

Prevalence of Systemic Lupus Erythematosus and Systemic Sclerosis in the First Nations Population of Alberta, Canada

CHERYL BARNABE,¹ LAWRENCE JOSEPH,² PATRICK BELISLE,² JEREMY LABRECQUE,²
STEVEN EDWORTHY,¹ SUSAN G. BARR,¹ MARVIN FRITZLER,¹ LAWRENCE W. SVENSON,³
BRENDA HEMMELGARN,¹ AND SASHA BERNATSKY²

Objective. To estimate the population-based prevalence of systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) in Alberta, Canada, stratified by First Nations status.

Methods. Physician billing claims and hospitalization data for the province of Alberta (1994–2007) were used to ascertain cases of SLE and SSc using 3 case definitions. A latent class Bayesian hierarchical regression model was employed to account for the imperfect sensitivity and specificity of billing and hospitalization data in case ascertainment. We accounted for demographic factors, estimating prevalence rates for the First Nations and non-First Nations populations by sex, age group, and location of residence (urban/rural).

Results. Our model estimated the prevalence of SLE in Alberta to be 27.3 cases per 10,000 females (95% credible interval [95% CrI] 25.9–28.8) and 3.2 cases per 10,000 males (95% CrI 2.6–3.8). The overall prevalence of SSc in Alberta was 5.8 cases per 10,000 females (95% CrI 5.1–6.5) and 1.0 case per 10,000 males (95% CrI 0.7–1.4). First Nations females over 45 years of age had twice the prevalence of either SLE or SSc relative to non-First Nations females. There was also a trend toward higher overall SLE prevalence in urban dwellers, and higher overall SSc prevalence in rural residents.

Conclusion. First Nations females older than 45 years of age have an increased prevalence of either SLE or SSc. This may reflect a true predominance of autoimmune rheumatic diseases in this demographic, or may indicate systematic differences in health care delivery.

INTRODUCTION

The health status of First Nations people in Canada is greatly affected by chronic rheumatic disease, with approximately 1 in every 4 individuals reporting a diagnosis

of arthritis or rheumatism (1). Although increased rates of rheumatoid arthritis in First Nations populations relative to the general population have been documented in cohort studies (2–5), less is known about rates of systemic autoimmune rheumatic diseases (SARDs), including systemic lupus erythematosus (SLE), systemic sclerosis (SSc), Sjögren's syndrome, and idiopathic inflammatory myopathies. Increased prevalence of SLE in First Nations populations relative to the general population has been identified in Canadian populations in one region in Alberta (6), one region in British Columbia (7), and in Manitoba (8), as well as in Alaskan Indian populations (9), and in the Crow, Arapahoe, and Sioux Nations in the US (10). Data on SSc prevalence are very limited and dated (7,11).

There are multiple steps involved in diagnosing SARD in individuals, including symptoms and signs presented to health care professionals, suspicion and/or recognition of

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¹Cheryl Barnabe, MD, FRCPC, Steven Edworthy, MD, FRCPC, Susan G. Barr, MD, MSc, FRCPC, Marvin Fritzler, PhD, MD, FRCPC, Brenda Hemmelgarn, MD, PhD, FRCPC: University of Calgary, Calgary, Alberta, Canada; ²Lawrence Joseph, PhD, Patrick Belisle, MSc, Jeremy Labrecque, MSc, Sasha Bernatsky, MD, PhD, FRCPC: McGill University, Montreal, Quebec, Canada; ³Lawrence W. Svenson, MSc: University of Calgary, Calgary, and Alberta Health and Wellness and University of Alberta, Edmonton, Alberta, Canada.

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Address correspondence to Cheryl Barnabe, MD, FRCPC, 3330 Hospital Drive NW, Calgary, Alberta T2N 4N1, Canada. E-mail: ccbarnab@ucalgary.ca.

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Significance & Innovations

- We provide population-based estimates of systemic lupus erythematosus and systemic sclerosis prevalence rates in a North American jurisdiction.
- First Nations females have twice the prevalence of systemic lupus erythematosus and systemic sclerosis relative to non-First Nations females (>45 years of age).
- Prevalence rates vary by demographic factors of race, sex, age, and location of residence.

a possible SARD by the health care provider, referral to a tertiary care specialist such as a rheumatologist, and, as is sometimes necessary, a period of observation to confirm a diagnosis. Demographic factors, such as an individual's age, sex, socioeconomic status, level of education, and location of residence, may therefore affect their propensity to be diagnosed with a SARD, as these factors influence symptom recognition, presentation to health care providers, and ongoing followup. The influence of demographic factors on SARD prevalence has been previously demonstrated (12–15). The effect of demographic factors on disease diagnosis and thus prevalence may be particularly amplified in the First Nations population, where differential access to health services has been documented for care in general (16,17), nephrology services (18), and rheumatologist care (3).

