Prevalence and Incidence of Rheumatoid Arthritis in Canadian First Nations and Non–First Nations People

A Population-Based Study

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Background: The aim of this study was to determine the prevalence, incidence, and onset age at rheumatoid arthritis (RA) diagnosis in First Nations (FN) and non-FN populations in Manitoba, Canada.

Methods: Population-based administrative health records from April 1, 1995, to March 31, 2010, were accessed for all Manitobans. The FN population was identified using the Federal Indian Registry File. Crude and adjusted RA prevalence and incidence rates (adjusted for age, sex, health region of residence) were compared using Poisson regression and reported as adjusted RA prevalence and incidence rates (adjusted for age, sex, health region of residence) were compared using Poisson regression and reported as

Results: Rheumatoid arthritis crude prevalence increased between 2000 and 2010 to 0.65%; adjusted RA prevalence in females was 1.0% and in males was 0.53%. The 2009/2010 adjusted RA prevalence was higher in FN than non-FN (RR, 2.55; CI, 2.08–3.12) particularly for ages 29 to 48 years (RR, 4.52; CI, 2.71–7.56). Between 2000 and 2010, crude RA incidence decreased from 46.7/100,000 to 13.4/100,000. Adjusted RA incidence remained higher in FN than non-FN (2000–2010 RR, 2.1; CI, 1.7–2.6; p < 0.0001) particularly for ages 29 to 48 years (RR, 4.6; CI, 2.8–7.4; p < 0.0001).

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The study was approved by the University of Manitoba Ethics Review Board (H2010:273), Manitoba Centre for Health Policy (MCHP 2012-026), and Manitoba Health Information Research Governance Committee (HIRGC 2010-2011-29) and was conducted with the support of the Assembly of Manitoba Chiefs (now the First Nations Health and Social Secretariat of Manitoba) under the auspices of the Health Disparity Research Program (PI2006-00209), principal investigator B.E.

The authors were unable to make the data set used in this study publicly available as they were not the custodians of the data, but rather obtained permission to access the data for this project.

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The authors declare no conflict of interest.

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The FN population was younger at diagnosis than the non-FN population (mean age, 39.6 years [CI, 38.3–40.8 years] vs. 53.3 years [CI, 52.7–53.9 years]; p < 0.0001). The FN population had more physician visits but fewer rheumatology visits than the non-FN population.

Conclusions: Rheumatoid arthritis prevalence is increasing, and RA incidence is decreasing in Manitoba. The FN population has a greater prevalence and incidence of RA and is younger at diagnosis than the non-FN population. When combined with fewer rheumatology visits, this significant care gap highlights the need to optimize rheumatology care delivery to the FN population.

Key Words: administrative health data, incidence, indigenous, prevalence, rheumatoid

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Prevalence estimates for rheumatoid arthritis (RA) vary across regions and populations, likely reflecting differences in population prevalence of RA susceptibility genes combined with variable exposure to RA-associated environmental risk factors. Globally, some indigenous people have among the highest reported prevalence of RA, with estimates ranging from 2 to 6 times greater than those reported in nonindigenous populations; other indigenous populations do not have higher rates, Central Canadian population-based estimates including those from the province of Manitoba found indigenous people were affected by RA 2 to 3 times more than the general population. However, these studies used variable methods and data sources to identify indigenous individuals with RA.1–5 Population-based trends in RA incidence and prevalence in Canadian indigenous people are lacking.

