Prevalence of Multiple Sclerosis in Canada: A Systematic Review

Alexandre Y. Poppe, Christina Wolfson, Bin Zhu

ABSTRACT: Background: Studies of the prevalence of multiple sclerosis (MS) in Canada have generally been isolated to specific regions. Given the importance of multiple sclerosis as a cause of disability in adults, a comprehensive review of Canadian MS prevalence examining current data, interregional variation, deficiencies in knowledge and frontiers for research is timely. Methods: A systematic review of all studies addressing the prevalence of MS in Canada or regions within Canada, published in English or French since 1985, was conducted. Studies were identified using MEDLINE, EMBASE and bibliographic review. Studies were evaluated for methodological rigour and a test of heterogeneity across studies was performed and a measure of consistency (I²) estimated. Results: Studies were generally of high quality. Nine were restricted to regions within Canada and one provided an estimated national prevalence based on self-reported cases. All reported a high prevalence (>50 per 100,000). Latitude and longitude gradients were not striking while assessment of heterogeneity confirmed that regional differences were unlikely to be the result of sampling variability. Conclusions: This review confirms Canada as a country of very high MS prevalence and it is the first study to demonstrate that variation in regional estimates represents true differences in prevalence within Canada. Avenues for future MS prevalence research, including adoption of a national MS registry, are proposed.

Multiple sclerosis (MS) is a chronic illness affecting the central nervous system. Through an inflammatory autoimmune process, there is injury to both myelin and axons resulting in myriad clinical features, including motor weakness, sensory disturbances, visual loss, gait ataxia, sphincter dysfunction and cognitive changes. While the etiology of multiple sclerosis remains unknown, current evidence suggests an interplay between environmental and genetic factors. Epidemiological studies of MS have demonstrated geographic and demographic variability in both prevalence and incidence. These results have in turn contributed to hypothesis generation with regard to MS etiology.

The existing literature suggests that Canada is an area of high MS prevalence. Canada is a vast nation comprised of ten provinces and three territories and lies at latitude 60N and longitude 95W. It has a population of 32,805,041, of which 70% is between 15 and 64 years of age. Two-thirds of the population is concentrated in urban centres and, while ethnically diverse in

Identification of Studies

This systematic review was designed in accordance with the Meta-analysis of Observational Studies in Epidemiology recommendations. Search terms of the medical literature (1965-October 2015) were conducted using MEDLINE with the broad subject headings “multiple sclerosis” and “Canada”, the latter as an exploded term. The search was conducted for articles written in French or English. A total of 228 references were found. Because single-database searching may have limited yield, the same search was conducted using EMBASE, but this provided no additional references. Titles were reviewed, potentially relevant articles were retained and full text obtained. The bibliographies of these articles were then hand searched for additional references. A total of 21 studies were found, four through bibliographic review and two through one author’s own files (CW). Six studies were published before 1985 and excluded. Of the remaining 15 studies, one was available only as an abstract, two as posters and one as a presentation; these were not included in the formal review. In one case, data were published twice, once as a paper and once as a poster and only the paper was included. Finally, one targeted an ethnic subpopulation and was excluded. This process yielded nine papers for inclusion in our systematic review (Figure 1).

The same search strategy was repeated using MEDLINE for the period from November 2005 to September 2007 to identify any additional relevant studies published during that period. This search yielded 24 results. A review of titles and abstracts confirmed two potentially relevant papers. One included data from a study available only as a presentation prior to November 2005. As it was devoted to a special subpopulation, this study was not included. The second study was included, bringing the total number of studies to ten (Table 1).

Table 1: Studies included in systematic review

<table>
<thead>
<tr>
<th>Reference</th>
<th>No.</th>
<th>Reference</th>
</tr>
</thead>
</table>
Inclusion Criteria

Inclusion criteria were broad and encompassed any study that reported primary data on MS prevalence in Canada, or regions therein, published in French or English between January 1985 and September 2007. All studies meeting inclusion criteria were published in English. We found two studies from the same group examining MS prevalence in the same territory (Newfoundland and Labrador) at different time points. Both studies were included for analysis.

