Review of report "Investigation of potential health effects from the use of herbicides and any herbicide-related contaminants, particularly dioxins used at CFB Gagetown from 1952 to the present: epidemiological study" by Dr. Judith Guernsey

General comments

This is an ecologic study to assess if the risks of cancer, diabetes or Parkinson's Disease are elevated among New Brunswick residents who may have been exposed to chlorophenoxy herbicides applied at CFB Gagetown primarily during June of 1966 and 1967. The author has taken a reasonable approach to study design, analysis and data interpretation.

Problems

There are several almost insurmountable problems that preclude firm or even fairly certain conclusions as to whether the use of chlorophenoxy or other herbicides at CFB Gagetown increased the risk of these diseases among the exposed population. These problems include:

1. Definition of exposed population. Although there was never any direct measurement of exposure (e.g., measurement of urinary 2,4-D or 2,4,5-T), the likelihood of non-trivial exposure must have been limited to those directly involved in the experimental applications and bystanders within the sprayed regions or the population living less than 1 km from such regions. These persons have never been identified and followed for several decades to assess chronic disease risks (more on this issue later). Instead, the author defined the potentially exposed population to include residents of a geographic region much larger than that likely to have been exposed as bystanders living near sprayed regions. In addition, it is virtually certain[1] that such herbicides (esp. 2,4-D) have been widely used by the New Brunswick forestry and agricultural industries during the past several decades. Following the same logic used by the author to define the study population in this report, it seems likely that low-level exposure to chlorophenoxy herbicides (esp. 2,4-D) was widespread in New Brunswick and was mainly attributable to forestry, agricultural and residential uses. Thus I believe that is almost certain that the study and comparison populations had similar, low-level exposure to 2,4-D and that any differences in disease risks are likely to be attributable to statistical variation and risk factors other than herbicide exposure.

2. Population mobility. The author notes the relatively high population mobility in the study region (e.g., only about half of Gagetown village residents in 2005 had lived at the same address in 2000). If one assumes the military personnel living near the experimentally sprayed regions were at highest risk of exposure to chlorophenoxy herbicides, then those exposed during 1966-67 would only represent a small fraction of the population at risk during the study period (1980 or 1984 to 2003). The likely effect

[1] I say "virtually certain" because I do not have access to herbicide use data for New Brunswick but I know that the forestry industry there used 2,4-D extensively and agricultural use of 2,4-D has been widespread in Canada for over 50 years.

of high mobility combined with the dilution imposed by the large geographic area selected for study (see #1 above) is to greatly reduce the chance of detecting any truly increased disease risks attributable to use of herbicides at CFB Gagetown.

3. Low statistical power. Despite the large geographic region selected for study, the "exposed" population was only about 120,000 persons (20% of New Brunswick) and the numbers of cases of cancers of interest were generally very small during any 5-year period. For rare cancers such as soft tissue sarcoma and nasopharyngeal cancer, the numbers of cases in the study population were too small to draw any firm conclusions. In general, the author recognizes this issue at several points in the text but still makes a few inferences that seem to go beyond the data (these are noted in the attached PDF file).

Maps

It would be helpful to include a map that shows both the boundaries of the study population and the areas where experimental applications were conducted during June of 1966 and 1967. If possible, it would be very helpful to also display the regions where forestry and agricultural uses of 2,4-D occurred during one or more years between 1966 and about 1973 (to allow a 10-year minimum latent period for cancer development during 1983 or later). Failing this, even semi-quantitative or qualitative statements on the extent of such uses during that time period would be helpful.

95% confidence intervals

Strongly recommend adding 95% CI's for all SIRs and SMRs cited in text. Similarly, I recommend adding the CI's and numbers of cases/deaths in all cells of Tables 5-8.

Recommendations for future research

This section needs to be expanded and strengthened. Specifically, I suggest adding these recommendations:

1. Assess the feasibility of using data in the Enhanced Cancer Surveillance system to identify risk factors including residence near CFB Gagetown for the selected cancer sites in New Brunswick. This database includes residential history information.
2. Re-implement the Enhanced Cancer Surveillance system with a major focus on residential, occupational and bystander pesticide exposure. This could be piloted in New Brunswick to build a clearer picture of the potential role of pesticide exposure and other environmental factors in human cancer.
3. Assess the feasibility of a record-linkage cohort study of CFB Gagetown military personnel and their families. This could include families based there before, during and after the experimental spray program.

Specific comments

See attached PDF file.

Investigation of potential health effects from the use of herbicides and any herbicide-related contaminants, particularly dioxins used at CFB Gagetown from 1952 to the present:

Epidemiological Study

In response to RFP 4500135700
PHAC – Health Promotion and Chronic Disease Prevention Cost Centre 215002

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June 2007

Acknowledgements

I would like to acknowledge the invaluable assistance I have received from Jillian Ashley-Martin and Mikiko Terashima who have assisted with organizing the geographic referencing, the data coding and data validation. Jillian also was invaluable in assistance with generation of the final incidence and mortality rates and with assistance in writing the final report. I would like to thank Dr. Christopher Balram and his staff, especially Wilfred Pilgrim, at the Province of New Brunswick Epidemiology Division for their cooperation and assistance with provision of mortality and cancer incidence data files upon which this study is based.

I also thank Dr. Howard Morrison, Senior Scientist and Project Authority, and Dr. Bernard Choi, Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada, and the Department of National Defence who have been supportive and accommodating throughout this project. All conclusions are my own, however, and I take full responsibility for the content of the document and for any errors or emissions.

Executive Summary

- The purpose of this descriptive epidemiologic study was to determine whether there is evidence of increased rates of chronic disease in residents of a region comprising CFB Gagetown and surrounding areas, that was identified by the community as being at risk of exposure to herbicides and herbicide-related contaminants that were used at CFB Gagetown from 1952 to the present (heretofore called the Gagetown Study Region, or GSR), compared to all residents of the Province of New Brunswick.

- Of special concern are the health risks that may have resulted from exposure to experimental applications of Agent Orange and Agent Purple during the specific test periods in June 1966 and June 1967 and other herbicides used at the base. Diseases were chosen on the basis of the results of a recently completed review of the current scientific literature that identified certain outcomes as being more likely to be associated with exposure to herbicides that were sprayed in the GSR. This list was further refined based upon the quality of diagnostic information related to these health effects and upon the availability of validated data in New Brunswick.

- Five year average age- standardized incidence and mortality rates and 95% confidence intervals were calculated (via the direct method) for the selected diseases for both males and females and for five year time intervals for the GSR and for the Province of New Brunswick for the time interval of 1980 (mortality) or 1984 (cancer incidence) to 2003. The time period was chosen on the basis of the period for which data were available. Standardized incidence and mortality ratios were compiled in order to present a composite picture of the comparative experience of Gagetown Study Region versus the Province of New Brunswick. Also population attributable risks for several diseases were generated to estimate the 'health impact' that are associated with living in and, hence, being exposed to the Gagetown region.

- For both men and women, Gagetown Study Region residents' overall experience with mortality and cancer incidence was similar to that calculated for the Province as a whole over the entire period of study. Men in the GSR had a slightly reduced risk of dying from cancer than the entire province. This was especially so during 1989-1998. For most of the specific disease outcomes, there were few differences between the GSR population and the Province of New Brunswick as a whole for both mortality and cancer incidence.

do you mean "compared to Canada as a whole" (assuming that the CCS rates were national)

- Differences were noted in the New Brunswick all-cause cancer mortality rates resulting from these analyses compared to the lower rates reported by the Canadian Cancer Society for the same time periods, which if applied to the rates for Gagetown, would indicate that the GSR residents were at increased risk for all cause cancer compared to the Province as a whole. As indicated in Appendix 2, there were some challenges associated with working with the all-cause cancer incidence file that we received. For the purposes of this report, we are assuming that the data that were sent to us were correct.

- Rates of nasopharyngeal cancer and soft tissue sarcoma incidence and mortality in both women and men in the Gagetown Study Region, though not significantly higher according to the statistical criteria set for this study, were consistently elevated compared to the New Brunswick population as a whole when there were sufficient numbers to calculate rates. These two diseases were also identified in the literature review as outcomes that are associated with exposure to herbicides. While the current findings are inconclusive due to the small numbers of cases observed in this study, it is possible that exposure to the conditions in the GSR enhanced the risk for development of these two diseases.

would help to specify what is meant by conditions (incl. known risk factors other than herbicides)

- We were not able to develop individual exposure profiles to the experimental sprays and measure subsequent individual risk for disease in this study. We were also not able to differentiate between health effects resulting from the experimental herbicides and others sprayed in routine applications at the base. Separation of health outcomes that resulted from exposure to the range of herbicides used at CFB Gagetown from those factors that may have been caused by other environmental or lifestyle and genetic factors was also not possible.

- This study makes no attempt to draw conclusions about the causes of a particular individual's disease or death. This is the responsibility of that individual patient's physician who is able, through collection of a careful clinical and environmental history and diagnostic information from the patient, to identify those etiological factors that are contributory to an individual's disease.

apart from tobacco and known occupational causes such as asbestos, I believe that physicians rarely speculate on the etiology of specific cancers of individual patients ... perhaps you mean the underlying cause of death which is based on anatomy/pathology as opposed to etiology?

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Introduction

The purpose of this descriptive epidemiologic study was to determine whether there is evidence of increased rates of chronic disease in residents of a region comprising CFB Gagetown and surrounding areas, that was identified by the community as being at risk of exposure to herbicides and herbicide-related contaminants that were used at CFB Gagetown from 1952 to the present (heretofore called the Gagetown Study Region, or GSR), compared to all residents of the Province of New Brunswick. The rates of disease for the Gagetown Study Region were compared to the provincial New Brunswick rates for the same time periods. The time period for this study was 1980-2003 for mortality and 1984 to 2003 for cancer incidence. An intensive effort was made by the investigator, in working with the Province, to obtain data for the earlier periods but this proved not to be possible within the time span that was available for this study.

These findings provide initial data to the community about the chronic diseases that are elevated in the GSR compared to the province as a whole. Of special concern are the health risks that may have resulted from exposure to experimental applications of Agent Orange and Agent Purple during the specific test periods in June 1966 and June 1967 and other herbicides used at the base. Diseases were chosen on the basis of the results of a recently completed review of the current scientific literature that identified certain outcomes as being more likely to be associated with exposure to herbicides that were sprayed in the GSR. This list was further refined based upon the quality of diagnostic information related to these health effects and upon the availability of validated data in New Brunswick. Five year average age- standardized incidence and mortality rates and 95% confidence intervals were calculated (via the direct method) for the selected diseases for both males and females and for the different time intervals for the GSR and for the Province of New Brunswick. These rates were then compared to each other to determine the extent to which the GSR rates differed from the provincial rates. These data also provide the number of disease and mortality occurrences for the GSR and the province by gender and time interval.

The underlying assumption of this study design is that the unique feature of the Gagetown Study Region that sets residents apart from the rest of the Province is their experience with the combination of the herbicides that were sprayed there over time. It is assumed that those who have lived the greatest proportion of their lives in this region will be at greatest risk for exposure to the herbicides in

question and hence were exposed and also diagnosed while still living in the region. There is a significant potential for bias, however, caused by people moving into and out of the region during the period of chronic disease latency (after exposure but before the disease actually appears). This is an unavoidable limitation of ecological study designs. Nevertheless, such studies do tell us whether there is suggestive evidence of higher rates of disease experienced by the community at risk compared to background populations- presumably attributable to the special features of exposures that the community of interest might have experienced over time.

or from any pesticides used by GSR residents at work or home.

We were not able to develop individual exposure profiles to the experimental sprays and measure subsequent individual risk for disease in this study. We were also not able to differentiate between health effects resulting from the experimental herbicides and others sprayed in routine applications at the base. Separation of health outcomes that resulted from exposure to the range of herbicides used at CFB Gagetown from those that may have been caused by other environmental or lifestyle and genetic factors also was not possible. All of these analyses would have required an intensive epidemiological study involving extensive follow-up, interviews and possibly collection of biological samples. This study is only an initial look at the health experience of residents in the Gagetown Study Region and whether there is suggestive evidence that they were at increased risk compared to the province as a

suggest "delayed" instead of "long time"

This study also builds upon an assumption that there is a ten to fifteen year or more latency of disease onset resulting from the or cumulative effects of late 1960's experimental spray exposure window to mortality. It also allows for a fifteen to twenty year or more latency period for cancer onset resulting from the or cumulative effects of experimental herbicide exposures. It is possible that the earlier health effects that might have occurred during the 1970's were missed by these analyses.

This study makes no attempt to draw conclusions about the causes of a particular individual's disease or death.

see prev. note re etiology vs anatomical/ pathologic cause of death

Objectives

The principal research questions are: 1) whether there is evidence of increased mortality risk for a range of health outcomes (identified by the review of herbicide-associated effects in the peer-reviewed, scientific literature) in relation to residence within the Gagetown Study Region, as defined below, at time of diagnosis for the period 1980 to 2003, compared to the Province of New Brunswick and Canada as a whole for the same time period, after adjusting for age and gender; and 2) whether there is evidence of increased cancer risk for a range of specific cancer diagnoses (identified by the review of herbicide-associated effects in the peer-reviewed, scientific literature) in relation to residence within the Gagetown Study Region, as defined below, at time of diagnosis for the period 1984 to 2003, compared to the Province of New Brunswick and Canada as a whole for the same time period, after adjusting for age and gender.

Methods

Identification of Geographic Regions

Target Population

The target population was comprised of residents living in a collection of census subdivisions (CSDs) in southern New Brunswick including the area that contains CFB Gagetown. The inclusion list of communities and regions was developed using three sources of information: 1) a 2005 map provided by the Department of National Defence that identified the CFB Gagetown range and training area[1] 2) data from the Department of National Defence Gagetown study Task 2A Report that lists agents, dates and locations of application that have been identified for this study by DND; and 3) the list of communities identified by the DND Gagetown Study Community Advisory Committee as those suspected to be at higher risk for exposure to the herbicides.

what criteria did the committee use to identify regions at high risk of exposure?

Census subdivision codes for each census year from 1971-2001 corresponding to the target population were examined (and mapped if digital shape files were available (years 1981-2001). With the exception of three new CSDs that were introduced in 1981 and more recently two new CSDs in 2001 (see table notation), for the most part, the boundary files have remained consistent. The communities

of interest and respective geocodes are displayed in Table 1. The map in Figure 1 displays the target communities and shows the location of the study area in relation to the entire province.

