Regional variation of multiple sclerosis prevalence in Canada

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Objective: *To describe the regional distribution of multiple sclerosis (MS) prevalence in Canada, controlling for age and sex.* **Methods:** *This study used data from the Canadian Community Health Survey, a large general health survey (n = 131,535) conducted in 2000/2001. Subjects aged 18 and over were included in the current analysis (n = 116,109). The presence of MS was determined by self-report. Prevalence was computed in five regions (Atlantic, Quebec, Ontario, Prairies and British Columbia). Logistic regression was used to compare regions and examine for confounding/interaction by age and sex.* **Results:** *The overall Canadian MS prevalence was 240 per 100 000 (95%CI: 210–280). Prevalence ranged from 180 (95%CI: 90–260) in Quebec to 350 (95%CI: 230–470) in Atlantic Canada. Logistic regression revealed no statistical difference between the odds of MS in Quebec, Ontario and British Columbia adjusted for age and sex. The adjusted odds of MS in the Prairies and Atlantic regions were significantly higher than in the other regions combined, with odds ratios of 1.7 (95%CI: 1.1–2.4, P <0.01) and 1.6 (95%CI: 1.1–2.4, P <0.05) respectively. Sensitivity analysis demonstrated similar prevalence in the nonaboriginal/nonimmigrant group (n = 96 219).* **Conclusion:** *Results suggest that Canadian MS prevalence differs by region. If validated, these regional differences may facilitate investigation of environmental influences.*
Multiple Sclerosis *(2005)* **11,** 516–519

Key words: *adult; Canada; epidemiologic studies; multiple sclerosis; prevalence*

Introduction

The causes of multiple sclerosis (MS) are unknown, but evidence points to a multifactorial aetiology involving both genetic and environmental components.[1,2] Identification of regional MS distribution could facilitate the generation of hypotheses regarding environmental factors. In Canada, MS prevalence is known to be high, with recent estimates ranging between 55 and 240 per 100 000.[3–5] It has, however, been unclear whether there are provincial or regional differences in prevalence, as there has been no systematic process in place to evaluate this. Comparison of prevalence between published regional studies has limited validity, due to differences in age distribution, ethnic composition and case ascertainment, as well as possible changes in prevalence over time.[4,6] The prevalence of MS has been shown to be lower in Canadian native peoples, and to differ in certain immigrant groups.[6] A population-based general health survey, the Canadian

Community Health Survey Cycle 1.1 (CCHS), provided data on MS as well as age, sex, immigration status and ethnicity in a large sample representing all regions of Canada ($n = 131 535$).[7] This allowed comparison of MS prevalence across regions at a single time point, taking demographics into account.

Methods

The CCHS was a cross-sectional nationally representative survey conducted between September 2000 and October 2001.[8] Participants aged 12 and older were selected from households in all ten provinces and three territories of Canada, using a sampling design developed by the Canadian national statistics agency (www.statcan.ca). Institutions, reserves (almost exclusively populated by aboriginal Canadians), crown lands, Canadian Forces bases and certain remote areas were excluded. The sample was constructed in two stages: first, households were selected, mostly by a multistage stratified cluster design (83%), but partially by random digit dialling (7%) and random sampling from telephone lists (10%). Secondly, one or two respondents were chosen within each household according to a defined strategy. Verbal informed consent was obtained from each participant. Analyses were performed in a secure Statistics Canada Data Centre designed to protect the confidentiality of participants. In these Centres, results must be vetted by a Statistics Canada analyst prior to leaving the Centre. The overall response

rate for the survey was 84.7%.[8] This ranged from 78.3% in the northern territories of Canada to 89.5% in Manitoba.