The prevalence of SLE and SSc among status First Nations peoples in Alberta, Canada, is unknown, and is ideally suited for study for 2 reasons. First, administrative data sets maintained by Alberta Health and Wellness allow identification of persons of First Nations status, validated on a case-by-case basis, which is not a universal feature of other health care databases across Canadian provinces or territories. Second, the Alberta Aboriginal population is rich in diversity with numerous Tribal Nations represented, including Blackfoot, Chipewyan, Cree, Dene, Sarcee, Saulteaux, and Sioux. Prevalence estimates from Alberta would therefore provide an overall view of the SLE and SSc landscape among First Nations populations in Canada.

The objective of our study was to calculate a population-based prevalence estimate for SLE and SSc in Alberta, stratified by First Nations status, using physician billing claims and hospitalization data. Individuals with the diseases of interest may be identified in neither, one, or both data sources, and may have a variable number of encounters for their condition. There is no reference gold standard to verify the true disease status. Therefore, rather than simply applying a diagnostic code algorithm to the raw data to identify prevalent cases, we employed a latent class Bayesian hierarchical regression model to estimate the probability of each individual having the condition of interest, based on the information at hand. Additionally, this model considers the expected underlying disease prevalence in the population of interest, the imperfect sensitivity and specificity of coding, and possible statisti-

cal dependence between ascertainment methods. We specifically stratified our results to account for the effects of demographic factors that may affect prevalence estimates, namely an individual's age, sex, and location of residence (rural versus urban).

MATERIALS AND METHODS

Data source. Alberta Health and Wellness maintains administrative databases for the Alberta Health Care Insurance Plan (AHCIP) registry, physician billing claims, and hospitalizations, covering approximately 3.7 million Alberta residents. The number of individuals registered with AHCIP only differs from census data by 0.1% (19). Approximately 6% of the Alberta population is of First Nations ancestry by census data (1), with 3.7% of the 2007 Alberta population having treaty status according to AHCIP (as defined below).

Study period. We ascertained cases of either SLE or SSc over a 14-year period (1994–2007). The numerator for the prevalence estimate for the year 2007 was based on cases defined over the entire 14-year study period but who were still registered with the AHCIP at any time that year, with the denominator being the midyear provincial population registered with the AHCIP.

Case definition. Physician billing claims in Alberta are coded according to the Ninth International Classification of Diseases, Clinical Modification (ICD-9-CM) system. We identified ICD-9-CM codes for SLE (710.0) or SSc (710.1). ICD-9-CM codes were also used for hospitalization data prior to April 2002, following which the International Classification of Diseases, Tenth Revision, Canadian Adaptation was instituted. Therefore, for hospitalization data prior to April 2002, we identified any hospital separations with codes 710.0 or 710.1 in any diagnosis position (up to 16 fields), and after April 2002, codes M32 (for SLE) and M34 (for SSc) in any diagnosis position (up to 25 fields). Three definitions were used to estimate the probability of an individual having either SLE or SSc, based on ≥ 1 billing code by a rheumatologist, ≥ 2 billing codes by any physician (≥ 8 weeks apart but within 2 years), or 1 hospitalization diagnosis.

Dependent variables. The Alberta Health and Wellness AHCIP file was used to determine patient sex, age (dichotomized as less than or greater than 45 years old), location of residence by postal code (rural or urban defined on census metropolitan area classifications) (20), and First Nations status. To determine First Nations status, we used validated methodology developed by Alberta Health and Wellness for health services research and adopted by the Alberta research community (18,21–23). In summary, First Nations and Inuit Health (FNIH) is responsible for the health care of First Nations people with treaty status, that is, individuals registered with the Government of Canada's Department of Indian and Northern Affairs. FNIH subsequently pays the AHCIP premiums for all individuals with

Table 1. Systemic lupus erythematosus prevalence estimates for First Nations and non-First Nations populations in Alberta, per 10,000 people*

