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Review Article

Indigenous Peoples Living with Multiple Sclerosis in Canada

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ABSTRACT: Indigenous Peoples in Canada are comprised of First Nations, Inuit and Métis and are the youngest and fastest growing population in the country. However, there is limited knowledge of how they are affected by multiple sclerosis (MS), the most common nontraumatic neurological disease of young adults, with Canada having one of the highest prevalences in the world. In this narrative review, we outline the limited studies conducted with Indigenous Peoples living with MS in Canada and the gaps in the literature. From the limited data we have, the prevalence of MS in Indigenous Peoples is lower, but the disease appears to be more aggressive. Given the dearth of Canadian data, we explore the worldwide MS studies of Indigenous populations. Lastly, we explore ways in which we can improve our understanding of MS among Indigenous Peoples in Canada, which entails building trust and meaningful relationships with these communities and acknowledging past and ongoing injustices. Furthermore, healthcare professionals conducting research with Indigenous Peoples should undergo training in cultural safety and data sovereignty, including principles of ownership, control, access and possession to have greater engagement with Indigenous communities to conduct more relevant research. With joint efforts between healthcare professionals and Indigenous communities, the scientific research community can be positioned to conduct better, more appropriate and desperately needed research, ultimately with improvements in the delivery of care to Indigenous Peoples living with MS in Canada.

RÉSUMÉ : La sclérose en plaques et les peuples autochtones au Canada. Les peuples autochtones au Canada se composent des Premières Nations, des Inuits et des Métis, et, ensemble, ils forment à la fois la population la plus jeune, qui connaît la plus forte croissance au pays. Malgré tout, on en connaît peu sur la manière dont cette maladie neurologique, non traumatique, la plus répandue affecte les jeunes adultes au Canada, là où la prévalence de la sclérose en plaques (SP) est l'une des plus élevées au monde. Dans la revue narrative ici présentée, il sera question du petit nombre d'études réalisées avec les Autochtones vivant avec la SP au Canada, et des lacunes relevées dans la documentation médicale. D'après le peu de données disponibles, la prévalence de la SP est plus faible chez les Autochtones, mais la maladie frapperait cette population avec plus d'intensité. Compte tenu du manque important de données sur la maladie au pays, l'équipe de recherche a examiné des études réalisées partout dans le monde parmi les populations autochtones. Enfin, l'équipe s'est penchée sur la manière d'améliorer la compréhension de la SP chez les peuples autochtones au Canada, ce qui suppose l'instauration d'un climat de confiance et l'établissement de relations significatives avec les communautés concernées, de même que la reconnaissance des injustices passées et présentes. De plus, les professionnels et professionnelles de la santé qui effectuent de la recherche avec les Autochtones devraient suivre de la formation sur la sécurité culturelle et la souveraineté des données, notamment sur les principes de propriété, de gestion, d'accès et de possession, afin de susciter un engagement plus ferme avec les communautés autochtones et, par le fait même, de faire de la recherche plus pertinente qu'autrefois. Ainsi, grâce aux efforts communs de coopération entre les professionnels de la santé et les Peuples autochtones, la communauté scientifique en recherche peut se trouver mieux placée pour effectuer des travaux de meilleure qualité et plus appropriés, qui répondent à des besoins criants, et finalement en arriver à une amélioration de la prestation des soins aux Autochtones vivant avec la SP au Canada.

Keywords: Canada; First Nations; Indigenous; Inuit; Métis; multiple sclerosis

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Introduction

As per the Canadian constitution, Indigenous Peoples comprise three distinct groups: First Nations, Inuit and Métis. There is great diversity within the Indigenous Peoples of Canada and their distinct cultures, laws, traditions and languages. Approximately 5% of Canada's total population (1.8 million people) identified as

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Table 1. Canadian studies on Indigenous Peoples living with MS

