposures  
\(^2\) \(n = 862\) exposures reported in medical records  
\(^3\) confirmed despite missing self-reported year

5.4.4. Years Elapsed Between Verification Mail date and Medical Record Exposure Year

The time elapsed between the verification mail date and the reported medical record year ranged from 0 to 42 years. Exposures documented in the same year as the verification form mail out (0 years elapsed) suggest that a subject incorrectly recalled the date of exposure - unlikely since many questionnaires were completed before verification began, or that the most recent documented exposure in the records was used for verification. The mean number of years elapsed was 10.2 years and the median, 8 years. Sixty percent of exposures found in medical records were within 10 years of the verification form mailout, suggesting that records were more readily available for recent exposures. Table 11 shows the exposure frequency in each elapsed time period.
Table 11: Years Elapsed between Verification Mail Out and Medical Record Year

<table>
<thead>
<tr>
<th>YEARS ELAPSED</th>
<th>FREQUENCY (PERCENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 5 Years</td>
<td>256 (30.0)</td>
</tr>
<tr>
<td>6 - 10 Years</td>
<td>259 (30.4)</td>
</tr>
<tr>
<td>11 - 14 Years</td>
<td>152 (17.8)</td>
</tr>
<tr>
<td>≥ 15 Years</td>
<td>186 (21.8)</td>
</tr>
</tbody>
</table>

n = 853 medical record exposures with reported year

5.4.5. Difference Between Self-Reported And Medical Record Year

Self-reported years of exposure were compared to medical record years of exposure to assess the accuracy of the self-reported year. This comparison assumed that the medical record was a "gold standard" and reflected the same exposure to which the respondent referred, and not an earlier or later one recorded in the accessed record. Both self-reported and medical record year were available for 793 exposures. Of these, 54.6% of exposures were reported in the same year, and 94.2% were within 5 years of each other. The verification form sent to medical sources stated that exposures to be verified could be within 5 years of the self-reported exposure year. Table 12 lists the distribution of year differences shown graphically in Figure 2.

Table 12: Comparison of Self-Reported and Medical Record Year Differences

<table>
<thead>
<tr>
<th>REPORTED YEAR - MEDICAL RECORD YEAR</th>
<th>FREQUENCY (PERCENT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; ( -10) Year Difference</td>
<td>12 (1.5)</td>
</tr>
<tr>
<td>- (6 - 10) Year Difference</td>
<td>26 (3.3)</td>
</tr>
<tr>
<td>- (1 - 5) Year Difference</td>
<td>174 (21.9)</td>
</tr>
<tr>
<td>Same Year</td>
<td>433 (54.6)</td>
</tr>
<tr>
<td>+ (1 - 5) Year Difference</td>
<td>140 (17.7)</td>
</tr>
<tr>
<td>+ (6 - 10) Year Difference</td>
<td>8 (1.0)</td>
</tr>
</tbody>
</table>

n = 793 exposures where both self-reported and medical record year were known
Figure 2: Reported Year versus Medical Record Year

Legend:
- SAME YEAR
- 1-5 YR DIFF
- 6-10 YR DIFF
- >10 YR DIFF

Distribution of Differences
Self-Reported Year of Exposure

- 1970-79 (n=2285)
- 1980 (n=401)
- 1990-99 (n=89)
- 1999 (n=18)

% of Self-Reported Exposures
II) MEDICAL RECORD AVAILABILITY

To ascertain medical record availability and explore the determinants of record availability, medical record responses (Table 6) were collapsed into two categories: 'No Record / Missing' which included no record of subject, no follow-up of medical source possible, and no reply from medical source, and 'Medical Record Available' which included agreement between self-report and medical record, medical record different from self-report, and medical record response of "Incorrect" without additional information. This dichotomy assumed that the appropriate medical source was accessed and that a response of "Incorrect" from a medical record source referred to the self-reported exposure rather than the absence of a subject record. Using this definition, medical records were available for 982 of 1,873 self-reported exposures. The proportion of record availability ('Medical Record Available' + "No Record / Missing") was 52.4%.

5.6. CASE-CONTROL STATUS

Medical records were available for 318 of 628 case-reported exposures (50.6%) and 664 of 1,245 control-reported exposures (53.3%). A $\chi^2$ test indicated that there was no significant association between case-control status and record availability ($p = 0.27$) (Table 13).
Table 13: Associations between Listed Variables and Medical Record Availability

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chi-square</th>
<th>Degrees of Freedom</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-Control Status</td>
<td>1.22</td>
<td>1</td>
<td>0.270</td>
</tr>
<tr>
<td>Sex</td>
<td>11.97</td>
<td>1</td>
<td>0.001</td>
</tr>
<tr>
<td>Age Group</td>
<td>5.67</td>
<td>3</td>
<td>0.129</td>
</tr>
<tr>
<td>Education</td>
<td>19.37</td>
<td>3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Self-Reported Exposure</td>
<td>31.90</td>
<td>6</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Self-Reported Year</td>
<td>144.81</td>
<td>3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Years since Self-Report</td>
<td>133.60</td>
<td>3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Medical Record Source</td>
<td>40.20</td>
<td>3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(excluding missing source)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.7. SOCIODEMOGRAPHIC VARIABLES

The study population included 604 females and 210 males. Records were available for 768 of 1,403 female-reported exposures (54.7%) and 214 of 470 male-reported exposures (45.5%). A \( \chi^2 \) test indicated that the association between sex and record availability was highly significant (\( p = 0.001 \)) (Table 13).

The highest proportion of medical records was available for respondents aged 34 years or less (55.3%). Records were available for 48.8% of exposures reported by respondents aged 35-49 years and for 26.8% of exposures reported by respondents aged 50-64 years. Medical records were available for 54.7% of exposures among respondents aged 65 years or older. A \( \chi^2 \) test indicated that there was no significant association between age and record availability (\( p = .129 \)) (Table 13).
Respondents with ≤ Grade 9 education reported 312 exposures, of which 193 (61.8%) had available medical records. Records were available for 314 of 624 respondents completing additional years of high school (50.3%) and 271 of 497 respondents with some technical, trade, or vocational school (54.5%). The lowest record availability rate was found for those with some university education, who reported 439 exposures, of which 204 (46.5%) had available records. The \( \chi^2 \) test indicated that the association between educational status and record availability was highly significant (\( p < 0.001 \)) (Table 13). A cross-tabulation of sex and education showed a higher proportion of males with higher educational levels.

5.8. SELF - REPORTS

5.8.1. Exposure Type

The highest proportion of record availability was found for heart, rib, and mammography exposures (73.7%). Records were available for 55 of 88 (62.5%) radionuclide exposures, and for 52% of both head, neck, and CT exposures (315 of 600) and barium swallows/enemas (286 of 549). Together, x-rays of the head and neck, and CT (n = 315) and x-rays involving barium swallow/enema (n = 286) accounted for 62.1% of the 982 available medical records (Figure 3). A \( \chi^2 \) test indicated a significant association between self-reported exposure type and record availability (\( p < 0.001 \)) (Table 13).

5.8.2. Year of Exposure

Record availability decreased in each earlier decade. Records were available for 64.4% of exposures reported in 1980 or later, 50.2% of exposures reported between 1970 - 1979, 38.2% of exposures reported between 1960 - 1969, and 18.1% of exposures reported in 1959 or earlier. An unanticipated finding was the availability of records for 73% of 89 exposures for which no exposure year was reported (Figure 4). A \( \chi^2 \) test (excluding exposures without a reported year) indicated a highly significant association between reported exposure year and record availability.
Figure 3: Distribution of Responses to Request for Medical Record Data

By Self-Reported Exposure Groups
A cross-tabulation between sex and year of self-report indicated that a higher proportion of males reported exposures in earlier years.

5.8.3. Years Elapsed Since Self-Reported Exposure

Years elapsed examined the effect of the passage of time on record availability and may be more generalizable to other studies than year of self-report. Records were available for 67.3% of exposures self-reported within 5 years of questionnaire mail out, 59% for exposures within 6-10 years, 51.9% for exposures within 11-14 years, and 35.2% for exposures at least 15 years earlier. Although record availability declined with each increasing 5 year interval, records were available for more than 35% of exposures reported at least 15 years earlier. A chi-square test (3 df) indicated a significant association between years elapsed and record availability (p < 0.001).

5.9. MEDICAL RECORD SOURCE

If a record source could not be pursued, the exposure was deleted (n=169) leaving 1,794 for subsequent analysis. Physicians, contacted for 821 exposures, were able to provide records for 523 exposures (63.7%). Hospitals were contacted for 806 exposures and had records for 408 (50.6%) self-reported exposures. Chiropractors were contacted for only 31 exposures but had records available for 27 exposures (87%). Clinics were contacted for 46 exposures and had records available for 24 (52%) of exposures. Although chiropractors were a superior source of records, only 31 exposures were reported from chiropractors. Record availability from physicians was high and they were a source of records for a large number of respondents. A chi-square test (3 d.f.) indicating a strong association between record availability and medical record source (p < 0.001) (Table 13). A cross-tabulation of sex and record source indicated that hospitals were contacted for a higher proportion of males than females.
Figure 4: Distribution of Responses to Request for Medical Record Data

By Self-Reported Year (All Exposures)

Total Self-Reports = 1,873
5.10. SUMMARY OF BIVARIATE ANALYSIS

An available medical record was defined as a verification response of ‘Agreement’ or ‘Incorrect’ (with or without additional exposure information). Using this definition, medical records were available for 982 self-reports. Characteristics related to exposure (type of exposure, reported year, years elapsed between questionnaire mail out and exposure, and medical record source) appeared to be more important determinants of record availability than some subject-related characteristics (case-control status, age group).

5.11. MULTIVARIATE ANALYSIS

Two definitions of medical record availability were used in multivariate analysis. The first, or ‘broad’ definition of record availability, used in bivariate analysis, considered the medical record to be available if the response from the medical record source indicated either medical record ‘Agreement’ with the self-report, or ‘Incorrect’ with or without additional exposure information.

Analysis was also carried out using a second, ‘narrow’ definition of record availability to eliminate the possibility that an ‘Incorrect’ response to a verification request might have referred to the subject rather than the exposure. ‘Incorrect’ responses without any exposure information were excluded. A medical record was considered available only if verification responses noted an exposure in the medical record. The following definitions were used in the ‘narrow’ definition of record availability:

1) No Record / Missing: included ‘No Follow-up / No Reply’ and ‘No Subject Record’
2) Medical Record Available: Exposure Record Only.

5.11.1. ‘Broad’ Definition of Medical Record Availability

To estimate the odds ratio of record availability, variables which were significantly associated with record availability in bivariate analysis (Table 13) were included in a logistic regression model, with ‘Record Availability’ as the outcome of interest. The referent category was ‘No Record Available’.
Analysis was limited to 1,620 of 1,873 reported exposures, after elimination of observations with missing values for any of the potential explanatory variables. Outcomes are shown in Table 14. The following equation best fit the data. As an informal test of the goodness-of-fit of the model, the residual deviance was divided by the degrees of freedom for a value of 1.29. Values close to 1 suggest that the model is a good fit to the data.

\[
\log \left( \frac{Pr(Record\text{Availability})}{1 - Pr(Record\text{Availability})} \right) = \alpha + \beta_1(\text{Clinic}) + \beta_2(\text{Physician}) + \beta_3(\text{Chiropractor}) + \\
\beta_4(6-10\text{ Years Elapsed}) + \beta_5(11-14\text{ Years Elapsed}) + \beta_6(\geq 15\text{ Years Elapsed}) + \\
\beta_7(\text{Female}) + \beta_8(\text{Some tech./trade/vocational}) + \beta_9(\text{Gr. 10-13}) + \beta_{10}(\leq \text{Gr. 9})
\]

Including 'Reported Year Group' instead of 'Years Elapsed between Questionnaire Mail out and Self-Reported Year' resulted in a model with a similarly good fit to the selected model. 'Years Elapsed' was preferred because it is more easily generalizable.

The odds of record availability were increased relative to hospital contact, if physicians or chiropractors were contacted. The narrow confidence interval for physician record availability suggests that the odds ratio estimate is relatively precise. The same cannot be said for chiropractor records, where the confidence interval ranges from 2 to nearly 20. The odds of record availability declined inversely to the number of years elapsed compared to the odds of record availability for exposures reported within 5 years of questionnaire mailout, being significantly lower for exposures reported more than 10 years earlier. The narrow confidence intervals again suggest the relative precision of the odds ratio estimates. The odds of record availability were higher if the respondent was female, or the respondent had Grade 9 or less education. However, confidence intervals for educational levels other than Grade 9 or less included '1', indicating that despite estimated odds ratios > 1, only ≤ Grade 9 education was a significant determinant of record availability. In bivariate analysis, a higher proportion of males than females reported early exposures, a higher
education, and reported hospital sources. These variables were all associated with a decreased odds of record availability in the model.