	Females		Males	
	First Nations	Non-First Nations	First Nations	Non-First Nations
<45 years old				
Rural dwellers	14.6 (10.6–19.7)	12.1 (10.5–13.9)	1.9 (0.8–3.7)	0.9 (0.5–1.5)
Urban dwellers	21.6 (14.8–31.1)	15.5 (14.1–16.9)	2.6 (1–5.4)	1.3 (0.9–1.8)
>45 years old				
Rural dwellers	89.7 (63.2–129.5)	44.3 (40.0–49.3)	6.6 (2.5–13.9)	7 (5.4–8.9)
Urban dwellers	105.3 (70.6–152.9)	50.6 (46.9–54.7)	10.5 (4.0–25.0)	6.5 (5.2–8.1)
Estimated cases, no.	407	8,892	41	1,050

* Values are the prevalence estimate (95% credible interval) unless otherwise indicated.

treaty status in the province of Alberta, and this payment history is available in the registry file. Thus, individuals identified to have premiums paid by FNIH at any time since 1994 were considered to be First Nations individuals. All other people were classified as non-First Nations individuals.

Statistical analysis. To account for the imperfect sensitivity and specificity of billing and hospitalization data in case ascertainment, as well as the influence of demographic factors on prevalence, we used the latent class hierarchical regression model (12,14) that has been developed based on a Bayesian approach (24). Latent class models are applicable in instances where there is no gold standard for determining cases, such as in administrative data sets. This method incorporates information from multiple case definitions that each provide information on a patient's probability of having the disease in question. Our models therefore combine divergent results from multiple case definitions and also account for possible correlation between the case definitions relying on physician billing claims (rheumatologist billing and any physician billing), as these are derived from the same source. In addition, disease diagnosis and thus prevalence may vary according to patient demographics. Therefore, a hierarchical model was used to account for population sampling variability (assigned a binomial distribution), misclassification error (adjusting for both false-positives and false-negatives), variation in prevalence according to patient demographics (age, sex, and rural versus urban residence) input as a logistic regression model on the binomial probabilities from the first level of the model, and variation in the sensitivity of case ascertainment according to patient demographics (age, sex, and rural versus urban residence), again input as a logistic regression model, but based on the sensitivity of case ascertainment. For all prevalence rates estimated by the Bayesian method, we calculated 95% credible intervals (95% CrIs) representing values between which there is a 95% probability of containing the parameter of interest, given the data at hand and any prior information input. Noninformative prior distributions were used through the analyses, except for the specificity of each case definition, which was assumed to be high given that experienced specialists, repeat visits, and trained hospital coders were assigning the diagnostic

codes. We thus used a beta (248.3, 1.65) prior density for the specificities, which cover the range from 0.98 to 1.0. Statistical analyses were programmed in WinBUGS, version 1.4.3 (MRC Biostatistics Unit).

The study was approved by the McGill University institutional ethics review board.

RESULTS

SLE. Accounting for the imperfect sensitivities and specificities inherent in administrative data sources by using a latent class Bayesian hierarchical regression model, the overall prevalence of SLE in Alberta was 27.3 cases per 10,000 females (95% CrI 25.9–28.8) and 3.2 cases per 10,000 males (95% CrI 2.6–3.8). The sex distribution reflected the known predominance of SARD in females versus males, with 32.2 cases per 10,000 First Nations females (95% CrI 26.5–39.2) and 27.1 cases per 10,000 non-First Nations females (95% CrI 25.7–28.6), compared to 3.2 cases per 10,000 First Nations males (95% CrI 1.8–5.4) and 3.2 cases per 10,000 non-First Nations males (95% CrI 2.6–3.8).

After stratification for age and location of residence, interesting trends emerged (Table 1). As expected, since SLE is a chronic condition that usually presents in midlife and beyond, SLE prevalence was elevated in the population >45 years of age relative to the prevalence of those <45 years of age. This was true for both females and males of First Nations and non-First Nations ancestry. However, First Nations females >45 years of age had twice the prevalence of SLE relative to non-First Nations females. There was a suggestion of a trend toward higher SLE prevalence in First Nations females and males living in an urban location relative to rural dwellers; however, the 95% CrIs for these estimates overlap and thus no strong conclusions could be made.