Self-report data were gathered on several health conditions, including MS. Presence of MS and other conditions was probed with questions of the form: 'We are interested in long-term conditions that have... been diagnosed by a health professional. Do you have *[specific condition]*?'.[9] There was no clinical confirmation, but the requirement of a diagnosis by a health professional would be expected to improve the validity of responses. Subtypes of MS were not differentiated. Statistics Canada did not conduct pilot studies validating the self-reported diagnoses.[10] However, self-report methodologies have been extensively researched, with comparisons against medical records and other data sources.[11–15] Most studies conclude that self-report is reasonably accurate for diseases that have clear diagnostic criteria, are easily communicated to patients, and affect function, particularly for the assessment of prevalence.[13–15] A recent study found that a comorbidity index constructed from baseline self-reported diagnoses was predictive of both mortality and hospitalizations.[16] MS has some of the characteristics that are associated with higher accuracy; namely, it refers to a specific disorder that is easily communicated, it has defined diagnostic criteria, and it is associated with disability.

The CCHS recorded age, sex, ethnicity and immigration status for each respondent. Subjects over age 17 that responded to the MS question and lived in one of the ten Canadian provinces were included in this analysis ($n = 116\,109$). The northern territories were excluded due to small sample size.

The prevalence of MS and 95% confidence intervals were calculated for Canada as a whole and for five regions (Atlantic Canada, Quebec, Ontario, Prairies and British Columbia). Table 1 presents the provincial composition of the regions. Although the CCHS provided more detailed geographical information at the provincial level, the low prevalence of MS would have made provincial prevalence estimates imprecise. Sampling weights and a bootstrap programme developed by Statistics Canada were employed for all analyses, to deal with the complex sampling strategy.

Logistic regression was used to compare MS prevalence among regions, and to examine for confounding or interaction by age or sex. As the prevalence of MS has been demonstrated to increase with age to a peak and then decline, the relationship between MS prevalence and age was examined with a generalized additive model (GAM) to determine an appropriate representation for age.[17,18] The logistic regression model initially included all interaction terms between age, sex and region. This model was reduced in a series of steps, resulting in the final model.

A number of secondary analyses were performed to assess the validity of the results. A sensitivity analysis was performed to evaluate the impact of potential differences in the prevalence of MS among aboriginals and immigrants to Canada (who might be unequally distributed across the country). This was done by repeating the above analyses while restricting inclusion to Canadian-born nonaboriginals ($n = 96\,219$). Next, to assess whether there was differential disease reporting among regions, the regional distribution of self-reported thyroid disease and migraine in the CCHS was also examined. Finally, the CCHS estimate of MS prevalence for the Prairies was compared to the prevalence for Alberta, as determined from diagnostic codes in physician billing data from the Alberta Health Care Insurance Plan. Of note, Alberta is one of the Prairie provinces. Data from 2.97 million residents of Alberta during 2001 were analysed. These Alberta residents were identified as having MS if an MS diagnostic code was assigned twice by a physician between 1991 and 2001.[19]

Results

Table 1 presents characteristics of the CCHS sample. Of the 116 109 eligible participants, 332 reported a diagnosis of MS. The overall weighted estimate of MS prevalence in Canada was 240 per 100 000 (95%CI: 210–280). Regional weighted prevalence ranged from 180 (95%CI: 90–260)

Table 1 Sociodemographic features of the study sample (unweighted)

Sample size	116 109
Age (years)	
18–24	10.1%
25–44	37.5%
45–64	31.6%
65–84	18.8%
85+	2.0%
Sex	
Male	45.7%
Female	54.3%
Region	
Atlantic (Prince Edward Island, New Brunswick, Nova Scotia, Newfoundland)	13.8%
Quebec	17.7%
Ontario	30.6%
Prairies (Alberta, Saskatchewan, Manitoba)	23.8%
BC (British Columbia)	14.2%
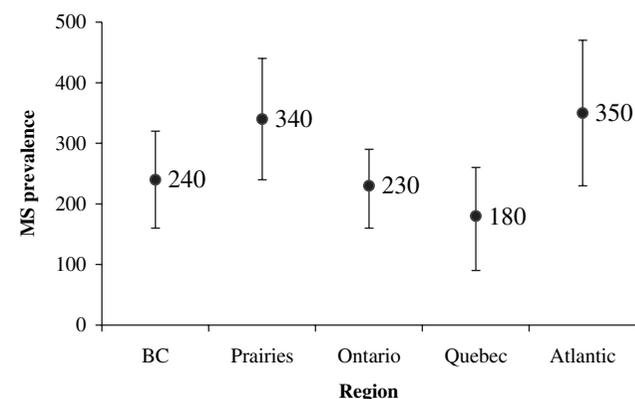
Figure 1 *Estimated MS prevalence* per 100 000 (and 95% CI[†]) in regions of Canada. *Weighted estimate. [†]95% bootstrap confidence interval.*

