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

To:

Dr. Howard Morrison
Project Authority
Centre for Chronic Disease Prevention and Control
Public Health Agency of Canada
120 Colonnade Road
Ottawa ON K1A 1B4

Submitted by:

Dr. Judith Guernsey
Associate Professor
Department of Community Health and Epidemiology
Dalhousie University
5790 University Avenue, room 406
Halifax NS B3H 1V7

(902) 494-1767 (ph)
(902) 494-1597 (fax)
Judy.Guernsey@Dal.Ca (email)

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Executive Summary

1. The purpose of this descriptive epidemiologic study was to determine whether there is evidence of increased chronic disease risk, particularly cancers, in residents of a region comprising CFB Gagetown and surrounding areas, that was identified by the community as being exposed to herbicides and herbicide-related contaminants used at CFB Gagetown from 1952 to 2004 (heretofore called the Gagetown Study Region, or GSR), compared to the risk for chronic disease in all residents of the Province of New Brunswick.

2. 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.

3. Five year average age- standardized mortality and cancer incidence 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 ratios (SIR) and standardized mortality ratios (SMR) and 95% confidence intervals were computed in order to present a composite picture of the comparative health experience of Gagetown Study Region residents versus the Province of New Brunswick residents during corresponding time periods. 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.

4. 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. 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. Breast cancer incidence was slightly but statistically significantly elevated for all four time periods for women. Because there was no information about the multiple risk factors for breast cancer, including environmental exposures, obesity and smoking, that may explain this finding, it was not possible to draw conclusions about what might be possible explanations for this result, or whether indeed this was clinically significant.

5. Nasopharyngeal cancer for female GSR residents compared to female Province of New Brunswick residents was observed to be significantly elevated in 1999-2003 and suggestively elevated in 1984-1988. This is a very rare form of cancer and subject to considerable statistical uncertainty. No Gagetown cases were observed for the other two time intervals. For the entire 20 year interval, the standardized incidence ratio was mildly elevated at 1.4 but this finding was not statistically significant. These data were also based on very few cases (total = 4). There were no nasopharyngeal cancer deaths in GSR women during the study period which prevented calculation of mortality rates for this outcome. Nasal sinus cancer incidence or mortality risk did not appear to be elevated in GSR women compared to New Brunswick women.

6. Nasopharyngeal cancer incidence appeared elevated for GSR men compared to New Brunswick men during 1984-1988 (SIR= 2.07) though the 95% confidence interval was large and was not statistically significant. Standardized incidence ratios were lower for other time periods and were not statistically significant. Statistically elevated SMRs for nasopharyngeal cancer mortality in GSR males were observed for 1984-1988, and the point estimates for nasopharyngeal cancer SMRs were of similar magnitude (SMR= 1.76, 1.96, 1.57; not statistically significant) during 1980-1984, 1989-1993 and 1994-1998 but not for the most recent time interval when there were no deaths from this cancer in men. These ratios are all based upon sparse data; there were only 3 nasopharyngeal cancer deaths observed in GSR for the 25 year span.

7. Development of individual exposure profiles to the CFB Gagetown experimental sprays was not possible due to lack of accessible, systematic information that would be required to perform this analysis. Differentiation between health effects resulting from the experimental herbicides and

others sprayed in routine applications at the base was also not possible due to the current lack of this information. 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 without complete exposure histories of those employed or otherwise exposed at the base.

8. This is an exploratory study that may lead to future research; feasibility of further work would depend upon the extent of documentation related to the identity of those exposed and the nature of those individuals' exposures. Possible studies might include a record-linkage cohort study of the health experience of CFB Gagetown personnel who worked as mixers, loaders, applicators or flaggers during the applications and CFB Gagetown civilian and military personnel who worked in post-herbicide-application brush cleaning operations. Prior to proceeding with such work, study design features, including an assessment of whether sufficient numbers of cases were likely to occur to support such an analysis. Other concerns would be loss of the ability to follow up cases due to fact that perhaps many of the most vulnerable subjects may no longer be living and the lack of adequate information about past personal exposures.

9. 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 factors that are contributory to the development and prognosis of an individual's disease.

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Introduction

The purpose of this descriptive epidemiologic study was to determine whether there is evidence of increased chronic disease risk, particularly cancers, in residents of a region comprising CFB Gagetown and surrounding areas, that was identified by the community as being exposed to herbicides and herbicide-related contaminants used at CFB Gagetown from 1952 to the present (heretofore called the Gagetown Study Region, or GSR), compared to the risk for chronic disease in all residents of the Province of New Brunswick. This is an exploratory study that may lead to future research; feasibility of further work would depend upon the extent of documentation related to the identity of those exposed and the nature of those individuals' exposures.

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.

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 exposure to the varying combination of the herbicides that were sprayed there over time. The study area is also quite large. The size accounts for the increased likelihood that those who came into contact with the CFB Gagetown environment at some point in their lives were likely to have settled in the general proximity of the Base, including Fredericton, but not necessarily on the Base, if they chose to remain in New Brunswick. There are some challenges and potential for bias with these study design assumptions, however. As people moved into and out of the region during the period of chronic disease latency (after exposure but before the disease actually appears), they are either attributed (falsely) as being an exposure-related case (for in-migrants) or as being loss to follow-up (exposure-related cases are not counted) for out-migrants. While these migration factors creates a potential for statistical bias, such descriptive studies provide preliminary information whether higher rates of disease experienced by

the community at risk, if demonstrated, might be attributable to the special features of exposures that the community might have experienced over time.

As documented in previous CFB Gagetown reports, there were significant differences in the types, quantities and toxicity of herbicide agents that were applied at the base at different time periods. In particular, Agent Orange and the other experimental sprays were limited to 1966 and 1967 and then later in 1990. To explore these temporal exposure variations, the data were stratified by gender into five year intervals. Some of the more toxic herbicides, used during these years, would likely have had their effects in earlier years but perhaps not in more recent times. Another study assumption is that there is a ten to fifteen year or more latency of disease onset resulting from the delayed or cumulative effects of late 1960's experimental spray exposure window. It is possible that some of the chronic effects that occurred in earlier years were missed by this analysis. Hence, stratifying the data into five year intervals allows one to explore these hypotheses in a preliminary way. Summary estimates for each disease for the entire study period were not calculated because they were seen as not meaningful due to this considerable variation in the herbicide exposures.