Study authors, year of publication	Study location	Type of study	Key findings
Oger and Lai, 1994	BC	Population-based using BC database	MS was present in those of mixed Indigenous/European ancestry, but none with sole Indigenous ancestry were found to have MS
Saeedi et al., 2012	BC	Population-based using BC database with additional case-control analyses	Indigenous MS group progressed more rapidly to EDSS 6
Svenson et al., 2007	AB	Population-based using AB government health databases	Greater increase in prevalence of MS among First Nations persons compared to the general population between 1994 and 2002
Warren et al., 1996	AB	Population-based with case-control comparisons	Negative association between having Indigenous ancestry and MS prevalence
Warren et al., 2007	AB	Population-based using AB government health databases	No change in incidence of MS among First Nations or general population between 1994 and 2002
Marrie et al., 2016	MB	Cross-sectional observational study	First Nations persons with MS had fivefold increased odds of having comorbid psychiatric disease compared to the general population and less likely to be HLA-DRB*1501 positive than the general population
Marrie et al., 2018	MB	Population-based using administrative (health claims) data	Incidence and prevalence of MS was twofold lower in First Nations population than non-First Nations population; and First Nations persons with MS were more likely to have diabetes and chronic lung disease than non-First Nations persons with MS
Mirsattari et al., 2001	MB	Retrospective case-control study	Those identified as First Nations were found to have more aggressive MS, though it may have been NMOSD, given that clinical features and response to MS treatment aligned more with NMOSD
Ramagopalan et al., 2009	Canada	Population-based	Index MS cases with a North American Indigenous father and Caucasian mother had a higher sibling recurrence risk and greater female-to-male sex ratio than having a Caucasian father and North American Indigenous mother

AB = Alberta; BC = British Columbia; EDSS = expanded disability status scale; MB = Manitoba; MS = multiple sclerosis; NMOSD = neuromyelitis optica spectrum disorder.

Indigenous in the 2021 Census,[1] with this number projected to increase to 5.4%–6.8% (2.5–3.2 million people) by 2041.[2] Notably, Indigenous Peoples are the youngest and fastest growing population in Canada.[1] Despite this, little is known about how Indigenous Peoples are affected by multiple sclerosis (MS), an immune-mediated demyelinating disease affecting the brain and spinal cord, which is the most common neurological condition affecting young adults.

This narrative/literature review aims to examine MS in Indigenous Peoples living with MS in Canada, to identify possible reasons for differing disease trajectories from those that do not identify as Indigenous and to propose how future studies could be appropriately conducted with this critical and growing population in Canada. We also focus on approaches to more respectfully engage with Indigenous Peoples given the history of intergenerational trauma, mistrust and inequitable engagement with the medical system for several possible reasons, including more limited access to care being located rurally, anti-Indigenous racism, healthcare providers' lack of understanding of Indigenous health and healing models and social determinants of health including racism, environmental degradation, wholism, unemployment and lower levels of education, among others.[3–5]

Search strategy

In collaboration with a health librarian at the University of Alberta (Edmonton, Alberta, Canada), our major search strategy undertaken in August 2024 comprised Indigenous terminology, Canada and MS, in combination with controlled vocabulary and keywords. Searches were conducted in Ovid Embase, Ovid MEDLINE, CINAHL and SCOPUS. Searches were limited to the English language. Titles of papers and abstracts were reviewed together, and appropriate studies from Canada were included in this targeted review. More specifically, inclusion criteria were as follows: (1) the study needed to include Indigenous Peoples in Canada and (2) the study needed to be on MS specifically. For the full search strategy, please refer to Supplemental Table 1.

Canadian studies on Indigenous Peoples with MS

Using the above search strategy, nine articles were deemed to be appropriate and were included; these are summarized in Table 1. Studies will be reviewed in order of provinces from West to East, followed by a review of pan-Canadian data. In cases where Indigenous Peoples were not explicitly identified as First Nations, Inuit or Métis, the term "Indigenous" will be used.

Two studies have been conducted in British Columbia (BC). Oger and Lai in 1994 examined MS prevalence at the University of British Columbia's MS Clinic and only found 46 cases ($n = 94{,}615$) who identified as mixed Indigenous and European ancestry with no participants who self-identified as Indigenous only[6]. A more contemporary study by Saeedi and colleagues identified 26 Indigenous Peoples with MS from the BC MS database.[7] They compared the identified Indigenous population to two groups – one including all definite MS cases in BC and a second group matched by age at onset, sex and initial disease course. With these comparisons, their key finding was that the Indigenous group progressed more rapidly to expanded disability status scale (EDSS) ≥6 (requirement of a unilateral gait aid).[7]

The few studies conducted in Alberta have focused primarily on the changing incidence and prevalence of MS in Indigenous Peoples. Warren and colleagues found a negative association

