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Original Article

Geographical Variation In Medication and Health Resource Use In Multiple Sclerosis

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ABSTRACT: ***Background:*** Understanding disease-modifying therapy (DMT) use and healthcare resource utilization by different geographical areas among people living with multiple sclerosis (pwMS) may identify care gaps that can be used to inform policies and practice to ensure equitable care. ***Methods:*** Administrative data was used to identify pwMS on April 1, 2017 (index date) in Alberta. DMT use and healthcare resource utilization were compared between those who resided in various geographical areas over a 2-year post-index period; simple logistic regression was applied. ***Results:*** Among the cohort ($n = 12{,}338$), a higher proportion of pwMS who resided in urban areas (versus rural) received ≥ 1 DMT dispensation (32.3% versus 27.4%), had a neurologist (67.7% versus 63.9%), non-neurologist specialist (88.3% versus 82.9%), ambulatory care visit (87.4% versus 85.3%), and MS tertiary clinic visit (59.2% versus 51.7%), and a lower proportion had an emergency department (ED) visit (46.3% versus 62.4%), and hospitalization (20.4% versus 23.0%). Across the provincial health zones, there were variations in DMT selection, and a higher proportion of pwMS who resided in the Calgary health zone, where care is managed by MS tertiary clinic neurologists, had an outpatient visit to a neurologist or MS tertiary clinic versus those who resided in other zones where delivery of MS-related care is more varied. ***Conclusions:*** Urban/rural inequalities in DMT use and healthcare resource utilization appear to exist among pwMS in Alberta. Findings suggest the exploration of barriers with consequent strategies to increase access to DMTs and provide timely outpatient MS care management, particularly for those pwMS residing in rural areas.

RÉSUMÉ : Variations géographiques de l'utilisation des médicaments et des ressources en santé dans le cas de la sclérose en plaques. ***Contexte :*** Comprendre l'utilisation des traitements modificateurs de la maladie (TMM) et l'utilisation des ressources en santé dans différentes zones géographiques peut permettre, dans le cas des individus vivant avec la sclérose en plaques (SP), d'identifier des lacunes en matière de soins. Ces dernières peuvent en retour être utilisées pour informer les politiques et les pratiques afin d'assurer des soins davantage équitables. ***Méthodes :*** Des données administratives ont été utilisées pour identifier les individus vivant en Alberta qui étaient atteints de SP en date du 1er avril 2017 (date de référence). L'utilisation de TMM et de ressources en santé a ainsi été comparée parmi les patients qui résidaient dans diverses zones géographiques, et ce, pendant une période de deux ans après la date de référence. À cet effet, une régression logistique simple a été appliquée. ***Résultats :*** Dans notre cohorte ($n = 12\ 338$), une proportion plus élevée d'individus atteints de SP résidant dans des zones urbaines (par rapport aux zones rurales) a reçu ≥1 dispensation de TMM (32,3 % contre 27,4 %), a consulté un neurologue (67,7 % contre 63,9 %), un spécialiste autre qu'un neurologue (88,3 % contre 82,9 %), a effectué une visite pour obtenir des soins ambulatoires (87,4 % contre 85,3 %) et une visite à un établissement tertiaire de la SP (59,2 % contre 51,7 %). Ajoutons aussi que ces mêmes individus des zones urbaines ont donné à voir une proportion plus faible de visites aux urgences (46,3 % contre 62,4 %) et d'hospitalisations (20,4 % contre 23,0 %). Dans les zones de santé à l'échelle de la province, on a noté des variations dans le choix des TMM. De plus, une plus grande proportion d'individus atteints de SP qui résidaient dans la zone de Calgary, là où les soins sont gérés par les neurologues d'un établissement tertiaire de la SP, ont effectué une visite ambulatoire chez un neurologue ou dans un établissement tertiaire de la SP par rapport à ceux qui résidaient dans d'autres zones où la prestation de soins liés à la SP est plus variée. ***Conclusions :*** Des inégalités urbaines/rurales dans l'utilisation des TMM et des ressources en santé semblent exister parmi les individus atteints de SP qui résident en Alberta. Nos résultats suggèrent d'explorer les obstacles et les stratégies qui en découlent afin d'améliorer l'accès aux TMM et de fournir une prise en charge ambulatoire de la SP en temps opportun, en particulier pour ceux et celles qui résident dans les zones rurales.