Five year average age- standardized incidence and mortality rates and 95% confidence intervals were calculated (via the direct method of standardization) for the selected diseases for both males and females for the GSR and for the Province of New Brunswick. These data also provide the number of disease and mortality occurrences for the GSR and the province by gender and time interval. 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 disease data for the earlier periods but this proved not to be possible within the time span that was available to complete this study.

Information regarding individual exposure profiles to the experimental sprays, risk factors and subsequent individual risk for disease in this study was not available. Differentiation between health effects resulting from the experimental herbicides and other herbicides sprayed in routine applications at the base or from any pesticides used by GSR residents at work or at home was not possible without an intensive survey of GSR residents. 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 determinants also was not possible in this study. Such analyses would have required an intensive epidemiological study involving extensive follow-up, interviews and possibly collection of biological samples, which would have taken years. Recommendations are made in the discussion section of the report with regards to future research involving more detailed analyses.

Finally, 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.

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, 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 in relation to residence within the Gagetown Study Region, 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 of concern was comprised of those residents who may have come into contact with the list of herbicides identified by DND that were purportedly used at CFB Gagetown from 1952 to 2003 through the direct mixing, loading or application of herbicides, through direct exposure to agents via inhalation, ingestion or dermal exposure on the Base or through indirect environmental exposure via food, water or dermal contact with clothing of spouses. This target population was translated to comprise 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 two sources of information:

1) a 2005 map provided by the Department of National Defence that identified the CFB Gagetown range and training area;

2) the Task 2A report that lists agents, dates and locations of herbicide applications, as identified for this study by DND.

The list of GSR census subdivisions and draft map was sent to the DND Gagetown Study Community Advisory Committee and they confirmed the list and expanded it to include other southern New Brunswick CSDs. The rationale for this decision was that they believed residents suspected to be at higher risk for exposure to the GSR herbicides lived in these areas. The GSR 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 by aggregating the GSR census subdivisions and calculating an overall rate for the region. It was not possible to calculate rates for smaller communities due to the lack of more precise geographic resolution of case records available from the New Brunswick Cancer Registry and from the Canadian Mortality Database. Census

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

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.

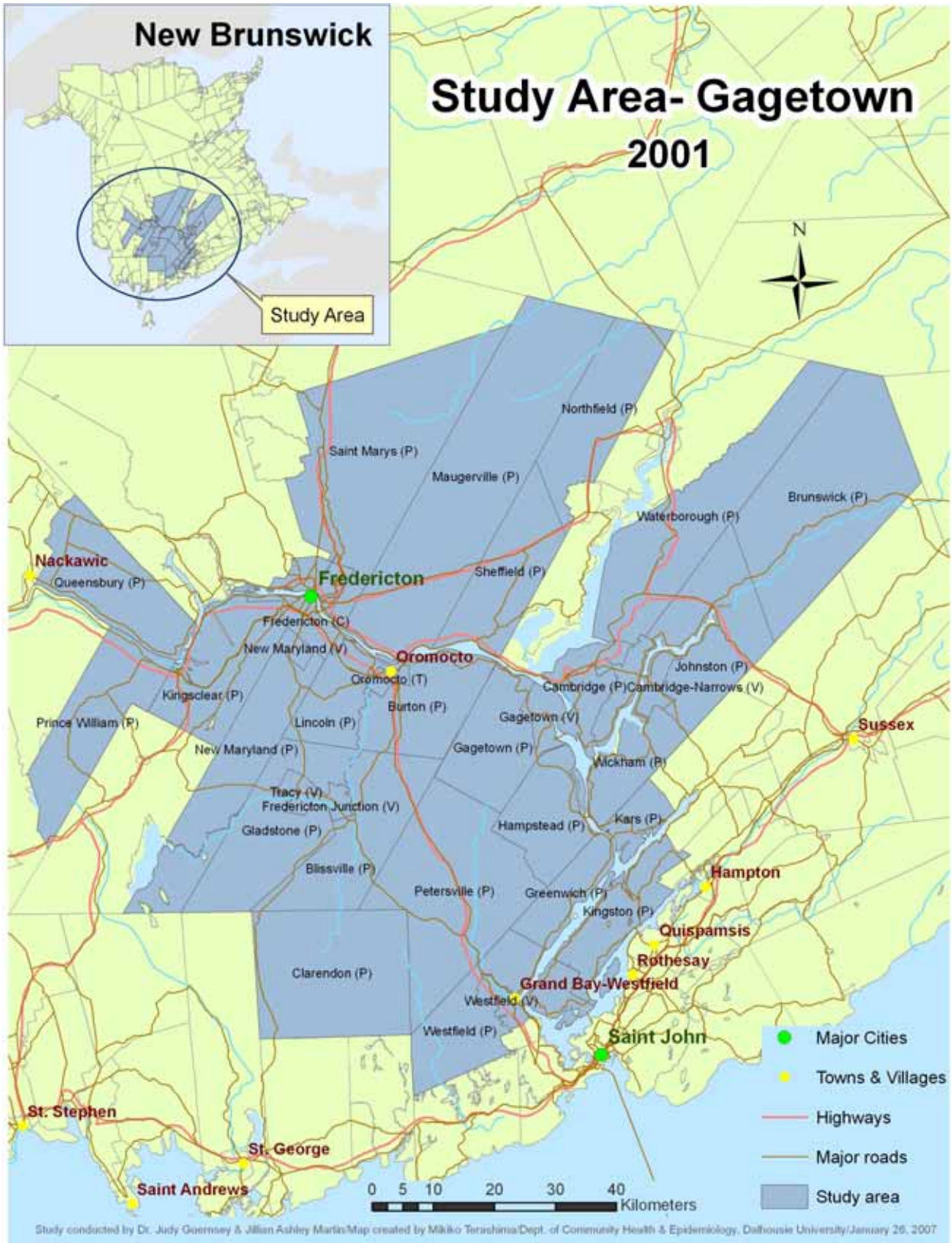
Reference Population

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 data are regularly reported to the Public Health Agency of Canada who then publicly releases this information on their website. 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. New Brunswick residents were seen as meeting these criteria.