The indigenous population residing in the Canadian province of Manitoba is comprised mainly of Cree, Ojibway, and Oji-Cree persons, hereafter referred to as First Nations (FN).6 In 2016, FN comprised 18% of the total Manitoba population, one of the highest provincial percentages in Canada outside Northern Canada. The First Nations population is one of the fastest-growing subpopulation groups in the province. Compared with all other Manitobans, this group has a younger age structure7 with higher rates of RA susceptibility genes.8 Using clinical data from the University of Manitoba Rheumatology Clinic (UMRC), we have shown that RA is more severe among Manitoba FN than non-FN populations, with a high articular burden of disease, more seropositive disease, and an earlier age at onset.9 Despite this greater disease severity, the FN population with RA experiences greater disparity in accessing rheumatology care.4,10 The younger FN population structure combined with increased disease severity suggests the burden of RA and related care needs will persist or increase for this population. Current estimates of the burden of RA are needed to inform health service planning. This study therefore estimated the prevalence, incidence, and age at RA onset comparing Manitoba FN and non-FN people and estimated health care access based on primary care and specialist physician visits because this care may affect the likelihood of an RA diagnosis.
METHODS

Data Sources

Manitoba is a central Canadian province with a population of approximately 1.2 million. Census data indicate 18% of the Manitoba population self-reports as FN. This study linked 3 data sources including health claims data, the Federal Indian Registry file, and clinical data from the UMRC. Universal health care coverage is provided to 98% of the Manitoba population. Records for nearly all health services accessed, including service date, medical provider accessed, and diagnosis, are recorded in the Manitoba Population Research Data Repository (MPRDR) housed at the Manitoba Centre for Health Policy (MCHP). Diagnoses are recorded using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) or International Classification of Diseases, Ninth Revision, Canada (ICD-10-CA) codes. The ICD-9-CM codes are used for ambulatory care visits. Health service data are available from 1984 onward. Data on prescription drug use regardless of payer are available from 1995, including date dispensed and Drug Identification Number; the Drug Identification Numbers are linked to the World Health Organization's Anatomic Therapeutic Chemical Classification System. Repository data are deidentified. Each resident has a unique scrambled identifier linked to all their service claims. For this study, we accessed health records from April 1, 1995, to March 31, 2010. In Manitoba, health privacy legislation requires that categories that contain fewer than 6 individuals are not reported, and these data are “censored.”

First Nations individuals were identified in the administrative data using the Federal Indian Registry file, which contains records for all registered FN for the purposes of legal entitlement. Permission to use the file was obtained from Indian and Northern Affairs Canada, the University of Manitoba Ethics Review Board, Manitoba Health Information Research Governance Committee, and the Assembly of Manitoba Chiefs Secretariat Inc. (now the First Nations Health and Social Secretariat of Manitoba), under the auspices of the Health Disparity Research Program (PI2006-00209, principal investigator B.E.). The file was linked to the MPRDR. Linkage was expanded based on familial kinship identifiers in the MPRDR to include individuals eligible but not registered in the MPRDR. Linkage was expanded based on familial kinship (PI2006-00209, principal investigator B.E.). The file was linked to the MPRDR. Linkage was expanded based on familial kinship identifiers in the MPRDR to include individuals eligible but not yet registered as FN and those of FN heritage and likely eligible to be registered as FN.11 Identification of FN in the MPRDR is improved significantly in the younger age groups using this algorithm and is therefore a more inclusive approach to identify FN in Manitoba.12,13

Since 1990, the UMRC has maintained a clinical database of all patients seen in the clinic, which includes rheumatologist-recorded diagnoses and visit dates. Records of patients seen between 2000 and 2010 (RA = 2281, non-RA n = 7044; 73% female, self-reported FN 13%) were linked to the MPRDR using scrambled identifiers. The linked data set was used to validate administrative definitions for RA. Self-reported ethnicity was not used in the validation studies or for population-based estimates of prevalence and incidence.