Table 14: Significant Determinants of Medical Record Availability*

<table>
<thead>
<tr>
<th>Variable</th>
<th>LRS** (p-value)</th>
<th>Odds Ratio Estimate</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Record Source (referent = hospital)</td>
<td>40.94 (&lt;.001)</td>
<td>1.00</td>
<td>0.61 - 2.24</td>
</tr>
<tr>
<td>Clinic</td>
<td></td>
<td>1.17</td>
<td>1.17 - 1.78</td>
</tr>
<tr>
<td>Physician</td>
<td></td>
<td>1.44</td>
<td></td>
</tr>
<tr>
<td>Chiropractor</td>
<td></td>
<td>6.70</td>
<td>2.28 - 19.67</td>
</tr>
<tr>
<td>Years Elapsed (referent = ≤ 5 years)</td>
<td>75.11 (&lt;.001)</td>
<td>1.00</td>
<td>0.57 - 1.03</td>
</tr>
<tr>
<td>6 - 10 Years</td>
<td></td>
<td>0.76</td>
<td>0.41 - 0.79</td>
</tr>
<tr>
<td>11 - 14 Years</td>
<td></td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td>≥ 15 Years</td>
<td></td>
<td>0.32</td>
<td>0.24 - 0.42</td>
</tr>
<tr>
<td>Sex (referent = Male)</td>
<td>9.49 (0.002)</td>
<td>1.00</td>
<td>1.13 - 1.81</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>1.43</td>
<td></td>
</tr>
<tr>
<td>Education (referent = university ± tech.)</td>
<td>9.95 (.019)</td>
<td>1.00</td>
<td>0.98 - 1.75</td>
</tr>
<tr>
<td>Some tech. / trade / vocational</td>
<td></td>
<td>1.31</td>
<td></td>
</tr>
<tr>
<td>Grade 10 - 13</td>
<td></td>
<td>1.07</td>
<td>0.81 - 1.40</td>
</tr>
<tr>
<td>≤ Grade 9</td>
<td></td>
<td>1.60</td>
<td>1.14 - 2.24</td>
</tr>
</tbody>
</table>

* 'Broad' Definition of Medical Record Availability  n = 1,620 exposures

** LRS = Likelihood Ratio Statistic

5.11.2. 'Narrow' Definition of Medical Record Availability

Of 982 self-reports with an available medical record using the 'broad' definition of availability, 120 were eliminated using the 'narrow' definition of availability because verification responses indicated 'Incorrect' without additional exposure information, leaving 862 self-reports for which medical records were considered available and 891 with no available record. The same variables were included in a logistic regression model using the narrower definition of record availability. Results were very similar to those obtained using the broad definition of record availability, with the exception of 'years elapsed between questionnaire mail out and self-reported year'. The odds of
record availability decreased significantly as early as 6 - 10 years prior to the questionnaire mail out, compared to the broad definition which showed a significant decrease in record availability only after 11-14 years had elapsed. Because the outcomes were similar using both ‘broad’ and ‘narrow’ definitions of record availability, ‘Incorrect’ verification responses without further exposure information likely referred to incorrect self-reports and not lack of a subject record. If the ‘broad’ definition of record availability had referred to a lack of subject records and included a mix of incorrect exposures and unavailable (no record of subject) medical records, odds ratios using the broader definition would have been reduced towards the null.

5.11.3. Evaluation of the Effect of Multiple Observations from Single Respondents

To check for possible problems in measurement precision due to multiple observations from individual respondents, logistic regression analyses were carried out using only the first observation, or only the last observation, from each respondent. Using the broader definition of record availability, and only the first self-report, record source and years elapsed remained significantly associated with record availability. No significant associations with sex or education were observed. These results were also seen using the narrower definition of record availability. Similar results were observed using only the last reported observation from each individual, and both the broad and narrow definitions of record availability. The sample size was reduced to 814 observations, the number of respondents, from 1,873 using first or last observations, which may have reduced the power to detect associations. Logistic regression analysis using a generalized estimating equation approach to compare standard errors before and after correction for multiple observations confirmed that multiple observations from single respondents did not modify the findings. In all cases, the number of years elapsed between questionnaire mail date and year of self report, as well as medical record source accessed, were significant determinants of record availability.
### Table 15: Significant Determinants of Medical Record Availability*

(Narrow Definition of Record Availability)

<table>
<thead>
<tr>
<th>Variable</th>
<th>LRS** (p-value)</th>
<th>Odds Ratio Estimate</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Record Source (referent = hospital)</td>
<td>51.53 (&lt;.001)</td>
<td>1.00</td>
<td>0.63 - 2.42</td>
</tr>
<tr>
<td>Clinic</td>
<td></td>
<td>1.23</td>
<td>0.63 - 2.42</td>
</tr>
<tr>
<td>Physician</td>
<td></td>
<td>1.65</td>
<td>1.33 - 2.05</td>
</tr>
<tr>
<td>Chiropractor</td>
<td></td>
<td>6.85</td>
<td>2.30 - 20.41</td>
</tr>
<tr>
<td>Years Elapsed (referent = ≤ 5 years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 - 10 Years</td>
<td>74.80 (&lt;.001)</td>
<td>1.00</td>
<td>0.55 - 1.00</td>
</tr>
<tr>
<td>11 - 14 Years</td>
<td></td>
<td>0.57</td>
<td>0.40 - 0.80</td>
</tr>
<tr>
<td>≥ 15 Years</td>
<td></td>
<td>0.31</td>
<td>0.23 - 0.41</td>
</tr>
<tr>
<td>Sex (referent = male)</td>
<td></td>
<td>6.34 (.012)</td>
<td>1.00 - 1.73</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>1.35</td>
<td>1.06 - 1.73</td>
</tr>
<tr>
<td>Education (referent = univ. ± tech.)</td>
<td></td>
<td>7.86 (.049)</td>
<td>1.00 - 1.77</td>
</tr>
<tr>
<td>Some tech./trade/vocational</td>
<td></td>
<td>1.31</td>
<td>0.97 - 1.77</td>
</tr>
<tr>
<td>Some high school only</td>
<td></td>
<td>1.04</td>
<td>0.78 - 1.38</td>
</tr>
<tr>
<td>≤ Grade 9</td>
<td></td>
<td>1.50</td>
<td>1.06 - 2.12</td>
</tr>
</tbody>
</table>

* n = 1,505 observations after elimination of observations with missing values
**LRS = Likelihood Ratio Statistic

### III) ACCURACY OF SELF-REPORTED EXPOSURES

To evaluate the accuracy of self-reported medical radiation exposures by comparison with exposures noted in medical records, the two response categories corresponding to unavailable records, "No Follow-up / No Reply" and "No Subject Record", were eliminated, leaving 982 self-reported exposures where medical records were available. The following 2 categories were determined by the response noted on the medical verification form:

1) Incorrect - exposure on medical verification form was noted only as 'Incorrect' or was specified, but not the same field as the self-reported exposure.

2) Agreement - exposure on medical verification form was noted as 'correct', or was specified and in the same field as self-reported exposure.
The overall proportion of agreement was \( \frac{824}{982} \) or 83.9%.

The assumption was again made that “Incorrect” referred to exposures and not subjects. However, there were too few exposures (38) noted outside of the self-reported exposure field to warrant analysis using a narrower definition of agreement limited to these 38 exposures.

5.12. SUMMARY OF BIVARIATE ANALYSIS

Contingency tables were used to examine the association between each variable and medical record agreement. Findings are shown in Table 16. Only two variables were significantly associated with record agreement - medical record source and type of self-reported exposure. The proportion of agreement between self-reports and exposures noted in the medical records of physicians was 88.9%, 83.3% for clinic records, 77.9% for hospital records, and 77.7% for chiropractic records. When the accuracy of specific types of exposures was examined, the proportion of agreement between self-reported X-rays of the heart, ribs, or mammography, and medical records was 89%. The lowest proportions of agreement were for arm or shoulder X-rays (77%), and X-rays of the head, neck, or CT scans (79%). The proportion of agreement for the remaining types of exposure (barium swallow / enema; abdomen / spine / hip; radiotherapy; and radionuclides) ranged between 86% and 88%.
Table 16: Associations between Listed Variables and Record Agreement in Bivariate Analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chi-square</th>
<th>Degrees of Freedom</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-Control Status</td>
<td>0.60</td>
<td>1</td>
<td>0.44</td>
</tr>
<tr>
<td>Sex</td>
<td>1.83</td>
<td>1</td>
<td>0.18</td>
</tr>
<tr>
<td>Age Group</td>
<td>4.35</td>
<td>3</td>
<td>0.23</td>
</tr>
<tr>
<td>Education</td>
<td>1.44</td>
<td>3</td>
<td>0.70</td>
</tr>
<tr>
<td>Medical Record Source*</td>
<td>21.21</td>
<td>3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Self-Reported Exposure</td>
<td>13.13</td>
<td>6</td>
<td>0.04</td>
</tr>
<tr>
<td>Self-Reported Years Elapsed</td>
<td>4.63</td>
<td>4</td>
<td>0.33</td>
</tr>
<tr>
<td>Medical Record Years Elapsed</td>
<td>0.90</td>
<td>3</td>
<td>0.83</td>
</tr>
<tr>
<td>Medical Record Exposure*</td>
<td>11.26</td>
<td>6</td>
<td>0.08</td>
</tr>
</tbody>
</table>

* 25% of cells had expected counts <5. $\chi^2$ may not be a valid test.
** n = 982 exposures

5.13. MULTIVARIATE ANALYSIS

Variables which showed a significant association with record agreement in bivariate analyses (Tables 16) were included in a logistic regression model of record accuracy. "Incorrect" was used as the referent category. After elimination of observations with missing values, analysis was based on 917 observations ("Agreement" = 770, "Incorrect" = 147). The initial model included self-reported exposure and medical record source, and was extended to include other variables such as case-control status, sex, age group, and education. After elimination of variables with p-values > .05, only medical record source remained (Table 17). The following equation represented the model which best fit the data. As an informal test of the goodness-of-fit of the model, the residual deviance was divided by the degrees of freedom for a value of 0.86. Values close to 1 suggest that the model is a good fit to the data.
\[
\log \left\{ \frac{\Pr(Record\,Agreement)}{1 - \Pr(Record\,Agreement)} \right\} = \alpha + \beta_1(\text{Clinic}) + \beta_2(\text{Physician}) + \beta_3(\text{Chiropractor})
\]

Table 17: Significant Determinants of Agreement between Self-Reports and Medical Records

<table>
<thead>
<tr>
<th>Variable</th>
<th>LRS** (p-value)</th>
<th>Odds Ratio Estimate*</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Record Source (referent = hospital)</td>
<td>25.64 (0.001)</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Clinic</td>
<td></td>
<td>1.40</td>
<td>0.46 - 4.23</td>
</tr>
<tr>
<td>Physician</td>
<td></td>
<td>2.57</td>
<td>1.76 - 3.74</td>
</tr>
<tr>
<td>Chiropractor</td>
<td></td>
<td>1.03</td>
<td>0.40 - 2.64</td>
</tr>
</tbody>
</table>

* 'Agreement' is the referent category ('0' outcome).
** LRS = Likelihood Ratio Statistic

The estimated odds of correctly reported exposures was significantly increased if physicians' records were accessed, and the relatively narrow confidence interval suggests that the odds ratio estimate is reasonably precise. Wider confidence intervals associated with odds ratio estimates for clinics and chiropractors both include '1', indicating that the odds of record accuracy are not significantly related to accessing records from these sources. The wider confidence intervals reflect the imprecision of the estimated odds ratios because of the small numbers in these two categories.

Self-reported exposure which was moderately associated with record accuracy in bivariate analysis (p = .04) showed no significant association with record accuracy in multivariate analysis (p = .10). However, when self-reported exposure was collapsed into 2 categories, 'head and neck x-ray, or CT scan', with all other types of exposures grouped together as the referent category, the estimated odds of record agreement were significantly decreased for 'head and neck x-ray, or CT scan' (Table 18). One of the lowest levels of accuracy was found for 'head and neck x-ray, or CT scan' (79%) in bivariate analysis.
Table 18: Significant Determinants of Agreement between Self-Reports and Medical Records (Using Two Categories of Self-Reported Exposure)

<table>
<thead>
<tr>
<th>Variable</th>
<th>LRS** (p-value)</th>
<th>Odds Ratio Estimate*</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Record Source (referent = hospital)</td>
<td>25.64 (&lt;.001)</td>
<td>1.00</td>
<td>0.44 - 4.08</td>
</tr>
<tr>
<td>Clinic</td>
<td></td>
<td>1.35</td>
<td></td>
</tr>
<tr>
<td>Physician</td>
<td></td>
<td>2.49</td>
<td>1.71 - 3.64</td>
</tr>
<tr>
<td>Chiropractor</td>
<td></td>
<td>1.15</td>
<td>0.44 - 2.95</td>
</tr>
<tr>
<td>Self-Reported Exposure</td>
<td>5.13 (0.02)</td>
<td>1.00</td>
<td>0.45 - 0.94</td>
</tr>
<tr>
<td>(referent = other exposures)</td>
<td></td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>Head and Neck X-ray, CT scan</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 'Agreement' is referent category ('0' outcome)
** LRS = Likelihood Ratio Statistic

Logistic regression analysis using a generalized estimating equation approach to compare standard errors before and after correction for multiple observations from single respondents. confirmed that multiple observations from single respondents did not alter the findings. Estimated odds ratios for clustered and unclustered data were similar.

IV) COMPARISON OF THE EFFECT OF EXPOSURE DATA FROM DIFFERENT SOURCES ON ESTIMATES OF THE RELATIVE RISK OF THYROID CANCER

Exposure data were summarized by subject for all of the 1,564 study respondents. Of these, 750 respondents reported either no exposure to medical radiation or no exposure eligible for verification. The remaining 814 respondents reported 1,873 verification-eligible exposures investigated in previous chapters. The subject-specific data set recorded subjects' sex, age, case-control status, and frequency of each self-reported exposure (where applicable), as well as the frequency of each medical record exposure, where records were available. Because exposure frequencies were used, the year of exposure was no longer a part of the record.
To compare the effect of exposure measurements from different data sources on estimates of the relative risk of thyroid cancer (Objective 3), a new exposure variable based on exposure to ‘Head and/or Neck X-ray, or CT scan’ was created for illustration purposes in subsequent analysis. The association of prior head and neck X-rays with thyroid cancer has been documented in the literature. In addition, it represented the exposure reported most frequently by study subjects (439 subjects reported some exposure to ‘Head and/or Neck X-ray, or CT scan’).

