Incidence and mortality trends and geographic patterns of follicular lymphoma in Canada

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ABSTRACT

Background Follicular lymphoma (FL) is the most common indolent lymphoma and the 2nd most common non-Hodgkin lymphoma, accounting for 10%–20% of all lymphomas in the Western world. Epidemiologic and geographic trends of FL in Canada have not been investigated. Our study’s objective was to analyze incidence and mortality rates and the geographic distribution of FL patients in Canada for 1992–2010.

Methods Demographic and geographic patient data for FL cases were obtained using the Canadian Cancer Registry, the Registre québécois du cancer, and the Canadian Vital Statistics database. Incidence and mortality rates and 95% confidence intervals were calculated per year and per geographic area. Rates were plotted using linear regression models to assess trends over time. Overall data were mapped using Microsoft Excel mapping software (Redmond, WA, U.S.A.) to identify case clusters across Canada.

Results Approximately 22,625 patients were diagnosed with FL during 1992–2010. The age-standardized incidence rate of this malignancy in Canada was 38.3 cases per million individuals per year. Geographic analysis demonstrated that a number of Maritime provinces and Manitoba had the highest incidence rates, and that the provinces of Nova Scotia and Quebec had the highest mortality rates in the nation. Regional data demonstrated clustering of FL within cities or regions with high herbicide use, primary mining, and a strong manufacturing presence.

Conclusions Our study provides a comprehensive overview of the FL burden and its geographic distribution in Canada. Regional clustering of this disease in concentrated industrial zones strongly suggests that multiple environmental factors might play a crucial role in the development of this lymphoma.

Key Words Follicular lymphoma, incidence, mortality, geographic clustering, epidemiology, pollutants, herbicides, mining, clustering


INTRODUCTION

Non-Hodgkin lymphomas (NHLs) are the 5th most commonly diagnosed cancers in Canadian adults1. Non-Hodgkin lymphoma is the general term for a heterogeneous group of malignancies arising from lymphoid tissues; it can involve extranodal sites such as skin, bone marrow, and spleen, among others. Since the late 1980s, multiple reports have documented an increasing incidence of NHL worldwide2.

In Canada, NHL accounts for nearly 90% of all lymphomas and for about 4% of all cancers in both sexes. There are more than 30 NHL subtypes, with follicular lymphoma (FL) being the most common form of indolent NHL and the 2nd most common form of NHL overall, accounting for approximately 20%–30% of all NHL cases3. Follicular lymphoma represents 10%–20% of all lymphomas in the Western world4.

Globally, the incidence of FL—like that of the other NHL subtypes—is rising, although the incidence rate varies by
geographic region and ethnic group. The incidence of FL has been observed to be significantly lower in Asian and sub-Saharan African countries than in the Western world, which is likely attributable to a combination of genetic and environmental factors and differences in life expectancy. In the United States, the incidence rate for FL is estimated to be approximately 31.8 cases per 1,000,000 person-years. Although the incidence of FL in the United States has remained stable in recent years, particularly for elderly patients (>75 years of age), it increased by 1.8% per year during 1992–2001. Marked predominance was found in white compared with African American or Asian populations. Unlike other NHL subtypes, FL has an incidence rate that is similar in men and women. Although the incidence of FL is lower in African American populations, the average age of diagnosis is approximately 10 years younger in African American than in white individuals. Follicular lymphoma is most commonly diagnosed in individuals more than 50 years of age.

The cause of FL remains poorly understood. Recent efforts have uncovered several environmental and genetic risk factors that could play a significant role in the pathogenesis of FL. Notably, FL risk is thought to have an important environmental component, given that its incidence has been found to be increased in individuals of Chinese and Japanese descent who were born in the United States, despite a lower overall FL incidence in China and Japan. A number of environmental exposures have been associated with the development of FL and NHL. They include exposure to insecticides, herbicides, hair dyes (before the 1980s), smoking, alcohol intake, and residence near certain industrial areas.