Validation of the Administrative Definition for RA

Administrative definitions for RA were validated in the MPRDR using the UMRC diagnosis as the criterion standard. We adapted validated administrative definitions currently used to identify other chronic immune-mediated diseases in the regional administrative data.14,15 Individuals were identified as RA if they were residents of Manitoba for 2 years or more with 5 or more physician visits or hospitalizations with ICD-9-CM/ICD-10-CA codes 714/M05, M06. For those who were residents for less than 2 years, 3 or more claims sufficed (definition 1). As a comparison, we applied other administrative definitions used in North American data sets during the study period16-18 (Supplementary Table 1, http://links.lww.com/RHU/A143 for ICD codes and definitions). Validity of the administrative definitions for RA was determined for use in the entire Manitoba population and then estimated separately for FN and non-FN populations. The κ, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) with 95% confidence intervals (95% CIs) and Youden J statistic (sensitivity + specificity – 1) * 10019 were calculated to determine the most appropriate definition to use in the MPRDR. We were most interested in specificity to minimize overdiagnosis. We further characterized the “false-positive” RA cases (FPs) identified by definition 1, by determining the diagnosis assigned in the clinical database and the use of prescribed arthritis medications (disease-modifying antirheumatic drugs, biologics, or corticosteroids).

Prevalence and Incidence

Definition 1 was applied to identify RA cases. Using end-year population figures as the denominators, crude prevalence rates for RA per 100 population (i.e., %) for each year from 2000 to 2010 were determined for all Manitobans. Rates were then stratified by FN status and by age group. Age groups were 0 to 18, 19 to 28, 29 to 38, 39 to 48, 49 to 58, 59 to 68, and older than 68 years. We included the 0- to 18-year age group as ambulatory visits in the MPRDR are coded with ICD-9-CM codes that do not reflect updated classification of juvenile chronic arthritis. This whole population approach was more inclusive and respectful of the younger provincial FN demographic. Using a 5-year run-in period to eliminate prevalent cases, incident RA cases were identified and then stratified by FN status, age group, and sex. Prevalence and incidence rates were modeled over time using Poisson regression models adjusted for age group, sex, and regional health authority (based on postal code of residence). All models fit well with the ratio of the model deviance to degrees of freedom close to 1 (range, 0.90–1.35). Comparisons between FN and non-FN populations are reported using relative rates (RRs) with 95% CIs.

Age at diagnosis, defined as the age at first RA code in the incident RA cohorts, was reported as mean years (SD) and duration followed (for incident RA) as months (SD). Health care utilization (physician visits) was identified by provider (any provider, nonrheumatology specialist provider, rheumatology specialist provider) and reported as mean number of visits/RA individual during the 10-year period. Age, duration followed, and physician visits were compared between FN and non-FN populations using Student t tests and reported with 95% CIs. Statistical significance for all comparisons was assessed using the criterion of α = 0.05. All data management, programming, and analyses were performed using SAS (SAS Institute Inc, Cary, NC).

The study was approved by the Ethics Review Board (H2010:273), the MCHP (2012-026), and the Heath Information Research Governance Committee (2010/2011-29) and was conducted with the support of the Assembly of Manitoba Chiefs Secretariat Inc. (now the First Nations Health and Social Secretariat of Manitoba).

RESULTS

Validation of RA Definition

The validation cohort included 2281 RA patients (432 FN) among 9325 total patients (1210 FN). Seventy-three percent were female. Definition 1 had the best specificity when applied to the entire Manitoba population (κ = 65.9 [95% CI, 64.1–67.6]; sensitivity, 77.1 [95% CI, 75.4–78.8]; specificity, 90.3 [95% CI,
89.6–91.0]; PPV, 72.0 [95% CI, 70.3–73.8]; NPV, 92.4 [95% CI, 91.8–93.0]; and Youden J of 67.4). This definition also had the best specificity of those tested when applied to the FN population, although it was less accurate than for the non-FN population (κ = 61.4 [95% CI, 56.8–66.0]; sensitivity, 74.8 [95% CI, 70.8–78.9]; specificity, 86.4 [95% CI, 84.0–88.8]; PPV, 75.7 [95% CI, 71.7–79.7]; NPV, 85.9 [95% CI, 83.4–88.3]; and Youden J of 61.3).

The validity of the alternative definitions to identify RA in the total and FN populations in Manitoba is reported in Supplementary Table 2, http://links.lww.com/RHU/A143. Based on performance in both the FN and total populations and to maintain consistency with other Manitoba studies, the administrative definition used to identify persons diagnosed with RA was definition 1.