SSc. The overall prevalence of SSc in Alberta was 5.8 cases per 10,000 females (95% CrI 5.1–6.5) and 1 case per 10,000 males (95% CrI 0.7–1.4). The overall prevalence of SSc in Alberta was comparable in First Nations and non-First Nations individuals, although the point estimates were somewhat higher in First Nations individuals (4.7 cases per 10,000 First Nations individuals, 95% CrI 3.3–

Table 2. Systemic sclerosis prevalence estimates for First Nations and non-First Nations populations in Alberta, per 10,000 people*

	Females		Males	
	First Nations	Non-First Nations	First Nations	Non-First Nations
<45 years old				
Rural dwellers	2.7 (1.1–5.7)	1.2 (0.7–2.0)	0.7 (0.1–1.8)	0.3 (0.1–0.6)
Urban dwellers	3.7 (1.2–9.5)	1.4 (1–2.1)	0.6 (0.5–2.1)	0.3 (0.1–0.5)
>45 years old				
Rural dwellers	29.1 (18.2–45.3)	13.6 (11.4–16.3)	3.6 (0.8–10.2)	2.2 (1.4–3.2)
Urban dwellers	23.6 (11.1–43.9)	12.4 (10.7–14.7)	4.0 (0.8–14.4)	2 (1.4–2.8)
Estimated cases, no.	100	1,870	17	295

* Values are the prevalence estimate (95% credible interval) unless otherwise indicated.

6.5 versus 3.3 cases per 10,000 non-First Nations individuals, 95% CrI 2.9–3.8). Stratified by sex, the prevalence was 7.9 cases per 10,000 First Nations females (95% CrI 5.5–11.3) and 1.3 cases per 10,000 First Nations males (95% CrI 0.5–2.7), while the prevalence was 5.7 cases per 10,000 non-First Nations females (95% CrI 5.0–6.5) and 0.9 cases per 10,000 non-First Nations males (95% CrI 0.7–1.3).

As seen with SLE, the prevalence of SSc was highest in the population >45 years of age (Table 2). In this age group, both rural- and urban-dwelling First Nations females had approximately twice the prevalence of SSc relative to non-First Nations females. In contrast to SLE, there appeared to be a slightly higher prevalence of SSc in the rural population, although the 95% CrIs for these estimates are wide and overlap.

DISCUSSION

Using a latent class hierarchical Bayesian model, and ascertaining cases from 1994–2007, we estimate that approximately 27 in every 10,000 females and 3 in every 10,000 males in Alberta have SLE. These results are consistent with those from the Third National Health and Nutrition Examination Survey, with case determination by self-report of physician diagnoses in the US between 1988–1994, with a prevalence estimate of 24.1 cases per 10,000 people (25). In addition, our data suggest that in Alberta, 6 in every 10,000 females and 1 in every 10,000 males have SSc. These rates are consistent with those reported from Quebec, Canada, using very similar methods to the current study, with 7 SSc cases per 10,000 females and 1 SSc case per 10,000 males (15). One study from the US found a similar prevalence of SSc of 4 cases per 10,000 females and 0.8 cases per 10,000 males (26), with another calculating an overall prevalence estimate of 3–5 per 10,000 individuals (27).

Prevalence estimates vary depending upon the methods of case ascertainment and the period over which cases are ascertained. A population-based study from Rochester, Minnesota, ascertained 48 SLE cases over a 12-year period, and estimated the 1993 SLE prevalence to be 12.2 cases per 10,000 people, adjusted by age and sex to the 1970 US white population (28). In the Canadian province of Manitoba, a prevalence estimate based on medical documenta-

tion was 2.1 cases per 10,000 for the general population, and 4.2 cases per 10,000 for the Aboriginal population (8). Using similar analysis methods to our current study, but with only hospitalization data, 1 billing data algorithm (2 codes), and a much shorter period for case ascertainment (1995–2003), the prevalence of SLE in Quebec was estimated at 4.5 cases per 10,000 people in 2003, with the highest prevalence group (women 45–64 years of age) approaching 10 cases per 10,000 people (13). The prevalence estimate from that study is likely an underestimate since many SLE patients do not require hospital admission. In contrast to other provinces, Alberta physicians may provide more than one ICD-9 billing code, which could increase the likelihood of identifying a chronic disease with administrative data. It seems unlikely that this affected our prevalence estimates since the majority of Alberta physicians only record 1 billing code.