**METHODS**

The present study was conducted in accordance with the CISS-RDC-668035 and 13-SSH-MCG-3749 protocols approved by the Social Sciences and Humanities Research Council of Canada and the Quebec Inter-university Centre for Social Statistics respectively. In accordance with institutional policy, the study received an exemption from the McGill University Research Ethics Board.

Clinical and geographic data were obtained from the Canadian Cancer Registry (CCR), the Registre québécois du cancer (RQC), and the Canadian Vital Statistics (CVS) databases, as previously described. The CCR is a dynamic database of Canadian cancer patients from 12 Canadian provinces and territories (excluding Quebec), who were diagnosed with primary tumours during 1992–2013. The RQC database was used to obtain corresponding data for patients residing in Quebec. Because the data from the RQC spans the years 1992–2010, we decided to analyze findings for that period so as to encompass all Canadian provinces and territories.

Geographic and clinical information—including patient sex, year of diagnosis, age at diagnosis, and forward sortation area (RSA) of residence (the first 3 digits of a postal code, which defines a geographic region), as well as the 3rd edition of the International Classification of Diseases for Oncology (ICD-0-3) code for the tumour—were obtained from the CCR and RQC databases. Unfortunately, the CCR and RQC registries do not collect certain demographic characteristics, including the ethnic background of patients.

Consistent with the updated 2016 World Health Organization classification of lymphoid neoplasms, FL cases were defined based on ICD-0-3 codes, and FL data were obtained using ICD-0-3 codes that reflect the stages of the disease: FL not otherwise specified (code 9690), FL grade 1 (code 9695), FL grade 2 (code 9691), FL grade 3 (code 9698).

The CVS mortality database was used to obtain cause of death. For the cause-of-death analysis, the 9th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-9) was used for deaths during 1992–1999 (code 202.0 for FL overall), and the 10th revision (ICD-10) was used for deaths during 2000–2010 (codes C82.9 [FL not otherwise specified], C82.0 [FL grade 1], C82.1 [FL grade 2], and C82.2 [FL grade 3]). Data for FL incidence and mortality were analyzed as a group and not individually. Unfortunately, the CCR and RQC databases are not linked to the CVS (mortality) registry, and hence, it was not possible to follow specific patients from the time of diagnosis to the time at which they succumbed to their lymphoma.

Population counts for incidence and mortality were obtained on national, provincial, city, and RSA postal code levels from Statistics Canada’s Census of Population for the years 1996, 2001, 2006, and 2011.

**Mandatory Data Rounding**

In accordance with data publication rules from the CCR, RQC, and CVS, the RQC meant to preserve patient privacy and confidentiality, random rounding of variables for FL cases as absolute numbers was undertaken for all values presented in this study. With respect to the random rounding of tabular data, the Social Sciences and Humanities Research Council of Canada and Statistics Canada require the use of an unbiased random rounding scheme that rounds each cell count, independent of other cells, to a lower or higher multiple of 5, with counts being more likely to be rounded to their nearest multiple of 5. Counts of 1–4 were restricted from publication, according to Social Sciences and Humanities Research Council of Canada regulation. Therefore, if the number of cases or deaths fell into the range of 1–4 per ICD-0-3 code, the related clinical and geographic information could therefore not be released to protect patient confidentiality. To assess low-incidence regional clusters, we were able to review communities in which zero FL cases or deaths were documented.

**Statistical and Mapping Analyses**

Unless otherwise specified, analyses of the rounded data for all patients with FL across Canada for the period 1992–2010 are presented throughout this report. Age-adjusted incidence rates and 95% confidence intervals (CIs) were calculated and are reported by year of diagnosis and for provincial or national incidence analysis. Crude incidence rates were calculated for cities and RSA. Unless otherwise specified, Canadian census averages from the years 1996, 2001, 2006, and 2011 were used for all population analyses. The CIs were calculated based on the exact Poisson distribution. Incidence rates were plotted using a linear regression model to assess trends over time. The coefficient of determination was calculated to
determine how closely the incidence rates corresponded to the regression line.