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


New Brunswick
Study Area
Study Area- Gagetown
2001
N
Northfield (P)
Saint Marys (P)
Maugerville (P)
Brunswick (P)
Waterborough (P)
Nackawic
Queensbury (P)
Fredericton
Sheffield (P)
Fredericton (C)
New Maryland (V)
Oromocto
Oromocto (T)
Johnston (P)
Cambridge (P)
Cambridge-Narrows (V)
Kingsclear (P)
Burton (P)
Prince William (P)
Lincoln (P)
Gagetown (V)
Sussex
New Maryland (P)
Gagetown (P)
Wickham (P)
Tracy (V)
Fredericton Junction (V)
Gladstone (P)
Hampstead (P)
Kars (P)
Blissville (P)
Hampton
Petersville (P)
Greenwich (P)
Kingston (P)
Quispamsis
Rothesay
Clarendon (P)
Grand Bay-Westfield
Westfield (V)
Westfield (P)
Saint John
Major Cities
Towns & Villages
Highways
Major roads
Study area
St. Stephen
St. George
Saint Andrews
0 5 10 20 30 40
Kilometers
Study conducted by Dr. Judy Guernsey & Jillian Ashley Martin/Map created by Mikiko Terashima/Dept. of Community Health & Epidemiology, Dalhousie University/January 26, 2007

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 residual herbicides that have bioaccumulated in the parents' bodies may have also occurred but such an analysis would have required serum samples and longitudinal data on all parental exposures in the region. These data were simply not available. Other reasons for not including birth outcomes include insufficient numbers to support a meaningful analysis.

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, yet the genesis of the disease may relate back to a past exposure. Hence, mortality data reflect both disease risk and likelihood of survival. 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 but not the external causes that caused the cancer or other disease. 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.

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 in the early 1900'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)			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 Disease	201 Hodgkin 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	NB Cancer Registry (incident cases); Statistics Canada (deaths)	Suf	Suf	include
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

Inad= Inadequate or insufficient evidence

Lim= Limited or suggestive evidence of an association

Suf = Sufficient evidence of a positive association

Sug No = Suggestive evidence of no association

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. Non Hodgkin's Lymphoma, Hodgkin's Disease, Multiple Myeloma and Leukemia were grouped together as 'Lymphoid Cancers' in the file returned to us by the Province of New Brunswick containing mortality counts.

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 prevented exploration of these effects.

Cancer incidence data were not available from the New Brunswick Cancer registry 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 were provided for the years 1984-2003 and were coded by the ICD-O classification system. Mortality data were provided for the years 1980-2003 and were coded by the ICD-9 classification system and included deaths from cancers, and other selected chronic diseases. Detailed data formats and instructions were provided to the Province of New Brunswick to facilitate data coding and transfer.

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 Rate: $A = \sum [I_{Ai} \times W_i] / \sum W_i$

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.

Variance = $\sum W_i^2$ (cases/population^2) / $[\sum (W_i)]^2$
where Wi = the age specific weights

Lower confidence limit = $\acute{\Gamma}^{-1} (x^2/v, 1) (\alpha /2)$
Where $\acute{\Gamma}^{-1}$ is the inverse of the gamma distribution, x is the age standardized rate, v is the variance and α = level of significance.

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

Where $\acute{\Gamma}^{-1}$ 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.

Standardized Incidence and Mortality Ratios

Standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs), and corresponding 95% confidence intervals, were then calculated 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. The significance of this value 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. Also, 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. Rates were determined to be statistically significantly different if the associated 95% confidence intervals did not include the null value (no effect) of 1.0. While a ratio may be statistically elevated, a ratio may not be regarded to be clinically significant until it attains a value of 1.5 or greater, due in part to the small numbers of cases or other uncertainty considerations.

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):

Population Attributable Risk (PAR) % $= [(IR_P - IR_{UE}) / IR_P] \times 100.$

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-level 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.

Consideration for testing for statistical associations when examining multiple outcomes

Because multiple rates were calculated for a range of health outcomes, it is possible that statistical significance was observed for some of the findings purely by chance alone.

Results

Cancer Incidence

Tables 5 and 6 present five year average standardized incidence ratios and 95% confidence intervals associated with various cancers for females and males respectively. These ratios were calculated from data provided in the tables 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.

Tables 7 and 8 present five year average standardized mortality ratios, 95% confidence intervals and counts 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.

<u>All causes of cancer: incidence and mortality</u>

Gagetown Study Region male residents experienced slightly elevated risks for all cause cancer incidence during 1984-1988 but then this trend reversed with a consistent pattern of slightly reduced incident risk of all cause cancer for the other three periods. Similarly, all-cause cancer mortality was consistently lower (borderline during the first two time periods) in GSR males across the five time intervals compared to New Brunswick males. Conversely, Gagetown Study Region female residents were at slightly but significantly increased risk for diagnosis of any cancer compared to New Brunswick females during 1989-1993 and 1999-2003 and at borderline increased risk during the other two time periods. The increased risk for all cause cancer incidence in GSR females did not transfer to an increased risk for all cause cancer mortality for GSR women; across all five time intervals the risk for cancer mortality was virtually the same for both GSR women and New Brunswick women.