per 100 000 in Quebec to 350 (95%CI: 230–470) per 100 000 in Atlantic Canada (Figure 1).

As expected, the general additive model demonstrated a nonlinear relationship between MS and age. Due to the relatively small number of MS cases, adequate stratification by age to describe this relationship was not possible. Age was therefore represented as age, age^2, age^3 and age^4. Logistic regression was performed with terms for region, sex, age and the higher powers of age.

The first logistic regression models compared the odds of MS in British Columbia, the Prairies, Ontario and the Atlantic region against the region of lowest prevalence (Quebec), adjusted for age and sex. There was no significant interaction between sex, region, or any of the age terms, so the interaction terms were removed from the model. Age and age^2 terms were retained, but higher order age terms were removed. The reduced model demonstrated that the odds of MS were not significantly different in Ontario or British Columbia than in Quebec, so these regions were combined.

In the final logistic regression model the odds of MS were significantly higher in the Prairies and the Atlantic region than in the other regions combined, adjusting for age and sex (Table 2).

The above results pertain to the entire sample ($n = 116\,109$). Consistent results were obtained when the analysis was repeated in the Canadian born, nonaboriginal group ($n = 96\,219$). The prevalence estimates in this less genetically heterogeneous sample were also higher in the Atlantic and Prairies than in the other regions. Thirty-five of the 332 subjects with MS were excluded in this sensitivity analysis. There was no similar pattern of regional variation for thyroid disease or migraine prevalence across Canada. The Alberta Health Care Insurance Plan sample included 8999 persons with MS, and MS prevalence was 386 per 100 000 (95%CI: 377–394).

Discussion

This study confirms the high prevalence of MS in Canada (240 per 100 000), consistent with previous reports that Canadian MS prevalence is among the highest in the world.[6] It also extends this finding by demonstrating

Table 2 Logistic regression results for MS as a function of region, age and sex

	Odds ratio* (95% CI[†])	Wald P
Prairie region	1.7 (1.1–2.4)	0.008
Atlantic region	1.6 (1.1–2.4)	0.022
Age	1.2 (1.1–1.3)	<0.001
Age squared	1.0 (1.0–1.0)[‡]	<0.001
Female sex	2.1 (1.4–3.1)	<0.001

*Weighted odds ratio estimate, rounded to one decimal place in keeping with Statistics Canada guidelines.
[†]95% bootstrap confidence interval.
[‡]Although the age squared term has an odds ratio of 1.0 when rounded to one decimal place, it was retained in the model because its contribution becomes important for higher ages.

regional differences in MS prevalence within Canada. The specific contribution of the work is to describe regional prevalence with a single method of ascertainment, adjusting for age and sex, and with a sensitivity analysis to address the issues of ethnicity and immigration status.

The use of self-report to assess MS prevalence, without clinical confirmation, is a limitation of this study. However, the fact that the prevalence of other chronic diseases was not similarly distributed argues against systematic regional reporting differences as an explanation for the regional variation in MS prevalence. Verification of diagnosis by chart review or diagnostic workup would address the magnitude and significance of this limitation. However, it is probably unrealistic to think that this could be done in a population-based study large enough to examine regional prevalence differences. Confirmation of the very high rate of MS in the Prairies (340/100 000; 95%CI: 240–340) using Alberta billing data (386/100 000; 95%CI: 377–394) partially addresses this limitation. These Alberta Health Care data were collected during the same year (2001) and relied on physician-reported diagnosis rather than self-report. Unlike the CCHS, the Alberta Health Care sample included institutions, potentially contributing to the slightly higher observed Alberta prevalence compared to the CCHS Prairies region.