The following definition of exposure was used in subsequent analyses:

“Exposed” subjects were those with one or more ‘head and/or neck X-ray, or CT scan’, with or without additional exposures.

“Unexposed” subjects were those with exposures other than ‘head and/or neck X-ray, or CT scan’, subjects reporting no verification-eligible exposures, or subjects reporting no medical radiation exposures of any kind.

When classification was based on medical record information, the record was considered to be missing if no medical record of any exposure was available. Otherwise, subjects were classified as “Exposed” or “Unexposed” according to the medical record data.

5.14. EXPOSURE DATA USED FOR COMPARISON

Epidemiologic studies often rely on self-reported data to estimate odds ratios. The verification component of this study provided an opportunity to evaluate the effect of exposure measurements from different data sources on estimates of the relative risk of thyroid cancer (Objective 3), and to assess the reliability of self-reports relative to medical records. Four subsets of exposure data were compared:
1) Self-Reports - Exposure classification in this group was determined by the self-reports of the 1,564 study respondents. Of these, 439 were classified as ‘Exposed’ (based on the above definition), and 1,125 were classified as ‘Unexposed’. Unexposed subjects included the 750 respondents who had not reported any (verification-eligible) exposures, as well as 375 subjects with medical radiation exposure but no reported ‘head, and / or neck X-ray, or CT scan’. This data set provided an estimate of the odds ratio of thyroid cancer based on self-reported information, as would normally occur in case-control studies reliant on self-reports.

2) Self-Reports with Available Medical Records - Exposure classification in this group was determined by the self-reports of subjects reporting exposures for which medical records were available. Subjects reporting verification-eligible exposures were eliminated (n = 320) if no medical records of any exposure were available, reducing the number of subjects in this group to 1,244. Of these, 292 were classified as ‘Exposed’. Unexposed subjects included the 750 respondents reporting no (verification-eligible) exposures, as well as 202 subjects with no reported ‘head, and / or neck X-ray, or CT scan’. This subgroup provided an estimate of the odds ratio of thyroid cancer using self-reports when medical records are available. These results are not of interest on their own, but allow for a comparison of relative risk estimates based on self-reports and medical records using the same subject population as in the subsequent group (3) which relies on medical record information.

3) Medical Records - The subjects (n=1,244) in this group were the same as in the second group, but exposure classification relied on the medical record reports, rather than the self-reports, of subjects reporting exposures for which records were available. This reduced the number of subjects classified as ‘exposed’ to 221. The 750 respondents reporting no (verification-eligible) exposures, as well as 273 subjects with no medical record of ‘head and / or neck X-ray, or CT scan’ comprised the ‘unexposed’ group. If
medical record data were used to determine exposure, this subgroup would provide the appropriate estimate of the odds ratio.

4) Self-Reports verified in Medical Records - This group was subdivided based on two definitions of exposure.

i) This group was restricted to study subjects whose exposure classification (‘Exposed’, ‘Unexposed’) was the same in both their self-reports and medical records. Subjects were eliminated (n = 75) if their self-reported exposure classification (‘Exposed’, ‘Unexposed’) was not the same as their medical record exposure classification, reducing the total number of subjects in this group to 1,169. The number of subjects classified as ‘Exposed’ in both self-reports and medical records was 219. The 750 respondents reporting no (verification-eligible) exposures, as well as an additional 200 subjects with no self-reported or medical record of ‘head and / or neck X-ray, or CT scan’ comprised the ‘Unexposed’ group (n = 950). Exposure measurements from this data subgroup are more accurate than those from the above-mentioned groups. Estimates of the odds ratio obtained using this data would be of interest where measurement of exposure was restricted to exposures confirmed in medical records.

ii) This subgroup classified subjects as ‘Exposed’ if the actual number of self-reported ‘head and / or neck X-ray, or CT scan’ was the same as the number verified in medical records. Subjects were eliminated if the number self-reported ‘head and / or neck X-ray, or CT scan’ was not the same as the number verified in the medical record (n=124). This reduced the number of ‘Exposed’ subjects to 170. The number of ‘Unexposed’ subjects remained 950. The total number of subjects was 1,120. This provides a more accurate measure of exposure than 4 i), because it addresses the total amount of confirmed exposure. Odds ratios estimated from this exposure data would be important where the quantity of exposure was of interest.
Table 19 shows the distribution of “Exposed” and “Unexposed” subjects, as well as the distribution of case-control status, sex, and age group in each of the data sets.

**Table 19: Distribution of Variables using Data from Different Data Subsets**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data Set *</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. (n=1,564)</td>
</tr>
<tr>
<td></td>
<td>Freq. (%)</td>
</tr>
<tr>
<td>Exposure:</td>
<td></td>
</tr>
<tr>
<td>Exposed</td>
<td>439 (28.1)</td>
</tr>
<tr>
<td>Unexposed</td>
<td>1.125 (71.9)</td>
</tr>
<tr>
<td>Case-Control Status:</td>
<td></td>
</tr>
<tr>
<td>Case</td>
<td>447 (28.6)</td>
</tr>
<tr>
<td>Control</td>
<td>1.117 (71.4)</td>
</tr>
<tr>
<td>Sex: Male</td>
<td>400 (25.6)</td>
</tr>
<tr>
<td>Female</td>
<td>1.164 (74.4)</td>
</tr>
<tr>
<td>Age Group:</td>
<td></td>
</tr>
<tr>
<td>≤ 34 Years</td>
<td>478 (30.6)</td>
</tr>
<tr>
<td>35 - 49 Years</td>
<td>448 (28.6)</td>
</tr>
<tr>
<td>50 - 64 Years</td>
<td>355 (22.7)</td>
</tr>
<tr>
<td>≥ 65 Years</td>
<td>283 (18.1)</td>
</tr>
</tbody>
</table>

* Data Set
1. Self-Reports
2. Self-Reports with Available Medical Records
3. Medical Records
4. Self-Reports verified in Medical Records
   i) Exposure Classification the same in both Self-Reports and Medical Records
   ii) Frequency of Self-Reported ‘Head and/or Neck X-ray, or CT scan’ same as Frequency verified in Medical Record

The highest proportion of subjects were classified as ‘Exposed’ (28.1%) based on self-reported exposure data (Data Set 1). The proportion of subjects classified as ‘Exposed’ declined in each
subsequent data subset with the exception of a slight increase from Data Set 3 to 4.i, due to a
decrease in the sample size and a negligible change in the number of ‘Exposed’ subjects in Data Set
4.i. Two subjects, classified as ‘Exposed’ using medical record data (Data Set 3) were classified as
‘Unexposed’ using self-reported data, reducing the number of subjects classified as ‘Exposed’ by 2
in Data set 4.i. An additional 73 subjects, classified as ‘Exposed’ using self-reported data and
‘Unexposed’ using medical record data, were eliminated from Data Set 4.i, further reducing the
sample size.

While the proportion of subjects classified as ‘Exposed’ decreased in each data subset, the
proportion of cases and controls remained relatively constant. Similarly the distribution of sex and
age, used as the basis of frequency matching in the selection of controls, remained relatively
constant in each data subset. The composition of data subsets 2 and 3 were the same, differing only
in the classification criteria for exposure.

5.15. BIVARIATE ANALYSIS

Bivariate analysis was used to examine associations between case-control status and age, sex, and
exposure using exposure data from each of the data subsets. Results are shown in Table 20.
Table 20: Association Between Variables and Case-Control Status in Bivariate Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>(d.f.)*</th>
<th>Data Set **</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=1,564)</td>
<td>(n=1,244)</td>
</tr>
<tr>
<td></td>
<td>$\chi^2$ (p-value)</td>
<td>$\chi^2$ (p-value)</td>
</tr>
<tr>
<td>Exposure</td>
<td>(1)</td>
<td>7.19 (0.01)</td>
</tr>
<tr>
<td>Age Group</td>
<td>(3)</td>
<td>2.83 (0.42)</td>
</tr>
<tr>
<td>Sex</td>
<td>(1)</td>
<td>0.31 (0.58)</td>
</tr>
</tbody>
</table>

* Degrees of Freedom
** Data Set
1. Self-Reports
2. Self-Reports with Available Medical Records
3. Medical Records
4. Self-Reports verified in Medical Records
   i) Exposure Classification the same in both Self-Reports and Medical Records
   ii) Frequency of Self-Reported ‘Head and/or Neck X-ray, or CT scan’ same as Frequency verified in Medical Record

Exposure based on self-reported data (Data Set 1), self-reported data with available medical records (Data Set 2), and self-reported exposure verified in medical records (Data Set 4.i), were significantly associated ($p < .05$) with case-control status. The p-value associated with $\chi^2$ test between exposures based on medical record reports (Data Set 3) and case-control status was marginally greater than .05. Exposure based on the number of self-reports matching the number of reports found in medical records (Data Set 4.ii) was not significantly associated with case-control status ($p=0.36$). Age Group and Sex, used as the basis of frequency matching in the selection of controls, showed no significant association with case-control status in any of the data subsets.

5.16. MULTIVARIATE ANALYSIS

Estimated odds ratios of thyroid cancer were compared using exposure measurements based on data from each data subset. Age Group and Sex were also included in the models because they
were the basis for frequency matching in the original study population and could be potential confounders. The following equation represents the model used for comparison of each subset:

\[
\log \left( \frac{\Pr(ThyroidCancer)}{1 - \Pr(ThyroidCancer)} \right) = \alpha + \beta_1(\text{Exposed}) + \beta_2(\text{Female}) + \beta_3(35-49 \text{ Years}) + \\
\beta_4(50-64 \text{ Years}) + \beta_5(\geq 65 \text{ Years})
\]

A comparison of the odds ratio estimates and 95% Confidence Intervals derived from this model using exposure measurements from each data set is shown in Table 21.
Table 21: Comparison of Odds Ratios and Confidence Intervals from Multivariate Analysis using Different Measures of Exposure

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data Set **</th>
<th>1. (n=1,564)</th>
<th>2. (n=1,244)</th>
<th>3. (n=1,244)</th>
<th>4.i. (n=1,169)</th>
<th>4.ii. (n=1,120)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>p OR est. (CI)*</td>
<td>p OR est. (CI)*</td>
<td>p OR est. (CI)*</td>
<td>p OR est. (CI)*</td>
<td>p OR est. (CI)*</td>
</tr>
<tr>
<td>Ref=Unexposed</td>
<td></td>
<td>.01 1.00</td>
<td>.003 1.00</td>
<td>.06 1.00</td>
<td>.03 1.00</td>
<td>.37 1.00</td>
</tr>
<tr>
<td>Exposed</td>
<td></td>
<td>1.38</td>
<td>1.54</td>
<td>1.35</td>
<td>1.43</td>
<td>1.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(1.09 - 1.76)</td>
<td>(1.16 - 2.04)</td>
<td>(0.99 - 1.84)</td>
<td>(1.04 - 1.96)</td>
<td>(0.81 - 1.67)</td>
</tr>
<tr>
<td>Sex: Ref=Male</td>
<td></td>
<td>.55 1.00</td>
<td>.77 1.00</td>
<td>.78 1.00</td>
<td>.96 1.00</td>
<td>.84 1.00</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>1.06</td>
<td>1.02</td>
<td>1.02</td>
<td>0.97</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.82 - 1.37)</td>
<td>(0.76 - 1.36)</td>
<td>(0.77 - 1.36)</td>
<td>(0.72 - 1.31)</td>
<td>(0.74 - 1.37)</td>
</tr>
<tr>
<td>Age Group:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ref ≤ 34 Years</td>
<td></td>
<td>.48 1.00</td>
<td>.49 1.00</td>
<td>.52 1.00</td>
<td>.22 1.00</td>
<td>.34 1.00</td>
</tr>
<tr>
<td>35 - 49 Years</td>
<td></td>
<td>1.07</td>
<td>0.99</td>
<td>1.02</td>
<td>0.99</td>
<td>1.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.80 - 1.42)</td>
<td>(0.72 - 1.36)</td>
<td>(0.75 - 1.40)</td>
<td>(0.72 - 1.37)</td>
<td>(0.75 - 1.46)</td>
</tr>
<tr>
<td>50 - 64 Years</td>
<td></td>
<td>0.93</td>
<td>0.86</td>
<td>0.89</td>
<td>0.86</td>
<td>0.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.69 - 1.27)</td>
<td>(0.61 - 1.22)</td>
<td>(0.63 - 1.26)</td>
<td>(0.60 - 1.22)</td>
<td>(0.65 - 1.35)</td>
</tr>
<tr>
<td>≥ 65 Years</td>
<td></td>
<td>0.82</td>
<td>0.77</td>
<td>0.79</td>
<td>0.68</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.59 - 1.15)</td>
<td>(0.53 - 1.13)</td>
<td>(0.54 - 1.14)</td>
<td>(0.46 - 1.02)</td>
<td>(0.49 - 1.09)</td>
</tr>
</tbody>
</table>

* 95% Confidence Interval
** Data Set
1. Self-Reports
2. Self-Reports with Available Medical Records
3. Medical Records
4. Self-Reports verified in Medical Records
   i) Exposure Classification the same in both Self-Reports and Medical Records
   ii) Frequency of Self-Reported 'Head and/or Neck X-ray, or CT scan' same as Frequency verified in Medical Record.
Estimates of the odds ratios were similar using measurements of exposure based on self-reports (Data Set 1 - OR 1.38), self-reports with available medical records (Data Set 2 - OR 1.54), medical record reports (Data Set 3 - OR 1.35), and self-reported exposure verified in medical records (Data Set 4 - OR 1.43). The estimated odds ratios were significant in Data Sets 1, 2, and 4. The p-value was only marginally greater than .05 (p=.06) using medical record exposure data (Data Set 3). The narrowest confidence interval was seen in data set 1 with the largest sample size. Confidence intervals were slightly wider in other subgroups, but this was primarily a function of the number of observations in each data subset. However, all confidence intervals overlapped.