The analyses of disease patterns in the target population were done at the level of Statistics Canada-defined census subdivisions. Finer geographic resolution is not possible due to the lack of finer geographic resolution of case records available from the New Brunswick Cancer Registry and from the Canadian Mortality Database. Census subdivisions- level of georeferencing also has the general advantage of consistent census geographic boundaries being applied from one national census to the next. This consistency was confirmed via a visual examination and plotting of these boundary files using GIS (geographic information system) software.

Reference Population

Incidence and mortality rates in the exposed communities were compared to provincial New Brunswick rates, as the reference population. The Province of New Brunswick was chosen for a number of reasons. First of all, provincial cancer rates are regularly reported to the Canadian Cancer Registry which are then publicly released in an annual national report. This provides a means to compare the provincial rates generated from data sent to us by the province with those that are publicly available. Thus, this is a mechanism to assess data quality and validate our study findings. Secondly, the ideal referent population will have similar demographic and lifestyle risk factor characteristics and, thus inherently controls, in a general way, for these 'background' characteristics in comparing the rates from the two regions.

Table 1. Geographic codes for Gagetown study: Census Subdivisions of Communities of Interest (1971-2001)*

Geography ID	CSDNAME	1971			1976			1981	1986	1991	1996	2001
		PR	CD	CSD	PR	CD	CSD	PRCDCSD	PRCDCSD	PRCDCSD	PRCDCSD	PRCDCSD
01	Blissville	13	3	1	13	3	1	1303001	1303001	1303001	1303001	1303001
02	Brunswick	N/A			13	4	16	1304016	1304016	1304016	1304016	1304016
03	Burton	13	3	11	13	3	11	1303011	1303011	1303011	1303011	1303011
04	Cambridge (P)	13	4	11	13	4	11	1304011	1304011	1304011	1304011	1304011
05	Cambridge-Narrow (V)	13	4	13	13	4	13	1304013	1304013	1304013	1304013	1304013
06	Clarendon	13	2	14	13	2	14	1302014	1302014	1302014	1302014	1302014
07	Fredericton Junction	13	3	6	13	3	6	1303006	1303006	1303006	1303006	1303006
08	Gagetown (P)	13	4	4	13	4	4	1304004	1304004	1304004	1304004	1304004
09	Gagetown (V)	13	4	5	13	4	5	1304005	1304005	1304005	1304005	1304005
10	Gladstone	13	3	4	13	3	4	1303004	1303004	1303004	1303004	1303004
11	Greenwich	13	5	38	13	5	38	1305038	1305038	1305038	1305038	1305038
12	Hampstead	13	4	6	13	4	6	1304006	1304006	1304006	1304006	1304006
13	Johnston	13	4	14	13	4	14	1304014	1304014	1304014	1304014	1304014
14	Kars (P)	13	5	36	13	5	36	1305036	1305036	1305036	1305036	1305036
15	Kingsclear (P)	13	10	18	13	10	18	1310018	1310018	1310018	1310018	1310018
16	Kingston (P)	13	5	14	13	5	14	1305014	1305014	1305014	1305014	1305014
17	Lincoln	13	3	8	13	3	8	1303008	1303008	1303008	1303008	1303008
18	Maugerville	13	3	16	13	3	16	1303016	1303016	1303016	1303016	1303016
19	New Maryland (P)	13	10	1	13	10	1	1310001	1310001	1310001	1310001	1310001
20	New Maryland (V)	N/A			N/A			N/A	N/A	N/A	1310002	1310002
21	Northfield	13	3	18	13	3	18	1303018	1303018	1303018	1303018	1303018
22	Oromocto	13	3	12	13	3	12	1303012	1303012	1303012	1303012	1303012
23	Petersville	13	4	1	13	4	1	1304001	1304001	1304001	1304001	1304001
24	Prince Willilam	13	10	16	13	10	16	1310016	1310016	1310016	1310016	1310016
25	Queensbury	13	10	21	13	10	21	1310021	1310021	1310021	1310021	1310021
26	Saint Marys (P)	13	10	31	13	10	31	1310031	1310031	1310031	1310031	1310031
27	Sheffield	13	3	14	13	3	14	1303014	1303014	1303014	1303014	1303014
28	Tracy (V)	13	3	5	13	3	5	1303005	1303005	1303005	1303005	1303005
29	Waterborough	13	4	18	13	4	18	1304018	1304018	1304018	1304018	1304018
30	Westfield (P)	13	5	11	13	5	11	1305011	1305011	1305011	1305011	1305011
31	Westfield (V)	13	5	13	13	5	13	1305013	1305013	1305013	1305013	N/A
32	Wickham	N/A			N/A			1304008	1304008	1304008	1304008	1304008
33	Fredericton city	13	10	32	13	10	32	1310032	1310032	1310032	1310032	1310032
34	Grand Bay	13	5	12	13	5	12	1305012	1305012	1305012	1305012	N/A
35	Grand Bay-Westfield	N/A			N/A			N/A	N/A	N/A	N/A	1305015

should state that the significance of the high-lighted areas.

Selection of Health Outcomes

Health outcomes were initially identified based on a critical analysis of epidemiological literature relevant to the herbicides purportedly used at CFB Gagetown from 1956-2004. The range of outcomes identified from the review was larger and time period longer than was subsequently studied in this investigation. Limiting factors relate primarily to the general challenges of capturing accurate diagnoses of the diseases of interest and to the availability and quality of province-wide primary data that would support such analyses over this extended period of time.

Reporting of the occurrences of cancers and several other diseases to a province-wide cancer surveillance program is required by law. These reports have been validated by the results of the pathologist's assessment. The presence of other diseases is generally identifiable only through physician visits or hospital separations administrative records; in these situations, one is not able to discern whether such a record is the first time that the case occurred without extensive research. If one were to rely on number of physician visits for a disease in Gagetown vs. other areas of the province, it would be impossible to sort out whether this was a factor of the differential availability of physician services or whether there was a true difference.

Birth outcome data, including the occurrence of congenital anomalies, are exceptions. Low birth weights, stillbirths, and other perinatal factors are now recorded in a province wide perinatal surveillance registry. Institution of this system in New Brunswick, with proper quality control procedures, has only recently occurred. Because the resulting data are only available for recent years, examination of these outcomes would have not been informative due to the insufficient time period to observe trends. Other considerations include the facts that there were no available data for period of greatest interest- the late 1960's and early 1970's and the several years that followed these exposures. Poor birth outcomes resulting from bioaccumulated parental exposures to herbicides may have also occurred but such an analysis would have required longitudinal data on all parental exposures in the region. These data were simply not available.

the study area seems huge and much larger than the region where even minimal exposure could occur...the inclusion of regions more than about 1 km from sprayed regions will tend to reduce the chance of observing true increased risks in the small regions likely to have had even minimal exposure.

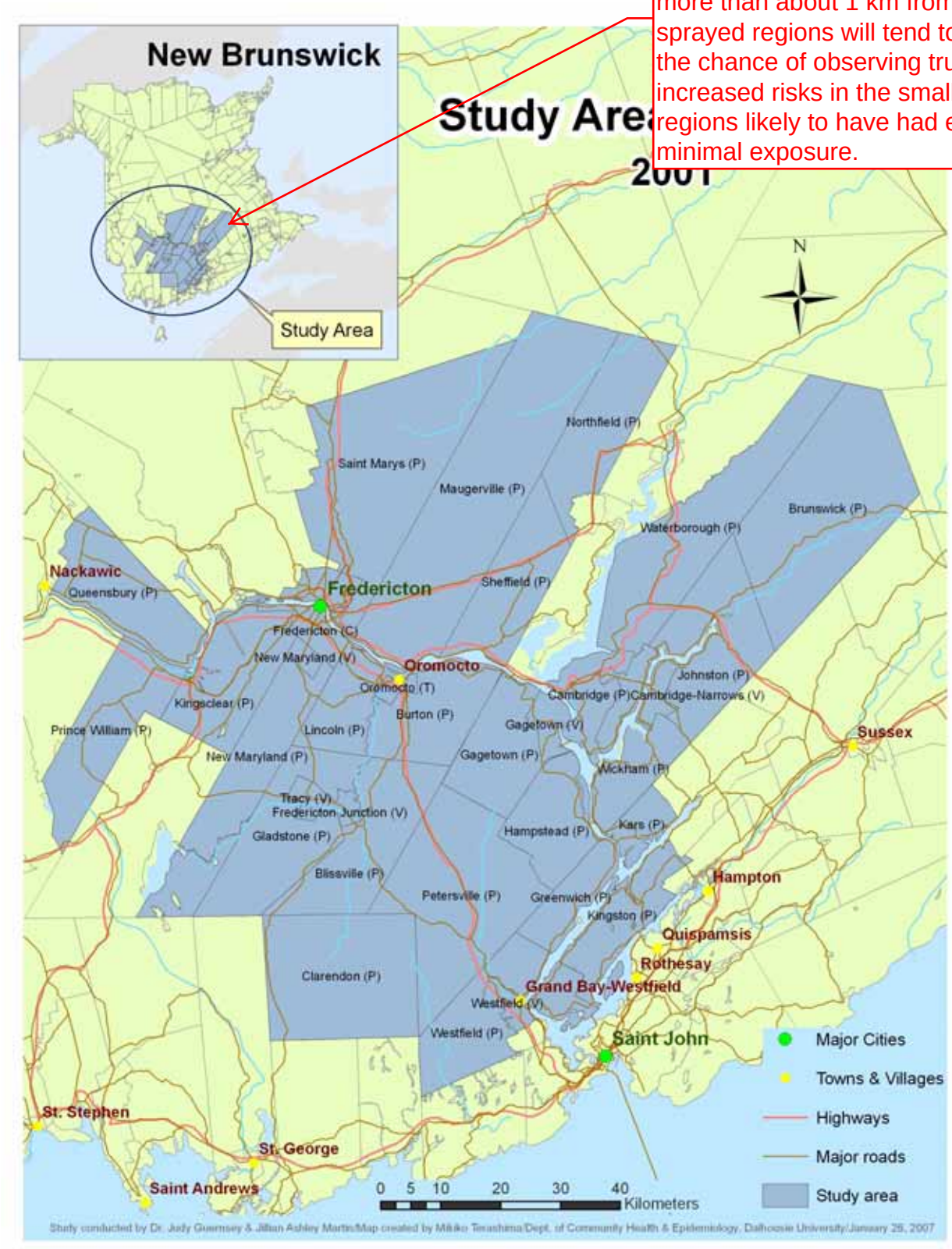

Figure 1: Map of Gagetown Study Region

suggest "mort. data reflect both disease risk and likelihood of survival and are also subject to..."

Other reasons for not including some diseases include insufficient numbers to support a meaningful analysis. This was especially the case for the rarer cancers.

In addition to certain cancers of interest, age standardized mortality data were calculated for several non-cancer outcomes. Incidence data are generally preferable to mortality data because they give a more complete picture of a population's experience with a disease. For example, people often survive cancer given appropriate treatment, yet the genesis of the disease may relate back to a past exposure. Mortality data are also subject to reporting bias due to the fact that they are derived from the information that is recorded on the death certificate. The coroner will record the apparent primary cause of death and any contributory factors that precipitated the death. Undiagnosed disease or long standing chronic conditions may not be known by the person attending the death and will thus go undocumented. Some diseases are more easily recognized at death than others, for example pulmonary insufficiency due to emphysema, is more likely to be recorded than an 'invisible' disease, such as peripheral neuropathy, that may or may not have significantly contributed to the person's death. Those diseases that are more difficult to diagnose will also be less likely to be recorded on a death certificate. Mortality data, hence, should be viewed with caution.

could reword to clarify that physicians identify the disease that caused death but not the external causes of chronic diseases such as cancer.

A decision matrix is provided in Table 2 that summarizes decisions for inclusion in the study according to each outcome.

Careful attention was given to selection of the International Classification of Disease (ICD) codes. The ICD is an international consensus system of disease classification established by the World Health Organization in the early 1950's. For the purposes of this investigation, the ICD 9th revision codes were in place. Selection of specific codes was made on the basis of maintaining consistency with disease outcomes listed in the US Institute of Medicine VAO report and with the Canadian Cancer Registry coding classification.

Table 2. Decision Matrix Related to Inclusion of Health Outcomes

Diagnosis	ICD Codes	Data source	IOM status	Lit review	Comment
All malignant neoplasms	140-209 - All malignant neoplasms (ICD8) 140-208 - All malignant neoplasms (ICD9)	NB Cancer Registry (incident cases); Statistics Canada (deaths)	NC		Assess general risk of cancer to set context
Nasopharynx	147 Malignant neoplasm of nasopharynx	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Inad	Inad	Nasopharyngeal cancer has different epi profile than nasal cancer; rare cancer (1-2 per 100,000 per year
Nasal Cavity	160 Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Inad	Inad	Cancer mortality coded differently than incidence
Larynx	161 Malignant neoplasm of larynx	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Lim	Lim	Number of cases limited
Lung	162.2-162.9 Malignant neoplasm of bronchus, and lung ICD-9 162.3 Upper lobe, bronchus or lung 162.4 Middle lobe, bronchus or lung 162.5 Lower lobe, bronchus or lung ICD-10 C34.1 Upper lobe, bronchus or lung C34.2 Middle lobe, bronchus or lung C34.3 Lower lobe, bronchus or lung C34.8 Overlapping lesion of bronchus and lung ICD-O	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Lim	Inad	Include

	Primary site codes: C340-C343,C348-C349 Histology codes (n=178) can be retrieved if necessary				
Bone	170 Malignant neoplasm of bone and articular cartilage	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Inad		Include Rare; metastatic tumours appear here, Number of cases in NB
Soft Tissue Sarcomas	171 Malignant neoplasm of connective and other soft tissue ICD-9 171 Malignant neoplasm of connective and soft tissue ICD-10 C46 Malignant neoplasms of Kaposi's sarcoma C49 Malignant neoplasms of other connective and soft tissue ICD-O M8800/3 Soft tissue sarcoma M9140/3 Kaposi's sarcoma	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Suf	Suf	Include
Breast	174 Malignant neoplasm of female breast (*ICD 8- female and male combined*) ICD-9 174 Malignant neoplasm of female breast ICD-10 C50 Malignant neoplasm of breast (female) ICD-O Primary site code: C500-C506 C508-509 Histology codes (n=186) not included	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Inad	Lim	include
Prostate	185 Malignant neoplasm of prostate ICD-9 185 Malignant neoplasm of prostate ICD-10 Malignant neoplasms of prostate	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Lim	Lim	include