Although the CCHS sample size was very large, the precision of our results was limited by the small number of participants with MS (only 332). This precluded prevalence reporting at the provincial level, and produced wide confidence intervals for regional prevalence. In spite of this, we were able to demonstrate significant regional prevalence differences, adjusting for age and sex.

Elucidation of such regional differences can help with hypothesis generation regarding environmental risks for MS, based on knowledge of the local attributes of regions with higher prevalence. This has been recognized by the Centers for Disease Control and Prevention in developing the National Environmental Public Health Tracking Program.[20] This programme has been set up to systematically track certain diseases thought to be related to environmental exposures, as well as numerous potential exposures. MS is specifically mentioned as an end point for tracking, along with other chronic neurodegenerative diseases. Naturally, resultant hypotheses must be seen as preliminary because they rely on ecological associations: that is, associations at the level of groups (for example, the regions in the current study) rather than individuals. However, contemporary surveys that include biological assessment such as serum and urine measures of nutrition and environmental toxins (e.g., vitamin D, mercury, lead) will allow testing of some of these hypotheses at the individual level.[21,22]

Consideration of the environmental attributes of the five regions analysed in this study does not immediately suggest a known candidate environmental risk factor for MS.[23,24] For example, there are no obvious differences in latitude that would explain the results; although on average the major cities in the Prairies are further north than in the other regions, this is not consistently true of

the Atlantic region. Average annual sunlight hours (potentially related to both vitamin D and actinic skin damage) are highest in the Prairies.[25] Socioeconomic status is generally high in all the Canadian provinces from an international viewpoint, but Quebec has the largest proportion of inhabitants below a defined low income cutoff, while Ontario has the smallest proportion.[26,27] Education level is similarly uninformative in that postsecondary education is least common in Quebec and most common in British Columbia.[27] However, the value of the study results is that they can be used to stimulate novel hypothesis generation regarding environmental influences in MS.

The considerable environmental variation found across Canada, in conjunction with the availability of similar systems for acquiring and reporting environmental data, the relatively homogenous population distribution, and the universal availability of health care present a tremendous opportunity to evaluate environmental factors for their association with MS prevalence.

Acknowledgements and Support

References

1 Dyment DA, Ebers GC, Sadovnick AD. Genetics of multiple sclerosis. *Lancet Neurol* 2004; **3**: 104–10.

2 Coo H, Aronson KJ. A systematic review of several potential non-genetic risk factors for multiple sclerosis. *Neuroepidemiology* 2004; **23**: 1–12.

3 Pryse-Phillips WE. The incidence and prevalence of multiple sclerosis in Newfoundland and Labrador, 1960–1984. *Ann Neurol* 1986; **20**: 323–28.

4 Svenson LW, Woodhead SE, Platt GH. Regional variations in the prevalence rates of multiple sclerosis in the province of Alberta, Canada. *Neuroepidemiology* 1994; **13**: 8–13.

5 Patten SB, Beck CA, Williams JV, Barbui C, Metz LM. Major depression in multiple sclerosis: a population-based perspective. *Neurology* 2003; **61**: 1524–27.

6 Rosati G. The prevalence of multiple sclerosis in the world: an update. *Neurol Sci* 2001; **22**: 117–39.

7 Statistics Canada. Details of the Canadian Community Health Survey (CCHS) Cycle 1.1. Overview. Retrieved 21 February 2005, from http://www.statcan.ca/english/concepts/health/cchsinfo.htm. Modified 18 December 2003.

8 Statistics Canada. Canadian Community Health Survey (CCHS) Cycle 1.1. Public Use Microdata File Documentation. Ottawa, Canada: Statistics Canada, Health Statistics Division, 2002.