When comparing overall prevalence estimates, we found that demographic factors of age, sex, and location of residence affected the estimates significantly. As can be expected for chronic conditions having a peak incidence in the third to fifth decades of life, both females and males older than age 45 years have more prevalent disease relative to those younger than age 45 years by approximately 3–5 times. However, our estimates are potentially underestimating the true equivalent disease prevalence between First Nations and non-First Nations individuals, given a reduced life expectancy in individuals of First Nations descent (29). We did not completely age standardize our estimates, but we did provide estimates by age group. It is unknown why First Nations females have twice the prevalence of SLE and SSc relative to non-First Nations females. This may reflect a true predominance of SLE and SSc among First Nations females, and is consistent with previous studies of SARD in First Nations populations, which also reported a genetic predisposition to autoimmune disorders and more severe disease phenotypes (7–11). It is interesting, however, to hypothesize that this increased prevalence is a result of environmental exposures in a population predisposed to SARD, since, for example, silica exposure has been suggested as an environmental trigger for SARD (30,31). Although a protective factor conferring improved survival could also increase prevalence estimates, this seems less likely given the more

severe disease phenotypes and difficulties accessing health care reported in First Nations populations.

We stratified our results by location of residence since we suspected that our prevalence estimates may be impacted by differential access to medical services. First Nations populations, largely based in rural locations, are less likely to have physician care. Aboriginal peoples in the Northwest Territories have higher use of nursing and social services compared to physician services, reflecting delivery of health services by nonphysicians in remote locations (17). Data based on a wider population from the 1991 Aboriginal Peoples Survey also revealed that Aboriginal peoples, particularly those living on a reserve, were less likely to use physician services compared to the general Canadian population (16). Differential access to medical services would result in fewer rural or First Nations individuals being diagnosed with a SARD, and an underestimate of prevalence based on administrative data sets since no billing claim or hospitalization separation would be generated. As a result, the high prevalence of SLE and SSc observed in our First Nations population may actually be an underestimate of the true value. Although the discrepancy between the urban and rural prevalence of SLE and SSc in our study may represent real regional effects, they may also reflect differences in whether and how these 2 conditions present for medical care, and/or differences in referral and diagnosis.

A limitation of this study is the possible misclassification of First Nations patients as being non-First Nations people, since the latter group includes people of First Nations ancestry who do not have treaty status, as well as the Métis population. This misclassification would be expected to dilute the observed difference in prevalence between groups, and therefore should not alter the main conclusions of this study.

Limitations of using administrative data for determining disease prevalence relate mainly to the sensitivity and specificity of case definitions. Also, all administrative data may contain errors related to coding accuracy. A current initiative by The Canadian Arthritis Network, with the endorsement of the Public Health Agency of Canada, will provide future guidance on the optimal use of administrative data for rheumatic disease research and surveillance (32).

It is unknown whether differential misclassification bias of disease status may have affected our prevalence estimates. In particular, there might be systematic differences in case identification between health care providers for First Nations and non-First Nations females. For example, First Nations females with an unexplained constellation of symptoms might be more likely to be misclassified as having a systemic autoimmune rheumatic disease compared to non-First Nations females. Our estimates could also be affected by an increased frequency of overlap syndromes in the First Nations group (7), in which patients may meet criteria for more than 1 rheumatic disease resulting in inaccurate ICD-9 coding. Finally, if First Nations females are less likely to access primary or specialist care, the prevalence of disease in this group compared to non-First Nations females may have been underestimated. A strength of our study, considering these limitations, was

the use of a modeling approach that combined the results of 3 case definitions in order to provide the best estimate of prevalence and 95% CrI based on the data at hand.

In conclusion, the overall prevalence of SLE and SSc is similar for First Nations and non-First Nations populations in Alberta; however, First Nations females over the age of 45 years have twice the prevalence of these diseases relative to non-First Nations females. This finding has important health service implications that warrant further research, since we need to ensure that these women have adequate access to necessary specialists and treatment. In addition, ongoing observation of SARD prevalence in our population will enable us to study temporal variations in environmental and genetic risk factors, which may yield further insight into disease pathogenesis.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Barnabe had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Svenson, Bernatsky.

Acquisition of data. Fritzler, Svenson, Bernatsky.

Analysis and interpretation of data. Barnabe, Joseph, Belisle, Labrecque, Edworthy, Barr, Svenson, Hemmelgarn, Bernatsky.

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