Geographic maps of Canada, divided by city and fsa, were generated using Microsoft Excel 3D (Redmond WA, U.S.A.) and ArcGIS Pro mapping software (Esri Canada, Toronto, ON). In mapping the ccr, rqc, and cvs results, only city and fsa regions with populations of at least 5000 individuals based on 1996, 2001, 2006, and 2010 census data were selected. The aim was reduce erroneous false-positive hits, in which a few cases of fl occurring within sparsely populated cities and postal codes (<5000 residents) might have artificially inflated the incidence and mortality rates. That rule was not applied to the national and provincial analyses, which included all patients. In our graphics, cities with a significantly high incidence or mortality rate are represented with red dots, and cities with a significantly low incidence or mortality rate are represented with green dots.

The ArcGIS mapping software was used to analyze the industrial presence in proximity to identified fsas. Industries were located using enhanced points of interest files produced by DMTI Spatial Inc. (Richmond Hill, ON). The enhanced points of interest file is a national database of more than 1 million Canadian businesses and recreational points of interest present during 2002–2010.

RESULTS

Approximately 22,625 patients were diagnosed with fl during 1992–2010. As summarized in Table 1, a significant proportion of those patients, 31.6%, were diagnosed with pathologic grade 1 FL (28.9% were diagnosed with grade 2 FL, and 15.1%, with grade 3 FL). No sex preponderance was found in the Canadian fl population. Mean age at the time of diagnosis for patients with fl in Canada during 1992–2010 was 60.8 ± 13.8 years, and the age ranges for the individual fl stages were similar (Table 1).

Incidence of FL in Canada During 1992–2010

The overall incidence of fl increased in Canada from 1992 to 2010, with a documented slope of 0.5 cases per million individuals per year [$R^2 = 0.7, p < 0.0001$, Figure 1(A)]. The age-standardized incidence rate for this malignancy in Canada during 1992–2010 was 38.3 cases per million individuals per year (95% cr: 37.8 cases to 38.8 cases). Data for the age-standardized incidence by province during

<table>
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<tr>
<th>TABLE 1</th>
<th>Demographics of patients in Canada with follicular lymphoma, analysis by sex and age</th>
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<tr>
<td>Follicular lymphoma subtype</td>
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<tr>
<td></td>
<td>(n)</td>
</tr>
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<td>Grade 3</td>
<td>9698</td>
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<tr>
<td>Overall</td>
<td>—</td>
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<sup>a</sup> According to the International Classification of Diseases for Oncology, 3rd edition.

<sup>b</sup> Rounded to nearest 5.

Dx = diagnosis; NOS = not otherwise specified.

FIGURE 1 Age-standardized incidence and mortality rates (cases per 1 million individuals per year) for all cases of follicular lymphoma during 1992–2010, with line of best fit and linear regression analysis of the incidence rate over time. (A) Incidence trend [coefficient of determination ($R^2 = 0.7; p < 0.0001$)]. The slope of the line represents 0.5 ± 0.08 cases per million individuals per year. The average age-standardized incidence rate for this malignancy in Canada during 1992–2010 was 38.3 cases per million individuals per year. (B) Mortality trend ($R^2 = 0.7; p < 0.0001$). The slope of the line represents 0.07 ± 0.009 cases per million individuals per year. The average age-standardized mortality rate for this malignancy in Canada during 1992–2010 was 1.3 cases per million individuals per year. CI = confidence interval.
1992–2010 reflect the overall Canadian trend [supplemental Figure 1(A–J)]. Notable increases in the FL incidence were demonstrated in the populous Canadian provinces of Ontario, Quebec, and British Columbia [supplemental Figure 1, panels B, I, and J respectively].