Exclusion Criteria

We excluded genetic epidemiological studies looking at prevalence of MS in family members of affected probands. Studies devoted to special subpopulations (such as First Nations or the Hutterites) were excluded. Economic burden and mortality studies were also excluded as were data presented only in posters, abstracts, letters or presentations.

Data Extraction

Once accepted for inclusion, studies were assessed using a quality assessment tool designed for studies of prevalence and relevant information was extracted using a data abstraction grid. Quality assessment parameters included proper definition of study population characteristics, method of case ascertainment (i.e. chart review, patient examination), reproducibility of case definition, clear statement of prevalence dates and description of statistical analyses used to derive prevalence figures. Check boxes permitted differentiation between “Very Good”, “Good” and “Poor” for each quality assessment parameter. “Very Good” was used when the parameter was addressed completely, “Good” when it was addressed but incompletely, and “Poor” when it was not addressed at all. Whichever descriptor was applied most often to a particular study determined the overall quality rating for that study. Two authors (AYP, CW) reviewed the studies independently and when necessary, disagreements were resolved by consensus.

Data abstraction included information about the study (authors, year of publication, region studied), information about study methods (study population, case definition, case ascertainment) and study results (crude prevalence rates, age- and sex-specific prevalence and other relevant results).

Data Analyses

Extracted data concerning study methodology and results were tabulated (Table 2). Several studies examined both prevalence and incidence of MS but given the aim of this review, only prevalence values were extracted. All studies provided prevalence as number of cases per 100,000 population and all but two provided confidence intervals. Age- and sex-standardization were not reported in all studies.

A test for heterogeneity across studies was conducted to test the null hypothesis that all studies are estimating the same parameter. Rejecting this null hypothesis would support the notion that there is in fact true variation in MS prevalence between the study populations not due to sampling error. Higgins et al provide a measure of consistency across studies that is derived from the $Q$ statistic and is not dependent on the number of studies included for comparison. This measure, $P$, is calculated as $P = 100\% * (Q - df)/Q$, where $df$ = degrees of freedom = number of studies - 1. The value is expressed as a value between 0 and 100\%, where 0 indicates no heterogeneity and increasingly larger values suggest increasing heterogeneity.

Generally, an $P$ of less than 25\% indicates low heterogeneity, 25\% to 50\%, moderate heterogeneity and over 50\%, high heterogeneity.

Given that the data are derived from different populations at different time points, pooling of these data may mask regional and temporal differences. A high degree of inconsistency across studies further argues against statistical pooling of results.

RESULTS

Study characteristics

Ten studies met inclusion criteria (Table 1). Publication dates ranged from 1986 to 2007 and all studies were considered of “Good” or “Very Good” quality. Four studies examined provincial MS prevalence, five examined prevalence within smaller geopolitical regions (cities or counties) and one examined national prevalence and prevalence within larger subdivisions of Canada. Of the provincial and regional studies, four were from Alberta, two from Newfoundland and Labrador, one from Saskatchewan, one from Ontario and one from British Columbia (Figure 2). The number of identified cases ranged from 7 to 5,548 (median = 274.5) and population denominators ranged from 6,912 to 2,791,398 (median = 742,592). It is likely that the same cases may have been “double counted” in separate studies of the same region. All studies estimated point-prevalence although two did not provide an exact prevalence date.

Cases were ascertained in a similar manner in all but two studies, that is, through MS registries, MS clinic charts, neurologists’ files, hospital admissions, MS society documents, mailing lists and other physicians. Patients were examined by a neurologist-investigator in only three of the ten studies. These methods are generally supported by a recent study on the thoroughness of MS case ascertainment in small communities. Intercase reliability for the diagnosis of MS was not reported, but agreement on such a diagnosis among neurologists is presumably high given defined diagnostic criteria. Comparisons of Poser and 2001 MacDonald criteria have suggested similar rates of MS diagnosis. One of the studies used billing data from the Alberta Health Care Insurance Plan (AHCIP) (ICD-9 code 340). The national study was based on self-report of an MS diagnosis among respondents to the Canadian Community Health Survey (CCHS).