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between having Indigenous ancestry and developing MS, with no patients in their MS Clinic being identified as having Indigenous ancestry with MS in 1996.[8] A 2007 study by Svenson and colleagues demonstrated a lower prevalence of MS in First Nations people compared to the general population.[9] However, there was a greater increase in prevalence among First Nations people with MS, with a 41.6% increase in prevalence from 56.3 per 100,000 in 1994 to 99.9 per 100,000 in 2002.[9] In comparison, the general population with MS was reported as having a 21.6% increase in prevalence from 262.2 per 100,000 in 1994 to 335.0 per 100,000 in 2002.[9] A separate study by Warren and colleagues did not find any significant change in MS incidence in First Nations people or the general population over the same time frame (1994–2002).[10]

In Manitoba, those of First Nations background (specifics of the First Nation community participants are not further described here to protect the identities of the group members due to the small sample size) were found to have more aggressive MS than non-Indigenous persons. However, these patients may have had neuromyelitis optica spectrum disorder (NMOSD) for a few reasons. First, the study was published in 2001,[11] which predated the discovery of aquaporin-4.[12,13] Second, clinically, those identifying as First Nations had more optic nerve and spinal cord involvement, with severe visual loss with visual acuities worse than 20/200 in one or both eyes. Third, those treated with interferon-beta had poor response to treatment,[11] features more typical of NMOSD than MS. Thus, it is uncertain how many patients in this cohort had MS. A study by Marrie and colleagues in 2018 showed similar findings to previous studies from Alberta, with the First Nations population having a twofold lower incidence and prevalence of MS than the non-First Nations population.[14] However, the prevalence of MS in the First Nations population in Manitoba is higher than in other Indigenous populations outside of Canada. Furthermore, this study described the key finding that diabetes and chronic lung disease were more common in First Nations persons with MS compared to non-First Nations persons with MS,[14] both of which can negatively impact ambulation and vision.[15,16] A previous study by Marrie and colleagues had shown that First Nations persons with MS had fivefold increased odds of having comorbid psychiatric disease compared to the general population.[17] These findings are important as the presence of comorbidities can increase MS relapse rate, contribute to more physical and cognitive impairment and are associated with increased mortality.[18–20]

Our review found no published studies east of Manitoba or the territories specifically examining Indigenous Peoples with MS. One study used data from across Canada from the Canadian Collaborative Project on Genetic Susceptibility to Multiple Sclerosis, which looked at the parent of origin effect in MS, finding that index cases with a North American Indigenous father and Caucasian mother had a higher sibling recurrence risk, along with greater female-to-male sex ratio than having a Caucasian father and North American Indigenous mother.[21] This could be due to the Carter effect (where fathers with MS transmit the disease to their children more often compared to mothers with MS)[22] being stronger in Indigenous men than non-Indigenous men.

Discussion

From our literature review, there is a lack of knowledge regarding the MS experience for Indigenous Peoples in Canada. Most studies to date have been undertaken with administrative data, with minimal data on long-term follow-up. From the few studies published, the trends that have emerged are that the prevalence and incidence of MS in Indigenous Peoples are lower than the general population. However, the historically reported lower prevalence and incidence may at least in part be due to ascertainment bias and undercounting. Regardless, the prevalence has been increasing over time. Increasing prevalence may in part be accounted for by modest improvements in access to specialist care and diagnostic tests (e.g., MRI, biomarkers) over the past decade.

However, it is important to consider sociocultural/political factors that may arise from a history of colonialism and the displacement of Indigenous Peoples in Canada. Pediatric obesity is associated with an increased risk of MS,[23] and rates of being overweight and obesity are disproportionately higher among Indigenous youth in Canada.[24] Higher rates of obesity among Indigenous youth are attributed to multiple factors, including food insecurity and a lack of access to traditional foods.[25] Smoking is also associated with increased risk of developing MS as well as with increased disability scores, and rates of cigarette smoking are significantly higher among First Nations, Inuit and Métis populations in Canada.[26] Lastly, increasing urbanization has been associated with rising rates of MS among otherwise genetically stable populations.[27] As of 2021, approximately 61% of the Indigenous Peoples of Canada reside in urban communities. Urban migration of Indigenous Peoples in Canada is multi-factorial, including sequelae of the residential school system, a lack of employment opportunities and access to healthcare and social services in home communities and disproportionate engagement with the justice system through incarceration and child welfare services, which result from anti-Indigenous racism and colonial practices in Canada.[28] An understanding of the factors that contribute to rising MS prevalence and severity among Indigenous Peoples in Canada underscores the importance of addressing social determinants of health in a culturally competent manner.