Data set 4 used a different measure of exposure than the other 4 groups, relying on the confirmed frequency of exposure rather than the fact of exposure as a basis for classification. Studies concerned with estimating the actual burden of radiation exposure may be more interested in assessing the frequency of exposure. The estimated odds ratio in this subset (1.17) was lower than the odds ratios calculated in the other subsets. Of 49 subjects lost from Data Set 4 because recorded frequencies of exposure did not match, 24 of 75 cases (32%) were classified as exposed in Data Set 4 and 25 of 144 controls (17%) were previously classified as exposed. The disproportionate loss of exposed cases reduced the odds ratio estimate to non-significant levels (p=.37).

V) ACCURACY OF REPORTED NON-EXPOSURE

To assess the possibility of false negative self-reports of radionuclides, a random sample of 10% of cases and 5% of controls reporting no radionuclide exposure on the subject questionnaire was selected. The sample included 36 cases and 52 controls (n = 88). Hospital responses were classified as:

1) No Record: No record of subject, which implied no radionuclide exposure at any of the contacted hospitals

2) No Radionuclide Record: Same as ‘No Record’ or record of subject, but no radionuclide record, and
3) Radionuclide Record: Record of radionuclide exposure.

Information on the sample and the results of the medical record search are shown in Table 22.

Only one record of radionuclide administration was found. The subject was a female case, aged 50-64, who had reported a radionuclide exposure in 1987. Radionuclide administration was noted in the medical record to have occurred in 1984, approximately 3 years prior to the diagnosis date. For the purposes of this study, the subject was considered unexposed. One of the eligibility criteria for the negative verification study required either no report of radionuclide exposure, or radionuclide exposure within 2 years of thyroid cancer diagnosis for cases, or after January 1, 1986 for controls.

If the subject had not reported any radionuclide exposure, 1 false negative report out of 88 negative reports (1.1%) could be a significant finding given the low prevalence of radionuclide exposure (the prevalence of radioiodine, a type of radionuclide is estimated to be 1% of the population). However, the false negative report may have been related to the eligibility criteria. Barring this report, a superficial look at the findings gives reasonable confidence to the accuracy of negative self-reports of radionuclide exposure.
**Table 22: Information Collected on Negative Verification Sample**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age Group:</strong></td>
<td></td>
</tr>
<tr>
<td>≤ 34 Years</td>
<td>29 (33.0)</td>
</tr>
<tr>
<td>35 - 49 Years</td>
<td>17 (19.3)</td>
</tr>
<tr>
<td>50 - 64 Years</td>
<td>21 (23.9)</td>
</tr>
<tr>
<td>≥ 65 Years</td>
<td>21 (23.9)</td>
</tr>
<tr>
<td><strong>Sex:</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>20 (22.7)</td>
</tr>
<tr>
<td>Female</td>
<td>68 (77.3)</td>
</tr>
<tr>
<td><strong>Status:</strong></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>52 (59.1)</td>
</tr>
<tr>
<td>Case</td>
<td>36 (40.9)</td>
</tr>
<tr>
<td><strong>Number of Hospital Contacts:</strong></td>
<td></td>
</tr>
<tr>
<td>1-10</td>
<td>28 (31.8)</td>
</tr>
<tr>
<td>11-20</td>
<td>16 (18.2)</td>
</tr>
<tr>
<td>&gt; 20</td>
<td>44 (50.0)</td>
</tr>
<tr>
<td><strong>Radionuclide Record:</strong></td>
<td></td>
</tr>
<tr>
<td>No Record</td>
<td>46 (52.3)</td>
</tr>
<tr>
<td>No RN Record</td>
<td>41 (46.6)</td>
</tr>
<tr>
<td>RN Given</td>
<td>1* (1.1)</td>
</tr>
</tbody>
</table>

* One record of radionuclide administration found for a female case, aged 50-64, in 1984, approximately 3 years prior to diagnosis date. The number of hospital contacts = 21.
6. DISCUSSION

Study data provided an opportunity to assess the availability of medical records and to explore the determinants of availability. In addition, where records were available, it was possible to evaluate the agreement between self-reported radiation exposures and exposures noted in the medical record, and to examine the determinants of agreement. Exposure data from medical records, commonly considered a ‘gold standard’, allowed for a comparison of relative risk estimates of thyroid cancer using exposure information collected from self-reports and medical records. Efforts to evaluate the prevalence of false negative reports were undertaken in a 10% sample of respondents (n=88) reporting no radionuclide exposure.

This chapter discusses the overall strengths and limitations of the study. conclusions based on the study objectives outlined in chapter 3. and closes with suggestions for further research.

6.1. STUDY STRENGTHS AND LIMITATIONS

6.1.1. Sample Size

Of 1,564 Ontario subjects who completed the study questionnaire, 814 subjects reported a total of 1,873 verification-eligible exposures. Verification was exposure-specific, with attempts made to verify each of the 1,873 self-reported exposures. There has been some discussion in the literature (18) regarding the appropriateness of basing agreement between two data sources on the respondent versus each episode reported by the respondent. A respondent incorrectly reporting multiple exposures might significantly influence episode-specific agreement, and have little impact on subject-specific agreement. Exposure-specific agreement was selected in the CCRERG verification study to address questions of availability and agreement because it allowed for the evaluation of a range of variables associated with each exposure (years elapsed, source, type of exposure). Analysis was based on 1,873 reported exposures, effectively increasing the sample size beyond 814 subjects. Analysis indicated that multiple observations from single respondents did not modify the findings.
Sample size is an important consideration in determining the power of a study to provide precise estimates and to detect meaningful differences. Generally, a larger sample has a greater ability (power) to detect smaller statistically significant differences. A comparison of sample sizes in selected verification studies is shown in Table 23. The CCRERG study is one of the largest, and thus more likely to detect meaningful effects of explanatory variables on medical record availability and accuracy of self-reports.

Only two other studies examined x-ray exposures (12, 33), each covering 200 or fewer study participants. In the Tristate Leukemia Study (12), agreement was evaluated between medical records and the number of X-rays reported by each respondent. The authors found that 80% of X-rays found in outpatient records had not been reported by respondents. Preston-Martin et al (33) evaluated agreement between dental records and the number of dental X-ray visits reported by each respondent. Recall accuracy was greatly enhanced because respondents were not asked to recall any specifics of exposure beyond an X-ray visit. However, the authors (33) speculated that if agreement with dental records was sought for the precise number of dental radiographs, interview information would have misclassified a high proportion of respondents.

6.1.2. Generalizability

In addition to sample size, Table 23 lists the sex, range of self-reported exposure years, and exposure of interest covered in other verification studies. Several studies incorporating a verification component have examined reproductive histories (21, 23, 27, 28, 29, 30, 31, 39) and been restricted to females. This study included both males and females.

The CCRERG study covered the broadest range of exposure years of any cited study. Self-reported exposure years ranged from 2 to 58 years prior to questionnaire mail out. The median number of years elapsed was 11. Four of the sixteen cited studies verified exposures occurring within the previous 5 years (14, 27, 28, 37) and of these, 3 verified exposures occurring within one year (14, 27, 28). Only 3 studies considered exposures occurring more than 30 years earlier (23, 33, 35) but the sample size was either smaller than the CCRERG study or restricted to females.
Table 23: Participants and Exposure Years Covered in Selected Verification Studies

<table>
<thead>
<tr>
<th>Study Number</th>
<th>Verification-Eligible Sample</th>
<th>Sex</th>
<th>Years Elapsed</th>
<th>Exposure of Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCRERG</td>
<td>814</td>
<td>M,F</td>
<td>2 to 58</td>
<td>medical radiation</td>
</tr>
<tr>
<td>12</td>
<td>200</td>
<td>M,F</td>
<td>not reported</td>
<td>x-ray</td>
</tr>
<tr>
<td>14</td>
<td>1,380</td>
<td>M,F</td>
<td>same year</td>
<td>medical history</td>
</tr>
<tr>
<td>21</td>
<td>334</td>
<td>F</td>
<td>mean = 12</td>
<td>drug use</td>
</tr>
<tr>
<td>22</td>
<td>338</td>
<td>M,F</td>
<td>1-14</td>
<td>med./surg. conditions</td>
</tr>
<tr>
<td>23</td>
<td>1,032</td>
<td>F</td>
<td>≥ 30</td>
<td>estrogen use</td>
</tr>
<tr>
<td>27</td>
<td>270</td>
<td>F</td>
<td>0.75</td>
<td>medical history</td>
</tr>
<tr>
<td>28</td>
<td>1,086</td>
<td>F</td>
<td>0.75</td>
<td>medical history</td>
</tr>
<tr>
<td>29</td>
<td>198</td>
<td>F</td>
<td>4 - 16</td>
<td>oral contraceptive use</td>
</tr>
<tr>
<td>30</td>
<td>911</td>
<td>F</td>
<td>10</td>
<td>Pap smear history</td>
</tr>
<tr>
<td>30</td>
<td>674</td>
<td>F</td>
<td>5</td>
<td>Pap smear history</td>
</tr>
<tr>
<td>31</td>
<td>1,702</td>
<td>F</td>
<td>&lt; 30¹</td>
<td>number of ovaries</td>
</tr>
<tr>
<td>33</td>
<td>204</td>
<td>M,F</td>
<td>&gt; 30</td>
<td>dental x-rays</td>
</tr>
<tr>
<td>35</td>
<td>207</td>
<td>M,F</td>
<td>&gt; 40</td>
<td>surgical history</td>
</tr>
<tr>
<td>37</td>
<td>90</td>
<td>M,F</td>
<td>0 to &gt; 5</td>
<td>medical history</td>
</tr>
<tr>
<td>39</td>
<td>75</td>
<td>F</td>
<td>3 - 17</td>
<td>oral contraceptive use</td>
</tr>
</tbody>
</table>

¹ Exposure Years covered not clear in study report

The age of participants in the CCRERG study was broadly distributed, ranging from 16 to 86 years, with a mean age of 47. Participants were distributed as evenly as possible within four age groups (≤ 34 years, 35-49 years, 50-64 years, ≥ 65 years) for analysis. These age ranges were broader than those in other verification studies, where participants' ages tended to be skewed either towards the elderly or pre-middle age. In a verification study of cataract patients (14), age was reported only as older or younger than 65 with 52% of subjects over 65 years of age. Another study (21) of agreement between interview and medical record data was restricted to women who entered a retirement community after age 60. The mean age of the study population was 72 years.
Age groupings of <60 years, 60-75 years, and 75+ years were used in the analysis of agreement between interview and medical record data in a case-control study of chronic lymphocytic leukemia (22), suggesting an older population. In another study (23), female participants were between 45 - 74 years of age. Similar age ranges, between 40 and 64, were studied in an evaluation of surgical history recall (35). In a study of oral contraceptive use (29), less than 25% of participants were over the age of 35. Age distribution was more evenly distributed in a verification study of cervical cancer patients (30) with ages ranging from 20 - 64, and in a dental X-ray study (33) where participants were between 25 and 64 years old. Narrow age groupings in some studies may explain why age has generally not had a demonstrated effect on recall.

Educational levels in the CCRERG study ranged from Grade 9 or less through university. Approximately 50% had ≤ Grade 13 education, while the remainder completed some technical, trade, or vocational school or university. In another verification study (14), two thirds of the participants had ≤ Grade 12 education. However, in a verification study of estrogen use (23), educational level was distributed relatively evenly between grammar, high school, and college.

The wide distribution of exposure years in the study population, as well as the inclusion of both sexes, considerable age variability and broad educational backgrounds, suggest that findings from this study are more readily generalizable to other populations.

6.1.3. Permission to Access Medical Records

Consent to access medical records was high for both cases (98%) and controls (93%) in the CCRERG study. Other verification studies found similarly high rates of consent. In one study comparing interview and medical record information on estrogen use (23), a consent rate of 96.7% among estrogen users and 89.7% among non-users was reported. In a cervical cancer study (30), 94% of cases and 82% of controls provided consent to contact their physicians. Consent was somewhat higher in a cervical dysplasia study (30), with 96% of cases and 87% of controls providing consent. In a dental X-ray validation study (33), approximately 6% of eligible case-control pairs were excluded because consent to contact their dentists was denied, primarily because of unpaid dental bills. The lowest consent rates were reported in a study of birth malformations
where consent was denied by 21% of case mothers with private obstetricians, and 40% of control mothers with private obstetricians. Cases generally provide higher rates of consent than controls, presumably because they have more of a vested interest in the study outcome. However, the high rates of consent for both cases and controls in the CCRERG study make it unlikely that verification ability was compromised by differences in record access permission.

6.1.4. Bias

Some studies have noted differences in recall accuracy between cases and controls (25-31). Generally, cases are thought to report exposures more accurately than controls, being either more aware of their medical history or more motivated to explore previous exposures.