Geographic Distribution of FL Cases in Canada
Age-standardized incidence rates for the Canadian provinces and territories revealed intriguing trends [Figure 2(A) and supplemental Table 1]. The provinces of New Brunswick, Prince Edward Island, Nova Scotia, and Manitoba had incidence rates that were notably higher than the national average. In contrast, the incidence rate in Newfoundland and Labrador was statistically significantly lower than the national average.

We examined the crude incidence rates for FL in Canadian cities [Figure 3(A), supplemental Table 2]. Most of the cities (56%) with significantly higher incidence rates were located in the province of Ontario: Peterborough, North Bay, Greater Sudbury, St. Catharines, and Thunder Bay [supplemental Table 2, Figure 3(A)]. Apart from Moncton, New Brunswick, and Winnipeg, Manitoba, cities with significantly higher incidence rates did not correspond to provinces with statistically higher incidences, as already reported. Other cities with incidence rates above the national average included Nanaimo and Kelowna, British Columbia. As expected, the total number of FL cases was higher in larger cities such as Montreal and Vancouver, but the incidence rates in those cities were on par with the Canadian average. However, Quebec City had fewer cases than expected (n = 160) given its large population of 504,000. Major cities in Ontario with low FL incidence rates included Ottawa, Mississauga, Toronto, North York, and Brampton. Calgary and Edmonton, the two major cities in Alberta, also had incidence rates that were lower than the national average [Figure 3(A), supplemental Table 2].

To further dissect the distribution of FL in Canada, we analyzed the crude FL incidence within cities by using FSA postal codes. Supplemental Table 3(A) lists FSAs with a statistically significant increased or decreased incidence of FL. In each high-incidence city, we were able to find statistically significant high-incidence FSAs that corresponded with specific neighborhoods. For example, FSAs V9R, V9S, and V9T are regions with significantly high incidences in Nanaimo, British Columbia, which has the highest per-city incidence in Canada (Nanaimo incidence: 65.0; 95% CI: 52.9 to 79.0). Interestingly, these high incidence FSAs in Nanaimo are geographically located side-by-side [supplemental Figure 3(AD)], as was the case with other multiple high-incidence FSAs within several high-incidence cities. That regional clustering of cases occurred elsewhere across the country [supplemental Figure 3(A–AF)]. In Nova Scotia, a clustering of patients was observed in FSAs B0H, B0K, B0J, B0N, and B0P, in a horseshoe formation [supplemental Figure 3(B)]. In the city of Moncton, New Brunswick, the high-incidence FSA regions E1E, E1C, and E1A were adjacent to one another [supplemental Figure 3(E)]. Significant FSA clustering was also found in northeastern Ontario [supplemental Figure 3(O)], particularly within the regions surrounding Peterborough, Nipissing, and Sudbury. Lastly, clustering of cases was found in London in southwestern Ontario for N0L, N0H, and N0J [supplemental Figure 3(S)] and in Thunder Bay in northern Ontario for P7C and P7B [supplemental Figure 3(T)]. Strikingly, many adjacent high-incidence FSAs within the city limits of Winnipeg, Manitoba, were located near industrial regions: R2Y and R3J; R2H and R2M; and R2V, R2G, and R0E [supplemental Figure 3(V)]. Contiguous regions of high incidence were also found in Edmonton, Alberta [FSAs T5W and T6A; supplemental Figure 3(AA)] and in the cities of Okanagan, Kelowna, and Kamloops in British Columbia [supplemental Figure 1(AC)]. The major metropolitan city of Surrey, British Columbia, also demonstrated a clustering of high-incidence FSA regions: V4A, V4B, and V4P [supplemental Figure 3(AD)].