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

Disease	1984-1988		1989-1993		1994-1998		1999-2003	
	n	**SIR**	**n**	**SIR**	**n**	**SIR**	**n**	**SIR**
All cancer causes	796	1.02 0.97-1.07*	948	**1.09** **1.05-1.13**	1005	1.03 0.99-1.07*	1168	**1.06** **1.03-1.10**
Bone	3	**3.21** **1.5-4.77**	1	0.75 0.04-2.29	3	**3.41** **1.38-4.61**	2	0.78 0.16-1.72
Brain	18	1.30 0.94-1.70*	23	**1.50** **1.15-1.88**	11	0.73 0.44-1.09*	17	1.08 0.76-1.43
Breast	219	**1.10** **1.01-1.19**	272	1.08 0.99-1.16*	324	**1.09** **1.01-1.16**	351	1.06 0.99-1.13*
Hodgkin's Disease	6	1.12 0.57-1.80	7	1.01 0.55-1.56	4	0.92 0.36-1.67	8	1.11 0.65-1.65
Larynx	0	--	6	**1.93** **1.10-2.81**	4	0.72 0.28-1.36	2	0.50 0.09-1.29
Lung	70	1.10 0.93-1.27	83	**0.85** **0.73-0.98**	91	**0.76** **0.65-0.87**	135	0.90 0.80-1.00*
Acute lymphocytic leukemia	6	**2.62** **1.64-3.54**	3	1.07 0.36-2.02	1	0.43 0.01-1.49	3	1.0 0.32-1.91
Acute myeloid leukemia	6	1.25 0.65-1.99	1	0.3 0.01-1.17	8	1.22 0.70-1.82	10	1.71 0.45-2.33
Chronic lymphocytic leukemia	0	--	3	0.56 0.16-1.22	4	0.62 0.22-1.23	6	0.67 0.31-1.15
Chronic myeloid leukemia	3	1.65 0.63-2.88	4	1.80 0.83-2.91	4	1.12 0.45-1.98	3	0.86 0.03-1.68
Multiple myeloma	7	0.73 0.73-1.20	16	**1.55** **1.11-2.02**	9	0.79 0.23-0.64	13	0.88 0.57-1.24
Nasopharynx	2	2.49 0.79-4.04	0	--	0	--	2	**2.85** **1.00-4.67**
Non Hodgkin's lymphoma	29	0.96 0.73-1.21	33	1.00 0.78-1.24	39	0.84 0.66-1.04*	42	0.93 0.66-1.04*
Other respiratory (including nasal cavity)	3	1.37 0.48-7.11	3	1.70 0.66-2.90	1	0.53 0.02-1.73	2	1.25 0.30-2.54
Soft tissue sarcoma	4	1.09 0.45-1.93	6	1.00 0.50-1.63	7	1.06 0.57-1.66	8	1.13 0.65-1.67

[1] n = number of Gagetown Study Region cases; * borderline but not statistically significant difference. -- = insufficient numbers to calculate ratio

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

Disease	1984-1988		1989-1993		1994-1998		1999-2003	
	n[1]	SIR	n[1]	SIR	n[1]	SIR	n[1]	SIR
All cancer causes	990	**1.04** **1.00-1.09**	999	**0.94** **0.90-0.98**	1112	**0.96** **0.91-0.98**	1228	0.99 0.96-1.03*
Bone	1	0.36 0.01-1.30	1	0.43 0.02-1.51	2	0.95 0.21-2.05	2	0.58 0.11-1.43
Brain	16	0.92 0.62-1.27	18	1.02 0.73-1.36	18	0.86 0.60-1.17	21	0.92 0.67-1.20
Hodgkin's Disease	3	**0.36** **0.09-0.81**	8	1.03 0.59-1.57	9	1.51 0.96-2.11*	6	0.82 0.40-1.35
Larynx	13	0.72 0.45-1.05	22	1.09 0.81-1.42	16	0.80 0.54-1.10	22	**1.49** **1.11-1.90**
Acute lymphocytic leukemia	5	1.28 0.61-2.09	3	0.76 0.23-1.56	3	0.81 0.25-1.65	5	1.38 0.71-2.16
Acute myeloid leukemia	9	**1.92** **1.23-2.69**	4	0.92 0.36-1.70	5	0.63 0.27-1.14	9	1.31 0.81-1.90
Chronic lymphocytic leukemia	0	--	5	0.62 0.26-1.13	1	**0.07** **0.003-0.32**	10	0.93 0.56-1.38
Chronic myeloid leukemia	5	1.80 0.95-2.74*	1	0.32 0.01-1.19	3	0.89 0.27-1.76	6	1.00 0.50-1.65
Lung	262	0.94 0.85-1.03	145	**0.64** **0.57-0.72**	186	0.79 0.71-0.87	219	**0.87** **0.80-0.95**
Multiple myeloma	12	0.93 0.58-1.35	12	0.98 0.63-1.40	18	1.26 0.91-1.65*	17	1.06 0.74-1.42
Nasopharynx	2	2.07 0.59-3.73	1	0.63 0.03-2.04	2	0.96 0.20-2.15	0	--
Non-Hodgkins Lymphoma	34	0.95 0.74-1.18	35	0.94 0.74-1.16	46	0.91 0.74-1.10	45	**0.81** **0.65-0.98**
Other respiratory (including nasal cavity)	6	**2.18** **1.31-3.04**	1	0.28 0.01-1.05	0	--	3	1.22 0.41-2.28
Prostate	176	**1.13** **1.02-1.24**	264	0.98 0.91-1.06	283	**0.85** **0.78-0.92**	319	0.96 0.89-1.03
Soft tissue sarcoma	7	1.03 0.55-1.62	5	1.09 0.52-1.81	6	0.94 0.47-1.55	5	0.65 0.28-1.17
Testicular	9	1.23 0.73-1.82	10	1.13 0.71-1.62	9	1.02 0.61-1.50	13	1.06 0.71-1.45

[1] n = number of Gagetown Study Region cases; * borderline but not statistically significant difference. -- = insufficient numbers to calculate ratio