In the CCRERG study, permission to access medical records was high for both cases and controls. Potential case-control differences in reporting may also have been limited by the cover letter accompanying the subject questionnaire (Appendix 1), which introduced the study as a ‘National Health Study’ rather than a study of thyroid cancer. No significant association between case-control status and record availability or accuracy was found in this study.

Analysis in this study was exposure- and not subject-specific. A subject incorrectly recalling multiple exposures may have biased the study outcomes. Logistic regression using a generalized estimating equation approach indicated no evidence that multiple observations from single subjects had biased the results in this study.

6.1.5. Accuracy of Measurement Instruments

The measurement instrument is particularly important for exposures which may in themselves have little significance to the respondent. Subjects’ lack of awareness of important, but non-invasive procedures such as X-rays, has been demonstrated in some studies (12, 16). Radiation exposures in the CCRERG thyroid cancer study were determined by responses to 3 questions (Appendix 1). A list of possible exposure choices was provided for X-rays.
however, the list was incomplete. No listing for X-rays of the back was provided. The only mention of back was in the listing for 'back of neck', and respondents may have included lumbar or thoracic X-rays of the spine in this category for lack of a more appropriate category. Similarly, there was no listing for mammography, and although a listing for 'other' was provided, respondents may have limited their responses to the categories provided. A listing for C.T. scans was available, but scans may have been to various body sites.

A further limitation of exposure measurement was related to the verification form sent to medical sources (Appendix 2). Check boxes for 'Correct', 'Incorrect', and 'Don't know' were provided, as well as an area in which to provide additional information such as the description and year of exposure, or corrections. While a 'correct' response was straightforward to interpret, an 'incorrect' response without additional exposure information may have implied that the self-reported exposure was incorrect or the accessed medical source was incorrect. Similarly a response of 'don't know' may have referred to no patient record or no record of exposure. The verification forms also indicated that a self-reported year could be ± 5 years of the medical record date. Although this was meant to broaden the scope of the medical record search, results suggest that in some cases the most recent exposure noted in the medical record was used to confirm a self-report (see 5.4.4.). The verification form did not request information on the years of medical record checked, nor ask hospitals whether both outpatient or inpatient records were checked. Thus the completeness of the medical record search is unknown.

No information on additional radiation exposures noted in medical records was requested. This would have provided an indication of the amount of false negative self-reports. Although the verification of non-exposure to radionuclides addressed the possibility of false negatives, it is not clear if these results are generalizable to other types of radiation exposures. Requesting additional medical information may have provided a more meaningful estimate of false negative radiation exposure. Finally, because of the sample size and geographic area covered in this study, multiple abstractors were involved in the medical record search. The accuracy and completeness of the information they provided is not known.
6.1.6. Self-Reported Exposure Patterns

‘Head, and / or Neck X-rays, and CT scans’ were reported with the greatest frequency (32%), followed by x-rays involving barium swallow or enema. These radiation exposures may occur with the greatest frequency in the population.

To jog subjects’ memories and to provide investigators with some indication of the significance of an exposure, subject questionnaires asked for the reason of the radiation exposure. Answers to this question were sparse, and the only indication of the significance of an exposure to a subject may be the frequency with which each type of exposure was reported. It is possible that exposures to Head, and / or Neck X-rays, and CT scans’ are the result of serious, acute conditions that are more likely to be recalled and that memory of x-rays involving barium swallow or enema are unpleasant enough to sustain recall.

There was evidence of a reporting year preference for years ending in ‘0’ or ‘5’. To assess the accuracy of the self-reported year, the medical record year was subtracted from the self-reported year to allow for the possibility of “telescoping”, which would result in a more recent self-reported year than the year noted in the medical record. In each reporting decade, the largest proportion of exposures occurred in the same year as the self-reported year of exposure, suggesting that respondents were able to accurately recall the year of exposure. The highest proportion of agreement between self-reported and medical record year occurred for exposures reported prior to 1960. This contradicts reports in the literature which suggest decreasing accuracy with increasing time spans. It may indicate that some respondents had long-standing contact with a medical source, or had access to their medical records allowing them to confirm the year of exposure. More than one quarter of exposures (26.7%) were reported at an earlier date (reported year - medical record year was a negative number) than indicated in the medical record. It is possible that because of the 5 year leeway allowed on the medical verification form, record abstractors provided the most recent record of a noted exposure. Over 94% of self-reported exposures verified in the medical record were within 5 years of each other. For this reason,
agreement between year of self-report and medical record was not used as a criterion of agreement.

6.1.7. Analysis

In addition to questionnaire weaknesses, certain aspects of the analysis could be improved. The first concerns the categories selected for each variable. For the most part, categories were chosen to be both meaningful and to distribute self-reported frequencies throughout the levels. For this reason, specific body sites of exposure were grouped into 7 categories. Educational levels were set at ≤ Grade 9, etc. because numbers did not justify perhaps more intuitive categories such as elementary, high school, university, etc.. The exception to this rationale of category groupings was record source, where throughout the analysis, four categories of record source were maintained despite extremely low numbers in two of the categories - clinics (n = 46) which should have been combined with hospitals. and chiropractors (n = 31) which should have been combined with physicians. As they were, numbers in these categories were too small to generate any meaningful information.

A useful adjunct to the analysis would have included calculation of the effect of various levels of exposure misclassification on the estimation of the odds ratio of thyroid cancer. That is, if a proportion of respondents reporting no exposure were in fact exposed, the impact on the estimated odds ratio and levels of significance could be determined for varying estimates of misclassification. This analysis could also be used for positive self-reports. In this way, the extent of differential recall bias that would be required to overturn a given inference of association could be determined (66). Unfortunately, the study did not provide comprehensive data on misclassification from which one could infer a range of likely values (being restricted essentially to the accuracy of self-reports).

6.1.8. Summary of Study Strengths and Limitations

In summary, this study is one of the larger verification studies with sufficient power to detect statistically significant effects. It is also the largest study to examine the accuracy of self-reported
radiation exposures. The inclusion of males and females, as well as the broad distribution of age and education, make results more easily generalizable to other populations. Consent to access medical records was high for both cases and controls, and verification ability is not likely to have been compromised by differences in record access permission. No case-control bias or bias from exposure-specific analysis was observed. This study is one of the very few to evaluate the accuracy of exposures from the distant past, and found that where records were available, agreement between self-reports and medical records did not decline with the passage of time. The trend to report exposure years ending in ‘0’ or ‘5’ could affect the definition of agreement in studies relying on year of report as a criteria of agreement.

The completeness of the exposure history is unknown in this study. The questionnaire, itself, may have contributed to the compilation of a less than complete history by omitting or combining exposure listings, resulting in either under-reporting or misclassification of exposures. Lack of clarity on the verification form may have led to misclassification of outcomes by suggesting that a reported exposure was incorrect when in fact there was no record of a subject. The completeness of the record search and the accuracy of the abstractors are also unknown. Most significantly, the extent of false-negative reporting, particularly of X-ray exposures, is not known. A negative verification study of radionuclide exposures was undertaken, but because the sample size was small and the prevalence of radionuclide exposure is low, results may not be generalizable to populations with a much higher prevalence of exposure. Complete medical records were available to Graham et al (12), who found that the amount of X-ray exposure discovered in the medical record was such large a part of the whole radiation experience of respondents that reliance on interview data alone could be completely invalid. Positive self-reports provided by respondents in the CCRERG study may not be a complete picture of true radiation exposure and according to the findings of Graham et al (12), is likely to be an underestimation of their true radiation exposure and there is no adequate measure of the accuracy of reports of no exposure. Thus, it is only possible to draw conclusions about the accuracy of recall for exposures reported by respondents. This has considerable implications for the CCRERG study of radiation exposures and thyroid cancer risk. Thyroid cancer risk estimates would be reduced towards the null if under-reporting was distributed evenly among cases and controls. Differential reporting among cases and controls would alter odds
ratio estimates depending on the distribution of the bias. Nevertheless, many epidemiologic studies rely on self-reports and verification studies restrict themselves to an evaluation of positive self-reports. This verification study while confirming the accuracy of positive self-reports, does not address issues regarding the completeness of self-reported radiation history.

Finally, it is possible that there was recall bias in reporting of certain exposures. However, without knowing the proportion of these exposures compared to the total radiological experience, this is only speculation.

6.2. DETERMINANTS OF MEDICAL RECORD AVAILABILITY

Records were available for 52.4% of self-reported exposures, calculated on a per-exposure basis. When analysis of the CCRERG study was subject-specific, records were available for at least some of the exposures reported by 494 of 814 respondents with verification-eligible exposures (60.7%). This is similar to the medical record retrieval rate of 61.5% reported by Irwin (31) in a large verification study covering approximately 30 years. Record retrieval rates were much higher in a dental X-ray validation study (33) where at least some information was available for 95/102 case-control pairs.

Sex, education, self-reported exposure type, self-reported year, and medical record source were associated with record availability, using both ‘broad’ (including all ‘incorrect’ responses) and ‘narrow’ definitions of availability. Neither case-control status nor age group showed any association with record availability. Records were more likely to be available for exposures reported by females (54.7%) than for those reported by males (45.5%). Females were also more likely to indicate a physician as a primary record source. Record availability from physicians was high (OR=1.44), and they were a source of records for a large number of respondents. Subjects may have had long term contact with a physician who may in turn, have maintained records for longer periods of time than hospitals. This may also be an artefact of the study protocol, which pursued physician records before hospital records when both sources were given. Hospitals may have been contacted when no other source was available. Record retrieval
was very high from chiropractors (OR=6.7), but they represented only 1.8% of the sample and confidence intervals were very broad (2.28 - 19.67).

The record source is an important consideration in future studies. Although medical record departments of hospitals are better equipped to search medical records, physician records were able to provide more complete information. Record availability was greater for exposures reported within 10 years of the questionnaire date than for earlier exposures. There was a significant decline in record availability for exposures reported 11-14 years earlier (OR=.57) and ≥ 15 years earlier (OR=0.32). Nevertheless, records were available for almost 20% of exposures reported prior to 1960 (see Figure 4). Preston-Martin et al (33) also found a decline in the availability of dental records with each 10-year period, with complete records available for 49% of cases and 44% of controls within 20 years of visiting a dentist, and declining to 22% of complete records available for cases and 9% for controls for dental visits more than 20 years earlier. Few other verification studies consider exposures reported more than 10 years earlier. The CCRERG study contributes to the body of knowledge on the verification of exposures going back more than 50 years.

Record availability was lowest for respondents with some university education, and highest for those with ≤ Grade 9 education (OR=1.6). While one might be tempted to speculate that subjects with ≤ Grade 9 education were younger, and therefore had less years of exposure and fewer medical sources to recall, in fact the oldest respondents reported the least education, and may have used medical services more often and had more readily available medical records. University-educated respondents may have been more mobile than other groups, and their medical records purged once minimum retention requirements were met.

Medical records were available for 315 of 600 self-reported ‘X-rays of the head and neck, and CT scan’ (52%) and 286 of 549 self-reports of x-rays involving barium swallow / enema (52%). Together, ‘X-rays of the head and neck, and CT scan’ and x-rays involving barium swallow / enema accounted for 62.1% of the 982 available medical records. The highest percentage of record availability (75%) was found for ‘x-rays of the heart and ribs, and mammography’. These exposures may have been more significant to respondents, or more recent, leading to improved
recall of the medical record source and increased likelihood of record availability. Recall of the medical record source is as dependent on the recall accuracy of respondents as the reported exposures.

6.3. DETERMINANTS OF AGREEMENT BETWEEN SELF-REPORTS AND MEDICAL RECORDS

The overall proportion of agreement between self-reports and medical records was 83.9%. Self-reports which did not agree with medical record reports were considered to be incorrect. Some true positive self-reported exposures may have been excluded because medical records were no longer available or the appropriate medical source was not contacted. The results of this study indicate that the source of medical records is an important determinant, not only of record availability, but also of agreement between self-reported radiation exposures and medical records. Records from physicians were more likely than hospital records to confirm a self-reported exposure. A continuing relationship with a medical practitioner not only extends the availability of records, but may also increase a subject’s awareness of their medical history. Subjects may also have confirmed radiation exposures with their physician before responding to the questionnaire. One study (16) reported more missing information in records from physicians’ offices than in records from clinics or hospitals, however, this was not the experience in this study.

Some investigators (22) found that the accuracy of self-reports was higher for males and for subjects with a better education. However, these subjects were also cases, with more advanced disease. Educational level has not shown consistent associations with recall accuracy. Sex and education were not significantly related to record accuracy in this study.

Age was did not show a significant association with report accuracy in this study, despite a wide variability in the age of the study population. Several other studies (14,21,22,24) were similarly unable to demonstrate an age effect on recall of either a medical source or a self-reported exposure. Concerns over the recall ability of elderly subjects have been expressed, but results in the literature are equivocal.
The years elapsed since self-report was not a significant determinant of record accuracy. In contingency table analysis, the proportion of accurate responses in each elapsed interval (≤ 5 years, 6-10 years, 11-14 years, ≥ 15 years) was over 80%, and numbers of exposures with available records were relatively constant in each interval. This suggests that the accuracy of self-reports is not dependent on the time of the report, and that even self-reports from earlier time periods can be relied on for accuracy.