The studies in this review span 20 years and earlier studies predate the routine inclusion of MRI criteria in the diagnosis of MS. Of those eight studies not relying on billing data or self-report, the two oldest studies utilized Schumacher criteria and two used modified Schumacher criteria (no age criterion). Three used Poser criteria (1983) and one used a combination of these, including the more recent MRI-based McDonald criteria.

Volume 35, No. 5 – November 2008

LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES
### Table 2: Prevalence of MS from studies included in systematic review

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Area</th>
<th>Methodology</th>
<th>Prevalence (MS group members, add)</th>
<th>Schumacher</th>
<th>Modified</th>
<th>Figures</th>
<th>Poser</th>
<th>Figures</th>
<th>Figures</th>
<th>Figures</th>
<th>Figures</th>
<th>Regional (%)</th>
<th>N/A</th>
<th>Regional (%)</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pryse-Phillips</td>
<td>1988</td>
<td>Newfoundland &amp; Labrador</td>
<td>Self-references (MS group members, add)</td>
<td>250</td>
<td>262,679</td>
<td>55.2</td>
<td>N/A</td>
<td>88.0</td>
<td>77-100</td>
<td>64-111</td>
<td>N/A</td>
<td>N/A</td>
<td>BC: 16.487 (14.2)</td>
<td>240</td>
<td>BC: 240 (160-320)</td>
<td>240</td>
</tr>
<tr>
<td>Hader*</td>
<td>1988</td>
<td>London</td>
<td>London MS clinic, Admission records</td>
<td>54</td>
<td>63,895</td>
<td>2.2:1</td>
<td>85.0</td>
<td>118-305</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Hader*</td>
<td>1988</td>
<td>Middlesex County</td>
<td>London MS clinic, Admission records</td>
<td>229</td>
<td>260,050</td>
<td>2.3:1</td>
<td>88.0</td>
<td>77-100</td>
<td>64-111</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Warren (9)</td>
<td>1992</td>
<td>Barrow County, Alberta</td>
<td>MS clinic, County medical society numbers</td>
<td>19</td>
<td>9,720</td>
<td>1:1</td>
<td>196.0</td>
<td>118-305</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Warren (12)</td>
<td>1993</td>
<td>Westlock County, Alberta</td>
<td>MS clinic, County medical society numbers</td>
<td>23</td>
<td>11,510</td>
<td>1.4:1</td>
<td>200.0</td>
<td>127-300</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Klein (11)</td>
<td>1994</td>
<td>Crowsnest, Alberta</td>
<td>MS clinic, Area CIs</td>
<td>15</td>
<td>6,912</td>
<td>2:1</td>
<td>217.0</td>
<td>121.5-356</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Klein (11)</td>
<td>1994</td>
<td>Cardston, Alberta</td>
<td>MS clinic, Area CIs</td>
<td>N/A</td>
<td>2,560,000</td>
<td>2.03:1</td>
<td>216.7</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Sverson (14)</td>
<td>1994</td>
<td>Alberta</td>
<td>AHCP records, ICD-9 code 340</td>
<td>N/A</td>
<td>5548</td>
<td>2.5:1</td>
<td>94.4</td>
<td>90.2-98.7</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Niake (5)</td>
<td>2005</td>
<td>Newfoundland &amp; Labrador</td>
<td>B/9 neurologist files, MS clinic</td>
<td>493</td>
<td>521,286</td>
<td>2.69:1</td>
<td>94.4</td>
<td>90.2-98.7</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Hader (15)</td>
<td>2007</td>
<td>Saskatoon, Saskatchewan</td>
<td>MS registry established in 1999 from Nursing homes, Home Care Program, MS Society, Saskatoon, MS Rehab Clinic, family physicians, neurologists and provincial records, Surveys repeated in 1996, 2006 and 2009. Admission and emergency records from 2001 to 2005 from 3 local hospitals.</td>
<td>587</td>
<td>196,815</td>
<td>2.4:1</td>
<td>298.3</td>
<td>274.7-323.9</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

* and § signify studies in which data for distinct regions were included in the same publication; V Figure not given in original paper (derived from Klein et al. 1994); V Figure not provided in original paper (derived from 1986 Alberta Census); £ Prevalence figures from this study are not crude prevalence estimates; MD=doctor of medicine; GP=general practitioner; LTC=long-term care; AHCP=Alberta Health Care Insurance Plan; ICD=International Classification of Diseases.
Results by region