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	
	n[1]	SMR	n[1]	SMR	n[1]	SMR	n[1]	SMR	n[1]	SMR
All cancer causes	233	0.99 0.91-1.08	335	0.97 0.90-1.04	421	1.00 0.94-1.06	471	1.00 0.94-1.06	488	0.99 0.93-1.05
Bone	1	0.89 0.03-2.68	1	1.02 0.05-2.91	0	1.41 0.14-3.37	1	1.86 0.17-4.13	0	--
Brain	6	0.93 0.45-1.54	8	0.93 0.52-1.45	9	1.06 0.62-1.58	12	1.12 0.72-1.58	9	0.85 0.49-1.30
Breast	44	0.93 0.75-1.13	60	**0.83** **0.69-0.98**	81	0.99 0.85-1.14	93	1.01 0.88-1.16	92	**1.16** **1.01-1.32**
Larynx	0	--	0	--	0	--	1	0.65 0.04-2.04	0	--
Leukemia	1	1.05 0.07-3.06	1	0.80 0.04-2.45	1	0.5 0.02-1.74	3	1.27 0.44-2.32	3	0.78 0.23-1.58
Lung	37	**1.35** **1.09-1.64**	46	0.94 0.76-1.13	69	0.91 0.76-1.06	73	**0.76** **0.64-0.90**	98	**0.84** **0.72-0.96**
Lymphoid	17	**1.43** **1.02-1.89**	21	1.25 0.92-1.62	34	**1.31** **1.05-1.60**	26	0.88 0.65-1.13	30	0.85 0.65-1.08
Nasal cavity	1	1.81 0.11-3.92	1	2.69 0.33-5.17	0	--	0	--	0	--
Nasopharynx	0	--	0	--	0	--	0	--	0	--
Soft tissue sarcoma	2	1.58 0.40-11.38	0	--	3	0.98 0.03-1.90	7	**2.48** **1.62-3.33**	2	1.42 0.52-2.45
Type 2 Diabetes	17	**0.64** **0.43-0.91**	36	0.83 0.65-1.19	43	0.92 0.74-1.13	62	1.24 0.92-1.29	76	**1.10** **1.06-1.42**
Parkinson's Disease	0	--	3	0.66 0.19-1.41	8	1.28 0.75-1.92	13	1.32 0.91-1.78	4	**0.45** **0.15-0.93**

[1] n = number of Gagetown Study Region deaths

* borderline but not statistically significant difference

-- = insufficient numbers to calculate ratio

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	
	n[1]	SMR	n[1]	SMR	n[1]	SMR	n[1]	SMR	n[1]	SMR
All cancer causes	289	0.93 0.86-1.01*	460	0.96 0.90-1.02*	474	**0.88** **0.82-0.93**	518	**0.87** **0.82-0.92**	551	**0.91** **0.86-0.96**
Bone	0	--	0	--	0	--	2	0.94 0.20-2.12	1	2.11 0.25-4.02
Brain	6	0.87 0.40-1.51	13	1.17 0.78-1.62	13	1.02 0.67-1.44	12	0.87 0.55-1.26	13	1.06 0.70-1.48
Prostate	35	1.07 0.84-1.34	33	**0.76** **0.58-0.96**	53	0.90 0.74-1.07	50	**0.71** **0.57-0.86**	54	**0.77** **0.63-0.92**
Larynx	2	0.46 0.08-1.22	5	0.97 0.45-1.63	5	0.87 0.39-1.52	5	0.69 0.30-1.24	4	0.57 0.21-1.13
Leukemia	1	0.56 0.005-1.79	3	1.24 0.43-2.29	4	1.27 0.55-2.17	1	0.35 0.01-1.31	4	1.25 0.53-2.14
Lung	81	**0.84** **0.71-0.98**	158	0.93 0.83-1.03	141	**0.73** **0.64-0.82**	147	**0.70** **0.62-0.78**	185	**0.88** **0.80-0.97**
Lymphoid	19	1.17 0.83-1.56	22	0.89 0.64-1.18	27	0.84 0.62-1.08	38	1.06 0.85-1.29	32	0.80 0.62-1.01*
Nasal cavity	0	--	0	--	0	--	0	--	0	--
Nasopharynx	1	1.76 0.13-4.20	2	**2.77** **1.0-4.36**	1	1.96 0.17-4.22	1	1.57 0.11-3.80	0	--
Soft tissue sarcoma	0	--	2	1.36 0.32-2.82	5	**1.99** **1.08-2.95**	0	--	5	1.58 0.81-2.46
Testicular	0	--	1	2.82 0.25-5.13	0	--	2	**5.0** **3.0-6.02**	0	--
Diabetes	24	**1.37** **1.01-1.77**	25	0.85 0.62-1.11	47	**1.25** **1.03-1.48**	53	0.96 0.79-1.14	76	1.07 0.92-1.23
Parkinson's Disease	1	0.47 0.02-1.77	4	0.80 0.29-1.54	12	**1.86** **1.28-2.48**	12	1.15 0.75-1.62	8	0.70 0.38-1.12

[1] n = number of Gagetown Study Region deaths

* borderline but not statistically significant difference

-- = insufficient numbers to calculate ratio

Nasopharyngeal and nasal cancer incidence and mortality

Results for nasopharyngeal cancer for female GSR residents were variable, likely due to small numbers. The standardized incidence ratio was observed to be elevated compared to female Province of New Brunswick residents during two of the four study periods (1984-1988 and 1999-2003). These findings are reflected in the elevated SIR values, albeit borderline for 1984-1988, when there were sufficient data to calculate an SIR. These data are based on very few cases (total = 4) and there were no cases observed for the other two time intervals, resulting in an overall nonstatistically significant SIR of 1.38 (95% CI: 0.61-2.37) for women for the twenty year span. There were no nasopharyngeal cancer deaths in GSR women during the study period which prevented calculation of mortality rates for this outcome.

Nasopharyngeal cancer incidence appeared elevated for GSR men compared to New Brunswick men during 1984-1988 (SIR= 2.07) but the 95% confidence interval indicated that this finding was not statistically significant. Standardized incidence ratios were lower for other time periods yet were not statistically significant. The overall standardized incidence ratio for men was 0.76 (95% CI: 0.34-1.37) suggesting a slightly reduced risk but this was not statistically significant. Statistically elevated SMRs for nasopharyngeal cancer mortality in GSR males were observed for the time period of 1984-1988, and the point estimates for nasopharyngeal cancer SMRs were of similar magnitude (SMR= 1.76, 1.96, 1.57; not statistically significant) during the earlier three study periods (1980-1984, 1989-1993 and 1994-1998) but not for the most recent time interval when there were no deaths from this cancer in men. These ratios are all based upon sparse data; there were only 5 nasopharyngeal cancer deaths observed in GSR for the 24 year span. The overall nasopharyngeal cancer standardized mortality ratio for males was 1.53 (95% CI: 0.78-2.45) but was not statistically significant.