	ICD-O Primary site code: C619 Histology codes (n=115) not included but can be retrieved				
Testis	186.0-186.9 Malignant neoplasm of testis ICD-9 Malignant neoplasm of testis ICD-10 C62 Malignant neoplasm of testis ICD-O Primary Site: C620-C621, C629	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Inad	Inad	include
Brain	191 Malignant neoplasm of brain	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Sug No	Inad	include
Non Hodgkins Lymphoma	200.0-200.8 Lymphosarcoma and reticulosarcoma ICD-9 200 Lymphosarcoma and reticulosarcoma 202 Other malignant neoplasms of lymphoid and histiocytic tissue 202.0 Nodular lymphoma 202.1 Mycosis fungoides 202.8 Other lymphomas 202.9 Other and unspecified malignant neoplasms of lymphoid and histiocytic tissue ICD-10 C82 Follicular Non-Hodgkins lymphoma (nodular) C83 Diffuse Non-Hodgkins lymphoma C84.0 Mycosis fungoides C85 Other and unspecified types of non-Hodgkin's lymphoma ICD-O M9591/3 Non Hodgkins Lymphoma (M9690/3) Follicular lymphoma (M9698/3) Follicular lymphoma (M9700/3) Mycosis fungoides (9710-9719) Other Specified Non-Hodgkin's lymphomas	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Suf	Suf	include
Hodgkin	201 Hodgkin disease	NB Cancer Registry (incident cases);	Suf	Suf	include

Disease	ICD-O (9650-9660) Hodgkin's disease ICD-10 C81 Hodgkins Disease (M9650/3) Hodgkin's disease, NOS (M9651/3) Lymphocyte-rich classical Hodgkin lymphoma (M9652/3) Mixed cellularity classical Hodgkin lymphoma (M9653/3) Lymphocyte-depleted classical Hodgkin lymphoma (M9659/3) Nodular lymphocyte predominant Hodgkin lymphoma (M966/3) Nodular sclerosis classical Hodgkin lymphoma	Statistics Canada (deaths)			
Multiple Myeloma	203 Multiple myeloma and immunoproliferative neoplasms ICD-9 203.0 Multiple Myeloma ICD-10 C90.0 Multiple Myeloma ICD-O 9732/3 Multiple Myeloma	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Lim	Lim	include
Leukemia	204 Lymphoid leukemia	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Inad	Inad	include
	204.0 Acute lymphoid leukemia		Inad	Inad	include
	204.1 Chronic lymphoid leukemia ICD-9 204.1 Chronic lymphocytic leukemia ICD-10 C91.1 Chronic lymphocytic leukemia ICD-O M9823/3 Chronic lymphocytic leukemia		Suf	Lim	include
	205 Myeloid leukemia		Inad	Inad	
	205.0 Acute promyelocytic leukemia		Inad	Inad	
	205.1 Chronic myeloid leukemia		Inad	Inad	

Non Cancer Outcomes	ICD Codes	Data source	IOM status	Lit review	Comment
Chloracne	No ICD-9 code No ICD-10 code	Not available	Suf	Not reviewed	Do not include no diagnostic code no specific diagnostic code that is systematically collected
Porphyria cutanea tarda	No ICD-9 code No ICD-10 code	Not available	Lim	Not reviewed	Do not include no specific diagnostic code that is systematically collected
Non insulin dependent diabetes (Type 2)	ICD-9 250.0 Diabetes mellitus type 2 250.2 Diabetes mellitus type 2 uncontrolled ICD-10 E11 Non-insulin dependent diabetes	Deaths: through 1) vital statistics (death certificates)	Lim	Lim	Do not include Difficult to elucidate etiology due to confounding from lifestyle factors (obesity, family history) and other comorbidities
Parkinson's Disease	332 Paralysis agitans (Parkinson's Disease)	Deaths: through 1) vital statistics (death certificates)	Inad	Lim	Do not include no specific diagnostic code that is systematically collected
	356.8 Other unspecified idiopathic peripheral neuropathy	Deaths: through 1) vital statistics (death certificates)	Lim	Lim	Do not include no specific diagnostic code that is systematically collected
Spina bifida	ICD-9 741 Spina bifida ICD-10 Q05 Spina bifida	Deaths: through 1) vital statistics (death certificates)	Lim	Lim	Do not include Data quality
Stillbirth	779.9 Unspecified condition originating in the perinatal period		Inad		Do not include Data quality
Low Birth Weight	Stillbirth NEC		Inad		Do not include Data quality

Table 3 ICD-O and ICD -9 and ICD 10 Codes for Cancer Incidence Outcomes

Cancer Site	ICD0 Codes	ICD Codes [1969-1974: ICD8; 1975-2003: ICD 9]
All malignant neoplasms	**C00-C80**	140-209 - All malignant neoplasms (ICD8) 140-208 - All malignant neoplasms (ICD9)
Nasopharynx	C11 Nasopharynx	147 Malignant neoplasm of nasopharynx
Nasal Cavity	C300 Nasal Cavity	160 Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
Larynx	C32 Larynx	161 Malignant neoplasm of larynx
Lung	C34 Lung	162.2-162.9 Malignant neoplasm of bronchus, and lung
Bone	C40-C41 Bone and articular cartilage	170 Malignant neoplasm of bone and articular cartilage
Soft Tissue	C38.0, C47, C49 Soft tissue (including heart)	171 Malignant neoplasm of connective and other soft tissue
Breast	C50 Breast	174 Malignant neoplasm of female breast
Prostate	C61 Prostate	185 Malignant neoplasm of prostate
Testis	C62 Testis	186 Malignant neoplasm of testis
Brain	C70-C72 Brain and Central Nervous System	191 Malignant neoplasm of brain
Non Hodgkins Lymphoma	C77 Non Hodgkins Lymphoma	200.0-200.8 Lymphosarcoma and reticulosarcoma 202.0-202.2, 202.8-202.9 Other malignant neoplasms of lymphoid and histiocytic tissue
Hodgkin's Disease	C77 Hodgkin disease	201.0-201.9 Hodgkin's disease
Multiple Myeloma		203.0, 203.2-203.8 Multiple myeloma
Leukemia	C42 Lymphatic leukemia Type 9820 Lymphoid leukemia	204 Lymphoid leukemia
	C42 Lymphatic leukemia	204.0 Acute lymphoid leukemia
	C42 Lymphatic leukemia	204.1 Chronic lymphoid leukemia
	C42 Lymphatic leukemia Type 9860 Myeloid Leukemia	205 Myeloid leukemia
	C42 Lymphatic leukemia Type 9866 Acute promyelocytic leukemia	205.0 Acute promyelocytic leukemia
	C42 Type 9863 Chronic myeloid leukemia	205.1 Chronic myeloid leukemia

Table 4. ICD Codes for Mortality Outcomes

Health Outcome	ICD Codes [1969-1974: ICD8; 1975-2003: ICD 9]
All malignant neoplasms	140-209 All malignant neoplasms (ICD8) 140-208 All malignant neoplasms (ICD9)
Cancer of nasopharynx	147 Malignant neoplasm of nasopharynx
Cancer of nasal cavity	160 Malignant neoplasm of nasal cavities, middle ear, and accessory sinuses
Cancer of larynx	161 Malignant neoplasm of larynx
Lung cancer	162.2-162.9 Malignant neoplasm of bronchus, and lung
Bone cancer	170 Malignant neoplasm of bone and articular cartilage
Cancer of soft tissue	171 Malignant neoplasm of connective and other soft tissue
Breast cancer (female)	174 Malignant neoplasm of female breast
Prostate cancer	185 Malignant neoplasm of prostate
Testicular cancer	186 Malignant neoplasm of testis
Brain cancer	191 Malignant neoplasm of brain
Non Hodgkin's lymphoma	200.0-200.9 Lymphosarcoma and reticulosarcoma 202.0-202.2, 202.8-202.9 Other malignant neoplasms of lymphoid and histiocytic tissue
Hodgkin's Disease	201.0-201.9 Hodgkin disease
Multiple Myeloma	203.0, 203.2-203.8 Multiple myeloma
Leukemia	204 Lymphoid leukemia 204.0 Acute lymphoid leukemia 204.1 Chronic lymphoid leukemia 205 Myeloid leukemia 205.0 Acute promyelocytic leukemia 205.1 Chronic myeloid leukemia
Diabetes mellitus	250 Diabetes mellitus
Parkinson's Disease	332 Paralysis agitans (Parkinson's Disease)
Disorders of the Peripheral Nervous System	350-359 Disorders of the Peripheral Nervous System
Anencephalus	740 Anencephalus and similar anomalies
Spina bifida	741 Spina bifida

Cancer outcomes and respective ICD-9 codes are listed in Table 3. ICD codes for mortality outcomes are listed in Table 4. These codes were sent to the Province of New Brunswick to assist them to select the appropriate records for this study.

Time Period

Herbicide spraying began in 1956 and continued until 2004. An assumption that the estimated average latency period between environmental exposures and diagnosis of cancers of ten years was

initially made (though this will vary from one cancer type to the next), and thus rates for the time period of 1966-the current time were of interest. Adverse reproductive outcomes occur with a much shorter latency, but the lack of data that has been fully validated for the study period prevented exploration of these effects.

Cancer incidence data were not available from the New Brunswick Cancer registry, unfortunately, for the earlier years or after 2003 so the decision was made to calculate rates for the period 1984-2003. Mortality data were available from 1980 to 2003.

In order to reduce the potential for fluctuating estimates that might result from using small numbers in single year periods, mean age standardized incidence rates and 95% confidence intervals for cancer incidence were calculated for five year time periods from 1984-2003 with the census year (1986, 1991, 1996 and 2001) forming the midpoint of the interval. Age standardized mortality rates and 95% confidence intervals were calculated for five-year periods from 1980-2003, with the exception of 1980-1983 where a four year time period was calculated.

Age Groups

Age specific rates were generated according to the following age groups: <1, 1-4, 5-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, 80+ years. Ten year age categorization was chosen because it increases counts within each strata while not markedly generating different results than would have resulted if five year age groups were used.

Population Count Data Source

Census year population data for each census subdivision were obtained from Statistics Canada population census records and aggregated into the respective population (GSR, New Brunswick).

Incidence and Mortality Data Sources

The province of New Brunswick Department of Health provided incidence and mortality data for the Gagetown Study Region and New Brunswick. Cancer incidence data was provided for the years

1984-2003 and was coded by the ICD-O classification system. Mortality data was provided for the years 1980-2003 and was coded by the ICD-9 classification system.

Cancer incidence data for the GSR were provided by the New Brunswick Cancer Registry. Mortality data were provided by the Province of New Brunswick. Detailed data formats and instructions were provided to the Province of New Brunswick to facilitate data coding and transfer.

source of mortality data already stated on previous page...could clarify on p. 16 that mortality data included cancer and the other selected chronic diseases.

Statistical Analysis

Incidence and Mortality Rates

Gender-specific, age-standardized incidence and mortality rates and 95% confidence intervals were calculated for each population using the direct method of standardization (Szklo & Nieto, 2004) using the 1991 Canadian population as the standard. The 1991 population weights were aggregated into ten year age intervals to match the age structure of the case and population data.

The adjusted rates were calculated using the following formula:

Age Adjusted Incidence Population A = $\sum [I_{Ai} \times W_i] / \sum W_i$

I_{Ai} = Age-specific incidence
W_i = Standard population age-specific weights
(Szklo & Nieto, 2004)

Annual rates were calculated by dividing the age adjusted rate by five to account for the fact that cases were aggregated over a five year time period. The exception is the 1980-1983 mortality data. Because data from 1979 were not available, the annual age adjusted rate for this time period was calculated by dividing the age adjusted rate by four.

Confidence intervals were calculated based on the gamma distribution. This method was chosen because it produces valid confidence intervals in situations where the cell count is low (Fay & Feuer, 1997). It is based on the assumption that the direct standardized rate is a linear combination of

independently distributed Poisson variables. The following formulas were used to calculate the variance and confidence intervals.

a statistician should assess this section...

Variance = W_i^2 (cases/pop^2) / [$(W_i)]^2$

where Wi = the age specific weights

Lower confidence limit = $^{-1}$ (x^2/v, 1) (/2)

Where $^{-1}$ is the inverse of the gamma distribution, x is the age standardized rate, v is the variance

Upper confidence limit = $^{-1}$ (x^2/v +1, 1) (1- /2)

Where $^{-1}$ is the inverse of the gamma distribution, x is the age standardized rate, v is the variance (Harvard School of Public Health, 2004).

The age standardized incidence and mortality data are presented in a series of tables included within Appendix 1.

Incidence and mortality rates for each health outcome and time period were then compared between New Brunswick and the Gagetown Study Region. Rates were determined to be statistically significantly different if the 95% confidence intervals for the two point estimates did not overlap. While this is standard epidemiological procedure for the direct method of standardization, the challenge with this approach is that the Gagetown rates were based upon small numbers which, in turn, generates wide confidence intervals. There were few instances in which the two rates were statistically different.

suggest re-wording to clarify what is meant by the high-lighted phrase and the sensitivity of indirect vs direct age-standardization when observed numbers are low.

Given this uncertainty and invoking the precautionary principle, instances where the Gagetown point estimates were of the New Brunswick confidence intervals are flagged. In this way, a theoretical approach that builds upon the indirect method of standardization for comparing rates from two populations (number of actual observed cases versus number of expected cases, based upon age-specific rates) was applied. In this manner, Gagetown rates that fell outside of the normal and expected range of New Brunswick rates were identified.

Example: Gagetown incidence rate	7.68	95% CI: 5.11-11.09
New Brunswick incidence rate	8.99	95% CI: 7.85-10.25

In this example, the Gagetown incidence rate is lower than the normal range for the New Brunswick incidence rate because the point estimate of 7.68 is less than the lower 95% confidence boundary of 7.85 but, because the two intervals overlap, it is not statistically significantly different.

Standardized Incidence and Mortality Ratios

Standardized incidence and mortality ratios were compiled in order to present a composite picture of the comparative experience of Gagetown Study Region versus the Province of New Brunswick. These were obtained by dividing the Gagetown rate by the New Brunswick rate for each time period and for each outcome and are presented in Tables 5-8. If the ratio is greater than 1, the rate in the Gagetown region appears to be higher than the corresponding rate in the New Brunswick region. For example, a standardized mortality ratio equal to 0.85 would be generated from a ratio of 7.68/8.99 as illustrated above. This would be constrained however, by the uncertainty associated with the point estimates for both the GSR and for New Brunswick, as discussed in the previous section. One might observe a SIR of 2.0, suggesting that the rate is twice as high in the GSR versus New Brunswick, but this could be the result of dividing a GSR rate of 2.0 per 100,000 by 1.0 per 100,000. It is important to refer to the width of the confidence intervals for the point estimates before drawing conclusions about such findings.