British Columbia

British Columbia (BC) is Canada’s westernmost and third most populated province. Central latitude and longitude are 55N, 125W and the population is primarily concentrated in Vancouver and its surrounding areas. One study found a crude prevalence of MS in BC of 93.3 per 100 000 on prevalence day July 1, 1982. When adjusted to the Canadian population, the prevalence was 91 per 100 000. A total of 2596 cases were found but no denominator (i.e. population of BC) or confidence interval was provided in the original paper. However, in a subsequent study, Klein et al. calculated the confidence interval to be 89.42 to 96.58 per 100 000 assuming a population of 2.97 million, a prevalence of 386 per 100 000 for males. This study used Schumacher criteria to classify cases as definite/probable MS and relied on neurologist chart reviews, communication with other physicians, long-term care facilities and self-referrals to identify cases.

The results were standardized to the population of Alberta from the 1986 census yielding a figure of 200 per 100 000 (95% CI: 127-300).

The study by Beck et al also provides estimates for BC, suggesting a much higher prevalence of 240 per 100 000 (95% CI 160 – 320). This study used data from a national population health survey (CCHS) conducted by telephone. Identification of cases was based on self-report in answer to the question “We are interested in long-term conditions that have…been diagnosed by a health professional. Do you have multiple sclerosis?” Diagnoses were not confirmed through chart review, physician contact or patient encounter. Because of small samples in the territories, only respondents living in one of the ten provinces were included in the analysis. A total of 116 109 respondents out of 131 535 were over 17 years-old and responded to the survey question pertaining to MS, making them eligible for analysis of MS prevalence.

Alberta

Alberta is the province for which there exist the most data regarding MS prevalence. In fact, four of the ten studies reviewed pertain to this westernmost Prairie province whose central geographical coordinates are 55N, 115W. The population is clustered primarily in two urban centres, Calgary and Edmonton, although there is also significant rural and aboriginal representation.

A study in Barrhead County, a rural area northwest of Edmonton, found a prevalence of 196 per 100 000 (95% CI: 118-305) in 1990. The authors of this study also examined MS prevalence in 1991 in a neighbouring region, Westlock County. The results were standardized to the population of Alberta from 1986 census yielding a figure of 200 per 100 000 (95% CI: 127-300).

The Crownsnest Pass region and Cardston and southern Alberta were studied in 1989 using MS society lists and patient files from general practitioners for case ascertainment. Modified Schumacher criteria were used and a prevalence of 217 per 100 000 (95% CI: 121.5-358) was found for Crownsnest and 88 per 100 000 (95% CI: 36-182) was found for Cardston.

Saskatchewan

Saskatchewan comprises the central Canadian Prairies and includes the major cities of Regina, Saskatoon and Prince Albert. It has a population of 1.07 million and its capital city is Regina. Only two studies of MS prevalence in Saskatchewan have been conducted, the study by Beck et al and a later study by W.L. Johns et al. (Beck et al study further examined MS prevalence in Alberta and used AHCIP data to confirm the validity of the CCHS results). Within the AHCIP, cases were identified if patients had been assigned a diagnostic code for MS twice between 1991 and 2001. Using this method and a total population of 2.97 million, a prevalence of 386 per 100 000 (95% CI: 377-394) was found.

Saskatchewan

Three MS prevalence studies in Saskatoon (52° 10' N, 106W), this province’s largest city, have been published. The
cases in London. Higher prevalence was noted among women, and the contribution of such studies to estimates of "background" MS prevalence has been questioned and the existence of genuine MS clusters or epidemics has been questioned and the absence of better case ascertainment has been questioned and the existence of such studies to estimates of "background" MS prevalence in the population is likely limited. 1

Ontario

Ontario is Canada's most populated province with central coordinates 50N and 86W. The population is primarily urban and concentrated in a corridor extending from Windsor to Kingston. Two studies published prior to 1985 were not included in our review: a survey of MS patients in Kingston in 1959 and in Ottawa in 1977. 2,27 Only one study has been published since 1985 examining MS prevalence in the region. 3 This study examined both prevalence and incidence of MS in London and nearby rural Middlesex County, both in southwestern Ontario. Case identification included using MS clinic records as well as review of local hospital admissions, long-term care facilities, home care programs and MS Society membership lists. Identified patients were examined by the authors. Crude prevalence for definite MS was 88 per 100 000 (95% CI: 77-100) for London and 85 per 100 000 (95% CI: 64-111) for Middlesex County. When adjusted to the 1981 Canadian population, a prevalence of 90 per 100 000 was found, making it the region with the lowest MS prevalence in Canada using that methodology.