Nasal sinus cancer incidence or mortality did not appear to be elevated in GSR women compared to New Brunswick women. There were no deaths at all from nasal cavity cancer in GSR men during the twenty year study period.

Soft Tissue Sarcoma

Soft tissue sarcoma incidence rates were not observed to be elevated in GSR females or males for the entire time period. Soft tissue sarcoma mortality rates were significantly elevated for both GSR males and GSR females compared to the province as a whole during 1989-1993 (SMR=1.99) for males and during 1994-1998 (SMR=2.48) for females. It is noteworthy 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.

Breast Cancer

Breast cancer age-standardized incidence rates were slightly higher for GSR women throughout the study period compared to the Province of New Brunswick, with SIR values ranging from 1.06 (1999-2003) to 1.10 (1984-1988) . Interestingly, this slight increase in risk did not transfer to increased breast cancer mortality for GSR women except during 1999-2003. Breast cancer mortality rates for the GSR region were either lower or on par with the rest of the Province for the other time intervals.

Prostate Cancer

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 slightly higher than for New Brunswick as a whole (SIR=1.13). Similarly, prostate cancer mortality was significantly lower in 1984-1988, 1994-1998, and 1999-2003 in GSR males than for the province as a whole.

Testicular Cancer

Standardized incidence rates for testicular cancer for GSR males were not significantly higher than New Brunswick males. However, during 1994-1998, the standardized mortality ratio was 5.0 and was significantly elevated. This observation was based upon only two testicular cancer

deaths for the GSR and could have been an anomalous finding. No testicular cancer deaths occurred during 1980-1983, 1989-1993 or 1999-2003.

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 ratio among GSR women in the earliest time period (1984-1988 SIR=1.10), the SIRs ranged from 0.76-0.90 from 1989-1993 among GSR women and from 0.64-0.94 among GSR men. Lung cancer mortality was also statistically significantly lower in 1980-1983, 1994-1998, and 1999-2003 for GSR women and for all time periods except 1984-1988 for GSR men.

Bone Cancer

Bone cancer incidence was significantly higher for GSR women for the time periods 1984-1988 (SIR=3.21) and 1994-1998 (SIR=3.41). These rates are based, however, upon small numbers of cases and this risk did not transfer to increased mortality rates. Standardized incidence ratios 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) but these findings were not statistically significant. 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

Brain cancer incidence was slightly higher for female Gagetown residents for the early years of the study [1984-1988 (SIR=1.30) and significantly higher during 1989-1993 (SIR=1.50) but the reverse was true for the more recent time period of 1994-1998 (SIR=0.73) (borderline but non significant). Brain cancer incidence and mortality rates for GSR males were not

significantly elevated or reduced compared to the rates for Province of New Brunswick males across the time span of the study.

Laryngeal Cancer

Incidence of laryngeal cancer was significantly elevated for women during 1989-1993 compared to New Brunswick women but this risk was not seen in the other time periods. Only one laryngeal cancer death occurred in the GSR women during the study period. The risk for laryngeal cancer was higher in GSR males during 1999-2003 but for the other periods not significantly different than New Brunswick males. Laryngeal cancer mortality risk in GSR males appeared lower than New Brunswick men but these results were not statistically significant.

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. Multiple myeloma incidence rates for GSR women were elevated during 1989-1993 (SIR=1.55) and slightly but not significantly elevated for GSR males during 1994-1998 but no other increased risks were observed for the other time periods. Non-Hodgkins Lymphoma incidence rates in the Gagetown Study Region 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). Risk for lymphoid cancer deaths was significantly higher for GSR women in 1980-1983 (SMR=1.43) and 1989-1993 (SMR=1.31) and suggestively higher in 1984-1988 (SMR=1.25) but the risk decreased in more recent years. Conversely, SMRs for lymphoid cancer deaths in males were lower than one for the most recent 20 years but these findings were not statistically significant.

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 GSR women (SIR=2.62). Incidence of acute myeloid leukemia (AML) was significantly elevated among GSR men in 1984-1988 (SIR=1.92). Chronic lymphocytic leukemia incidence rates were significantly lower in 1994-1998 in GSR males (SIR= 0.07). Similarly, the chronic myeloid leukemia incidence rate for GSR men was significantly lower in 1989-1993 (SIR=0.32) than for the province of New Brunswick. 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 Type 2 Diabetes and Parkinson's Disease were analyzed. Diabetes mortality in GSR women was significantly lower during the early years of the study (1980-1983: SMR=0.64) but was generally on par with the rest of the Province for the remaining years until 1999-2003 when the risk for Type 2 Diabetes mortality was slightly higher in GSR women (SMR= 1.10) . The mortality risk for diabetes in the Gagetown Study Region men was significantly higher during 1980-1983 (SMR=1.37) and during 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 Study Region experienced slightly heightened risk of mortality during 1994-1998 (SMR 1.32) yet decreased mortality during 1999-2003 (SMR=0.45).

Standardized mortality ratios among GSR men were elevated in 1989-1993 (SMR=1.86). These ratios are based on low rates of mortality for these diseases.

Population Attributable Risk

Percent population attributable risks (PAR) were calculated for both incidence rates and mortality rates. Diseases are presented if the risk of following diseases was heightened or decreased in Gagetown for most of the time intervals. It is important to keep in mind that these data do not account for the statistical uncertainty and broad confidence intervals that are associated with these numbers. 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 marked fluctuations in these data and this is most likely due, once again, to the uncertainty and low number of cases that were observed- causing significant fluctuations in the rates. These results should thus 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	51.69%	- 57.78%	- 4.44%	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 elevated in 1984-1988 and 1994-1998 but 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.

Population attributable risks for nasopharyngeal cancer incidence and mortality varied for 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.