Population Attributable Risk

The difference between the incidence of disease in the target population and in the province was used to calculate the population attributable risk for different diseases that are associated with the 'experience of living', in the most general sense, in the Gagetown region. This statistic was calculated by the following formula (Oleckno, 2002):

POP AR% = $[(IR_P - IR_{UE}) / IR_P] \times 100$. where $IR_{P:}$ Incidence rate in population

$IR_{UE:}$ Incidence rate among unexposed

Consideration for confounding influences of lifestyle or other demographic factors

Because this is an ecological study, there is no capacity to control for the confounding influences of individual lifestyle or demographic factors. An elevated incidence rate in the exposed population may be indicative of the influence of herbicide exposures but the impact of other risk factors cannot be excluded.

Results

Cancer Incidence

would help greatly to incl. observed numbers in Tables 5-8

Tables 5 and 6 present five year average standardized incidence ratios associated with various cancer for females and males respectively. These ratios were calculated from data provided in the tables that are included in Appendix 1. The Appendix 1 tables contain the age-standardized incidence rates and 95% confidence intervals for each specific outcome by gender and time period.

Cancer

suggest a column for full time period

Table 5. Five Year Standardized Incidence Ratios- Gagetown vs. NB Females - 1984-2003

Disease	Time period			
	1984-1988	1989-1993	1994-1998	1999-2003
All causes	1.02	1.00	0.97	1.07
Bone	3.21	0.75	3.41	0.78
Brain	1.30	1.50	0.73	1.08
Breast	1.10	1.08	1.09	1.06
Hodgkin's Disease	1.12	1.01	0.92	1.11
Larynx	--	1.93	0.72	0.50
Lung	1.10	0.85	0.76	0.90
Acute lymphocytic leukemia	2.62	1.07	0.43	1.0
Acute Myeloid leukemia	1.25	0.3	1.22	1.71
Chronic lymphocytic leukemia	--	0.56	0.62	0.67
Chronic myeloid leukemia	1.65	1.80	1.12	0.86
Multiple myeloma	0.73	1.55	0.79	0.88
Nasopharynx	2.49	--	--	2.85
Non Hodgkin's lymphoma	0.96	1.00	0.84	0.93
Other respiratory (including nasal cavity)	1.37	1.70	0.53	1.25
Soft tissue sarcoma	1.09	1.00	1.06	1.13

-- = insufficient numbers to calculate ratio

Table 6. Five Year Standardized Incidence Ratios- Gagetown vs. NB Males - 1984-2003

Disease	Time period			
	1984-1988	1989-1993	1994-1998	1999-2003
All causes	1.04	0.91	0.92	1.01
Bone	0.36	0.43	0.95	0.58
Brain	0.92	1.02	0.86	0.92
Hodgkin's Disease	0.36	1.03	1.51	0.82
Larynx	0.72	1.09	0.80	1.49
Acute lymphocytic leukemia	1.28	0.76	0.81	1.38
Acute myeloid leukemia	1.92	0.92	0.63	1.31
Chronic lymphocytic leukemia	--	0.62	0.07	0.93
Chronic myeloid leukemia	1.80	0.32	0.89	1.00
Lung	0.94	0.64	0.79	0.87
Multiple myeloma	0.93	0.98	1.26	1.06
Nasopharynx	2.07	0.63	0.96	--
Non-Hodgkins Lymphoma	0.95	0.94	0.91	0.81
Other respiratory (including nasal cavity)	2.18	0.28	--	1.22
Prostate	1.13	0.98	0.85	0.96
Soft tissue sarcoma	1.03	1.09	0.94	0.65
Testicular	1.23	1.13	1.02	1.06

-- = insufficient numbers to calculate ratio

"all cancers" (to distinguish from "all causes of death")

Table 7. Five Year Average - Standardized Mortality Ratios- Gagetown vs. NB Females 1980-2003

Disease	Time Period				
	1980-1983	1984-1988	1989-1993	1994-1998	1999-2003
All causes	0.99	0.97	1.00	1.00	0.99
Bone	0.89	1.02	1.41	1.86	--
Brain	0.93	0.93	1.06	1.12	0.85
Breast	0.93	0.83	0.99	1.01	1.16
Larynx	--	--	--	0.65	--
Leukemia	1.05	0.80	0.5	1.27	0.78
Lung	1.35	0.94	0.91	0.76	0.84
Lymphoid	1.43	1.25	1.31	0.88	0.85
Nasal cavity	1.81	2.69	--	--	--
Nasopharynx	--	--	--	--	--
Soft tissue	1.58	--	0.98	2.48	1.42
Diabetes	0.64	0.83	0.92	1.24	1.10
Parkinsons Disease	--	0.66	1.28	1.32	0.45

-- = insufficient numbers to calculate ratio

same comment as T. 7

Table 8. Five Year Average - Standardized Mortality Ratios- Gagetown vs. NB Males 1980-2003

Disease	Time Period				
	1980-1983	1984-1988	1989-1993	1994-1998	1999-2003
All causes	0.93	0.96	0.88	0.87	0.91
Bone	--	--	--	0.94	2.11
Brain	0.87	1.17	1.02	0.87	1.06
Prostate	1.07	0.76	0.90	0.71	0.77
Larynx	0.46	0.97	0.87	0.69	0.57
Leukemia	0.56	1.24	1.27	0.35	1.25
Lung	0.84	0.93	0.73	0.70	0.88
Lymphoid	1.17	0.89	0.84	1.06	0.80
Nasal cavity	--	--	--	--	--
Nasopharynx	1.76	2.77	1.96	1.57	--
Soft tissue	0.82	1.36	1.99	--	1.58
Testicular	--	2.82	--	5.0	--
Diabetes	1.37	0.85	1.25	0.96	1.07
Parkinsons Disease	0.47	0.80	1.86	1.15	0.70

-- = insufficient numbers to calculate ratio

plus diabetes and Parkinson's Disease

Tables 7 and 8 present five year average standardized mortality ratios associated with various cancer types for females and males respectively. These ratios were calculated from data provided in Appendix 1. The Appendix 1 tables include the age standardized mortality rates and 95% confidence intervals for each specific outcome by gender and time period.

did the CCS report age/sex-specific all cancer mort. rates for New Brunswick? if yes, must clarify reason for discrepancy with data used in this report.

All causes of cancer: incidence and mortality

For both men and women, Gagetown Study Region residents' overall experience with mortality and cancer incidence was similar to that calculated for the Province as a whole over the entire period of study. Men in the GSR had a slightly reduced risk of dying from cancer than the entire province. This was especially so during 1989-1998. There were differences, however, in the New Brunswick all-cause cancer mortality rates resulting from these analyses and which if applied to the rates for Gagetown, would indicate that the GSR residents were at increased risk for all cause cancer compared to the Province as a whole. For the purposes of this report, we are assuming that the data that were sent to us were correct.

would help to quantify the problems somewhat, e.g., what % of cancer case reports lacked such info?

Nasopharyngeal and nasal cancer incidence and mortality

but only 2 cases observed in study area..suggest rewording and not claiming consistent

These findings are reflected in the elevated SIR values, when there were sufficient data to calculate an SIR. Nasal cavity cancer mortality was also higher in GSR females during 1980-1984 and 1985-1989 than the province of New Brunswick. There were no nasopharyngeal cancer deaths in GSR women during the study period which prevented calculation of mortality rates for this outcome. Also, no deaths for nasal cancer in women were identified in the more recent time intervals.

but only 3 cases observed...not sufficient to claim "consistent" pattern...

for GSR men emerges in relation to nasopharyngeal cancer incidence. Elevated point estimates for nasopharyngeal cancer mortality in males were higher than the higher limit identified for the 95% confidence interval for the province for 1980-1983, 1984-1988, 1989-1993 and

should state "GSR", not Gagetown

reader needs to be reminded that the ASIR data are shown in Appendix 1 and the SIR data are shown in text tables...

1994-1998 but not for the most recent time interval when there were no deaths from this cancer in men. There were no deaths at all from nasal cancer in GSR men during the twenty year study period.

even this wording seems too strong to describe rates based on 0-2 deaths; suggest stating that there were too few cases or deaths for meaningful analysis/inferences

Soft Tissue Sarcoma

Soft tissue sarcoma incidence rates were not observed to be elevated in GSR females or males for the entire time period; however soft tissue sarcoma mortality rates were for both males and females in the Gagetown Study Region males compared to the province as a whole when there were sufficient data to calculate these rates (except for 80-83 males and 89-93 females). It is that the soft tissue sarcoma point estimate for males was lower than the 95% normal range for the Province of New Brunswick during the most recent time interval of 1999-2003 and that soft tissue sarcoma incidence rates were slightly elevated for the GSR men and women for the early years (1984-88).

suggest that the results are not noteworthy because of very small numbers involved

Breast Cancer

Breast cancer age-standardized incidence rates were only slightly, but consistently, higher for GSR women throughout the study period compared to the Province of New Brunswick, with SIR ranging from 1.06 (1999-2003) to 1.10 (1984-1988). In all cases, the point estimates for GSR women were higher than the upper bound of the 95% confidence intervals for New Brunswick women. Interestingly, this slight increase in risk did not transfer to increased breast cancer mortality for GSR women. Breast cancer mortality rates for the GSR region were on par with the rest of the Province.

? higher breast cancer screening rates in GSR compared to rest of province?

Prostate Cancer

Point estimates for rates of prostate cancer incidence and mortality were lower in Gagetown Study Region males than for the Province of New Brunswick, with the exception of 1980-1983 in which the rate was higher than for New Brunswick as a whole.

should describe testic. ca. incidence data as this section describes only the mortality data

Testicular Cancer

For the most part, the sparse data available for this relatively rare form of cancer prevented calculation of standardized ratios for all the time intervals. Nevertheless, the GSR testicular cancer

mortality

these data are those for testicular cancer mortality

incidence rate was observed to be higher during 1984-1998 and during 1994-1998 compared to the Province of New Brunswick, with SIRs equal to respectively. No cases of testicular cancer were observed for the GSR during the other time intervals.

Lung Cancer

Lung cancer incidence was generally lower for both men and women in the Gagetown Study Region compared to the Province of New Brunswick across the twenty year study period. Other than a slightly elevated rate among GSR women in the earliest time period (1984-1988 SIR=1.10), the SIR ranged from 0.76-0.90 from 1989-1993 among GSR women and from 0.64-0.94 among GSR men.

Bone Cancer

suggest stating 1-3 cases per time period to reinforce reader's understanding of just how small the numbers are...

Bone cancer incidence appeared higher among GSR women for the time periods 1984-1988 (SIR=3.21) and 1994-1998 (SIR=3.41). These rates are based, however, upon cases. Rates for men in the Gagetown Study Region suggested a significantly decreased risk of bone cancer incidence for the time periods: 1984-1988 (SIR=0.36), 1989-1993 (SIR=0.43) and 1999-2003 (SIR=0.58). These are also based on low number of cases. Bone cancer age standardized mortality rates for GSR men were even lower. Only three deaths from bone cancer were observed in males from the Gagetown Study Region during the entire period of study.

Brain Cancer

The rate of brain cancer incidence was higher for female Gagetown residents for the early years of the study [1984-1988 (SIR=1.30), 1989-1993 (SIR=1.50)] but the reverse was true for the more recent time period of 1994-1998 (SIR=0.73). Brain cancer incidence rates in the GSR were similar to the Province of New Brunswick across the time span of the study.

Laryngeal Cancer

The risk for laryngeal cancer mortality was reduced for GSR men especially in the most recent time periods. With the exception of the 1989-1993 time period, the risk for laryngeal cancer among GSR women was also lower.

Lymphohaematopoetic Cancers

No consistent trends were evident for Hodgkin's disease, multiple myeloma, or Non-Hodgkin's lymphoma. Other than a considerably lower risk observed for GSR men in the time period 1984-1988 (SIR=0.36), rate of Hodgkin's disease were not significantly different between the Gagetown region and New Brunswick. There was no apparent trend in multiple myeloma risk over time. Rates for women were both elevated (1989-1993: SIR=1.55) and decreased (1984-1988: SIR =0.73; 1994-1998 SIR= 0.79). Non-Hodgkins Lymphoma incidence rates in Gagetown were similar to New Brunswick for all time periods except for a significantly reduced risk among men in the most recent time period (1999-2003: SIR=0.81).

Leukemia

Incidence rates for the four leukemia subtypes (acute lymphocytic, acute myeloid, chronic lymphocytic and chronic myeloid) were examined. Due to the small number of cases within each subtype, there is considerable variation in incidence rates over time. The SIR for acute lymphocytic leukemia was notably elevated in 1984-1988 among women (SIR=2.62) yet an inverse relationship was observed for women in 1994-1998 (SIR=0.43). In contrast, no significant differences in incidence rates among men in Gagetown and New Brunswick were observed. Incidence of acute myeloid leukemia (AML) was significantly decreased among Gagetown women in 1989-1993 (SIR=0.3) and significantly increased in 1999-2003 (SIR=1.71). Among men, the results were similarly variable; Gagetown residents experienced significantly elevated incidence rates in 1984-1988 (SIR=1.92) and 1999-2003 (SIR=1.31) and decreased incidence rates in 1994-1998. Chronic myeloid leukemia rates also fluctuated over time. Incidence rates appeared higher among GSR women in 1989-1993 (SIR=1.80) and among GSR men in 1984-1988 (SIR=1.80). The age standardized chronic myeloid leukemia incidence rate for GSR men was lower in 1989-1993 (SIR=0.32) than for the province of New Brunswick.

this has to be an artifact and must be explained

Chronic lymphocytic leukemia (CLL) incidence rates were consistently lower for GSR women and men than the province of New Brunswick throughout the study period.

Similarly, the number of male cases in New Brunswick identified in 1989-1993 was 61, 88 in 1994-1998, and 82 in 1999-2003.

As noted in Appendix 2, the ICD diagnostic coding for the lymphatopoietic cancers and leukemias provided in the data files were not clear and this created some challenges for sorting the data in order to complete the final analysis. This situation might have created some misclassification errors resulting in biased estimates and may partially explain the rather divergent results we obtained for the different time intervals for these diseases.

Mortality from Diabetes and Parkinson's Disease

Mortality rates due to diabetes and Parkinson's disease were analyzed. Diabetes mortality in women was lower in women during the early years of the study (1980-1983: SMR=0.64, 1984-1988: SMR=0.83) but was generally on par with the rest of the Province for the remaining years. The mortality risk for diabetes in the Gagetown Study Region men was higher but not significantly so during 1980-1983 (SMR=1.37) and 1989-1993 (SMR=1.25) but was similar to the Province as a whole for the other time periods.

Considerable variability in mortality due to Parkinson's disease was observed. Female residents of the Gagetown region experienced slightly heightened risk of mortality during 1994-1998 (SMR 1.32) yet decreased mortality during 1984-1988 (SMR=0.66) and 1999-2003 (SMR=0.45). Standardized mortality ratios among men were elevated in 1989-1993 (SMR=1.86) and decreased in 1980-1983 (SMR=0.47) and 1999-2003 (SMR=0.70). These ratios are based on low rates of mortality. The fluctuations in the mortality ratios is partially due to these small numbers.

Population Attributable Risk

I do not find this section helpful; since most incid and mortality differences were not formally statistically significant, use of PAR seems dubious

Percent population attributable risks (PAR) were calculated for both incidence rates and mortality rates. Diseases are presented if 1) the risk of following diseases was heightened or decreased in Gagetown for most of the time intervals or 2) the rates of disease in Gagetown fell outside the bounds of the New Brunswick confidence interval for at least two time periods. Tables 9-12 present

percent population attributable risks for females and males for both the incidence and mortality data. A positive PAR may be interpreted as the percentage of the risk for the disease that is specifically attributable to the experience of living in the Gagetown Study Region. A negative PAR may be interpreted as the percentage of reduced risk that is attributable to living in Gagetown. There are quite marked fluctuations in these data and this is most likely due, once again, to the low number of cases that were observed- causing marked fluctuations in the rates. This suggests there is uncertainty in the findings and these results should be viewed with caution.

Table 9: Percent Population Attributable Risks- Incidence - Females

Disease	Time period			
	1984-1988	1989-1993	1994-1998	1999-2003
Bone Cancer	68.94	-32.5	70.64	-28.5
Brain Cancer	23.05	33.22	-36.18	7.28
Breast Cancer	9.06	6.79	7.93	5.75
Nasopharyngeal Cancer	59.78	NA	NA	64.94
Laryngeal Cancer	NA	48.31	-38.3	-98.57
Acute Lymphocytic Leukemia	61.76	6.90	-134.14	0
Acute Myeloid Leukemia	20.23	-233.33	17.98	41.50
Lung Cancer	8.75	-17.88	-31.32	-11.59
Soft Tissue Sarcoma	7.95	0.44	5.36	11.21

Table 10 % Population Attributable Risks- Mortality - Females

Disease	Time period				
	1980-1983	1984-1988	1989-1993	1994-1998	1999-2003
Diabetes	- 55.13%	- 19.11%	- 8.11%	9.01%	19.18%
All lymphoid cancers (NHL, HD, MM)	30.11	20.20	23.75	-14.95	-17.06
Soft tissue sarcoma	36.75%	NA	- 1.90%	59.73%	29.41%

Table 11 % Population Attributable Risks- Incidence - Males

Disease	Time period			
	1984-1988	1989-1993	1994-1998	1999-2003
Laryngeal Cancer	- 38.57	8.64	-25.68	32.86
Acute Myeloid Leukemia	48.02	-8.38	-59.22	23.51
Lung Cancer	- 6.8%	-55.66	-26.82	-14.41
Nasopharyngeal Cancer	46.69%	- 112.78%	- 14.4%	NA
Prostate Cancer	11.38	-1.72	-17.87	-4.6
Testicular Cancer	18.6	11.34	2.35	5.5

Table 12 % Population Attributable Risks- Mortality - Males

Disease	Time period				
	1980-1983	1984-1988	1989-1993	1994-1998	1999-2003
Diabetes	26.76	-17.61	19.81	-4.41	6.37
Parkinson's Disease	- 112.39	-24.80	46.12	13.27	-42.95
Nasopharyngeal Cancer	43.21	63.86	48.89	36.36	NA
Soft Tissue Sarcoma	NA	-74.75	49.76	NA	36.76
Testicular Cancer	NA	64.58	NA	80.00	NA

The PAR data suggest that the percent risk of developing bone cancer in women is markedly elevated in 1984-1988 and 1994-1998 but markedly reduced in 1989-1993 in the GSR region compared to the Province as a whole. A similar variable pattern emerges for brain cancer and laryngeal cancer incidence for women.

A consistent and moderate elevation of risk may be observed for nasopharyngeal cancer incidence and mortality in both women and men across the time intervals studied. The exception would be the middle time intervals where there were so few cases for women that it was not possible to calculate SIRs. Similarly, soft tissue sarcomas and breast cancer PARs were slightly positively elevated for women across the study period. The PAR for soft tissue sarcoma mortality for men was also elevated for two of the five time intervals, reduced for one and not available for the other two. It is also noteworthy that the population attributable risk for testicular cancer was higher in the two time intervals that it was possible to calculate an estimate.

Table 13. Age Standardized Cancer Incidence Rates per 100,000 Females – NB and Canada- 1996-2001

Disease	1996		2001	
	New Brunswick	Canada	New Brunswick	Canada
	Rate	Rate	Rate	Rate
All causes	336.88	339.47	350.43	348.73
Bone	NA	0.78	NA	0.70
Brain	3.59	5.23	3.70	5.59
Breast	99.84	98.60	96.24	99.62
Hodgkin's Disease	1.56	2.42	NA	2.23
Larynx	1.41	1.29	1.43	1.07
Leukemia				
Acute lymphocytic	1.72	1.25	NA	1.09
Acute myeloid	3.12	2.24	NA	2.12
Chronic lymphocytic	NA	2.74	1.98	2.74
Chronic myeloid	NA	1.01	NA	0.91
Lung	41.31	41.90	48.99	44.51
Multiple myeloma	3.50	3.51	3.76	4.07
Nasopharynx	NA	0.35	NA	0.32
Non-Hodgkin's	18.72	13.08	NA	13.33
Other respiratory	NA	1.17	1.50	1.10
Soft Tissue Sarcoma	2.12	2.12	2.41	2.05

Table 14. Age Standardized Cancer Incidence Rates per 100,000 Males – NB and Canada-1996-2001

Disease	1996		2001	
	New Brunswick	Canada	New Brunswick	Canada
	Rate	Rate	Rate	Rate
All causes	499.41	457.62	508.52	477.24
Bone	NA	1.01	NA	1.16
Brain	7.20	7.83	6.98	7.34
Hodgki's Disease	1.63	3.04	NA	2.82
Larynx	9.79	6.93	5.59	5.95
Leukemia				
Acute lymphocytic	1.90	1.60	NA	1.58
Acute myeloid	2.91	2.87	NA	2.97
Chronic lymphocytic	NA	5.52	4.45	5.42
Chronic myeloid	NA	1.88	NA	1.82
Lung	99.54	82.00	93.70	75.68
Multiple Myeloma	4.66	5.54	6.35	5.80
Nasophaynx	NA	0.85	NA	1.01
Non-Hodgkin's	22.02	18.33	20.84	18.96
Other respiratory	NA	3.43	4.28	3.31
Prostate	128.97	109.99	135.80	132.30
Soft Tissue Sarcoma	1.89	2.65	4.52	2.70
Testis	4.23	4.86	5.65	5.46

Table 15. Age Standardized Cancer Mortality Rates per 100,000 Females – NB vs Canada- 1986-2001 [1]

Disease	1986		1991	
	New Brunswick	Canada	New Brunswick	Canada
	Rate	Rate	Rate	Rate
All causes	152.24	154.35	150.20	153.53
Brain/ Nervous system	3.75	3.87	5.26	3.93
Breast	33.86	32.02	26.49	30.07
Leukemia	5.61	5.20	5.39	4.95
Lung, trachea, bronchus	20.79	24.01	27.62	29.53
Non-Hodgkin's	4.83	5.09	5.50	5.72

Disease	1996		2001	
	New Brunswick	Canada	New Brunswick	Canada
	Rate	Rate	Rate	Rate
All causes	157.52	155.18	148.11	148.22
Brain/ Nervous system	3.56	3.88	3.15	NA
Breast	33.29	28.94	21.17	25.00
Leukemia	4.90	4.94	4..82	4.38
Lung, trachea, bronchus	32.86	33.66	36.77	34.44
Non-Hodgkin's	5.75	5.82	7.67	5.73

1. Data downloaded from Cancer Surveillance on-line (http://dsol-smed.hc-sc.gc.ca/dsol-smed/cancer/index_e.html). Bone, Hodgkins disease, larnynx, multiple myeloma, nasopharynx, nasal cavity, soft tissue sarcoma mortality data not available on this site.

Table 16. Age Adjusted Cancer Mortality Rates (1986&1991) per 100,000 Males[1]

Disease	1986		1991	
	New Brunswick	Canada	New Brunswick	Canada
	Rate	Rate	Rate	Rate
All causes	255.96	248.99	258.06	247.17
Brain/ Nervous system	5.27	5.87	5.51	5.43
Leukemia	9.52	9.19	9.38	9.14
Lung, trachea, bronchus	85.67	78.95	91.68	78.75
Non-Hodgkin's	7.64	7.74	8.04	8.09
Prostate	29.66	29.37	28.90	31.15

Table 16. Age Adjusted Cancer Mortality Rates (1996 & 2001) per 100,000 Males[1]

Disease	1996		2001	
	New Brunswick	Canada	New Brunswick	Canada
	Rate	Rate	Rate	Rate
All causes	249.82	236.50	237.88	224.00
Brain/ Nervous system	6.94	5.89	4.63	5.36
Leukemia\	6.44	8.89	6.86	8.06
Lung, trachea, bronchus	86.46	73.03	79.82	64.64
Non-Hodgkin's	10.58	8.44	12.23	9.06
Prostate	27.65	28.99	32.67	26.67

Data downloaded from Cancer Surveillance on-line (http://dsol-smed.hc-sc.gc.ca/dsol-smed/cancer/index_e.html). Bone, Hodgkins disease, larnynx, multiple myeloma, nasopharynx, nasal cavity, soft tissue sarcoma, testis mortality data not available on this site.

Comparison of New Brunswick Cancer Rates Generated in this Study vs. Cancer Rates from National Sources

Province-wide age-standardized cancer rates for 1996 and 2001 from the Canadian Cancer Society (CCS) annual reports were compared with the estimates for the five year average age standardized cancer rates for the intervals 1994-1998 and 1999-2003 that generated in this study. The CCS data are provided in Tables 13-16.

Data were not available for all of the specific cancer diagnoses and time periods of interest. Some variation between the CCS results and the results from the present analysis is expected because 1) the present analysis is based on a five year average whereas the CCS provided annual rates and 2) the present analysis is based on ten year age groupings whereas the CCS uses five year age groupings. The rates calculated in the present analysis and the reported rates were generally consistent for the health outcomes and time periods of interest with a few notable exceptions.

All-cause cancer incidence

For both 1996 and 2001, the all-cause cancer incidence rates (per 100,000) for New Brunswick males generated from the current analysis (1996: 695.05; 95% CI: 682.81-707.44, 2001: 669.39; 95% CI: 657.96-680.97) are higher than the rate reported for New Brunswick (1996: 499.41, 2001: 508.52 (no confidence intervals provided)) by the CCS. The females rates are similarly elevated in the current study (1996: 470.95; 95%CI: 461.77-480.27; 2001: 469.74; 95%CI: 460.85-478.74) compared to the CCS reported rates for New Brunswick (1996: 336.88, 2001: 350.43 (no confidence intervals provided)). All-cause cancer incidence CCS data for earlier years were not available on-line.

The reasons for this difference are not immediately apparent. The all-cause cancer incidence files that were sent to us by the Province of New Brunswick for the most recent ten years were generated separately than the cause-specific data. It may be that the all- cause data set included benign cases in addition to malignancies. As discussed in Appendix 2: Technical Notes, the all-cause cancer files included counts only and did not provide ICD coding so we were not able to investigated this possibility.

this assumption does not appear to be justified; recommend that further analysis be done to resolve this issue (if not now, then as a follow-up to this report).

Other respiratory cancer incidence

Data that were generated for the category of 'other respiratory cancer' (includes nasal cancer) incidence rates in the present analysis are lower than the reported rates for Canada or New Brunswick. Data from this study indicate that, for New Brunswick males, the 2001 other respiratory cancer incidence rate is 0.87 per 100,000 (95% confidence interval: 0.51-1.37). The CCS data suggest that the 2001 'other respiratory cancer' incidence rate is 4.28 per 100,000 males. For females, the current analysis resulted in an 'other respiratory cancer incidence rate' of 0.52. The CCS data report a New Brunswick rate of 2.41 per 100,000 females. These divergent findings suggest that 'other respiratory' coding for these data in this study is not fully consistent with the CCS data coding for this cancer site. The original ICD codes for this site were not provided to us.

Leukemia mortality

mortality

Leukemia mortality rates were also consistently lower in the present analysis compared those reported by the CCS. For males, the age standardized rate was 1.16 per 100,000 males yet the CCS reported rate was found to be 6.86 per 100,000. For females, the age standardized incidence rate was 0.92 per 100,000 but the CCS reported a New Brunswick age standardized mortality rate equal to 4.82 per 100,000. Differences of similar magnitude persisted in other time periods. However, incidence rates for leukemia subtypes were not notably different from the CCS reports. Rates for leukemia mortality were created using the broad category leukemia as detailed in the technical notes.

Notable differences also exist in the leukemia cancer mortality results. It is likely that leukemia coding from the downloaded data is more inclusive that the leukemia data in our analysis.

this seems a likely explanation and should be pursued

Discussion

suggest stating "cancer, diabetes and Parkinson's Disease..."

The purpose of this descriptive epidemiologic study was to determine whether there is evidence of increased rates of [redacted] in residents of the Gagetown Study Region, comprising CFB Gagetown and surrounding areas, compared to all residents of the Province of New Brunswick. The time period for this study was 1980-2003 for mortality and 1984 to 2003 for cancer incidence. An intensive effort was made by the investigator, in working with the Province, to obtain data for the earlier periods but this proved not to be possible within the time span that was available for this study.