Although 'Head, neck, and CT' exposures, 'barium swallow / enema', and 'abdomen, spine, or hip' exposures were frequently reported, other categories had less than 75 observations each. These numbers may have affected the power of the study to assess the accuracy of these exposures. When self-reported exposures were collapsed into 2 categories ('head and neck x-ray, and CT scan'; all other exposures) the estimated odds of record agreement was significantly decreased for 'head and neck x-ray, and CT scan' compared to all other exposures. Thus records were more likely to be available, but less likely to be accurate for 'head and neck x-ray, and CT scan'.

No case or control differences were noted for record accuracy. This confirms that there was no reporting bias by status, despite the lower study response rate for controls. Although it is generally believed that case recall is better, other studies (32,33) have found no case-control reporting differences.

6.4. COMPARISON OF THE EFFECT OF EXPOSURE DATA FROM DIFFERENT SOURCES ON ESTIMATES OF THE RELATIVE RISK OF THYROID CANCER

Estimated odds ratios of thyroid cancer were compared using exposure measurements from self-reports and medical records in four data subsets to illustrate their effect on odds ratio estimates.

Based on study findings and a review of the literature, exposure was determined by a history of 'Head and / or Neck X-ray, or CT scan'. An association between pelvic radiation and case-control
status was also noted, but this category may have inadvertently included x-rays of the thoracic or cervical spine because a separate listing for 'back x-rays' was not available on the subject questionnaire. If these subjects were randomly distributed among those classified as exposed and unexposed, odds ratio estimates would be reduced towards the null. Conversely, if they were not randomly distributed, results could be biased in either direction depending on the distribution of these exposures. Radionuclide and radiotherapy exposures also showed an association with case-control status, and although there has been some interest in these exposures as possible risk factors for thyroid cancer in the literature, the number of these exposures reported in this study was small.

The 'Unexposed' group in each data set was comprised of subjects reporting no history of any medical radiation exposure or no exposure to 'Head and / or Neck X-ray, or CT scan'. The negative verification component of the CCRERG study was restricted to a sample of negative self-reports of radionuclide exposure, thus the accuracy of respondents' reports of no exposure are not known.

Data Set 1 relied on self-reported exposures, like many epidemiologic studies. The accuracy of the reports is unknown and reports may include both false negatives (incorrect reports of no exposure) and false positives (incorrect reports of exposure). The estimated odds ratio of 1.38 (95% C.I. 1.09 - 1.76) represents the estimate that would be obtained in case-control studies relying on self-reported information.

Data Set 2 relied on the self-reports of subjects with available medical records, eliminating subjects who reported exposure but for whom medical records were unavailable. This subgroup would not normally be of interest, but provided a measure of internal validity between Data Set 2 and Data Set 3 which was comprised of the same subjects but relied on medical record exposure data. The estimated odds ratio for exposure in Data Set 2 was 1.54 (95% C.I. 1.16 - 2.04), higher than the odds ratio estimate in Data Set 1 and with wider confidence intervals. Cross-tabulation showed that proportionally more controls classified as exposed in Data Set 1, were excluded, leading to an increase in the odds ratio estimate.
Data Set 3, comprised of the same subjects as in Data Set 2, relied on medical record data, allowing for a comparison of the estimated odds ratios using self-reports and medical records among the same study group. If no exposure was documented in the medical record, subjects were classified as ‘Unexposed’. Cross-tabulation showed an 8% drop in the number of cases classified as exposed by medical records and a 5% drop in the number of exposed controls between Data Sets 2 and 3. The disproportionate shift of exposed cases resulted in a lower odds ratio estimate of 1.35, and a concomitant shift in the C.I. (0.99 - 1.84) that included 1. Although medical record information is considered more accurate, the absence of information in an accessed record is not necessarily a confirmation of non-exposure. Apparent over-reporting by a subject may indicate that medical records were incomplete or that the appropriate records were not accessed (14).

Data Set 4 was comprised of subjects whose self-reported exposure agreed with the medical record of exposure, providing the most accurate measure of exposure. Subjects who reported exposure were excluded if no medical record was available or if the medical record did not agree with the self-report. Thus, subjects with true positive self-reports not documented in the medical record may have been excluded. The data set was subdivided into 2 groups. The first group (4 i) used the same definition of exposure as used in Data Sets 1 - 3, based on ever / never exposure to ‘head, neck x-ray, or CT scan’. The odds ratio estimate was 1.43 (95% C.I. 1.04 - 1.96). A stricter measure of exposure was adopted in Data Set 4ii), based on agreement between the frequency of self-reported ‘Head and / or Neck X-ray, or CT scan’ exposures and the frequency noted in the medical record. This subgroup would be of interest to investigators concerned with the total burden of exposure, for example those wanting to estimate the amount of radiation to which a person has been exposed. However, the elimination of subjects with some documented exposure and the sacrifice in sample size would likely be unacceptable to most investigators. The odds ratio estimate dropped to 1.17 (95% C.I. 0.81 - 1.67) in Data Set 4 ii). A disproportionate number of cases classified as exposed in Data Set 4i) were excluded in Data Set 4ii) reducing the odds ratio estimate to non significant levels (p=.37).

Estimated odds ratios of thyroid cancer in each data set were lower, ranging from 1.35 to 1.54 (excluding Data Set 4 ii which used a different definition of exposure) than odds ratio estimates for
prior medical radiation exposure reported in the literature (Table 1). These ranged from 2.8 to 42.2 in cited case-control studies (3,6,7,32). Analysis in this portion of the CCRERG study relied on simplified measures of exposure and estimated odds ratios were calculated for illustration purposes only. No attempt was made to control for confounders or to find a model which best fit the data. Other reported case-control studies of thyroid cancer may have included additional variables in their model and made efforts to control for confounders. Better quality exposure data may have been collected and more comprehensive measures of exposure developed using anthropomorphic phantoms to estimate radiation dose to the thyroid. Radiation exposure may have occurred in early childhood, a significant risk factor for thyroid cancer. Early exposures were not included in this part of the CCRERG study. Generally, radiation exposures occurring within 5 years of thyroid cancer diagnosis have been excluded in reported studies of thyroid cancer (32). The CCRERG study included exposures up to 2 years prior to the diagnosis date. While these factors undoubtedly contributed to the lowered odds ratio estimates, the observed odds ratio estimates in this study were still significantly increased.

Restricting the measure of exposure to agreement between self-reports and medical record data (Data Set 4) provides the most accurate measure of exposure. However, this study provided no evidence of any extra value in using medical record-verified information. Odds ratio estimates were very similar using self-reports (1.38), medical record-confirmed reports (1.43), or medical record data (Data Set 3, OR = 1.35). Confidence intervals were narrowest using self-reports, suggesting a more precise estimate of the odds ratio because of the larger size of the available study population. Confidence intervals were wider using medical record data, and included 1 in Data Set 3. These findings suggest that the price for “accuracy” may be too high, and future studies should put more faith in self-reported data. Self-reports are a reliable and expedient source of information on radiation exposures, particularly for exposures occurring in the distant past for which records may no longer be available. Restricting the analysis to reports confirmed in the medical record, while improving data quality, may unacceptably reduce the sample size (17). Self-reports are a cost-effective method of data collection, and these results suggest that in the absence of a ‘gold standard’ for determining complete exposure history, positive self-reports are accurately recalled and investigators relying on self-reported data should have confidence in the accuracy of
the data. However, the extent of under-reporting in self-reports as well as medical records which partially depend on a subject’s recall of the appropriate source is unknown. Similarly the extent of any bias related to those reports that are unavailable (and whose accuracy can therefore not be checked) is unknown.

Harlow and Linet (18) reviewed agreement between questionnaire data and medical records in 30 studies reported in the literature. Their review illustrated that substantive literature on agreement between self-reports and medical records is scarce. They found that the medical record was more complete for certain illnesses and medications, and for exposure to diagnostic X-rays, but was subject to under-reporting for conditions not necessarily requiring medical attention. They could offer no advice on the choice of self-reports or medical records as a source of exposure information, but strongly endorsed continued evaluation of agreement between self-reports and medical records as a means of validating exposure information. Horwitz (17) commented that since it is not clear if medical records or interviews provide more accurate data, information from each source should be evaluated and presented.

6.5. VERIFICATION OF REPORTED NON-EXPOSURE TO RADIONUCLIDES

A negative verification component was included in the CCRERG study to assess the prevalence of false negative reports of radionuclide exposure. A random sample was selected of 10% of cases and 5% of controls reporting either no radionuclide exposure, or exposure within 2 years of thyroid cancer diagnosis for cases or after 1986 for controls. The sample included 36 cases and 52 controls. Only one report of radionuclide exposure was found in medical records for the 88 subjects. The subject, a case who reported radionuclide exposure in 1987 on the subject questionnaire, was considered ‘unexposed’ by study criteria. The subject’s medical record noted radionuclide exposure in 1984, suggesting that the time of exposure had not been accurately recalled by the subject leading to the subject’s misclassification as ‘unexposed’. The self-reported date of radionuclide exposure was assumed to be correct when subjects with recent exposure were included in the negative verification sample. However, verification requests for positive self-reports (see Appendix 2) allowed for ±5 years from the date of self-report. However, eliminating subjects
with any reported radionuclide exposure may have excluded cases from the negative verification sample, because thyroid cancer cases were likely to have had some radionuclide exposure around the time of diagnosis.

If the subject misclassified as 'unexposed' is excluded, and limitations of the selection criteria are overlooked, negative medical record findings suggest that negative self-reports are accurate and increase confidence in the reliability of the self-reported data. However, the inferences that can be made about the prevalence of false negative self-reports of radionuclide exposure based on a sample size of 88 subjects are limited. The sample size of the original CCRERG thyroid cancer study was determined by the prevalence of radioiodine exposure, a type of radionuclide, estimated to be about 1% of the population (61). Only 65 of 1,564 study respondents (4.2%) reported (verification-eligible) radionuclide exposures. Thirty exposures were reported among 447 case respondents (6.7%) and 35 among 1,117 control respondents (3.1%). These estimates suggest that the prevalence of radionuclide exposure is low and inferences about under-reporting drawn from a sample size of 88 subjects may be uninformative.

One positive observation from a sample of 88 subjects with unreported radionuclide exposure is consistent with a true percent unreported of 0.03 to 6.0% (95% C.I.) (from binomial tables (67)). If the subject with a positive record is deleted because of incorrect exposure classification, then an observation of no positive records would be consistent with a true percent of 0 to 4.0% (95% C.I.) (67). Since the prevalence of radionuclide exposure in the study population is 4%, the sample is of limited power and tells us little about the extent of under-reporting in the sample.

In addition, results of a validation study of negative self-reports of radionuclide exposure may not be generalizable to other types of negative radiation reports. The prevalence of radionuclide exposure is substantially less than the prevalence of x-ray exposure. It is possible that chance alone could account for the apparent verification of non-exposure to radionuclides. The prevalence of false negative reports of x-ray exposure may be considerably higher.
Considerable time and effort was involved in the conduct of this study. Sensitivity calculations, using different estimates of the prevalence of false negative self-reports (e.g. 1% of self-reported negative exposure is misclassified; 2% is misclassified, etc.) to determine the stability of the odds ratio estimate, would be a more cost-effective approach, and would provide a more valid estimate of the true effect of false negative radionuclide exposure.

Few studies incorporate a negative verification component. Werler et al (27) noted that when reviewing records, the absence of an event or exposure in the medical record cannot necessarily be interpreted as unexposed. Absence of an exposure or illness is rarely documented, rather the appropriate record may not have been accessed.

6.6 CONCLUSIONS

The CCRERG thyroid cancer study included a large number of subjects, resulting in a sample size with sufficient power to reveal differences in odds ratio estimates of record availability and accuracy and to illustrate the impact of exposure measurements from different sources on estimates of the odds ratio of thyroid cancer.

Design limitations in the subject questionnaire may have contributed to incomplete ascertainment of exposure. No listing for either back X-rays or mammography was provided, and there was one catchall listing for all types of C.T. exposure. A category for ‘other’ was available and some respondents used this space to report back or mammography exams. Nevertheless it is possible that some exposures were not reported because appropriate categories were not available on the subject questionnaire.

Determinants of record availability (Objective 1) included the medical record source, years elapsed since exposure, sex, and education. The study protocol, which sought information from physicians first, may have increased the estimated odds ratio of record availability from physicians. However, results also suggest that physician records are a more reliable source of medical information than hospital records. Doctors may maintain their records for longer periods of time than hospitals.
because of on-going relationships with patients. Despite established procedures in hospital medical record departments to abstract medical record information, there may be less ‘red tape’ involved in accessing physician records. Not unexpectedly, the odds ratio estimate of record availability decreased inversely to the number of years elapsed since a reported exposure. Nevertheless, records were available for almost 20% of reports prior to 1960. Sex and education were also related to record availability with records available for more female-reported exposures. Females tended to visit physicians more frequently than males who reported more frequent hospital visits.

Where records were available (Objective 2), over 83% of self-reports were found to be accurate when compared to the medical record. Only record source was a determinant of record accuracy, with the greatest number of self-reports verified by physician records. This may be related to continued care between physicians and patients, resulting in records being maintained for longer periods of time in doctors’ offices than in hospitals. While the majority of exposures reported by subjects were accurate, the extent of under-reporting by subjects is not known.

Odds ratios of thyroid cancer were estimated using exposure measurements from four data subsets (Objective 3). The odds ratio estimates based on self-reports and medical records were very similar. Each data set was a subset of the self-reported group, so that odds ratio estimates were unlikely to change dramatically given that case-control status was not associated with either record availability or agreement. However, the extent of measurement error in our data is unknown, and depending on the direction of the misclassification, odds ratio estimates may be biased either toward or away from the null value. Neither self-reports or medical records, dependant on subjects’ recall and record availability, can be assumed to provide a complete radiation exposure history. The assessment of both under- (false negatives) and over-reporting (false positives) in this study was inadequate. Substantial biases have been shown to occur in the presence of a large amount of measurement error, particularly when relatively strong associations are detected (OR’s different from 1). Methods to correct for both random and systematic exposure measurement (68) are available, but are beyond the scope of this study. However, the implications for this study are that measurement error is unlikely to have a large impact on the relatively modest odds ratio estimates.
Findings in the CCRERG study suggest that exposures which are reported and which can be cross-checked with medical records, are reported accurately. Odds ratio estimates based on self-reported exposures were comparable to odds ratio estimates based on exposure information from the more highly regarded medical record. The study illustrates that self-reports, even for long-ago events, are a reliable source of radiation exposure information. This finding is of great importance not only to the CCRERG study, but also to the many studies relying on self-reported information. Few studies have attempted to verify self-reported radiation exposures. One study (12) found medical record evidence of extremely high rates of under-reporting by subjects. Another study (16) reflected on the diminished ability of subjects to recall X-ray exposures with such little personal significance to the subject. An important caveat of this study is that although radiation exposures were reported accurately by study participants, their total exposure history is unknown. Nevertheless, self-reports may be preferable in some circumstances because subjects are contacted directly and exposure information is more readily available than from medical records, potentially increasing the sample size and power of a study to detect associations. Findings are generalizable not only to other populations, but possibly to other exposures with similar prevalence and significance to the subject.

Finally, a sample of respondents with no reported exposure to radionuclides was selected to assess the possibility of false negatives (Objective 4). The definition of ‘unexposed’ was broad and included subjects who reported exposure late in the study period. This led to the discovery of one positive report in the medical record for a subject who reported exposure, but was classified as ‘unexposed’ according to the study criteria. The sample size was very small, and the prevalence of radionuclides very low, thus it is not clear if findings were due to chance, or if they are generalizable to other populations or exposures.

6.7. FURTHER RESEARCH

Despite the study strengths, two limitations suggest improvements for the future. The first relates to the accuracy of the two measurement instruments, the subject questionnaire and the verification form sent to medical sources. The questionnaire provided an incomplete list of exposure choices for respondents, and the number of responses which were misclassified or not reported as a result
of this oversight is unknown. Prompts have sometimes been included as memory aids, and a diagram of a torso divided into x-ray regions (much like the coding categories, Appendix 5) may have been easier for respondents to fill out, and avoided potential difficulty in describing medical exposures.

The verification form included check boxes for ‘Correct’, ‘Incorrect’ and ‘Don’t Know’. The latter two responses were misleading and clearer indications of the intent of these check boxes would be welcome. A box indicating ‘Incorrect Exposure’ or ‘No Record of Subject’ would go a long way in clarifying responses. In addition, the completeness of information provided on the verification form was unknown, and it is recommended that further studies incorporate a question indicating the years of medical record search. For hospital-directed forms, an indication as to whether searches included inpatient and outpatient records would also help to evaluate the completeness of the medical record search. Because the record source was a determinant of both record availability and accuracy, considerable attention should be given to the selection of an appropriate record source.

Finally, an adequate assessment of false negative reports has not been achieved. The negative verification study looked at a small sample of subjects to determine their accuracy in reporting no exposure to radionuclides. Findings are not likely generalizable to other studies. The prevalence of radionuclide exposure is low and in this study of Ontario subjects, few subjects reported exposure. False negative reports of X-ray exposure would be more informative. One approach would involve a request for complete medical record exposure information from a sample of subjects for whom verification is being sought for a reported exposure. Using this approach, the medical record source is known, and with luck, correct and available. The number of self-reported exposures compared to the total exposures reported in the medical record would provide an estimate of the extent of under-reporting. Alternatively, a negative verification study examining the prevalence of false negative reports of ‘head and neck X-ray, or CT scan’ could be initiated.

Analysis of record availability and report accuracy was exposure-specific, not subject-specific. Both exposure and subject-specific approaches have been used in two previous studies verifying
radiation exposures (12,33). Exposure-specific agreement was selected to address the questions of availability and agreement because it allowed for the evaluation of a range of variables associated with each exposure (years elapsed, source, type of exposure). Preston-Martin (33) evaluated agreement between the number of dental X-ray visits reported by each respondent. In the Tristate Leukemia Study, Graham et al (12) evaluated agreement between the number of x-rays reported by respondents. Where the total radiation exposure experienced by each person is of interest, subject-specific exposures should be used.

This study included a broad range of variables that allowed assessment of their effect on both record availability and agreement between self-reports and medical records. The source of medical records had a significant impact on both availability and agreement. Physician records were the most likely to be available and to confirm self-reports. While record availability was improved for exposures within 10 years of questionnaire mailout, this study is one of the few to include exposures in the distant past. A comparison of self-reported exposure (head, neck, CT) to medical record and medical record verified self-reports of exposure on thyroid cancer status illustrated that estimates of the odds ratio of thyroid cancer remained relatively stable.
7. REFERENCES


Appendix 1

Explanatory letter to case
- accompanies main questionnaire
- final version - November 17/87

Cancer is a health problem that concerns many of us. Although progress
is being made in the understanding of the disease, much more remains to be
done. One method of study that has proved effective in adding to our
knowledge has been the comparison of people who have cancer with the general
population. The more information we can gather from people with varying
medical histories, the better able we will be to understand and prevent this
disease.

We are currently conducting such a study in Ontario. Your physician,
Dr., has given us permission to send you a research questionnaire. It
should take only about 15 minutes to complete. In order for the results of
this study to be informative and truly representative of the people of
Ontario it is important that every questionnaire be completed and returned.
Since your name has been chosen, it is important that you complete the
questionnaire yourself (with assistance if necessary); please do not pass it
on to a friend or relative.

All responses will be treated as confidential and will be used only for
research purposes. The front sheet of the questionnaire which contains your
name and address will be removed as soon as the questionnaire arrives in our
office. The information you provide will be analyzed and reported in terms
of groups so that identification of individuals will never be possible. The
results of our study will be combined with those of similar studies being
conducted across Canada.

If you have any questions about this study or if you have difficulty in
filling out the questionnaire, please contact me or Isabel Fan, the study
coordinator at 416-978-7365 (call collect).

Thank you for your assistance.

Sincerely,

Nancy Kreiger, M.P.H., Ph.D.
Assistant Professor

Encl.
Cancer is a health problem that concerns many of us. Although progress is being made in the understanding of the disease, much more remains to be done. One method of study that has proved effective in adding to our knowledge has been the comparison of people who have cancer with the general population. The more information we can gather from people with varying medical histories, the better able we will be to understand and prevent this disease.

We are currently conducting such a study in Ontario. You have been randomly selected from municipal rolls, which are publicly available, to receive a research questionnaire. It should take only about 15 minutes to complete. In order for the results of this study to be informative and truly representative of the people of Ontario it is important that every questionnaire be completed and returned. Since your name has been chosen, it is important that you complete the questionnaire yourself (with assistance if necessary); please do not pass it on to a friend or relative.

All responses will be treated as confidential and will be used only for research purposes. The front sheet of the questionnaire which contains your name and address will be removed as soon as the questionnaire arrives in our office. The information you provide will be analyzed and reported in terms of groups so that identification of individuals will never be possible. The results of our study will be combined with those of similar studies being conducted across Canada.

If you have any questions about this study or if you have difficulty in filling out the questionnaire, please contact me or Isabel Fan, the study coordinator at 416-978-7365 (call collect).

Thank you for your assistance.

Sincerely,

Nancy Kreiger, M.P.H., Ph.D.
Assistant Professor
NATIONAL HEALTH STUDY

This sheet will be removed from the questionnaire as soon as it is received in the study office, and will be filed separately to ensure confidentiality.

Name: ___________________________ ___________________________ ___________________________ ___________________________
last name first name second name previous surname(s) (if any)

Address: ___________________________ ___________________________ ___________________________ ___________________________
street number city/town postal code telephone number

CONSENT

I give permission to the researchers to approach hospitals and physicians, for the purpose of this study only. I understand that all information will be confidential and published in statistical form only.

Signed: ___________________________ Date: ___________________________

Because you may not be aware of your early medical history, we would like to send your mother a brief questionnaire. If you give us permission to contact your mother, please write her name and address in the space provided.

Consent to contact mother: Yes__ No__ If no, please state reason: Deceased__ Other_____________________________

Mother's name: ___________________________ Telephone #: ___________________________

Address: ___________________________ ___________________________ ___________________________ ___________________________
street number city/town province country postal code

Thank you for your help: Ontario Cancer Treatment and Research Foundation Epidemiology Research Unit
Department of Preventive Medicine and Biostatistics
Faculty of Medicine, University of Toronto
Toronto, Ontario M5S 1A8
Telephone: (416) 978-7365
In order to look at variations in health and disease, consideration of medical history is important.

1. Have you ever had tuberculosis? Yes No Don't Know

2. Have you ever had any of the following diseases of the thyroid gland? (Please check the appropriate columns.)

<table>
<thead>
<tr>
<th>Disease Description</th>
<th>Yes</th>
<th>No</th>
<th>Don't Know</th>
<th>Surgery</th>
<th>Drugs</th>
<th>Radioiodine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Underactive Thyroid</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Hypothyroidism, Myxoedema)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>2. Thyroid Cancer</td>
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<td>3. Goitre</td>
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<tr>
<td>4. Hyperthyroidism</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Overactive Thyroid, Grave's Disease, Thyrotoxicosis)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Hashimoto's Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(Thyroiditis)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

How was it treated?

- For Off"Use Only
Has any member of your immediate family (that is, your parents, children, sisters or brothers) ever had any of the following diseases of the thyroid gland? (Please check appropriate columns.)

<table>
<thead>
<tr>
<th></th>
<th>Mother</th>
<th>Father</th>
<th>Children</th>
<th>Sisters</th>
<th>Brothers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underactive Thyroid (Hypothyroidism, Myxoedema)</td>
<td>Don't</td>
<td>Yes</td>
<td>No</td>
<td>Know</td>
<td></td>
</tr>
<tr>
<td>Thyroid Cancer</td>
<td>Don't</td>
<td>Yes</td>
<td>No</td>
<td>Know</td>
<td></td>
</tr>
<tr>
<td>Goitre</td>
<td>Don't</td>
<td>Yes</td>
<td>No</td>
<td>Know</td>
<td></td>
</tr>
<tr>
<td>Overactive Thyroid (Hyperthyroidism, Graves' Disease, Thyrotoxicosis)</td>
<td>Don't</td>
<td>Yes</td>
<td>No</td>
<td>Know</td>
<td></td>
</tr>
<tr>
<td>Hashimoto's Disease (Thyroiditis)</td>
<td>Don't</td>
<td>Yes</td>
<td>No</td>
<td>Know</td>
<td></td>
</tr>
</tbody>
</table>

Please estimate how often in your life, you have had the following X-rays and your age at the time. (Omit X-rays taken within the last 2 years.)

<table>
<thead>
<tr>
<th>Estimated age group</th>
<th>No. of X-rays of teeth</th>
<th>No. of X-rays of chest</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-19 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-39 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-49 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>60-69 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>70-79 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80+ years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5. Have you ever had any of the following X-ray examinations?
   If yes, please give the year(s), the hospital(s) or clinic(s) and city/town in which they were done, the name of the physician who referred you for X-rays and describe the reason for the X-rays.

<table>
<thead>
<tr>
<th>Year(s)</th>
<th>Hospital(s) or Clinic(s)</th>
<th>City/Town</th>
<th>Referring Chiropractor(s) or Physician(s)</th>
<th>Reason for X-ray</th>
<th>Don't Know</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head (eg. skull, sinuses)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back of neck (eg. cervical spine for whiplash)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barium swallow or barium meal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart or arteries (with injection)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdomen (without barium, pills or injection)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arm or shoulder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barium enema for bowel X-ray</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C.T. Scan</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (please describe part of body treated)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None of the above</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6. Have you ever had X-ray treatment, or radiotherapy, for conditions such as acne, hair removal, swellings in the neck, removal of moles or birthmarks, cancer?

Yes __  No __  Don't Know __

If yes, please give details:

What condition(s): _____________________________

Type of treatment: ______________________________

Hospital/Clinic: ________________________________ city/town

Year: __________

7. Have you ever been given radioactive drugs for diagnosis or treatment (nuclear medicine)?

Yes __  No __  Don't Know __

If yes, please give details:

Condition treated: _____________________________

Year: __________

Hospital/Clinic: ________________________________ city/town

Name of physician who referred you for diagnosis or treatment: ________________
8. We would like to ask you some questions about your smoking habits:
   Do you now or did you ever smoke cigarettes daily? Yes _____ No _____
   At what age did you start smoking cigarettes daily? _____
   About how many cigarettes do/did you smoke daily? _____
   At what age did you stop smoking daily? _____

9. Please list from the time you were born the places you have lived for at least one year. (Do not count moves within the same town or city.)
   Please start with where you live now and work backwards.

<table>
<thead>
<tr>
<th>Town or City</th>
<th>Province or Country</th>
<th>Approximate Years of Residence</th>
<th>C.S.</th>
<th>C.D.</th>
<th>Prov.</th>
<th>Country</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>19__ to 19__</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
10. We would like to ask about the jobs you have had during your life.

Please describe occupation and industry as specifically as possible, e.g. wheat farmer, plastics plant operator, road construction labourer, accountant in an oil refinery, etc.