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

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	1.72	1.25	NA	1.09
Acute lymphocytic	3.12	2.24	NA	2.12
Acute myeloid				
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

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

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

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
Hodgkin's Disease	1.63	3.04	NA	2.82
Larynx	9.79	6.93	5.59	5.95
Leukemia	1.90	1.60	NA	1.58
Acute lymphocytic	2.91	2.87	NA	2.97
Acute myeloid				
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
Nasopharynx	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

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

Table 15. Age Standardized Cancer Mortality Rates per 100,000 Females – NB vs Canada- 1986-2001(PHAC)[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), Public Health Agency of Canada. Bone, Hodgkin's disease, larynx, multiple myeloma, nasopharynx, nasal cavity, soft tissue sarcoma mortality data are not available on this site.

Table 16. Age Adjusted Cancer Mortality Rates (1986&1991) per 100,000 Males-(PHAC) [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, Hodgkin's disease, larynx, 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 Public Health Agency of Canada (PHAC) website 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 PHAC 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 PHAC results and the results from the present analysis is expected because 1) the present analysis is based on a five year average whereas the PHAC provided annual rates and 2) the present analysis is based on standardized incidence rates using ten year age groupings whereas the PHAC 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.

<u>All-cause cancer incidence</u>

For both 1996 and 2001, the all-cause cancer incidence rates (per 100,000) for New Brunswick males generated from the current analysis (1994-1998: 500.28; 1999-2003: 471.40) are consistent with the rates reported for New Brunswick (1996: 499.41; 2001: 508.52) by the Public Health Agency of Canada though the 2001 rate appears slightly lower. This slight variation could be the difference in comparing a five year mean rate (for the current study) covering the time interval of interest versus a single year rate from the year forming the midpoint of the interval. The rates from the current study for New Brunswick females are highly consistent (1994-1998: 338.33; 1999-2003: 338.98) with the reported rates for New Brunswick (1996: 336.88, 2001: 350.43 (no confidence intervals provided)). All-cause cancer incidence data for the earlier years were not available on-line from the Public Health Agency of Canada.

Other respiratory cancer incidence

Data that were generated for the category of 'other respiratory cancer' (includes nasal cancer but not lung cancer) incidence rates in the present analysis are lower than the PHAC 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 PHAC 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 PHAC 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 PHAC data coding for this cancer site. The original ICD codes for this site were not provided to us.

Leukemia mortality

Leukemia mortality rates were also consistently lower in the present analysis compared those reported by the PHAC. For males, the age standardized incidence rate was 1.16 per 100,000 males yet the PHAC-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 PHAC 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 PHAC reports. Rates for leukemia mortality were created using the broad category 'lymphoid cancers' as detailed in the technical notes. However, it is possible that the leukemia data that were provided to us only included the 4 subtypes of interest. Notable differences also exist in the leukemia cancer mortality results.

Discussion

The purpose of this descriptive epidemiologic study was to determine whether there is evidence of increased rates of chronic disease 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 to 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 historical 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. It is possible also that some of the statistically significant findings occurred purely by chance; since many ratios were calculated in this study, some significant results may have been anomalous.

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. Rates of nasopharyngeal cancer incidence in the Gagetown Study Region women were elevated compared to New Brunswick as a whole in the two time intervals in which there were sufficient numbers to calculate rates. For the two other time intervals, no cases were observed. A standardized incidence ratio was calculated for the entire 20 year period, while slightly elevated (SIR = 1.4), this finding was not significant. No nasopharyngeal cancer deaths were observed in women.

A SIR of 2.07 for nasopharyngeal cancer for the period 1984-1988 for GSR men compared to New Brunswick men was also found. Again this was based upon only two cases. Mortality from other respiratory cancers (including nasal cavity but not including lung cancer) was also higher for males during this same period and suggestively higher for GSR women during 1980-1983 (SMR= 1.81, not significant) and 1984-1988 (SMR=2.69, not significant). Associations between exposures to chlorophenoxy and chlorophenolic compounds and the development of nasopharyngeal cancers have been suggested by researchers since the 1960's. The conclusion of the recent review of current evidence from the literature by this researcher was that there remains inadequate or inconsistent information to determine an association between exposures to chlorophenoxy herbicides and nasopharyngeal cancer. A more complete investigation of this outcome in New Brunswick cases, as a future research initiative, may provide some further insights about the potential etiological role of herbicide exposures for this disease during this period. Potential problems with moving forward with this study include the need for a large number of subjects due to the rarity of this form of cancer and the need for excellent documentation of past exposure histories.

Breast cancer incidence was also slightly elevated in GSR women though the magnitudes of these ratios were only slightly higher than 1.0. In contrast, breast cancer mortality appeared to be slightly lower in the GSR than in the rest of the province. The risk for breast cancer has been associated with a full range of factors, including smoking, fertility, obesity and many other genetic, lifestyle and environmental factors. It was not possible to identify what might explain the slightly higher rates observed in CFB Gagetown. Issues of access to diagnostic and treatment services might also be contributory. Living near Fredericton, women in the GSR region may have been more likely to have access to mammography screening services and early diagnostic services than in the more remote areas of the province. This might then translate to reduced risk for mortality. This hypothesis is purely speculative and would require further research to examine. The recent literature review of herbicides did reveal limited or suggestive evidence of an association between chlorophenoxy herbicide exposure and breast cancer risk.

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 results for other diseases that have been most often linked to the GSR herbicides, 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 for the lymphopoietic cancers.

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[i] reveals that current smoking rates were 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 provide preliminary evidence that the residents of the GSR versus the Province of New Brunswick are quite similar in socio-economic status and lifestyle. The lower rates for lung cancer incidence in both men and women do suggest that smoking rates for GSR residents were slightly lower than the province as a whole.

The inclusion of Fredericton as part of the GSR likely influenced the findings. The population of New Brunswick during the study period ranged from 500,000 to 600,000. The GSR 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 enhanced the robustness of the statistical analysis due to the increase in sample size but may have diluted some of the more localized exposure effects that may have been primarily restricted to CFB Gagetown. It is possible that many former employees of CFB Gagetown and their family members are now currently living in Fredericton. As noted, the

Gagetown Community Advisory Committee advised the investigators about the study region boundaries.