Atlantic Provinces

The Atlantic provinces on Canada’s eastern coast include Newfoundland and Labrador, as well as New Brunswick, Nova Scotia and Prince Edward Island. Overall, these provinces are less populated than central and western Canada and are composed primarily of people of British, Irish and Scottish ancestry with both a rural and urban distribution. Other ethnic groups, including Acadians and Natives also contribute to the local demography.

Newfoundland and Labrador

The island of Newfoundland lies between latitudes 46 and 52N and longitudes 52 and 59W and Labrador is situated between 52 and 61N and 56 and 67W. The island of Newfoundland the population is primarily clustered near St. John’s and in large part, inhabitants are of southern English and Irish descent.

Two studies conducted by the same group examined MS prevalence in the island from that found in those studies specifically examining Nova Scotia and Newfoundland and Labrador.

Newfoundland and Labrador

Two studies conducted by the same group examined MS prevalence in the island from that found in those studies specifically examining Nova Scotia and Newfoundland and Labrador.

The 2001 study sought to update the previous data and took advantage of billing data using diagnostic codes, files from the only MS clinic in the province and three previously compiled databases to achieve more thorough case ascertainment. 5 A total of 493 cases were found on prevalence day (December 31st, 2001) using Poser criteria, giving a crude prevalence of 94.4 per 100 000 (95% CI: 90.2-98.7).

Other Atlantic Provinces

Other than Newfoundland and Labrador only Nova Scotia has been studied with regards to MS prevalence. One study focusing on Nova Scotia's capital, Halifax, was published in 1960 and excluded from this review. 3 A more recent study was also excluded because data were published only as a poster. 4 In this study, provincial prevalence in 2001 was ascertained using records from the only MS clinic in the province in conjunction with family physicians, neurologists and provincial records. Medical records for admissions and emergency department visits between 2001 and 2005 were also screened. Uniform diagnostic criteria were not applied to all patients since different criteria have been used over time in admitting patients to the MS registry. On prevalence day, 598 living cases were identified. With a city population of 196 815, a crude prevalence figure of 298.3 per 100 000 (95% CI: 274.7 to 323.6) was calculated. A female to male ratio of 2.4:1 was found and when age- and sex-adjusted to the 1981 Canadian population, the prevalence was 329 per 100 000. The authors similarly standardized their results to the world 2000 population (240.4 per 100 000), as has been suggested by others. 37 Such standardized figures allow for more meaningful comparisons between regional prevalence studies than do crude prevalence values.

Quebec

Quebec has central coordinates 52N and 73W, and despite being Canada's second-most populous province, there is surprisingly little data regarding the prevalence of MS in this region. In fact, no prevalence studies isolated to Quebec as a whole or Quebec communities were identified in our literature search. Quebec's population resides primarily in the southwestern region between Montreal and Quebec City and is also ethnically different in that the majority of its inhabitants are of French ancestry. The only provincial prevalence information available comes from the CCHS study in which a prevalence of 180 per 100 000 (95% CI: 90-260) was found, making it the region with the lowest MS prevalence in Canada using that methodology.

The most recent study estimated MS prevalence on January 1st, 2005. 15 The authors ascertained cases using an MS registry started in 1969 as well as information from nursing homes, home care programs, the MS Society of Saskatchewan, family physicians, neurologists and provincial records. Medical records for admissions and emergency department visits between 2001 and 2005 were also screened. Uniform diagnostic criteria were not applied to all patients since different criteria have been used over time in admitting patients to the MS registry. On prevalence day, 587 living cases were identified. With a city population of 196 815, a crude prevalence figure of 298.3 per 100 000 (95% CI: 274.7 to 323.6) was calculated. A female to male ratio of 2.4:1 was found and when age- and sex-adjusted to the 1981 Canadian population, the prevalence was 329 per 100 000. The authors similarly standardized their results to the world 2000 population (240.4 per 100 000), as has been suggested by others. 37 Such standardized figures allow for more meaningful comparisons between regional prevalence studies than do crude prevalence values.