Increasing prevalence and aggressiveness of MS in those who self-identify as Indigenous Peoples in comparison to non-Indigenous White people appears to potentially be more aggressive. One clear limitation of the studies published to date is that four of the studies were published before 2004 when aquaporin-4 was discovered, in relation to NMOSD. Thus, those studies may have inadvertently included NMOSD rather than MS.[29] There has also been a lack of separation of what the term Indigenous is referring to in most studies: First Nations, Inuit or Métis. Studies delineating the specific classification of Indigenous Peoples have only studied First Nations people with MS; there is no description of Inuit or Métis persons specifically with MS.

The most recent study looking at Indigenous Peoples with MS was published over six years ago, in 2018. Thus, any new changes in MS in the Indigenous population – diagnostically and with respect to clinical trajectory, also in relation to the COVID-19 pandemic – are unknown. Furthermore, when it comes to provincial and territory-specific data, only data from three provinces has been published: BC, Alberta and Manitoba. Given that these are not the regions where most Indigenous Peoples reside in the country, there is a large gap in our understanding of MS in the majority of the Indigenous population. In part, understanding MS in the Yukon, Northwest Territories and Nunavut is hampered by the fact that there are no permanent neurologists in these areas; small teams of neurologists from other places in Canada (e.g., Calgary) visit each of these regions every few months to provide care, some of whom are MS specialists, making continuity of care an issue. Even when neurologists are available, there is no nursing support nor allied health professionals available – critical parts of a multidisciplinary

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MS Clinic to help optimize care.[30] When possible, MS care takes place in capital cities in the territories. Thus, those who live more remotely need to take multiple means of transportation to get to the capital city, to get to the clinic – this can entail a combination of plane and bus travel, which can take several hours. With respect to prescribing disease-modifying therapies (DMTs), neurologists have been educating primary care providers/family physicians on how to prescribe and carry out monitoring lab work (S. Jarvis, personal communication, August 13, 2024). However, wait times to even be seen by a primary care provider are longer for Indigenous Peoples living in remote areas,[31] and First Nations peoples living off reserve, Métis and Inuit have experienced difficulty being referred to a specialist.[32] Marrie and colleagues have created a case definition for MS that can be applied to persons with MS receiving primary care,[33] which could be very applicable in the case of Indigenous Peoples with MS that are mainly being managed by primary care providers. In that study, with application of their case definition, they identified 37 cases out of 13,673 persons,[33] though the percentage of those identifying as Indigenous was unknown. For MS care to become more readily available and streamlined for Indigenous Peoples in the territories, we need to be able to identify the population with MS – how many Indigenous Peoples have MS and the severity of their disease. Ideally, this would be followed by the establishment of a specialty MS Clinic, which would require the support of the local health authority in making neurologic care a priority.

For the data currently available, there are several unanswered questions in the areas of DMT use, biomarkers (serum, cerebrospinal fluid, MRI), long-term clinical trajectories and access to care, among others, for Indigenous Peoples living with MS. Knowledge of DMT use is particularly important given the known benefits of contemporary DMTs on the relapsing aspect of the disease. The status of DMT access in Indigenous Peoples living with MS is unknown. DMTs are prohibitively expensive for most patients, and the cost is typically covered by a combination of provincial drug plans and patient support programs through the pharmaceutical company creating the DMT. Enrolling patients in patient support programs and obtaining coverage for these medications require significant administrative support that is rarely available in rural or remote healthcare settings. As an attempt to mitigate access issues, First Nations and Inuit patients enrolled in the Non-insured Health Benefits program can access DMTs in all provinces under "Limited Use" codes rather than "Special Authorization," as is required under all provincial drug plans. Determining the level of DMT use and subsequently improving DMT use is increasingly important with the advent of oral DMTs and high efficacy subcutaneous DMTs, as these may be easier to access, and infusion-based medications, which can be completed every 6 months in the cases of ocrelizumab, rituximab and ublituximab, are highly effective at reducing the chance of clinical relapse and/or new MRI activity.