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 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)[ii]. 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. The extent of this mobility is not clear however; it is possible that Fredericton residents moved across town or had moved in from Gagetown or other local rural community. However this mobility may have contributed to lack of detection of cases that were truly exposed 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. To fully explore this hypothesis, a longitudinal study of GSR residents would be required. Prerequisites for such an investigation would include a systematic list with complete documentation of who had worked at the base and when (identification of the cohort), and full details about current health status of all these individuals. Of interest would be the nature of the person's exposure: was the person ever employed as a mixer, applicator or flagger, and if so what herbicides were applied? Did the person engage in military training activities in which he or she came into direct contact with herbicide treated plants or soil? Was the person involved in forestry or agriculture related activities, unrelated to CFB Gagetown, during which exposures to herbicides occurred? 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 a major undertaking.

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. Breast

cancer incidence in women was observed to be slightly higher for all four study periods but it was not possible to draw conclusions about the factors that might be causing this slightly increased risk. There was also suggestive evidence that the incidence rates for nasopharyngeal cancers were higher for the female GSR residents compared to females from the Province of New Brunswick for two of the four study periods, but this analysis was based upon very few cases and no cases were observed for the other two study periods. Nasopharyngeal cancers for male GSR residents were also elevated for one of the four study periods (1980-1984). Further research could be explored in order to determine whether it is feasible to study these exposure-disease associations in detail; such work would be feasible only if there were sufficient cases with no loss to follow-up and accompanied by high quality exposure and individual risk factor information. Other potential study design concerns include the potential for loss of follow up due to the fact that those most vulnerable cases are no longer living and possible differential recall of previous exposure histories and lifestyle factors.

Finally, this study has made 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 factors that are contributory to the development and prognosis of an individual's disease.

Recommendations for future research

Further research could be explored to determine whether there is any evidence of associations between exposure to the herbicides used at CFB Gagetown and health effects. One possible approach is to assess feasibility of conducting a nested case-control epidemiological study after assembling a cohort comprising the CFB Gagetown military personnel and their families, herbicide applicators, mixers, and loaders, other civilian employees who worked at the base, and Canadian Forestry Service workers and others who were involved either directly with the herbicide spray operations or with brush clean-up operations. The exposure period of interest is from the early 1960's to 2000. Essential elements for such a study to go forward are the current existence of complete and formal lists of who worked and lived at the base and determination of whether there is sufficient statistical 'power' to test the hypotheses of interest.

If sufficient records exist to create this cohort, and if there is good documentation about times at which these individuals were working on the base and dates of individual herbicide spraying activities, then the next step would be to link this file to the Canadian Cancer Registry and the National Mortality database to find all occurrences of cancers and deaths in the cohort. Then, by using a nested case-control epidemiological study design, cases and controls, who would be selected randomly from the cohort but matched to cases by age and gender, will be carefully compared to each other in relation to agent-specific 'burden of herbicide exposures' and with regard to multiple agent exposure profiles. An external control group might also be included. The CFB Gagetown Task 2A report does identify some uncertainties related to information recording and data availability pertaining to exposures; it is not clear to the extent to which this applies to the employment and military personnel records.

The comparisons that would result from this study might yield patterns of herbicide-health effects associations related to the experience at CFB Gagetown. The challenge will be whether there are sufficient cases in order to establish such associations. As seen in the current study, the number of cases especially for rarer diseases likely will be sparse. If it is possible to create the cohort, then using the age-gender distribution information, one can estimate the probability of disease occurrence (thus number of cases) using national rates of disease. If this study goes

forward, such a study might help to answer questions long asked by members of the CFB Gagetown community.

References

Fay, M.P. & Feuer, E.J. (1997). Confidence intervals for directly standardized rates: A method based on the gamma distribution. Statistics in Medicine, 16, 791-801.

Harvard School of Public Health, 2004. Public Health Disparities Geocoding Project Monograph. Available on-line: http://www.hsph.harvard.edu/thegeocodingproject/webpage/monograph/methods.htm)

Oleckno, WA (2002). Essential Epidemiology. Waveland Press. Long Grove, Illinois.

Szklo, M. & Nieto, F.J. (2004). Epidemiology. Beyond the Basics. Jones & Bartlett Publishers, Sudbury, Massachusetts.

Appendix 1.

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

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 cancer causes	796	345.91 (322.25-370.85)	6242	339.50 (331.05-348.11)	948	359.70 (337.06-383.45)	6653	330.35 (322.38-338.47)
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)

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)

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 cancer causes	1005	348.91 (327.32-371.55)	7398	338.33 (330.54-346.26)	1168	360.78 (339.93-382.56)	8122	338.98 (331.40-346.68)
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)	2240	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)

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)

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 cancer causes	990	529.38 (496.46-563.90)	7631	507.70 (496.26-519.31)	999	463.32 (434.86-493.14)	8135	492.39 (481.71-503.23)
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)

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)

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 cancer causes	1112	471.19 (444.40-500.58)	8883	500.28 (489.90-510.83)	1228	468.81 (442.77-495.97)	9315	471.40 (461.80-481.15)
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)

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)

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)
Parkinson's 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 (11.57-11.62)	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)
Parkinson 's 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)

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)
Parkinson 's 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)
Parkinson's 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)

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 cancer 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)

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 cancer 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)

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)

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 cancer 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)

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 cancer 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)

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 Sarcoma	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)

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)

****

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 Public Health Agency of Canada 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	Age group	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 MS 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 age group 0-4 was given). A request for data in the requested age groups 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.

[i] http://www.statcan.ca/english/freepub/82-221-XIE/00502/tables/html/226.htm)

[ii] Source: 2001 Community Profiles: Available on-line http://www12.statcan.ca/english/profil01/CP01/Details/Page.cfm?Lang=E&Geo1=CSD&Code1=1304005&Geo2=PR&Code2=13&Data=Count&SearchText=gagetown&SearchType=Begins&SearchPR=13&B1=All&Custom=