We examined those cases identified by definition 1 as RA, who had a non-RA criterion-standard diagnosis in the clinical database, that is, FPs. Of the 681 FPs, 250 had other inflammatory arthropathy diagnoses, 91 had noninflammatory diagnoses, and 93 had connective tissue disease. A total of 247 non-RA cases did not have a known rheumatologic diagnosis or could not be classified as the number of individuals with the diagnosis was censored because of health privacy legislation in Manitoba. For more than 400 of the FP claims, a diagnosis of RA was assigned by a rheumatologist at a subsequent visit (after the date of initial UMRC diagnosis). This later diagnosis suggests that some of these FPs may represent an evolving arthropathy. A large number of these patients were prescribed disease-modifying antirheumatic drugs, corticosteroids, and even biologics, which suggests that many evolved into RA or had another true inflammatory disease. For most of the FPs, RA claims continued to persist in the administrative data set, even if another diagnosis was given by a rheumatologist (Supplementary Table 3, http://links.lww.com/RHU/A143).

Prevalence

Between 2000 and 2010, we identified 8095 prevalent RA cases (1095 FN, 7000 non-FN) in Manitoba. During this period, the total Manitoba population increased from 1,151,811 in 2000 to 1,223,221 in 2010, and the total FN population increased from 105,549 to 125,289. The crude prevalence of RA in Manitoba for 2009/2010 was 0.65% (FN 0.85%, non-FN 0.63%). The adjusted prevalence of RA was higher in females than males in all years.

Between 2000 and 2010, we identified 4159 incident RA cases (FN 566, non-FN 3593). In 2009/2010, the crude RA incidence was 13.4/100,000 population (FN 21.6/100,000; non-FN 12.5/100,000). Crude RA incidence declined over the study period but remained higher for FN than non-FN populations in each year (Supplementary Table 5, http://links.lww.com/RHU/A143). For the period from 2000–2010, FN had a 2.1-fold increased adjusted incidence of RA compared with non-FN. This increased RA incidence was particularly high for ages 19 to 48 years (Table). The adjusted RA incidence in 2009/2010 was 2.4-fold higher for females than males (RR all males vs. all females, 0.41; 95% CI, 0.25–0.67; p < 0.0001) and 2.2-fold higher for FN compared with non-FN (RR 2.2; 95% CI, 1.26–4.99). Adjusted RA incidence declined for most years between 2000 and 2010. No RA cases were diagnosed in FN older than 68 years in 2004 or 2008. Adjusted incidence rates remained higher for FN than non-FN populations especially for ages 19 to 48 years, which had RRs of RA diagnosis 2.5- to 4.6-fold higher in FN than non-FN populations (Fig. 2, Supplementary Table 4, http://links.lww.com/RHU/A143). This finding is consistent with the higher prevalence in these age groups.

Incidence

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TABLE. Relative Rates (RRs) and 95% Confidence Intervals (95% CI) of Rheumatoid Arthritis (RA) Incidence for FN Versus Non-FN Populations 2000–2010

| RR    | 95% CI         |
|-------|----------------|
| All Ages | 2.10  | 1.70–2.58 |
| 0–18 y   | 1.11  | 0.63–1.95 |
| 19–28 y  | 3.80  | 2.21–6.52 |
| 29–38 y  | 4.61  | 2.86–7.45 |
| 39–48 y  | 2.74  | 1.72–4.36 |
| 49–58 y* | 1.77  | 1.09–2.87 |
| 59–68 y* | 1.80  | 1.06–3.05 |
| >68 y    | 1.05  | 0.51–2.17 |

Bold estimates are statistically significant, \( p < 0.0001 \).
*Estimates are statistically significant, \( p < 0.03 \).