Of special concern are the health risks that may have resulted from exposure to experimental applications of Agent Orange and Agent Purple and other herbicides during the specific test periods in June 1966 and June 1967. Diseases were prioritized on the basis of a recently completed review of the current scientific literature related to herbicides and health effects. The underlying hypothesis tested in this study was that Gagetown Study Region residents were at increased risk for these diseases as a result of their [redacted] exposures to the herbicides in question. Because we had no information about other environmental exposures or lifestyle considerations for these two populations, we were not able to control for these influences in the analyses.

...their possible historical...

For the most part, rates of specific disease and mortality occurrence that were observed for the Gagetown Study Region were similar to the experience of New Brunswick as a whole. There were two notable exceptions. [redacted] These two diseases were also identified in the literature review as outcomes that were frequently linked to herbicide exposures in previous epidemiological studies. While the current findings are inconclusive for these two outcomes due to the small numbers involved in this study, it is possible that exposure to the conditions in the GSR enhanced the risk for development of these diseases. Further research would be required to fully test this hypothesis. In contrast, the other [redacted] that have been most often linked to herbicide exposures, i.e. non-Hodgkin's lymphoma, chronic lymphocytic leukemia and Hodgkin's disease, showed variable results and no consistent pattern of elevation. As discussed in the results section, the data for these outcomes contained some inconsistencies which were difficult to resolve; hence these rates may not be fully accurate.

I think this statement is too strong and should be reworded to acknowledge the very low case/death numbers; "consistently elevated" is, I believe, misleading.

suggest stating "the cancers other than soft tissue sarcoma that have been...."

Consideration was given to possible co-existing factors that might have increased the risk for these diseases. A comparison of lifestyle characteristics of the Gagetown Study Region versus the Province of New Brunswick provided by the 2005 Canadian Community Health Survey[2] reveals that current smoking rates were very similar (23.3% for NB and 24.4% for Health Region 3, including a large portion of western New Brunswick) and that the percent of residents with a body mass index of greater than 27 was only slightly higher in Health Region 3 (39.8% versus 39.2% for New Brunswick). Also, the incidence of low income in 1995/1996 was only slightly lower in the Health Region 3 (14.2% versus 16.5% in New Brunswick). These data suggest that the residents of the GSR versus the Province of New Brunswick are quite similar for standard disease risk factors.

The population of New Brunswick during the study period ranged from 500,000 to 600,000. The study population was approximately 20% of the total New Brunswick population. Between 44 and 48% of the Gagetown Study Region residents lived in the City of Fredericton. Inclusion of Fredericton residents may have helped to enhance the robustness of the study from a sample size perspective but diluted some of the more localized exposure effects that may have been primarily restricted to CFB Gagetown.

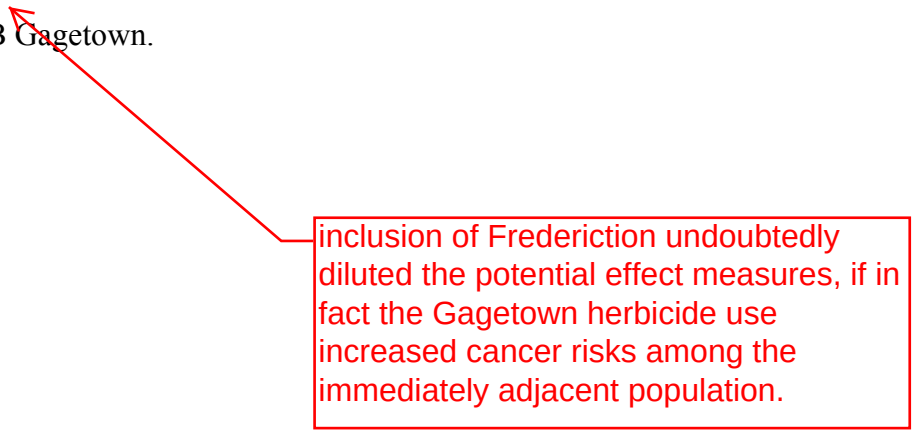

Table 17. Percent of Gagetown Study Region population residing in Fredericton

	1981		1986		1991		1996		2001	
	Fredericton	**GSR Area[1]**	**Fredericton**	**GSR Area***	**Fredericton**	**GSR Area***	**Fredericton**	**GSR Area***	**Fredericton**	**GSR Area***
Number (%)	43720 (48.0%)	91195 (100%)	44370 (46.0%)	96450 (100%)	46485 (45.2%)	102725 (100%)	46485 (44.1%)	105430 (100%)	47880 (44.4%)	107765 (100%)

1. The GSR area encompasses all 35 CSDs identified as part of the target community including Fredericton.

I believe that StatsCan also has data on mobility in/out of CSDs over the 5 years before a census; if available, it would be useful to cite such data for the GSR.

Differences were noted between GSR and the Province of New Brunswick in relation to mobility. Given the military nature of Gagetown Study Region residents, it is not surprising to learn that the mobility in Health Region 3 was much higher than the rest of New Brunswick (51.8% of Gagetown village had lived at the same address five years ago versus 67.2% of New Brunswick residents)[iii]. These 2005 data likely mirror earlier mobility patterns. The City of Fredericton residents were also quite mobile; 54.8% of residents had lived at the same address five years ago. Mobility may have contributed to lack of detection of cases because those who had been exposed may have left the area and then subsequently became ill. These cases would not have been reported as GSR cases. A detailed questionnaire survey with interviews of all participants would also be necessary once it had been established that a complete cohort existed. Loss to follow up is a considerable challenge in such studies. Even with good follow-up, such an investigation is an undertaking.

the difficulty seems overstated; suggest a term such as "major" rather than "enormous"

Conclusions

The results of this descriptive epidemiologic study revealed that there was little evidence to suggest that residents of the Gagetown Study Region were at increased risk for chronic disease incidence or mortality compared to all residents of the Province of New Brunswick. The exception to this finding is that the rates for both nasopharyngeal cancers and soft tissue sarcoma incidence are for the GSR residents compared to the Province of New Brunswick. While these observations were not statistically significant, the uncertainty of these findings is related to the rare nature of these diseases and the few cases that were identified in this small population. Further research would need to be done in order to examine these exposure-disease associations in detail; such work would only be feasible if there were sufficient cases with no loss to follow-up and accompanied by high quality exposure and individual risk factor information.

see previous comments about this issue...

suggest "cancer, diabetes or Parkinson's disease" rather than "chronic disease incidence or mortality"

the author should recommend at least 1-2 specific study designs that could improve the risk assessment done here

References

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Appendix 1.

Gagetown Area (Target Community) and New Brunswick Incidence and Mortality Rates

pt. estimate is not higher than the prov. upper CL

Table 1. Age Standardized Cancer Incidence Rates (1984-2003) per 100,000 Females

Disease	84-88				89-93			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
All causes	796	345.91 (322.25-370.85)	6242	339.50 (331.05-348.11)	1151	436.19 (411.23-462.26)	8803	435.7449 (426.59-445.03)
Bone	3	1.32* (0.27-3.86)	8	0.41 (0.18-0.81)	1	0.40 (0.01-2.22)	10	0.53 (0.25-0.97)
Brain	18	7.68* (4.54-12.15)	107	5.91 (4.83-7.15)	23	9.00* (5.70-13.52)	116	6.01 (4.96-7.21)
Breast	219	96.48* (84.11-110.17)	1557	87.74 (83.39-92.25)	272	104.47* (92.38-117.71)	1921	97.38 (93.03-101.87)
Hodgkin's Disease	6	2.45 (0.89-5.34)	40	2.18 (1.55-2.97)	7	2.61 (1.05-5.37)	48	2.59 (1.91-3.44)
Larynx	0		22	1.24 (0.77-1.88)	6	2.36* (0.86-5.14)	24	1.22 (0.78-1.83)
Leukemia								
Acute lymphocytic	6	2.38* (0.87-5.20)	17	0.91 (0.53-1.47)	3	1.16 (0.24-3.40)	20	1.08 (0.66-1.68)
Acute myeloid	6	2.62 (0.96-5.70)	39	2.09 (1.48-2.86)	1	0.42 (0.01-2.36)	29	1.40 (0.93-2.01)
Chronic lymphocytic	0	0	0	0	3	1.22 (025-3.56)	47	2.19 (1.61-2.92)
Chronic myeloid	3	1.17* (0.24-3.43)	14	0.71 (0.38-1.19)	4	1.60* (0.43-4.11)	18	0.89 (0.52-1.41)

* point estimate for Gagetown Study Region is not contained within 95% confidence limits for the corresponding New Brunswick rate. While the two confidence limits overlap, the small numbers of cases for the Gagetown Study Region have created some statistical uncertainty.

pt. est. < prov. upper CL

Table 1. Age Standardized Cancer Incidence Rates (1984-2003) per 100,000 Females (cont'd 2)

Disease	84-88				89-93			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Lung	70	31.08* (24.22-39.27)	518	28.36 (25.96-30.93)	83	32.39* (25.78-40.17)	757	38.18 (35.49-41.02)
Multiple myeloma	**7**	2.91* (1.17-6.00)	76	3.98 (3.13-4.99)	16	6.04* (3.44-9.84)	81	3.90 (3.09-4.86)
Nasopharynx	2	0.92* (0.11-3.32)	6	0.37 (0.14-0.82)	0		5	0.27 (0.09-0.62)
Non-Hodgkin's	29	12.48 (8.35-17.94	242	13.04 (11.44-14.81)	33	12.03 (8.26-16.92)	250	12.0 (10.54-13.62)
Other respiratory	3	1.34 (0.28-3.91)	18	0.98 (0.58-1.55)	3	1.14* (0.23-3.34)	13	0.67 (0.35-1.15)
Soft Tissue Sarcoma	4	1.76 (0.48-4.52)	28	1.62 (1.07-2.34)	6	2.27 (0.83-4.97)	45	2.26 (1.65-3.04)

* point estimate for Gagetown Study Region is not contained within 95% confidence limits for the corresponding New Brunswick rate. While the two confidence limits overlap, the small numbers of cases for the Gagetown Study Region have created some statistical uncertainty.

Table 1. Age Standardized Cancer Incidence Rates (1984-2003) per 100,000 Females (cont. 3)

Disease	94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
All causes	1332	457.82* (433.15-483.52)	103 45	470.95 (461.77-480.27)	16622	500.76* (476.16-526.30)	11409	469.74 (460.85-478.74)
Bone	3	1.09* (0.22-3.18)	6	0.32 (0.16-0.69)	2	0.70 (0.083- 2.53)	17	0.90 (0.51-1.47)
Brain	11	3.98 (1.97-7.16)	111	5.42 (4.44-6.54)	17	5.63 (3.25-9.10)	113	5.22 (4.27-6.32)
Breast	324	113.56* (101.34-126.81)	224 0	104.56 (100.22-109.04)	351	108.17* (96.94-120.34)	2428	101.95 (97.83-106.20)
Hodgkin's Disease	4	1.45 (0.38-3.79)	30	1.58 (1.06-2.27)	8	2.70 (1.13-5.45)	43	2.43 (1.74-3.30)
Larynx	4	1.41 (0.39-3.63)	40	1.95 (1.39-2.66)	2	0.70* (0.08-2.55)	32	1.39 (0.94-1.98)
Leukemia								
Acute lymphocytic	1	0.41* (0.01-2.30)	17	0.96 (0.56-1.54)	3	1.18 (0.23-3.53)	20	1.18 (0.71-1.85)
Acute myeloid	8	2.67 (1.13-5.34)	47	2.19 (1.60-2.93)	10	3.47* (1.65-6.40)	44	2.03 (1.46-2.75)
Chronic lymphocytic	4	1.33* (0.35-3.48)	49	2.14 (1.57-2.84)	6	1.76* (062-3.91)	65	2.64 (2.02-3.40)
Chronic myeloid	4	1.49 (0.40-3.83)	28	1.33 (0.88-1.93)	3	0.86 (0.18-2.53)	24	1.00 (0.63-1.51)

* point estimate for Gagetown Study Region is not contained within 95% confidence limits for the corresponding New Brunswick rate. While the two confidence limits overlap, the small numbers of cases for the Gagetown Study Region have created some statistical uncertainty.

Table 1. Age Standardized Cancer Incidence Rates (1984-2003) per 100,000 Females (cont'd 4)

Disease	94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Lung	91	32.70* (26.22-40.29)	934	42.94 (40.19-45.82)	135	42.97* (35.90-51.02)	1142	47.95 (45.15-50.89)
Multiple myeloma	9	3.03* (1.36-5.82)	85	3.83 (3.05-4.76)	13	3.48 (1.82-6.02)	98	3.95 (3.19-4.84)
Nasopharynx	0		5	0.24 (0.08-0.56)	2	0.77* (0.09-2.80)	6	0.27 (0.09-0.60)
Non-Hodgkin's	39	13.42 (9.48-18.46)	357	15.94 (14.28-17.74)	42	13.39 (9.59-18.19)	355	14.43 (12.90-16.10)
Other respiratory	1	0.34 (0.01-1.89)	14	0.64 (0.35-1.09)	2	0.65* (0.08-2.34)	12	0.52 (0.27-0.92)
Soft Tissue Sarcoma	7	2.61 (1.04-5.40)	51	2.47 (1.83-3.26)	8	2.32 (0.96-4.70)	44	2.06 (1.47-2.81)

* point estimate for Gagetown Study Region is not contained within 95% confidence limits for the corresponding New Brunswick rate. While the two confidence limits overlap, the small numbers of cases for the Gagetown Study Region have created some statistical uncertainty.

Table 2. Age Standardized Cancer Incidence Rates (1984-2003) per 100,000 Males

Disease	84-88				89-93			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
All causes	990	529.38* (496.46-563.90)	7631	507.70 (496.26-519.31)	1307	603.33* (570.86-637.16)	10915	660.06 (647.69-672.59)
Bone	1	0.46* (0.01-2.56)	21	1.28 (0.79-1.97)	1	0.41* (0.01-2.29)	18	0.96 (0.57-1.52)
Brain	16	7.66 (4.34-12.54)	132	8.33 (6.96-9.88)	18	7.49 (4.43-11.85)	126	7.31 (6.08-8.70)
Hodgkin's Disease	3	1.17* (0.23-3.47)	55	3.27 (2.46-4.26)	8	3.21 (1.38-6.37)	55	3.12 (2.35-4.07)
Larynx	13	6.56* (3.47-11.28)	143	9.09 (7.65-10.71)	22	9.84 (6.14-14.92)	152	8.99 (7.62-10.54)
Leukemia								
Acute lymphocytic	5	2.09 (0.66-4.92)	29	1.63 (1.09-2.35)	3	1.27 (0.26-3.73)	30	1.67 (1.12-2.39)
Acute myeloid	9	4.81* (2.16-9.24)	38	2.50 (1.76-3.44)	4	1.79 (0.48-4.66)	33	1.94 (1.34-2.74)
Chronic lymphocytic	0	0	0	0	5	2.33* (0.75-5.48)	61	3.76 (2.87-4.83)
Chronic myeloid	5	2.49* (0.81-5.81)	21	1.38 (0.85-2.12)	1	0.48* (0.01-2.66)	25	1.51 (0.97-2.23)

* point estimate for Gagetown Study Region is not contained within 95% confidence limits for the corresponding New Brunswick rate. While the two confidence limits overlap, the small numbers of cases for the Gagetown Study Region have created some statistical uncertainty.