We then conducted an incidence rate analysis to identify areas that had no FL (that is, zero cases) during 1992–2010. Our analysis documented 13 FSAs that had a statistically significant low incidence of FL [supplemental...
Table 3(B)]. Those fSAs are depicted in grey on the maps in supplemental Figure 3. Most of those regions (8 of 13 fSAs) were in Quebec (G3C, G3H, G3J, G3K, G4V, J1R, J2M, J9B). As depicted in supplemental Figure 3(I), a scattering of low-incidence fSAs can be found particularly in eastern Quebec, for the G3C, G3H, G3J, and G3K fSAs. The other 5 low-incidence communities were located in New Brunswick (E3G), Alberta (T8X), British Columbia (V8B), the Northwest Territories and Nunavut (X0A), and the Yukon Territory (Y0B).

To evaluate the potential influence of external triggers on FL carcinogenesis, we conducted an analysis of industrial presence in proximity to the identified fSAs, which revealed several notable trends (supplemental Figures 3 and 4). We used ArcGIS to assess the presence of industrial and mining lands, as well as a number of industrial facilities. We investigated a potential association between the proximity of such industries and FL incidence. Differences in industrial presence in the high- and low-incidence regions were highlighted in the generated maps, as shown in supplemental Figure 4. Notably, significantly more industrial land use was evident in the high-incidence regions compared with the low-incidence regions, as depicted in supplemental Figure 4 in the cities of Moncton, New Brunswick (panel A); Thunder Bay, Ontario (panel I); Winnipeg, Manitoba (panel J); and Nanaimo, British Columbia.

FIGURE 3  Maps illustrating the distribution of follicular lymphoma (FL) incidence and mortality per million individuals per year in Canadian cities. Red indicates cities with a significantly high incidence of FL. Green indicates cities with a low incidence. (A) Distribution of FL incidence per city in Canada. (B) Distribution of FL mortality per city in Canada. Microsoft Bing maps reprinted with permission from Microsoft Corporation (https://www.microsoft.com/en-us/maps/product/print-rights).
(panel K). In eastern Quebec, where multiple low-incidence fsas had been found, the proximity analysis showed little industrial land use within 5 km of those fsas. The trend was further supported when mapping results were subjected to a quantitative analysis of the overall land use by city, which demonstrated a significant increase in adjacent industrial and mining land use in high-incidence fsas compared with low-incidence fsas \( p < 0.01 \), supplemental Table 4(A).

We then investigated the presence of the following industries per FSA: gas and oil production; emitting chimneys; herbicide facilities and crop farms; metal factories; plastics manufacturing; and power plants. When those industrial facilities were mapped, as shown in supplemental Figure 5, a clustering of high-incidence fsas was evident in regions of high industrial density—particularly in supplemental Figure 5 in the cities of Winnipeg, Manitoba (panel B); Edmonton, Alberta (panel C); and Okanagan, Kelowna, Kamloops, and Nanaimo, British Columbia (panels D and E). Analysis of the mean density of those industrial facilities near noteworthy fsas suggests a significantly higher number of gas and oil production facilities; chimneys; herbicide and crop facilities; metals manufacturing; and plastics manufacturing factories within 5 km of high-incidence fsas compared with low-incidence fsas \( p < 0.01 \), supplemental Table 4(B)). However, the number of power plants had no significant association with high-incidence fsas.

**Analysis of FL Mortality Across Canada**

Mortality data were analyzed to corroborate the incidence trends. Data were obtained using an independent population-based cvs database. Like the diagnostic characteristics of FL, FL mortality showed no sex preponderance, with the male-to-female mortality ratio being approximately 1:1. Deaths from FL (72.8%) occurred mainly in individuals more than 60 years of age, and mean age at death was 68.1 years (Table II).

The age-standardized mortality rate for FL during 1992–2010 was 1.3 cases per million individuals per year (95% CI: 1.2 cases to 1.4 cases). A linear regression analysis of FL mortality documented an increase of approximately 0.07 deaths per million individuals per year during 1992–2010 in Canada [Figure 1(B)]. Analysis of mortality rates by province per year demonstrated a slight increase in mortality, particularly in the populous provinces of Ontario and British Columbia (supplemental Figure 2, panels B and H respectively). Notably, Manitoba demonstrated a steady decrease in mortality from 1992 to 2010.