Age at Diagnosis

The largest percentage of FN were diagnosed between ages 29 and 48 years, whereas the largest proportion of non-FN were diagnosed between ages 49 and 68 years (Fig. 3). The First Nations population in the incident RA cohort was on average 13 years younger at RA diagnosis than the non-FN population (FN 39.6 [95% CI, 38.4–40.8 years] vs. non-FN 53.3 [95% CI, 52.7–53.9 years]; \( p < 0.0001 \)). This was true for females (FN 39.3 [95% CI, 37.9–40.6 years] vs. non-FN 52.4 [95% CI, 51.7–53.2 years]) and males (FN 40.7 [95% CI, 37.9–43.3 years] vs. non-FN 55.3 [95% CI, 54.3–56.4 years]; both \( p < 0.0001 \)). Age at diagnosis did not change over the study period.

Physician Visits

Using the prevalent RA cohort, we compared total physician visits, nonrheumatology specialist visits, and rheumatology specialist visits between FN and non-FN populations over the study period. First Nations with RA had more total physician visits compared with non-FN with RA (mean visits/person 6.9 [95% CI, 6.4–7.4] vs. 8.2 [95% CI, 8.0–8.4]; \( p < 0.0001 \)). While we did not have person-years of follow-up, FN and non-FN populations in the incident cohort (2000–2010) had a similar duration of follow-up (FN 66.2 months [95% CI, 63.5–68.8], non-FN 64.6 months [95% CI, 63.5–65.7]; \( p = 0.29 \)).

DISCUSSION

The prevalence of RA in Manitoba increased steadily in the period 2000 to 2010, with 0.65% of the Manitoba population living with RA including 164 Manitobans diagnosed in that year. In 2009/2010, the adjusted prevalence of RA was 2.6 times higher in FN than in non-FN, whereas the adjusted incidence of RA was 2.2 times higher in FN than in non-FN. This increased RR of prevalent and incident RA for FN compared with non-FN was particularly striking for young females of childbearing age (ages 19–48 years). Over the study period, the adjusted RA prevalence increased and the adjusted RA incidence decreased, but both remained higher for FN than non-FN. Compared with the non-FN population, the FN population was younger at diagnosis and had fewer rheumatology visits.

The overall 2009/2010 prevalence of RA in Manitoba was comparable to reports from other Canadian provinces. Variability in RA prevalence rates in Canada likely reflects provincial variations in population characteristics, rheumatology resources, or administrative definitions used for case ascertainment as previously reported. The increasing prevalence of RA in Manitoba is consistent with a recent report from Quebec and was seen for both FN and non-FN populations in Manitoba. At the same time, RA incidence declined sharply in both FN and non-FN populations in Manitoba. These trends, along with a stable age at diagnosis, suggest longer disease duration because of improved survival.

Whereas some studies have also reported declining RA incidence, other studies have reported stable or increased RA incidence. This discrepancy may be due to population-specific differences in exposures to environmental factors known to contribute to RA risk, variable awareness of RA among the public and general practitioners affecting patients presenting for care and referral rates to rheumatology, or population migration trends. For most years of this study, the Manitoba population increased mainly from births. However, from 2007 to 2010 international immigration, mainly economic immigrants aged 20 to 54 years contributed more to provincial population growth than births. Thus, when...
combined with our definition requiring a 5-year disease-free period, immigration may have led to an underestimation of incident RA after 2007. Repeating our analysis with contemporary data would confirm this.

Consistent with a similar Alberta (Canada) population-based study using administrative health data,8 the adjusted prevalence of RA in the Manitoba FN population is more than twice that of the non-FN population. While declining over the study period, adjusted incidence rates remained higher for FN than non-FN populations for most years. This study also confirmed our previous reports of an earlier RA diagnosis age in FN compared with non-FN populations.