Table 2. Age Standardized Cancer Incidence Rates (1984-2003) per 100,000 Males (cont'd 2)

Disease	84-88				89-93			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Lung	262	99.13* (85.50-114.31)	1623	105.87 (100.76-111.18)	145	67.58 (56.98-79.59)	1746	105.20 (100.31-110.27)
Multiple myeloma	12	6.69 (3.41-11.79)	107	7.20 (5.89-8.71)	12	5.42 (2.80-9.48)	93	5.54 (4.47-6.79)
Nasopharynx	2	0.89* (0.10-3.32)	7	0.43 (0.17-0.89)	1	0.45 (0.01-2.53)	12	0.71 (0.36-1.24)
Non-Hodgkin's	34	17.32 (11.94-24.30)	280	18.26 (16.17-20.55)	35	15.82 (10.99-22.04)	285	16.85 (14.94-18.93)
Other respiratory	6	2.90* (1.06-6.31)	20	1.33 (0.81-2.07)	1	0.39* (0.01-2.16)	23	1.37 (0.87-2.06)
Prostate	176	100.89* (86.35-117.17)	1295	89.41 (84.55-94.47)	264	127.26 (112.31-143.64)	2105	129.45 (123.96-135.11)
Soft Tissue Sarcoma	7	2.95 (1.17-6.14)	49	2.86 (2.11-3.80)	5	2.04 (0.66-4.77)	32	1.87 (1.28-2.64)
Testis	9	3.87 (1.71-7.52)	53	3.15 (2.35-4.13)	10	3.88 (1.86-7.15)	61	3.44 (2.63-4.42)

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Table 2. Age Standardized Cancer Incidence Rates (1984-2003) per 100,000 Males (cont'd 3)

Disease	94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
All causes	1511	640.21* (608.16-673.48)	12378	695.05 (682.81-707.44)	1789	678.78 (647.45-711.22)	13287	669.3944 (657.96-680.97)
Bone	2	0.73 (0.09-2.65)	14	0.77 (0.42-1.29)	2	0.80 (0.10-2.91)	25	1.37 (0.88-2.04)
Brain	18	7.42 (4.38-11.78)	154	8.60 (7.29-10.08)	21	7.55 (4.65-11.58)	161	8.22 (6.99-9.62)
Hodgkin's Disease	9	3.52* (1.60-6.68)	41	2.33 (1.67-3.17)	6	2.38 (0.87-5.19)	52	2.92 (2.17-3.85)
Larynx	16	6.62* (3.78-10.79)	150	8.32 (7.04-9.77)	22	9.83* (6.14-14.92)	130	6.60 (5.51-7.85)
Leukemia								
Acute lymphocytic	3	1.27 (0.26-3.72)	28	1.56 (1.04-2.26)	5	2.09 (0.68-4.88)	24	1.51 (0.96-2.26)
Acute myeloid	5	2.06* (0.66-4.84)	59	3.28 (2.49-4.24)	9	3.53* (1.61-6.72)	52	2.70 (2.00-3.54)
Chronic lymphocytic	1	0.35* (0.01-1.97)	88	4.96 (3.97-6.11)	10	3.81 (1.82-7.02)	82	4.08 (3.24-5.08)
Chronic myeloid	3	1.25* (0.25-3.67)	25	1.41 (0.91-2.09)	6	2.38 (0.86-5.22)	47	2.37 (1.73-3.17)

* point estimate for Gagetown Study Region is not contained within 95% confidence limits for the corresponding New Brunswick rate. While the two confidence limits overlap, the small numbers of cases for the Gagetown Study Region have created some statistical uncertainty.

Table 2. Age Standardized Cancer Incidence Rates (1984-2003) per 100,000 Males (cont'd 4)

Disease	94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Lung	186	79.26* (68.23-91.57)	1784	100.52 (95.90-105.31)	219	83.88* (73.07-95.83)	1892	95.97 (91.66-100.42)
Multiple myeloma	18	7.66* (4.53-12.13)	108	6.08 (4.99-7.35)	17	6.32 (3.66-10.16)	121	5.99 (4.97-7.17)
Nasopharynx	2	0.90 (0.11-3.24)	17	0.94 (0.55-1.51)	0	0	13	0.66 (0.35-1.15)
Non-Hodgkin's	46	18.60 (13.58-24.85)	373	20.38 (18.35-22.58)	45	16.76* (12.19-22.48)	422	20.79 (18.81-22.91)
Other respiratory	0	0	11	0.61 (0.31-1.10)	3	1.06 (0.21-3.12)	18	0.87 (0.51-1.37)
Prostate	283	122.69* (108.76-137.90)	2535	144.61 (139.02-150.36)	319	122.55* (109.38-136.86)	2521	128.26 (123.26-133.39)
Soft Tissue Sarcoma	6	2.37 (0.86-5.19)	46	2.51 (1.83-3.35)	5	1.92* (0.62-4.51)	54	2.94 (2.20-3.85)
Testis	9	3.41 (1.56-6.47)	60	3.33 (2.54-4.30)	13	5.10 (2.70-8.75)	80	4.82 (3.80-6.02)

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Table 3. Age Standardized Mortality Rates (1980-2003) per 100,000 Females

Disease	80-83				84-88			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Diabetes	17	10.56* (6.15-16.92)	231	16.38 (14.33-18.64)	36	15.45* (10.81-21.40)	372	18.51 (16.67-20.50)
Parkinsons Disease	0	NA	18	1.25 (0.74-1.98)	3	1.27* (0.26-3.70)	40	1.93 (1.38-2.63)

Table 3. Age Standardized Mortality Rates (1980-2003) per 100,000 Females (cont'd)

Disease	89-93				94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Diabetes	43	16.02 (11.57 21.62)	397	17.32 (15.64-19.13)	62	20.30* (15.47 26.15)	463	18.47 (16.79-20.28)	76	23.52* (18.52 29.45)	571	19.01 (17.41-20.72)
Parkinsons Disease	8	2.59 (1.12 5.12)	50	2.02 (1.49-2.66)	13	3.09* (1.64 5.30)	67	2.34 (1.80-2.97)	4	1.05* (0.27 2.75)	80	2.35 (1.85-2.95)

* point estimate for Gagetown Study Region is not contained within 95% confidence limits for the corresponding New Brunswick rate. While the two confidence limits overlap, the small numbers of cases for the Gagetown Study Region have created some statistical uncertainty.

Table 4. Age Standardized Mortality Rates (1980-2003) per 100,000 Males

Disease	80-83				84-88			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Diabetes	24	**22.27*** (14.06-33.54)	171	16.31 (13.93-18.99)	25	**14.77*** (9.49-21.92)	250	17.38 (15.27-19.70)
Parkinsons Disease	1	1.13* (0.03-6.32)	24	2.40 (1.53-3.58)	4	2.42 (0.64-6.30)	43	3.02 (2.18-4.08)

Table 4. Age Standardized Mortality Rates (1980-2003) per 100,000 Males (cont'd)

Disease	89-93				94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Diabetes	47	23.17* (16.99-30.86)	298	18.58 (16.52-20.82)	53	22.91 (17.14-29.99)	419	23.92 (21.68-26.33)	76	29.21 (22.99-36.60)	543	27.35 (25.09-29.76)
Parkinsons Disease	12	6.18* (3.18-10.82)	52	3.33 (2.49-4.37)	12	5.35 (2.76-9.34)	80	4.64 (3.68-5.78)	8	3.19* (1.38-6.30)	90	4.56 (3.66-5.61)

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Table 5. Age Standardized Cancer Mortality Rates (1980-2003) per 100,000 Females

Disease	80-83				84-88			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
All causes	233	146.34 (128.12-166.44)	1992	147.01 (140.57-153.66)	335	144.67 (129.55-161.04)	2822	149.30 (143.80-154.96)
Bone	1	0.62 (0.01-3.48)	10	0.70 (0.34-1.30)	1	0.44 (0.01-2.47)	8	0.43 (0.18-0.85)
Brain	6	3.70 (1.35-8.04)	53	3.99 (2.98-5.23)	8	3.51 (1.52-6.92)	70	3.78 (2.94-4.78)
Breast	44	27.81 (20.19-37.38)	396	29.90 (27.0-33.02)	60	26.20 (19.98-33.73)	576	31.56 (29.01-34.27)
Larynx	0		4	0.31 (0.08-0.81)	0		13	0.71 (0.37-1.21)
Leukemia	1	0.66 (0.02-3.67)	9	0.63 (0.29-1.20)	1	0.43 (0.01- .38)	11	0.54 (0.27-0.97)
Lung	37	23.11* (16.26-31.88)	228	17.07 (14.91-19.46)	46	20.47 (14.98-27.31)	400	21.85 (19.75-24.11)
Lymphoid	17	10.76* (6.26-17.23)	103	7.52 (6.13-9.13)	21	8.91 (5.51-13.63)	138	7.11 (5.97-8.41)
Nasal cavity	1	0.58 (0.01-3.25)	4	0.32 (0.09-0.83)	1	0.43* (0.01-2.38)	3	0.16 (0.03-0.46)
Nasopharynx	0		3	0.21 (0.04-0.62)	0		2	0.11 (0.01-0.41)
Soft tissue	2	1.17 (0.14-4.21)	10	0.74 (0.35-1.37)	0		12	0.63 (0.32-1.09)

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Table 5. Age Standardized Cancer Mortality Rates (1980-2003) per 100,000 Females (cont'd 2)

Disease	89-93				94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%C)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
All causes	421	155.47 (140.88 171.15)	3280	155.85 (150.5 161.34	471	155.57 (141.53-170.62)	3614	155.82 (150.68-161.09)	488	142.64 (129.94-156.25)	3801	144.16 (139.42-149.01)
Bone	1	0.31 (0.01-1.72)	5	0.22 (0.07-0.51)	1	0.39 (0.01-2.15)	5	0.21 (0.06-0.52)	0		8	0.32 (0.13-0.65)
Brain	9	3.67 (1.68 6.97)	70	3.47 (2.70-4.40)	12	4.43 (2.27 7.78)	83	3.95 (3.14-4.91)	9	2.85 (1.29 5.44)	79	3.34 (2.62-4.20)
Breast	81	30.17 (23.93 37.55)	622	30.46 (28.08-32.97)	93	30.77 (24.75 37.86)	689	30.33 (28.06-32.72)	92	26.74 (21.42 32.99)	602	23.02 (21.15-25.02)
Larynx	0		9	0.44 (0.20-0.84)	1	0.35 (0.01-1.94)	12	0.54 (0.28-0.95)	0		10	0.43 (0.20-0.79)
Leukemia	1	0.37* (0.01-2.05)	17	0.74 (0.43-1.18)	3	0.80 (0.16-2.37)	17	0.63 (0.36-1.02)	3	0.72 (0.14-2.17)	27	0.92 (0.60-1.37)
Lung	69	26.83* (20.86 33.99)	598	29.62 (27.27-32.11)	73	25.75* (20.09-32.50)	745	33.73 (31.31-36.28)	98	29.59* (23.90 36.22)	873	35.40 (33.03-37.91)

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Table 5. Age Standardized Cancer Mortality Rates (1980-2003) per 100,000 Females (cont'd 3)

Disease	89-93				94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Lymphoid	34	12.38* (8.55-17.34)	202	9.44 (8.17-10.86)	26	7.86 (5.06 11.67)	214	8.98 (7.79-10.29)	30	7.68* (5.11 11.09)	244	8.99 (7.85-10.25)
Nasal cavity	0		4	0.20 (0.05-0.51)	0		3	0.14 (0.03-0.41)	0		1	0.07 (0.001-0.39)
Nasopharynx	0		4	0.19 (0.05-0.49)	0		2	0.09 (0.01-0.33)	0		2	0.06 (0.01-0.24)
Soft tissue	3	1.05 (0.21 3.07)	22	1.07 (0.67-1.62)	7	2.21* (0.86 4.66)	19	0.89 (0.53-1.40)	2	0.85 (0.16 2.57)	13	0.60 (0.31-1.05)

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Table 6. Age Standardized Cancer Mortality Rates (1980-2003) per 100,000 Males

Disease	80-83				84-88			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
All causes	289	225.64* (199.71-254.01)	2666	241.51 (232.31-250.98)	460	248.31* (225.83-272.41)	3822	258.05 (249.85-266.44)
Bone	0	0	9	0.65 (0.29-1.25)	0	0	11	0.70 (0.35-1.27)
Brain	6	4.77 (1.70-10.57)	53	5.48 (4.21-7.00)	13	6.35 (3.38-10.87)	86	5.41 (4.32-6.69)
Prostate	35	30.54 (21.06-42.83)	290	28.41 (25.20-31.91)	33	20.23* (13.86-28.53)	365	26.65 (23.95-29.57)
Larynx	2	1.40* (0.16-5.14)	35	3.03 (2.10-4.23)	5	2.31 (0.75-5.39)	37	2.39 (1.68-3.30)
Leukemia	1	0.66 (0.02-3.70)	12	1.18 (0.61-2.07)	3	1.53 (0.31-4.47)	18	1.23 (0.72-1.95)
Lung	81	62.37* (49.23-77.93)	846	74.10 (69.12-79.30)	158	82.99* (70.44-97.14)	1365	89.58 (84.86-94.49)
Lymphoid	19	13.93 (8.23-22.07)	134	11.93 (9.97-14.16)	22	11.83 (7.33-18.06)	197	13.26 (11.45-15.26)
Nasal cavity	0	0	1	0.091 (0.002-0.51)	0	0	1	0.06 (0.001-0.34)
Nasopharynx	1	0.81 (0.02-4.49)	5	0.46 (0.15-1.07)	2	0.83* (0.10-3.05)	5	0.30 (0.10-0.70)
Soft Tissue	0		15	1.22 (0.67-2.03)	2	0.99 (0.12-3.61)	12	0.73 (0.37-1.28)
Testicular	0		6	0.47 (0.17-1.03)	1	0.48 (0.01-2.67)	3	0.17 (0.04-0.52)