Overall mortality rates varied by province [supplemental Table 5, Figure 2(B), supplemental Figure 2]. Quebec had the highest mortality rate, at 1.8 deaths per million per year. Unexpectedly, Manitoba had a significantly lower mortality rate [0.2 deaths per million per year (95% CI: 0.0 deaths to 0.5 deaths)] despite having a significantly higher provincial incidence rate. The total number of FL deaths was low in Prince Edward Island and in Newfoundland and Labrador, and so to protect patient confidentiality, data for those jurisdictions could not be published.

Analysis of mortality by city indicated that Nanaimo, British Columbia, and Medicine Hat, Alberta, had the highest mortality rates [supplemental Table 6, Figure 3(B)], which is consistent with the incidence findings. We observed that several cities (8 of 11) in the provinces of Quebec and Ontario had significantly higher mortality rates, including Granby, Laval, Sherbrooke, and Montreal in Quebec and Kingston, London, Hamilton, and Ottawa in Ontario [supplemental Table 6, Figure 3(B)].

**DISCUSSION**

Our study is the first to evaluate FL incidence, mortality, and geographic distribution in Canadian patients diagnosed during 1992–2010. In all cases, clustering of high-incidence fsas was found in high-incidence cities. Identification of those geographic clusters can lead to the development of specific hypotheses to explain the pattern of risk and could reveal important clues about the causes of this disease\(^{22,23}\). Strikingly, we noticed that high industrial presence coincided with high-incidence fsas, while the opposite was true for the low-incidence fsas. Furthermore, clustering of high-incidence fsas was observed in areas of high industrial land use, which suggests that residents living in those geographic areas might be susceptible to regional and common external triggers influencing FL development. Similar spatial variations and geographic clustering have been demonstrated for an analysis of NHLs in the province of Manitoba, where clustering was shown to be indicative of variations in genetic and environmental risk factors\(^{24}\).

This type of geographic analysis is unprecedented for FL.

**TABLE II** Mortality characteristics of patients in Canada with follicular lymphoma, analysis by sex and age

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<th>Follicular lymphoma subtype</th>
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\(^a\) According to the International Classification of Diseases for Oncology, 3rd edition.

\(^b\) Rounded to nearest 5.

NOS = not otherwise specified.
in Canada and strongly suggests that industrial exposures might play an important role in the pathophysiology of this cancer.

It was previously reported that exposure to agricultural and food industries (hunting and forestry), manufacturing industries (metallurgy and metalworking), and production and distribution of electricity, gas, and water were associated with NHL.23,25,26 With respect to FL, exposure to herbicides used on crops and residential proximity to industrial facilities have particularly been linked to higher risk for this cancer.

Exposure to herbicides has been linked to the development of a particular translocation between chromosomes 14 and 18 that is associated with systemic FL. During a 9-year period, the frequency of that translocation was found to be increased by 253% in a pesticide-exposed group compared with 87% in a control group.27 Another study linked periods of high herbicide use with a higher prevalence and frequency of BCL2-IGH translocation in farmers.28 Our evaluation of the use of pesticides on a geographic level in the present study demonstrated that a number of herbicide facilities and crop farms were significantly positively associated with an increased incidence of FL within specific regions of Canada.

An association of proximity to industrial facilities or pollution with an increased risk of NHL has been documented internationally.29-34 Increased risk of NHL has been associated with living near a petroleum refinery for a decade or more. An increased risk of NHL was also found to be associated with proximity to primary metals industries. Specifically, the present study showed that FL risk was higher in individuals living within 2 miles of such a facility. In addition to the geographic clustering of NHL, results from American and Swedish studies have remarked on space–time clustering and risk of NHL.30,35 Although we were not able to investigate the temporal–spatial relationship between industries and the incidence of FL, our results mirror findings from earlier studies and indicate that proximity to industrial lands within Canadian cities corresponds to an increased FL incidence. The mean density of industrial facilities within 5 km of high-incidence SAS was also very high. Those results are strongly suggestive that more than 1 industrial risk factor could play a role in the development of FL. That hypothesis is further supported by our results showing that low-incidence FL regions have a low industrial presence.