A particularly important finding is that the increased RRs of prevalent and incident RA for FN versus non-FN were highest for females in the childbearing years. The postpartum and perimenopause life stages are known to be high-risk periods for the development of RA. We have previously demonstrated early age at first pregnancy, and that the postpartum period increased the risk of RA onset, whereas greater parity reduced RA risk in FN populations.28 Census data indicate FN women are generally younger at the time of their first pregnancy and have higher fertility rates.29 Whether fertility patterns contribute to the increased incidence of RA is unclear; however, this research suggests that the high burden of disease in young FN females will contribute to more difficult parenthood decisions, more complicated medical management, and potentially more impact on functional capacity as a parent.30

The reasons for the increased prevalence, incidence, and disease severity of RA in FN people are likely multifactorial. The high frequency of human leukocyte antigen shared epitope alleles in the FN population, combined with high rates of smoking, parity, and other environmental exposures reported to be associated with RA, may contribute to the increased risk of developing disease.8 Whether additional social and historical factors play a role in the increased burden of RA is not known but requires further study.

The notable exception to the increased prevalence of RA in the FN population was seen in the younger age group. While this phenomenon is well described in other settings and is likely multifactorial in etiology,4,37 primary care providers often lack confidence in musculoskeletal assessment leading to potential underrecognition of articular pathology and underreferral.38 Distance to care has been described as a significant contributor to care inequities.39 A disproportionate number of Manitoba FN patients reside in remote rural communities, some accessible only by air or in winter by seasonal ice roads. Because rheumatology care is centralized in Winnipeg, located in the southern part of the province, FN patients often travel significant distances and have multiday stays in Winnipeg for each rheumatology appointment. The high burden of other acute and chronic diseases, sociocultural concerns, and inherent mistrust of institutional medical systems and providers40 may also contribute to disparate access to rheumatologic care. Ongoing Manitoba studies are attempting to further describe barriers faced by FN attending rheumatology clinics. Increased rheumatology resources and innovative culturally appropriate systems for rheumatology care provision are needed to meet anticipated increasing demands.41,42

Overall, our study has several strengths including its large size, population-based design, and inclusive identification of FN. Like other studies, it is subject to the limitations of administrative data including imprecise diagnosis coding. Our case definition was validated for this data set, performed well compared with other published definitions available at the time of the analysis (and published recently52) and was separately validated in FN. Our population estimates of RA in the general population were similar to those found in other Canadian provinces using the same or similar definitions.17,20 Differences in the accuracy of administrative definitions for FN and the general population highlight the limitations when administrative definitions based on physician claims data are used for case ascertainment. This is particularly relevant in
settings where discrepancies in access to care or health care utilization exist between population groups. The reduced access to rheumatology services by FN with RA suggests our ascertainment of FN with RA may be incomplete. Thus, although our RA estimates for the FN population are an improvement from those previously published for Manitoba, the reported RA prevalence and incidence rates in this population may actually be underestimated.

Our administrative data do not contain patient-reported measures contributing to the overall burden of disease. However, we have previously reported severe disease in the FN RA population, and disease severity associates with poor physical function and quality of life. First Nations populations in Manitoba are generally more socioeconomically disadvantaged when compared with non-FN populations. This may impact both health care access (despite universal health care) and exposures to environmental factors associated with RA risk such as smoking and psychological stress. This complex interaction between disease, physical function, quality of life, and socioeconomic status and its impact on health inequality in rheumatic disease is consistent with what has been described for other indigenous populations.44

CONCLUSIONS

Compared with the general population, FN people in the province of Manitoba have a disproportionate burden of RA, with higher prevalence and incidence rates particularly for young females, a demographic group that is increasing in size both regionally and nationally. Despite the overall decline of RA incidence, the burden of RA will likely increase significantly for FN Manitobans, along with an increased need for rheumatology services to address disparities in accessing rheumatology care. Strategies to identify and address modifiable factors contributing to this excess RA burden are urgently needed. Moreover, rheumatology resources must be optimized and novel methods of culturally appropriate care delivery explored to improve outcomes for this population group.

KEYPOINTS

1. The prevalence of RA is increasing and the incidence of RA is decreasing in the Canadian province of Manitoba.
2. The FN population has a higher prevalence and incidence of RA and an earlier age at RA onset compared with the non-FN population.
3. The FN population has fewer rheumatology visits demonstrating a gap in rheumatology care delivery, which needs to be addressed.

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