Starting with your present job, please list all the jobs you have had for one year or more by occupation and industry and the length of time each job was held.

<table>
<thead>
<tr>
<th>Job Description</th>
<th>Length of Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupation</td>
<td>Industry</td>
</tr>
<tr>
<td>From</td>
<td>To</td>
</tr>
</tbody>
</table>

Have you ever worked at a job in which you were exposed to radiation of any kind?

Yes _____ No _____ Don't Know _____

Type of radiation (e.g. X-rays, gamma rays) __________________________
4. Marital Status: (please check one)

- Single
- Married
- Widowed
- Divorced/Separated
- Other

5. Occupational or Vocational Training:

- Elementary or Secondary: 12 3 4 5 6 7 8 9 10 11 12 13
- University: 1 2 3 4 5 6 7 8 9 10 11 12 13 14
- Technical / Trade: 1 2 3 4 5 6 7 8 9 10 11 12 13

6. How many years have you completed at each of the following types of schools?

- Elementary or Secondary
- University
- Technical / Trade

7. Sex: Male     Female

8. Date of Birth:

- Day: 
- Month: 
- Year: 

9. Place of Birth: 

10. Province: 

11. Country: 

12. Personal History: 

(7)

-- FOR OFFICE USE ONLY --
15. How many brothers have you had? (Please include half brothers but not adopted brothers.) Number ________

How many sisters have you had? (Please include half sisters but not adopted sisters.) Number ________

Please circle one:

Were you the 1st child your mother had?
2nd child?
3rd child?
4th child?
5th child?
6th child?
7th child?
8th child?
Other (Please specify) ________

16. How many children (live and stillborn) have you had? Number ________
For each child, please complete the following. (Omit adopted children.)

How old were you when the baby was born? What was the baby's sex?

1) ________  ________
2) ________  ________
3) ________  ________
4) ________  ________
5) ________  ________
6) ________  ________
7) ________  ________
8) ________  ________
17. **FOR FEMALES ONLY**

We would like to ask you some questions about your menstrual and reproductive history.

At what age did you have your first period (monthly bleeding, menstrual)?

Years __

Are you currently menstruating?

Yes ___ No ___

At what age did you have your last period?

Years __

What is the reason you are no longer menstruating?

Currently pregnant __

Periods stopped naturally __

Periods stopped after surgery (e.g. hysterectomy, because uterus (womb) removed, oophorectomy, because ovaries removed) __

Periods stopped after irradiation __

Have you ever been pregnant?

Yes ___ No ___

How many times have you been pregnant? ___
THANK YOU.

This is the end of the questionnaire.

---

When did you use them?

Year To Year

From To

---

Did you ever take any contraceptives (e.g., birth control pills) or take any suppressants (i.e., hot flushes, menstrual irregularities), for any reason?

Yes

No

Other

MISCARRIAGE

Stillbirth

LIVEBIRTH

What was the outcome of your first pregnancy?

---

17. cont'd.

(10)
Letter to physician named by subject regarding additional information
- accompanies exposure verification form(s)
- final version - August 17, 1987

We are currently conducting a study of thyroid cancer across Canada. We are mailing questionnaires to patients diagnosed with thyroid cancer and to a non-cancer comparison group. One of the participants in our study, seen by you is:

(Name, address, and also maiden name)

In response to the questionnaire, the patient noted procedures which are important for our study. As indicated on the enclosed consent form which the patient signed, permission has been given to us to contact you for additional information. All information is strictly confidential and will be used only for research purposes.

Would you please confirm the information listed on the attached form. If possible, it would be useful if you could also supply the number and strength of exposure for the procedure(s) given, in order to approximate the body dose received.

If you have any questions please call me or Isabel Fan, the study coordinator at 978-7365.

Thank you very much for your co-operation.

Sincerely,

Nancy Kreiger, M.P.H., Ph.D.
Assistant Professor

Encl.
We are currently conducting a study of thyroid cancer across Canada. We are mailing questionnaires to patients diagnosed with thyroid cancer and to a non-cancer comparison group. One of the participants in our study, is a former patient at your hospital.

(Name, address, and also maiden name)

In response to the questionnaire, the patient noted procedures which are important for our study. As indicated on the enclosed consent form which the patient signed, permission has been given to us to contact you for additional information. All information is strictly confidential and will be used only for research purposes.

Would you please confirm the information listed on the attached form. If possible, it would be useful if you could also supply the number and strength of exposure for the procedure(s) given, in order to approximate the body dose received.

If you have any questions please call me or Isabel Fan, the study coordinator at 978-7365.

Thank you very much for your co-operation.

Sincerely,

Nancy Kreiger, M.P.H., Ph.D.
Assistant Professor

Encl.
N.B. DATE GIVEN COULD BE ±5 YEARS

Patient: ____________________________
Birthdate: ____________________________

Please Indicate Whether the Information in Section(s) A is Correct; Please Complete Section(s) B.

(1) A. X-ray (description and year) ____________________________

[ ] Correct [ ] Incorrect [ ] Don't Know

Corrections if required: ____________________________

B. View: ____________________________ Number of x-rays: __________

Dose (described in milliamperes, seconds and kilovolts) ____________________________

(2) A. X-ray (description and year) ____________________________

[ ] Correct [ ] Incorrect [ ] Don't Know

Corrections if required: ____________________________

B. View: ____________________________ Number of x-rays: __________

Dose (described in milliamperes, seconds and kilovolts) ____________________________

(3) A. X-ray (description and year) ____________________________

[ ] Correct [ ] Incorrect [ ] Don't Know

Corrections if required: ____________________________

B. View: ____________________________ Number of x-rays: __________

Dose (described in milliamperes, seconds and kilovolts) ____________________________
Patient: ____________________________
Birthdate: ____________________________

Please indicate whether the information in Section(s) A is correct; please complete Section(s) B.

(1) A. Radiotherapy: (description of site and year) ____________________________

   ☐ Correct ☐ Incorrect ☐ Don't Know

   Corrections if required: ____________________________

B. Tumour dose: ____________________________

   Number of fractions: ___________ Number of days: ___________

   Machine type: ____________________________ Radiation type: ____________________________

(2) A. Radiotherapy: (description of site and year) ____________________________

   ☐ Correct ☐ Incorrect ☐ Don't Know

   Corrections if required: ____________________________

B. Tumour dose: ____________________________

   Number of fractions: ___________ Number of days: ___________

   Machine type: ____________________________ Radiation type: ____________________________

(3) A. Radiotherapy: (description of site and year) ____________________________

   ☐ Correct ☐ Incorrect ☐ Don't Know

   Corrections if required: ____________________________

B. Tumour dose: ____________________________

   Number of fractions: ___________ Number of days: ___________

   Machine type: ____________________________ Radiation type: ____________________________

OCTR, 12 Queen's Pk. Cr. W., Toronto, Ontario M5S 1A8 Tel: 416-978-7765
Patient: ________________________________
Birthdate: ______________________________

Please indicate whether the information in Section(s) A is correct; please complete Section(s) B.

(1) A. Radionuclides: (description and year) ________________________________

☐ Correct ☐ Incorrect ☐ Don't Know

Corrections if required: _____________________________________________________

B. Dose: ________________________________________________________________

Reason for dose: ☐ Diagnosis ☐ Treatment

(2) A. Radionuclides: (description and year) ________________________________

☐ Correct ☐ Incorrect ☐ Don't Know

Corrections if required: _____________________________________________________

B. Dose: ________________________________________________________________

Reason for dose: ☐ Diagnosis ☐ Treatment

(3) A. Radionuclides: (description and year) ________________________________

☐ Correct ☐ Incorrect ☐ Don't Know

Corrections if required: _____________________________________________________

B. Dose: ________________________________________________________________

Reason for dose: ☐ Diagnosis ☐ Treatment
Appendix 3

HOSPITALS IN ONTARIO WITH NUCLEAR MEDICINE FACILITIES, BY REGION

Eastern Ontario Region

Belleville   - Belleville General Hospital  
Kingston    - Hotel Dieu Hospital  
            - Kingston General Hospital  
Ottawa      - Ottawa Civic Hospital  
            - Ottawa General Hospital

East-Central Ontario Region

Barrie       - Royal Victoria Hospital  
Newmarket    - York County Hospital  
Orillia      - Soldiers Memorial Hospital  
Peterborough - Peterborough Civic Hospital  
            - St. Joseph's General Hospital

Metropolitan Toronto Region

Doctor’s Hospital  
Etobicoke General Hospital  
* Hospital for Sick Children  
Humber Memorial Hospital  
* Mount Sinai Hospital  
North York Branson Hospital  
* North York General Hospital  
Northwestern General Hospital  
* Princess Margaret Hospital  
Queensway General Hospital  
St. Joseph’s Health Centre  
* St. Michael’s Hospital  
** Scarborough Centenary Hospital  
** Scarborough General Hospital  
* Sunnybrook Medical Centre  
Toronto East General Hospital  
* Toronto General Hospital  
* Toronto Western Hospital  
* Wellesley Hospital  
* Women’s College Hospital  
York Finch General Hospital

* = Major Referral Hospital  
** = Major Referral Hospital for Patients from East of Toronto only
Suburbs of Toronto

Brampton - Peel Memorial Hospital
Missauga - Mississauga Hospital
Oakville - Oakville-Trafalgar Memorial Hospital
Oshawa - Oshawa General Hospital
Richmond Hill - York Central Hospital

Hamilton and Burlington

Burlington - Joseph Brant Memorial Hospital
Hamilton - Chedoke-McMaster Hospitals
- Hamilton General Hospital
- Henderson General Hospital
- St. Joseph’s Hospital

Niagara Region

Niagara Falls - Greater Niagara General Hospital
St. Catharines - Hotel Dieu Hospital
- St. Catharines General Hospital

West-Central Ontario Region

Brantford - Brantford General Hospital
- St. Joseph’s Hospital
Kitchener-Waterloo - Cambridge Memorial Hospital
- St. Mary’s General Hospital
London - St. Joseph’s Hospital
- University Hospital
- Victoria Hospital
Owen Sound - Grey Bruce Regional Health Centre
- St. Thomas-Elgin General Hospital
- Stratford General Hospital
Southwestern Ontario Region

Chatham  - Public General Hospital
         - St. Joseph’s Hospital
Sarnia   - St. Joseph’s Hospital
         - Sarnia General Hospital
Windsor  - Hotel Dieu Hospital
         - Metropolitan General Hospital
         - Salvation Army Grace Hospital

Northern Ontario Region

North Bay - St. Joseph’s Hospital
Sault Ste. Marie - Plummer Memorial Public Hospital
Sudbury   - Sudbury General Hospital
Thunder Bay - McKellar General Hospital
         - St. Joseph’s Hospital
Dear &status& &surname&:

The Ontario Cancer Treatment and Research Foundation, in association with the Department of Preventive Medicine at the University of Toronto, is currently conducting an epidemiologic study of cancer. A summary of the study is enclosed.

Attached are the names of &num& study participants who may have been patients at your hospital. Some of these people have had cancer while others are population-based controls. It is important for our research to know if any of these patients ever received radioactive drugs (radionuclides) for treatment or diagnosis before January 1, 1986.

These patients have signed consent forms, giving us permission to contact you for medical information. All information is strictly confidential and will be used only for research purposes. If you require photocopies of the consent forms, please contact Janice Fleury, our research assistant, at 416-978-2979.

Please check both inpatient and outpatient files and complete the attached form returning it in the envelope provided. If you prefer, Ms Fleury who has sworn an oath of confidentiality, is available to review the charts. She will call you in a week to confirm the arrangement. If you have any questions please call Ms Fleury or Isabel Fan, the study coordinator at 978-7365.

Your assistance is greatly appreciated.

Sincerely,

Nancy Kreiger, M.P.H., Ph.D.
Assistant Professor

Encl. (3): Summary of Study Protocol
Patient List
Return Envelope
Dear &status& &surname&

The Ontario Cancer Treatment and Research Foundation, in association with the Department of Preventive Medicine at the University of Toronto, is currently conducting an epidemiologic study of cancer. A summary of the study is enclosed.

Attached are the names of &num& study participants who may have been patients at your hospital. Some of these people have had cancer while others are population-based controls. It is important for our research to know if any of these patients ever received radioactive drugs (radionuclides) for treatment or diagnosis before January 1, 1986. As indicated on the enclosed signed consent forms, the patients have given us permission to contact you for medical information. All information is strictly confidential and will be used only for research purposes.

Please check both inpatient and outpatient files and complete the attached form for each patient, returning it in the envelope provided. If you have any questions, please call Ms Janice Fleury, our research assistant, or Isabel Fan, the study coordinator at 978-7365.

Your assistance is greatly appreciated.

Sincerely,

Nancy Kreiger, M.P.H., Ph.D.
Assistant Professor

Encl. (4): Summary of Study Protocol
Consent Forms
Patient List
Return Envelope
<table>
<thead>
<tr>
<th>Name (Previous Surname)</th>
<th>Radioactive Drugs? (Radionuclides)</th>
<th>Date(s) of Use:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes:____  No:____  No Records:____</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date(s) of Use:__________________</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes:____  No:____  No Records:____</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date(s) of Use:__________________</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes:____  No:____  No Records:____</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date(s) of Use:__________________</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes:____  No:____  No Records:____</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date(s) of Use:__________________</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes:____  No:____  No Records:____</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date(s) of Use:__________________</td>
<td></td>
</tr>
</tbody>
</table>

OCTRFF, 12 Queen's Pk. Cr. W., Toronto, Ont. M5S 1A8, Tel: 416-978-7365