Given the lack of data on Indigenous Peoples in Canada, one can look to Indigenous populations in other parts of the world including the USA, Australia, New Zealand and northern Europe. A systematic review of Indigenous persons with MS in the Americas[29] described one administrative data-based study, finding the age-adjusted prevalence of MS in US Indigenous persons as 50.1 per 100,000, with a reported prevalence rate ratio of MS in Indigenous persons compared to White Americans as 0.39,[34] aligning with Canadian studies showing a lower prevalence of MS in Indigenous persons. In a contemporary study looking at the Indigenous populations of Australia and New Zealand, the New Zealand Māori population MS prevalence fell between that of Southeast Asian and European ancestry, while MS was found to be uncommon in the Australian Indigenous and Torres Strait Islander populations.[35] A study from 2014 looking specifically at the New Zealand/Aotearoa Māori population compared to the general New Zealand population did not find any differences between the groups regarding the percentage of persons with relapsing MS, EDSS or MS severity score.[36] Among the northern European Indigenous Sámi population in Norway, there is a much lower prevalence of MS compared to the rest of the Norwegian population, which was felt to be in part due to the reduced frequency of the HLA-DRB1*15-DQB1*06 haplotype in the Sámi population.[37] Interestingly, Marrie and colleagues found that Indigenous Peoples in Manitoba were less likely to be HLA-DRB1*1501 positive.[17] Taken together, studies from across the world report a lower prevalence of MS among diverse Indigenous populations, which may partly relate to the lower frequency of MS genetic risk variants in these populations. However, clinical disease, biomarkers and long-term outcomes are very understudied in the Indigenous populations worldwide.

Research with Indigenous Peoples living with MS across Canada needs to be approached thoughtfully and with training in handling data sensitively and following principles of data sovereignty. One excellent resource is the First Nations Information Governance Centre (https://fnigc.ca/), with courses on ownership, control, access and possession (OCAP), a set of principles that should be applied when conducting research using First Nations' data. At present, the First Nations Information Governance Centre does not cover the Inuit or Métis populations, but there is work ongoing by these groups. Upon developing an understanding of OCAP principles and data sovereignty, trust must be built with the diverse Indigenous communities, which can only occur with recognition of past and ongoing injustices. To this effect, the Canadian Medical Association delivered a public apology to Indigenous Peoples in September 2024 and published a formal apology document stating that they had systematically embedded and upheld anti-Indigenous racism in healthcare, creating an unsafe environment for Indigenous patients and communities.[38] Ideally, apologies from other healthcare establishments are forthcoming that will be backed up with accountability and relationship building.

There is a pressing need for reconciliation and advocacy to improve Indigenous health and research. A dedicated MS advocacy and research group for Indigenous Peoples in Canada should include Indigenous Elders, health representatives, neurologists, primary care providers, researchers and policy experts to address disparities in diagnosis, treatment and access to culturally safe care. Despite the lower prevalence of MS, the group would focus on disease severity, social determinants of health and Indigenous-led research to improve health outcomes and equitable healthcare solutions. Such a group would collaborate directly with Indigenous communities, not only to foster meaningful inclusion in research but also to offer healthcare professionals diverse perspectives on wellness. It would provide education on Indigenous health within the medical profession, addressing the overreliance on Western frameworks of medicine and embracing alternative approaches to health and wellness. This knowledge translation would flow from healthcare professionals to Indigenous communities, and vice versa – needing to be reciprocal, with openness – to provide true translation and to make room for diverse interpretations. There is a need to consider knowledge and research in terms of the phenomena being studied but also to consider other elements

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surrounding this, thinking from a collective rather than individual perspective.[39,40] Lastly, to enhance care for Indigenous Peoples living with MS across Canada, clinics should adopt a multidisciplinary approach tailored to the unique needs of Indigenous Peoples. This includes integrating nurses, social workers and language interpreters trained in cultural safety, creating a supportive and controlled environment that fosters trust and ensures culturally responsive care for Indigenous patients.

Conclusions

With the growing Indigenous population in Canada and studies finding that they may have a more aggressive MS disease course, more work needs to be done studying Indigenous Peoples living with MS in Canada to ensure we provide them with the most informed and appropriate care possible to mitigate future morbidity. Research with Indigenous Peoples requires sensitivity and an understanding of data sovereignty, with the need for reciprocal engagement between professionals and the community for appropriate interpretation of data, and advocacy by all to optimize research, delivery of care and outcomes. An understanding of the factors that contribute to rising MS prevalence and severity among Indigenous Peoples in Canada underscores the importance of addressing social determinants of health in a culturally competent manner.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/cjn.2025.42.

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