We also note that the clinical characteristics of FL in our study are similar to those in the United States.3,7 In both countries, FL had no significant sex preponderance, and the average age at diagnosis was approximately 60 years. Further, an increase in the FL incidence was demonstrated in both the Canadian and the American populations—particularly in individuals more than 75 years of age. Those results highlight clinical characteristics and epidemiologic trends that transcend the American–Canadian border.

Since the start of the 2000s, significant progress has been made in the treatment of NHL, including FL. One of the most important treatment advances is perhaps the discovery and approval of rituximab for FL and other NHLs. Rituxan (Hoffmann–La Roche Ltd., Mississauga, ON) was the first form of rituximab to be approved in Canada in 2000.36 Rituximab is a chimeric monoclonal antibody directed against the B cell antigen CD20; it depletes B cells by various mechanisms, including direct antibody-dependent cellular cytolysis, complement-mediated cell death, and apoptosis signalling.37 Indeed, many studies have demonstrated an improvement in overall survival and treatment efficacy with the use of rituximab alone or in combination with conventional chemotherapy.38-40 The mortality rate and overall survival of patients with FL in our cohort might have been influenced by the introduction of rituximab, although such an effect was not distinctively observed in the study. Consistent with a study by Ye et al.,41 we similarly found a decline in FL mortality in Manitoba over time; however, that trend was not observed in other populous provinces of Canada that ultimately determined the overall Canadian mortality trend. Further epidemiology studies are required to confirm and quantify the impact of rituximab on the survival rates of patients with FL in Canada.

Our study had several limitations. Because of an inability to acquire residential history data, we were not able to conduct an in-depth temporal–spatial analysis. It has previously been shown that an elevated risk of NHL is associated with geographic clustering during the latency period of approximately 20 years.30 Another important limitation is that only industries present between the years 2002–2010 were included in our analysis. Historical manufacturing facilities, which might now be closed, could not be subjected to analysis. For example, the city of Peterborough, Ontario, which has a statistically high FL incidence rate, was previously a home to the now-closed facilities of General Electric Motors and of Westclox, where clock faces were painted with radium. Those factories might have been influential in the development of FL because of potential residual contamination in the region. Further studies are required to confirm that hypothesis. Patient occupation, chemical exposure, socioeconomic status, and residence history are also important factors that could not be analyzed in the present report.

It was previously shown that FL was markedly predominant in white compared with African American or Asian American individuals in the United States; further, it was also noted that age at diagnosis was 10 years younger for African American than for white individuals.8 Unfortunately, because data about the ethnic background of patients were not available in the databases used for the analysis, we were unable to confirm that trend.

CONCLUSIONS

The present study is the first to analyze the geographic distribution, incidence, and mortality for FL in Canada over a 19-year period. Our work confirms the clinical characteristics of FL that transcend North American borders. Furthermore, national data demonstrate a steady increase in both FL incidence and mortality despite its indolent nature. Follicular lymphoma has geographic niches in multiple industrial regions in Canada, suggesting that multiple environmental and social factors might play a role in the risks for and pathophysiology of this disease. High FL-associated mortality rates in certain areas might indicate that the disease is underdiagnosed or diagnosed
at later stages, or that patients in affected communities are not able to access treatments. Further studies are required to confirm those trends.

ACKNOWLEDGMENTS
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CONFLICT OF INTEREST DISCLOSURES
We have read and understood Current Oncology’s policy on disclosing conflicts of interest, and we declare that we have none.

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REFERENCES