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Table 6. Age Standardized Cancer Mortality Rates (1989-2003) per 100,000 Males (cont'd 2)

Disease	89-93				94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
All causes	474	224.67* (204.78-245.97)	4182	256.36 (248.62-264.27)	518	224.17* (205.22-244.39)	4546	258.26 (250.78-265.90)	551	210.74* (193.40-229.22)	4606	232.08 (225.39-238.92)
Bone	0	0	11	0.64 (0.32-1.14)	2	0.81 (0.10-2.94)	16	0.86 (0.49-1.39)	1	0.38 (0.01-2.09)	3	0.18 (0.04-0.52)
Brain	13	5.75 (3.04-9.86)	95	5.61 (4.53-6.86)	12	4.95 (2.54-8.68)	103	5.68 (4.63-6.89)	13	4.82 (2.55-8.27)	91	4.53 (3.64-5.58)
Prostate	53	26.97* (20.17-35.33)	467	30.04 (27.37-32.91)	50	22.25* (16.51-29.34)	535	31.34 (28.74-34.12)	54	21.46* (16.11-28.02)	554	27.90 (25.62-30.33)
Larynx	5	2.22 (0.72-5.19)	43	2.54 (1.84-3.42)	5	2.14* (0.69-5.00)	55	3.09 (2.32-4.02)	4	1.62* (0.44-4.16)	57	2.83 (2.14-3.67)
Leukemia	4	1.86 (0.51-4.77)	23	1.46 (0.92-2.19)	1	0.45* (0.01-2.52)	22	1.27 (0.79-1.92)	4	1.45 (0.39-3.72)	23	1.16 (0.73-1.74)

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Table 6. Age Standardized Cancer Mortality Rates (1980-2003) per 100,000 Males (cont'd 3)

Disease	89-93				94-98				99-03			
	Gagetown Area		New Brunswick		Gagetown Area		New Brunswick		Gagetown Area		New Brunswick	
	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)	N	Rate (95%CI)
Lung	141	66.35* (55.81-78.31)	1505	91.19 (86.64-95.94)	147	63.71* (53.80-74.92)	1610	91.28 (86.86-95.86)	185	70.83* (60.94-81.88)	1580	80.24 (76.31-84.32)
Lymphoid	27	12.66* (8.32-18.46)	251	15.16 (13.34-17.17)	38	16.23 (11.47-22.31)	273	15.31 (13.54-17.25)	32	12.00* (8.18-16.99)	295	14.94 (13.27-16.76)
Nasopharynx	1	0.45 (0.01-2.53)	4	0.23 (0.06-0.60)	1	0.44 (0.01-2.47)	5	0.28 (0.09-0.65)	0	0	6	0.29 (0.11-0.64)
Nasal cavity	0	0	3	0.19 (0.04-0.55)	0	0	2	0.11 (0.01-0.40)	0	0	1	0.05 (0.001-0.27)
Soft Tissue	5	2.05* (0.66-4.81)	18	1.03 (0.61-1.63)	0	0	13	0.74 (0.39-1.28)	5	1.85* (0.59-4.35)	23	1.17 (0.73-1.77)
Testicular	0	0	4	0.23 (0.06-0.60)	2	0.80* (0.09-2.89)	3	0.16 (0.03-0.48)	0	0	5	0.26 (0.08-0.61)

* point estimate for Gagetown Study Region is not contained within 95% confidence limits for the corresponding New Brunswick rate. While the two confidence limits overlap, the small numbers of cases for the Gagetown Study Region have created some statistical uncertainty.

Appendix 2 Technical Notes

1. Data protocol

A data protocol that explicitly laid out the mortality and cancer incidence data requirements, coding and formats this study was sent to the Province of New Brunswick, with a copy to the Public Health Agency of Canada, to aid in creating the needed data files to support this analysis. Population denominator format requirements were also sent at this time.

2. Case Data

Data files for each relevant disease and time period were created by the Province and sent to the team. There were some differences between what was requested by the team and what was sent to the team; these differences relate mainly to the manner in which the data were coded for disease diagnoses (ICD-O coding vs ICD9 coding) Files were extracted to facilitate the analysis of disease-time specific incidence and mortality rates. Diseases are detailed below. The time period for the cancer incidence data was 1984-2003. The entire time period for the mortality data was 1980-2003. Rates for each of the following five year intervals were calculated (1980-1983, 1984-1988, 1989-1993, 1994-1998, 1999-2003). Counts were aggregated over these five year intervals.

3. Cancer Incidence Coding of NB files

Cancer incidence data (1984-2003) were stratified based on SEER Cancer Description. This data was coded in ICD-O (International Classification of Diseases- Oncology) format. The diseases listed below were analyzed. The province of NB provided separate files for NB and the Gagetown target community. Data were further stratified into 1989-2003 as one file and 1984-1988 as a second file.

Disease	ICD-O Site Description	Notes
Bone	Bones and joints	
Brain	Brain	
Breast	Breast	
Hodgkins Disease	Hodgkins Disease	
Larynx	Larynx	
Acute lymphocytic leukemia	Acute lymphocytic leukemia	
Acute myeloid leukemia	Acute myeloid leukemia	
Chronic lymphocytic	Chronic lymphocytic	
Chronic myeloid	Chronic myeloid	
Lung	Lung and bronchus	
Multiple myeloma	Multiple myeloma	
Nasopharynx	Nasopharynx	
Non-Hodgkins	Non-Hodgkins lymphomas	
Other respiratory	Other respiratory	According to SEER coding manual, includes nasal cavity, trachea, inner ear, mediastinum.
Prostate	Prostate	
Soft Tissue sarcoma	Soft Tissue sarcoma (including heart)	
Testis	Testis	

4. Cancer mortality coding of NB files

Cancer mortality data were extracted using cancer description or ICD-9 and ICD-10 codes. The mortality data received on April 6, 2007 contained the following diseases (brain, breast, prostate, leukemia, lymph, lung). A file for Gagetown and a file for NB were received from the province of NB. These data were stratified by disease description.

Disease	**Description**
Brain	Cancer of the Brain (191) Cancer of the Brain (C71)
Breast	Malignant neoplasm – Breast (C50) Malignant Neoplasm – Female breast (174)
Prostate	Malignant Neoplasm – Prostate (185) Malignant Neoplasm – Prostate (C61)
Leukemia	Leukemias (204-208) Leukemias (C91.0-C91.3, C91.5-C91.9, C92, C93, C94.0-C94.3, C94.7, C95)
Lymph	Lymphoid Cancer (200-203) Lymphoid Cancer (C46.3, C81-85), C88.1-C88.9, C90, C91.4, C96)
Lung	Malignant Neoplasm – Trachea, bronchus and lung (162) Malignant Neoplasm – Trachea, bronchus, and lung (C33-C34)

Data received on May 4, 2007 included mortality for the other cancer cases of a priori interest (testicular, nasopharynx, larynx, bone, soft tissue sarcoma). This file also contained mortality data for all cancer cases for all of NB. It contained CSD place of residence data for each case. A separate file for the Gagetown region was created by extracting relevant cases using the CSD place of residence variable. Many of the diseases of interest were labeled as 'other neoplasms'. As such, it was not possible to extract cases by description. Disease-specific files were created using the ICD-9 and ICD-10 codes included in the file and extracting these from this main data set.

Disease	**ICD-9 Codes**	**ICD-10 Codes**
Testicular	1869	C629
Nasopharynx	1479	C119
Nasal Cavity	1600, 1602, 1603, 1609	None
Larynx	1610, 1611, 1613, 1618, 1619	C320, C321, C322, C329
Bone	1701, 1702, 1703, 1704, 1706, 1707, 1709	C400, C402, C414, C419
Soft tissue sarcoma	1710, 1712, 1713, 1714, 1715, 1716, 1718, 1719,	C490, C92, C493, C494, C495

5. Non-Cancer mortality coding of NB data

The selected mortality outcomes were initially identified using the disease description and ICD codes were verified using the WHO ICD manuals and confirmed for consistency, using the Institute of Medicine VAO report. The data received from New Brunswick contained separate files for NB and Gagetown. These files included data for Parkinson's Disease, congenital anomalies, certain conditions originating in the perinatal period, and other diseases of the nervous system and sense organs. Data for diabetes were sent to us as separate files at a later date (May 4). NB diabetes data was received in a file that only contained diabetes data (1980-2004). Gagetown diabetes data was received in a file that contained all causes of mortality. Gagetown diabetes data was extracted using site description (listed below). Based upon the numbers of records for perinatal mortality, congenital anomalies, and nervous system disorders, the decision was made not to proceed with analysis due to insufficient sample sizes.

Selected Mortality Coding

Disease Site Description	**ICD-9**	**ICD-10**	**Notes**
Certain conditions originating in the perinatal period (760-779)	7650 7651	None	Age <=1 **N=8** for Gagetown region (1980-2003), N=5 when age<1
Congenital anomalies (740-759)	7410 7419	Q059	Age restricted to <1: **N=5** for all of NB, **0** for Gagetown region (1980-2003)
Other disease of the nervous system and sense organs	3568	None	****N= 5** for all of New Brunswick, N=1 for Gagetown region (1980-2003)
Parkinson's Disease (332, G20, G21.1-G21.9, G22)	3320	G20	Analysis performed
Diabetes (250) Diabetes (E10-E14)	2501, 2502, 2503, 2504, 2506, 2509	E103, E105, E109, E110, E115, E117, E119, E149, E149	Analysis performed

6. All-Cause Cancer Incidence Data

The all-cause cancer incidence file contained solely the total number of annual counts for all causes by sex and age group for the periods relating to 1989-2003. The ICD coding was not provided. The provided table simply gave raw counts numbers that corresponded to year, age, and sex. Age groups were as follows (0,1,2,3,4,5-9,10-14,15-19,20-24….95-99, 100+years). These age groups were collapsed to match the age group structure chosen for the analysis (<1, 1-4, 5-9, 10-20, 20-30… 80+). When the file was in the appropriate format, it was imported into SAS and the age-adjusted rate macro was used to generate the all cause rates for each five year time period (89-93, 94-96, 99-03).

The data for 1984-1988 were provided in a file that listed all neoplasms for this time period (n=13874). This file contained SEER cancer description, morphology code, place of residence code, age, and gender. After formatting age into the appropriate age groups, the macro was used to generate the age-adjusted rate for this time period.

7. All Cause Cancer Mortality Data

The mortality file received contained all cases of cancer mortality for the time period 1980-2003. This file was the same file used to generate the mortality rates for the selected diseases of interest. The macro was used to generate the all-cause cancer mortality rates.

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In cases where there were cases with inappropriate gender coding, the records were not included in the analysis. (For example, a prostate or testicular cancer cases coded as female)

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8. Population Data

- Statistics Canada age and sex-specific census year population data were received for census years from 1981-2001 (1981, 1986, 1991, 1996, 2001). Aggregated data were provided at the level of census subdivision and in following five year age groups (<1, 1-4, 5-9, 10-14, 15-19, …80-84, 85-89). 2001 population data included the age group 90+. The oldest age group in files from previous year was 'ages 85+ years'.

- The total population for Gagetown region was calculated by aggregating the population of 35 CSDs that were identified as being part of the target community. Total numbers within each of the age categories for each census subdivision were randomized to within +/- 5 units. This has the potential to create bias. A custom run of the Statistics Canada census data would have allowed for a more accurate estimate of the total population within the region but may have not been necessary. Because the diseases of interest are chronic and rare occurrences, some variation in the size of the denominators would not likely significantly influence the resulting point estimates and 95% confidence intervals.

- Age groups were collapsed to match the population structure of the analysis (<1. 1-4. 5-9. 10-20, … 80+).

9. 1991 Standard Population Data

The weights pertaining to the 1991 standard population were obtained from the glossary of the Canadian Cancer Society Annual report (http://www.cancer.ca). The weights were collapsed into age groups to match the case and population data. Weights used for males and females were the same and are presented in the table below:

Sex	Agegroup	Weight
1	0	1428.7
1	1	5517.7
1	2	6945.4
1	3	13652.9
1	4	16496
1	5	17578.8
1	6	13559.9
1	7	9169
1	8	8089.6
1	9	5178.6
1	10	2383.2
2	0	1428.7
2	1	5517.7
2	2	6945.4
2	3	13652.9
2	4	16496
2	5	17578.8
2	6	13559.9
2	7	9169
2	8	8089.6
2	9	5178.6
2	10	2383.2

10. Other Data Issues

Questions that arose during the course of completing these analyses are as follows. For the most part, Dr. Balram and Wilfred Pilgrim were highly responsive in assisting with clarification of these issues as they arose.

- The raw data files sent from the Province of New Brunswick were not categorized according to the initially requested age groups. This was dealt with as part of data preparation prior to analysis.

- Cancer incidence data were provided in excel spreadsheets. Data for the time periods 1984-1988 and 1989-2003 were provided in two separate spreadsheets. The raw 89-03 data did not contain data for the category ‘all malignant neoplasms’ (ICD 9 140-209). When this data was requested, it was promptly received. The ‘all neoplasm’ data received for NB were not stratified into the age

groups <1 and 1-4 as requested (the agegroup 0-4 was given). A request for data in the requested agegroups was met.

- The 1984-88 cancer incidence excel spreadsheet contained a worksheet for Gagetown and a worksheet for NB. The ICD coding in these two worksheets were different. This became evident when it was observed that there were 3 cases of chronic lymphocytic leukemia in Gagetown but none in NB. As the Gagetown data is a subset of the NB data, this finding highlighted an issue with the data. Inquiry regarding this matter was made and a Gagetown file with coding consistent with the NB file was promptly received.

- Cancer mortality data for all the requested diagnosis were not initially provided (cancer of the larynx, nasal cavity, nasopharynx, soft tissue sarcoma, testicular, bone, and 'all malignant neoplasms'). The data for these diagnoses were provided upon request and were labeled as containing data for the years 1980-2003 but only contained data for 1986-2003. Data for the time period 1980-1986 was requested and received promptly. The provided data contained ICD codes in several different formats (1869, 1869.00, 186.9). As such it was a challenge to ensure that all cases were included in the extracted file.

- Mortality data for diabetes were not included as part of the initial data files. The data for NB and Gagetown were received subsequently upon request.

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