Claims of a cluster-focus of MS in the hamlet of Henribourg, Saskatchewan due to a postulated common environmental exposure have also been extensively studied. 38 The existence of genuine MS clusters or epidemics has been questioned and the absence of better case ascertainment has been questioned and the existence of such studies to estimates of "background" MS prevalence in the population is likely limited. 1

Ontario

Ontario is Canada's most populated province with central coordinates 50N and 86W. The population is primarily urban and concentrated in a corridor extending from Windsor to Kingston. Two studies published prior to 1985 were not included in our review: a survey of MS patients in Kingston in 1959 and in Ottawa in 1977. 2,27 Only one study has been published since 1985 examining MS prevalence in the region. 3 This study examined both prevalence and incidence of MS in London and nearby rural Middlesex County, both in southwestern Ontario. Case identification included using MS clinic records as well as review of local hospital admissions, long-term care facilities, home care programs and MS Society membership lists. Identified patients were examined by the authors. Crude prevalence for definite MS was 88 per 100 000 (95% CI: 77-100) for London and 85 per 100 000 (95% CI: 64-111) for Middlesex County. When adjusted to the 1981 Canadian population, a prevalence of 90 per 100 000 was found, making it the region with the lowest MS prevalence in Canada using that methodology.

The 2001 study sought to update the previous data and took advantage of billing data using diagnostic codes, files from the only MS clinic in the province and three previously compiled databases to achieve more thorough case ascertainment. 5 A total of 493 cases were found on prevalence day (December 31st, 2001) using Poser criteria, giving a crude prevalence of 94.4 per 100 000 (95% CI: 90.2-98.7).

Other Atlantic Provinces

Other than Newfoundland and Labrador only Nova Scotia has been studied with regards to MS prevalence. One study focusing on Nova Scotia's capital, Halifax, was published in 1960 and excluded from this review. 3 A more recent study was also excluded because data were published only as a poster. 4 In this study, provincial prevalence in 2001 was ascertained using records from the only MS clinic in the province in conjunction
with government administrative databases. The authors suggest that the best estimate is likely in the range of 200 to 218 per 100,000.

Canada

No single study examined national MS prevalence before the Beck et al study. In this study, 332 respondents reported a diagnosis of MS among the 116,109 eligible to participate. This produced a national prevalence of 240 per 100,000 (95% CI: 210-280) and this has engendered an upward revision of traditional national MS prevalence figures forwarded in years past.

Prevalence studies have often been compromised by small sample sizes and therefore large, overlapping confidence intervals that raise the possibility of there being no true regional differences within the country (Figure 3). Determining whether finding a single national prevalence for MS is meaningful rests in large part on whether interregional differences are real. If so, then a single national prevalence estimate may in fact underestimate the burden of disease in some Canadian territories, while overestimating it in others.

In addition, although a latitude gradient of MS prevalence has been found in other parts of the world, including the USA, Australia and Italy, none could be demonstrated within Canada (Table 3). Presumably, this is because the large majority of the Canadian population lives within a relatively narrow latitude corridor in the southern part of the country.

Heterogeneity among studies

For the computation of $P$ to examine variability, two studies were excluded due to major differences in methodology.\textsuperscript{15,16} Also, the earlier Newfoundland and Labrador study\textsuperscript{6} was excluded from the analysis given that more recent data for that province likely better reflect true MS prevalence. In two other studies, separate data were provided for neighbouring regions and these were considered as distinct data sets in our analysis.\textsuperscript{4,11}

Therefore, nine sets of data were included in the analysis and a high degree of heterogeneity ($P^2=98.86$) was found with a very large Q statistic: $Q=703.30$, df=8, p<0.0001. Studies published more recently generally yielded higher prevalence estimates.