9 Statistics Canada. Canadian Community Health Survey (CCHS) Questionnaire for Cycle 1.1. Retrieved 21 February 2005, from http://www.statcan.ca/english/concepts/health/index.htm. Modified 18 December 2003.

10 Statistics Canada. Canadian Community Health Survey: validity of self reported chronic conditions. Electronic communication. 20 December 2004.

11 Martin LM, Leff M, Calonge N, Garrett C, Nelson DE. Validation of self-reported chronic conditions and health services in a managed care population. *Am J Prev Med* 2000; **18**: 215–18.

12 Kehoe R, Wu SY, Leske MC, Chylack LT Jr. Comparing self-reported and physician-reported medical history. *Am J Epidemiol* 1994; **139**: 813–18.

13 Simpson CF, Boyd CM, Carlson MC, Griswold ME, Guralnik JM, Fried LP. Agreement between self-report of disease diagnoses and medical record validation in disabled older women: factors that modify agreement. *J Am Geriatr Soc* 2004; **52**: 123–27.

14 Haapanen N, Miilunpalo S, Pasanen M, Oja P, Vuori I. Agreement between questionnaire data and medical records of chronic diseases in middle-aged and elderly Finnish men and women. *Am J Epidemiol* 1997; **145**: 762–69.

15 Metzger MH, Goldberg M, Chastang JF, Leclerc A, Zins M. Factors associated with self-reporting of chronic health problems in the French GAZEL cohort. *J Clin Epidemiol* 2002; **55**: 48–59.

16 Fan VS, Au D, Heagerty P, Deyo RA, McDonell MB, Fihn SD. Validation of case-mix measures derived from self-reports of diagnoses and health. *J Clin Epidemiol* 2002; **55**: 371–80.

17 Hastie T, Tibshirani R. Generalized additive models. Retrieved 21 February 2005, from http://www-stat.stanford.edu/software/gam/index.html. Modified 30 September 2004.

18 Hastie T, Tibshirani R. *Generalized additive models*. London: Chapman and Hall, 1990.

19 Svenson LW, Warren SA, Schopflocher DP, Metz LM. High incidence and prevalence of multiple sclerosis in Alberta, 1999–2001. Halifax, NS, Canada: Canadian Society for Epidemiology and Biostatistics, 2003.

20 Litt J, Tran N, Malecki KC, Neff R, Resnick B, Burke T. Identifying priority health conditions, environmental data, and infrastructure needs: a synopsis of the Pew Environmental Health tracking project. *Environ Health Perspect* 2004; **112**: 1414–18.

21 Statistics Canada. Canadian Health Measures Survey. Retrieved 21 February 2005, from http://www.statcan.ca/english/concepts/hs/measures.htm. Modified 19 March 2004.

22 Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey (NHANES); 1999–2004 Survey Content. Retrieved 21 February 2005, from http://www.cdc.gov/nchs/nhanes.htm. Modified 28 January 2005.

23 Marrie RA. Environmental risk factors in multiple sclerosis aetiology. *Lancet Neurol* 2004; **3**: 709–18.

24 Kurtzke JF, Page WF. Epidemiology of multiple sclerosis in US veterans: VII. Risk factors for MS. *Neurology* 1997; **48**: 204–13.

25 Government of Canada. Environment Canada. UV Index and Sun Protection! –All About Ozone Layer-Sunshine. Retrieved 21 February 2005, from http://www.msc-smc.ec.gc.ca/education/uvindex/about_uvradiation/sunshine_e.html. Modified 18 February 2002.

26 Statistics Canada. 1996 Census: Sources of income, earnings and total income, and family income. Retrieved 21 February 2005, from http://www.statcan.ca/Daily/English/980512/d980512.htm. Modified 12 May 1998.

27 Statistics Canada. Census of Canada 1996, Individual Public Use Microdata File. Catalogue No. 95M0013XCB. Ottawa, Canada, 1999.