DISCUSSION

Several regional studies of MS prevalence have been conducted and suggest wide variation within the country. Our review suggests a range from a low of 55.2 per 100,000 in Newfoundland and Labrador to a high of 350 per 100,000 (95% CI: 230-470) in the Atlantic provinces.\textsuperscript{5,13} Of course, the Newfoundland study has since been repeated and yielded a higher prevalence while the methodology of the CCHS study which has suggested by far the highest prevalence figures to date, differs immensely from the other publications included for review. The $P$ value obtained confirms that the different prevalence estimates in the studies likely constitute true differences. This lends strong credence to the assertion that arriving at a single point estimate of national prevalence is a difficult and possibly misleading enterprise.

It is clear that more recent studies are producing higher prevalence figures than older ones. One might speculate that this reflects an increased incidence of disease, although other explanations are also plausible. In particular, improved case ascertainment via better access to neurologists and diagnostic tests likely explain the increased prevalence found in more recent studies as it did in the later Newfoundland study. Improved medical care leading to longer life spans among MS patients may also account for this apparent increase in prevalence. Analysis of sex ratios of MS by year of birth in a longitudinal population based dataset of over 29,000 Canadian MS patients (Canadian Collaborative Project on Genetic Susceptibility to Multiple Sclerosis) suggests an increasing ratio of female to male cases.\textsuperscript{18-20} This might imply an increasing disease incidence over the last 50 years, particularly in women, the cause of which may be environmental.

Most prevalence studies reviewed here reported a female to male ratio of approximately 2:1, from a low of 1:1 in Barrhead County, Alberta to a high of 2.69:1 in Newfoundland and Labrador. This suggests a higher female to male ratio than the general population and adds weight to the assertion that females are particularly at risk in those provinces with the highest prevalence.


table: Canadian regional MS prevalence estimates from included studies, by latitude and longitude

<table>
<thead>
<tr>
<th>Location</th>
<th>Latitude</th>
<th>Longitude</th>
<th>Prevalence per 100,000 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labrador</td>
<td>-77°59'</td>
<td>-56°59'</td>
<td>211 (182-240)</td>
</tr>
<tr>
<td>Newfoundland</td>
<td>-50°10'</td>
<td>-66°29'</td>
<td>240 (160-320)</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>-50°41'</td>
<td>-66°56'</td>
<td>217 (121-358)</td>
</tr>
<tr>
<td>Prince Edward Island</td>
<td>-46°57'</td>
<td>-64°39'</td>
<td>88 (77-100)</td>
</tr>
<tr>
<td>Nova Scotia</td>
<td>-51°15'</td>
<td>-66°29'</td>
<td>180 (90-260)</td>
</tr>
<tr>
<td>New Brunswick</td>
<td>-52°47'</td>
<td>-67°12'</td>
<td>200 (127-300)</td>
</tr>
<tr>
<td>Newfoundland</td>
<td>-51°15'</td>
<td>-66°56'</td>
<td>55 (29-94)</td>
</tr>
<tr>
<td>Prince Edward Island</td>
<td>-49°35'</td>
<td>-63°41'</td>
<td>52 (45-60)</td>
</tr>
</tbody>
</table>

Estimated geographical centre of territory: *geographical coordinates not provided in paper.
current knowledge of MS prevalence in Canada and confirms that this country has a national prevalence among the highest in the world of at least 100 per 100 000, and likely much higher. It also confirms that the regional variation in prevalence suggested in previous studies is genuine. Perhaps most importantly, it makes evident the gaps in knowledge that still exist concerning Canadian MS epidemiology. Future studies of MS prevalence should use more uniform case definition and ascertainment methods and provide prevalence values standardized to the Canadian population (by age and sex) to facilitate comparisons between regional studies. In addition, values standardized to the world population would help with comparisons between national studies, as has been advocated by others.29-34 Canada serves as an ideal territory for the study of MS epidemiology given the high prevalence of disease, regional variation, the presence of a well-established community of MS researchers and publicly-funded, universally accessible healthcare establishment. A national MS registry, as has been done in Norway, would further strengthen such research efforts.35

REFERENCES
Volume 35, No. 5 – November 2008

601

LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES