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Keywords: Administrative data; disease-modifying therapy; healthcare utilization; multiple sclerosis; retrospective; urban/rural residence

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Introduction

Multiple sclerosis (MS) is a chronic disorder of the central nervous system and a major cause of non-traumatic disability among working-age adults in Canada.[1] The prevalence of MS in Canada is one of the highest in the world, with the province of Alberta reported to have a particularly large population living with MS (358 cases per 100,000 population).[2–4] The most common form of MS is relapsing-remitting in which individuals experience periods of neurologic disability followed by complete or partial recovery over weeks to months.[5] Frequency and severity of relapses negatively impact the physical and psychosocial well-being of people living with MS (pwMS), as well as increase healthcare resource utilization, and associated costs.[6–8]

PwMS require complex care management that evolves over decades; care involves pharmacologic and nonpharmacologic interventions to control symptoms and delay disease progression or accumulation of disability, symptom management and coping, as well as management of comorbid conditions that are commonly present.[9] Integrated multidisciplinary teams, where comprehensive care is provided by MS specialist neurologists and nurses, physiatrists, psychiatrists and other health professionals, have been recommended as the gold standard for outpatient MS management.[10] Furthermore, treatment with disease-modifying therapies (DMTs) is the current pharmacological standard of care based on evidence that these treatments reduce the frequency and severity of relapses and may reduce disability over the long-term.[11–15] In Canada, government-funded specialized multidisciplinary MS tertiary clinics are located in most provinces, and these clinics facilitate government-funded access to DMTs, requiring assessment by a neurologist with specific expertise in MS. Therefore, access to DMTs and specialized MS care is of great importance for pwMS.

Ensuring universality and portability of healthcare, as required by the Canada Health Act, is particularly challenging in provinces with a large geographic area and low population density, such as Alberta (a geographical land area of 634,658 km^2 with a density of 6.7 persons per km^2).[16] Previous studies have identified geographic disparities in access to specialized care for other chronic conditions in Canada, which tends to be concentrated in urban areas.[17] However, studies identifying potential barriers to accessing optimal MS care and treatment are lacking, particularly within the Canadian health system.[18] Understanding DMT use and healthcare resource utilization by different geographical areas among pwMS may identify potential gaps in care that can be used to inform policies and individual practice to ensure the best possible care for all pwMS. The objectives of this study were to measure DMT use and healthcare resource utilization among pwMS according to urban/rural residence in Alberta; considering that MS care settings and resources vary by geographical health zones in the province, outcomes were also determined according to these zones of residence.

Methods

The University of Alberta institutional review board approved this study (Pro00101070). This study used administrative health data without any intervention. No study participants were placed at risk as a result of the study, and a waiver of consent was applied. This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.[19]

Study design

A retrospective, observational, population based cohort study was conducted using administrative health data from Alberta between April 1, 1993 and March 31, 2019. PwMS on April 1, 2017 (index date) were identified (using data between April 1, 1993 and March 31, 2019), and their DMT use and healthcare resource utilization were described over a 2-year observation period between April 1, 2017 and March 31, 2019.

Data source

Canadian provinces provide publicly funded health care for all residents. In Alberta, the fourth most populous Canadian province (4.2 million people in 2017), health care is administered under the Alberta Health Care Insurance Plan (AHCIP), of which over 99% of Albertans participate.[20] Each participant is assigned a unique person-level identifier (Personal Health Number); this was used to link individuals across datasets. Hospital admissions and ambulatory care visits were obtained from the Discharge Abstract Database (DAD) and the National Ambulatory Care Reporting System (NACRS; previously the Alberta Ambulatory Care Reporting System), respectively. These databases contain primary and secondary diagnostic codes according to the International Classification of Disease – Version 10 – Canadian Enhancement (ICD-10-CA). Physician visits were obtained from the Practitioner Claims database including patient, provider, and service information such as demographics, physician specialty, and health service and diagnostic codes; up to 3 ICD – Version 9 – Clinical Modification (ICD-9-CM; Alberta specific) diagnostic codes can be used per visit. The Pharmaceutical Information Network (PIN) contains information on all dispensed prescription medications from community pharmacies.

Cohort selection

Among individuals who had ≥ 1 healthcare encounter for MS (ICD-9 340 or ICD-10 G35 located in any diagnostic field) between April 1, 1993 and March 31, 2019, the following criteria were applied: (1) met the case definition for MS, defined as having ≥ 1 hospitalization or ≥ 5 ambulatory care visits and/or physician visits with a recorded code for MS (ICD-10-CA G35, ICD-9-CM 340) located in any diagnostic field within a 2-year period between April 1, 1993 and March 31, 2019 (multiple outpatient visits by an individual within the same day were considered as one visit),[21] (2) the MS incident date, defined as the first healthcare encounter with a recorded diagnostic code for MS or a related demyelinating disease of the central nervous system (see Supplementary Table 1), occurred by April 1, 2017 (index date), (3) alive on the index date, and (4) had AHCIP coverage for ≥ 2 years before the index date, and (5) had AHCIP coverage for ≥ 2 after the index date or until death whichever occurred first.

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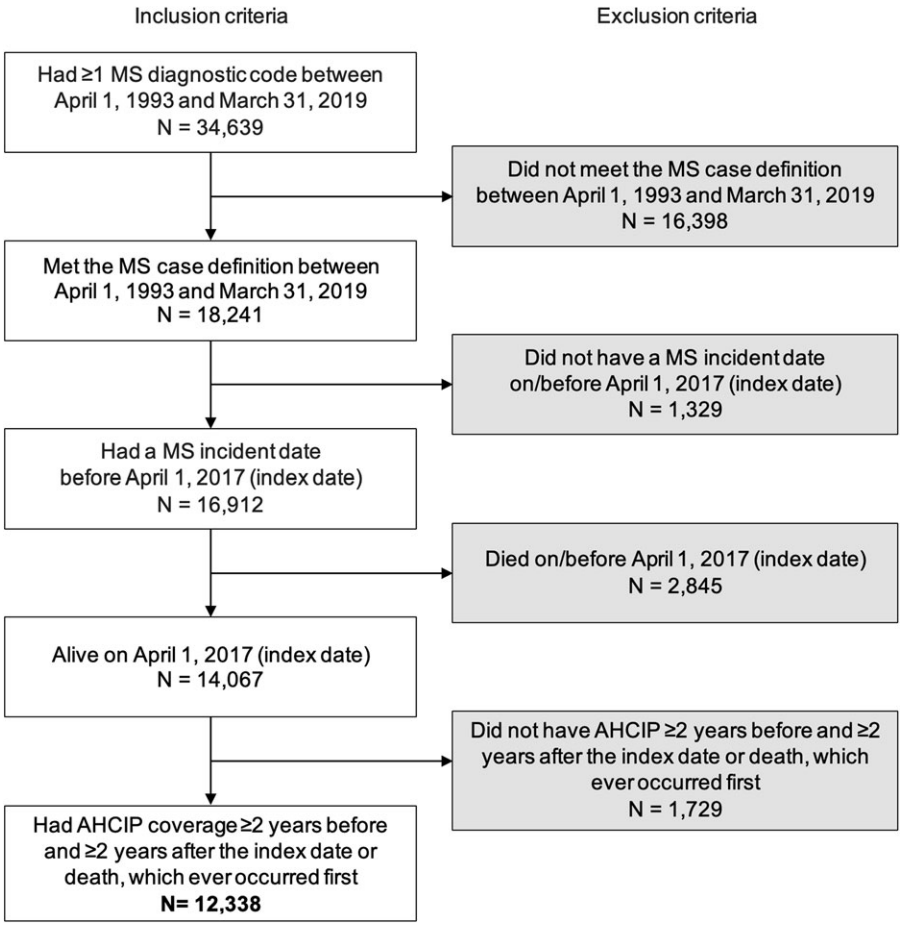

Figure 1. Cohort selection diagram. AHCIP = Alberta health care insurance plan; MS = multiple sclerosis.

Study measures

Study measures (baseline characteristics, DMT use and healthcare resource utilization) were presented for the total cohort and grouped according to geographical residence (urban/rural and Alberta Health Services zone [Edmonton, Calgary and Other] based on postal code) on the index date. Alberta Health Services is the single health authority in Alberta, organized into five geographical zones (North, Edmonton, Central, Calgary and South; see Supplementary Figure 1).

Demographic characteristics included age, sex and residence on the index date. Socioeconomic status was determined by the Pampalon material deprivation index (MDI; includes education, employment status and average income) and social deprivation index (SDI; includes marital status, single-parent family and living alone status) on the index date; indices were derived from the Alberta general population at the dissemination area level that was linkable to postal code and presented based on quintiles from most privileged (quintile 1) to most deprived (quintile 5).[22] The number of years living with MS before the index date (time between the MS incident date and the index date) was reported.[23]

DMT use and healthcare resource utilization (proportion with ≥ 1 dispensation and visit, respectively) were reported during the 2-year observation period (April 1, 2017 to March 31, 2019). DMT use was presented overall and according to drug type (older platform injection therapies: glatiramer acetate, interferon beta-1a and -1b, and peginterferon beta-1a; first line oral therapies: dimethyl fumarate and teriflunomide; higher-efficacy therapies: fingolimod, ocrelizumab and natalizumab; induction therapies: alemtuzumab and cladribine; other therapies: rituximab, cyclophosphamide, daclizumab and mitoxantrone). All-cause and MS-related (ICD-10 G35 in the most responsible diagnostic field; ICD-9 in any diagnostic field) physician visits (overall and according to speciality), non-emergent ambulatory care visits, emergency department (ED) visits and hospitalizations were presented; MS tertiary clinic visits were also reported (identified by the functional center code within NACRS or had a MS-related neurologist visit located at a health facility where MS tertiary clinics are located [Edmonton, Red Deer and Calgary]).

Statistical analyses

Descriptive statistics were reported as counts and percentages. Simple logistic regression was employed for statistical comparison of DMT use and healthcare resource utilization between pwMS who resided in urban and rural areas, and across geographical health zones. Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA).

Results

Cohort selection

Of the 34,639 individuals with ≥ 1 recorded diagnostic code for MS between 1993 and 2019, 12,338 were included in the cohort (Fig. 1). Within the cohort, 84.9% lived in urban areas and 15.1% lived in rural areas; across the health zones, 36.5% lived in the Calgary zone (93.1% urban, 6.9% rural), 32.5% lived in the Edmonton zone

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Table 1. Baseline characteristics of the cohort, presented overall and according to geographical residence

	Overall		Urban/rural residence				Health zone of residence					
			Urban		Rural		Calgary		Edmonton		Other	
	N	(%)	*N*	(%)	*N*	(%)	*N*	(%)	*N*	(%)	*N*	(%)
	12,338	100	10,475	84.9	1,863	15.1	4,498	36.5	4,011	32.5	3,829	31.0
Demographic												
Age, years												
Mean (SD)	53 (14)		52 (14)		54 (14)		52 (14)		53 (14)		53 (14)	
Missing, *n*	<10		<10		0		<10		<10		0	
Sex												
Female	8,851	71.7	7,522	71.8	1,329	71.3	3,232	71.9	2,874	71.7	2,745	71.7
Male	3,487	28.3	2,953	28.2	534	28.7	1,266	28.1	1,137	28.3	1,084	28.3
Socioeconomic status												
Material deprivation index												
1 (most well-off)	2,143	18.5	2,089	21.1	54	3.2	1,096	25.7	843	22.3	204	5.8
2	2,276	19.6	2,102	21.3	174	10.2	1,011	23.7	715	18.9	550	15.5
3	2,372	20.5	2,072	21.0	300	17.6	814	19.1	802	21.2	756	21.3
4	2,546	22.0	1,971	19.9	575	33.6	746	17.5	732	19.3	1,068	30.2
5 (most deprived)	2,253	19.4	1,647	16.7	606	35.5	598	14.0	692	18.3	963	27.2
Social deprivation index												
1 (most well-off)	1,847	15.9	1,714	17.3	133	7.8	908	21.3	632	16.7	307	8.7
2	1,737	15.0	1,607	16.3	130	7.6	715	16.8	625	16.5	397	11.2
3	2,243	19.4	1,864	18.9	379	22.2	773	18.1	789	20.9	681	19.2
4	2,651	22.9	2,078	21.0	573	33.5	864	20.3	800	21.1	987	27.9
5 (most deprived)	3,112	26.9	2,618	26.5	494	28.9	1,005	23.6	938	24.8	1,169	33.0
Clinical												
MS duration, years												
≤1–5 years	2,755	22.3	2,369	22.6	386	20.7	1,068	23.7	824	20.5	863	22.5
>5–10 years	2,276	18.4	1,950	18.6	326	17.5	840	18.7	701	17.5	735	19.2
>10–15 years	2,355	19.1	2,004	19.1	351	18.8	906	20.1	744	18.6	705	18.4
>15 years	4,952	40.1	4,152	39.6	800	42.9	1,684	37.4	1,742	43.4	1,526	39.9

IQR = interquartile range; MS = multiple sclerosis SD = standard deviation.
In accordance with data custodian privacy standards, outcomes with one to nine individuals were reported as < 10.

(96.9% urban, 3.1% rural) and 31.0% lived in the other zones (62.7% urban, 37.3% rural) (Table 1).

Baseline characteristics

The mean age of the cohort was 53 years (SD 14) and 71.7% were female; these demographic characteristics were similar across geographical areas (Table 1). PwMS residing in urban areas (versus rural) were more likely to be materially well-off (21.1% versus 3.2% had a MDI score of 1, the most well-off quintile of the Alberta general population) and less likely to be deprived (16.7% versus 35.5% had a MDI score of 5, the most deprived quintile of the Alberta general population). Those living in the Calgary health zone were most likely to be materially well-off (MDI 1: 25.7% versus 22.3% in the Edmonton and 5.8% in other health zones) and least likely to be deprived (MDI 5: 14.0% versus 18.3% in the Edmonton and 27.2% in the other health zones). Overall, pwMS were less likely to be socially well-off and more likely to be deprived (SDI 1: 15.9%; SDI 5: 26.9%) compared to the Alberta general population; those living in rural areas (versus urban) and other regions (versus Calgary and Edmonton) were less likely to be socially well-off and more likely to be deprived (Table 1). Most of the overall cohort had been living with MS for ≤ 15 years (60%; ≤ 1–5 years: 22%, > 5–10 years: 18%, > 10–15 years: 19%) and 40% had been living with MS for > 15 years (Table 1).

DMT use

Overall, 31.5% of pwMS had ≥ 1 DMT dispensation during the 2-year observation period. A 1.2-fold higher proportion of those living in urban areas received a DMT compared to those living in rural areas (32.3% versus 27.4%). Across the health zones,

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Table 2. Disease-modifying therapy use during the 2-year observation period (between April 1, 2017 and March 31, 2019), presented overall and according to geographical residence

	Overall		Urban/rural residence				Health zone of residence					
			Urban		Rural		Calgary		Edmonton		Other	
	N	(%)	*N*	(%)	*N*	(%)	*N*	(%)	*N*	(%)	*N*	(%)
	12,338	100	10,475	84.9	1,863	15.1	4,498	36.5	4,011	32.5	3,829	31.0
≥1 DMT dispensation	**3,892**	**31.5**	**3,381**	***32.3**	**511**	**27.4**	**1,446**	**[a]32.1**	**1,314**	**[a]32.8**	**1,132**	**[b]29.6**
Among those with ≥1 DMT dispensation												
Older platform	***2,037***	***52.3***	***1,763***	***52.1***	***274***	***53.6***	***747***	***51.7***	***688***	***52.4***	***602***	***53.2***
Glatiramer acetate	1,442	37.1	1,241	36.7	201	39.3	546	37.8	472	35.9	424	37.5
Interferon beta-1a	501	12.9	439	13.0	62	12.1	153	[a]10.6	193	[b]14.7	155	[b]13.7
Interferon beta-1b	79	2.0	<70	<2.1	<15	<2.9	29	2.0	26	2.0	24	2.1
Peginterferon beta-1a	62	1.6	<60	<1.8	<10	<2.0	38	[a]2.6	13	[b]1.0	11	[b]1.0
First line oral	***1,193***	***30.7***	***1,046***	***30.9***	***147***	***28.8***	***420***	***29.1***	***424***	***32.3***	***349***	***30.8***
Dimethyl fumarate	879	22.6	777	23.0	102	20.0	336	23.2	310	23.6	233	20.6
Teriflunomide	340	8.7	291	8.6	49	9.6	89	[a]6.2	125	[b]9.5	126	[b]11.1
Highly effective	***967***	***24.9***	***846***	***25.0***	***121***	***23.7***	***385***	***[a]26.6***	***302***	***[b]23.0***	***280***	***[a,b]24.7***
Fingolimod	722	18.6	631	18.7	91	17.8	360	[a]24.9	161	[b]12.3	201	[c]17.8
Ocrelizumab	206	5.3	188	5.6	18	3.5	<40	[a]<2.8	115	[b]8.8	<60	[c]<5.1
Natalizumab	81	2.1	65	1.9	16	3.1	<10	[a]<0.7	43	[b]3.3	<35	[b]<3.1
Induction	***206***	***5.3***	***186***	***5.5***	***20***	***3.9***	***70***	***4.8***	***83***	***6.3***	***53***	***4.7***
Alemtuzumab	137	3.5	<125	<3.7	<20	<3.9	41	[a]2.8	68	[b]5.2	28	[a]2.5
Cladribine	69	1.8	<69	<1.9	<10	<2.0	29	[a,b]2.0	15	[a]1.1	25	[b]2.2
Other therapies	***96***	***2.5***	***86***	***2.5***	***10***	***2.0***	***<10***	***[a]<0.7***	***58***	***[b]4.4***	***<35***	***[c]<3.1***

DMT = disease-modifying therapy.
In accordance with data custodian privacy standards, outcomes with one to nine individuals were reported as < 10 and associated results censored so that those with few outcomes could not be calculated. The "other therapies" consisted of rituximab, cyclophosphamide, daclizumab and mitoxantrone.
*Significantly different between urban and rural.
[a,b,c]Significantly different between each of the geographical health zones of residence; zones sharing the same letter were not significantly different from each other. Statistical comparisons between groups were conducted using simple logistic regression; statistical significance was set at $p < 0.05$.

the proportion who received ≥ 1 DMT dispensation in the urban/population-dense Calgary (32.1%) and Edmonton (32.8%) zones was significantly higher than the other health zones (29.6%; Table 2).

Among those who received ≥ 1 DMT dispensation, the most common (>10%) DMT category types were older platform injection therapies (52.3%), followed by first line oral therapies (30.7%), followed by higher-efficacy therapies (24.9%); these were similar between those who resided in urban and rural areas, and those who resided in the Calgary health zone had a 1.2-fold higher proportion who received a higher-efficacy therapy compared with those who resided in the Edmonton health zone (26.6% versus 23.0%) (Table 2). Regarding specific types of DMTs, use was similar between urban and rural areas, and varied across health zones. A significantly higher proportion of pwMS who resided in the Calgary health zone (versus the other zones) received peginterferon beta-1a (2.6% versus the Edmonton [1.0%] and other [1.0%] health zones) and fingolimod (24.9% versus 12.3% and 17.8%), and a significantly lower proportion received interferon beta-1a (10.6% versus 14.7% and 13.7%), teriflunomide (6.2% versus 9.5% and 11.1%), ocrelizumab (<2.8% versus 8.8% and < 5.1%) and natalizumab (<0.7% versus 3.3% and < 3.1%). A significantly higher proportion of pwMS who resided in the Edmonton health zone received alemtuzumab (5.2% versus the Calgary [2.8%] and other [2.5%] health zones) and other therapies (4.4% versus < 0.7% and < 3.1%) (Table 2).

Healthcare resource utilization

Overall, 97.1% and 77.4% of pwMS had ≥ 1 all-cause and MS-related healthcare resource visit during the 2-year observation period, respectively; a 1.1-fold higher proportion of those who resided in urban areas had a MS-related visit compared with those who resided in rural areas (78.0% versus 73.9%) (Table 3). A significantly higher proportion of pwMS who resided in urban areas (versus rural) visited a neurologist (all-cause: 67.7% versus 63.9%; MS-related: 62.2% versus 56.9%) or a non-neurologist specialist (all-cause: 88.3% versus 82.9%; MS-related: 20.1% versus 15.6%), and had a MS-related ambulatory visit (54.7% versus 41.8%) or MS tertiary clinic visit (59.2% versus 51.7%), and a significantly lower proportion had an ED visit (all-cause: 46.3% versus 62.4%; MS-related: 4.6% versus 6.6%) or hospitalization (all-cause: 20.4% versus 23.0%; MS-related: 2.1% versus 2.9%) (Table 3).

Across the health zones, a significantly higher proportion of pwMS who resided in the urban/population-dense Calgary and Edmonton zones (versus the other zones) visited a non-neurologist specialist (all-cause: 88.8% and 89.9% versus 83.6%; MS-related: 22.0% and 19.6% versus 16.2%), and a significantly lower proportion had an all-cause ED visit (45.6% and 45.6% versus 55.7%) or MS-related hospitalization (1.9% and 2.1% versus 2.6%). PwMS who resided in the Calgary zone (versus the Edmonton and other zones)

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Table 3. Healthcare resource utilization during the 2-year observation period (between April 1, 2017 and March 31, 2019), presented overall and according to geographical residence

	Overall		Urban/rural residence				Health zone of residence					
			Urban		Rural		Calgary		Edmonton		Other	
	N	(%)	*N*	(%)	*N*	(%)	*N*	(%)	*N*	(%)	*N*	(%)
	12,338	100	10,475	84.9	1,863	15.1	4,498	36.5	4,011	32.5	3,829	31.0
Had ≥ 1 healthcare encounter												
All-cause												
Total	11,981	97.1	10,164	97.0	1,817	97.5	4,350	96.7	3,904	97.3	3,727	97.3
Physician visit	11,968	97.0	10,152	96.9	1,816	97.5	4,345	96.6	3,902	97.3	3,721	97.2
General Practitioner	11,792	95.6	10,002	95.5	1,790	96.1	4,284	95.2	3,835	95.6	3,673	95.9
Other type	10,798	87.5	9,254	*88.3	1,544	82.9	3,992	[a]88.8	3,604	[a]89.9	3,202	[b]83.6
Neurologist	8,279	67.1	7,089	*67.7	1,190	63.9	3,178	[a]70.7	2,619	[b]65.3	2,482	[b]64.8
Ambulatory visit	10,563	85.6	8,934	*85.3	1,629	87.4	3,922	[a]87.2	3,330	[b]83.0	3,311	[a]86.5
Emergency department	6,014	48.7	4,852	*46.3	1,162	62.4	2,050	[a]45.6	1,830	[a]45.6	2,134	[b]55.7
Hospitalization	2,566	20.8	2,138	*20.4	428	23.0	875	[a]19.5	854	[b]21.3	837	[b]21.9
MS-related												
Total	9,551	77.4	8,174	*78.0	1,377	73.9	3,628	[a]80.7	3,068	[b]76.5	2,855	[c]74.6
Physician visit	9,368	75.9	8,014	*76.5	1,354	72.7	3,583	[a]79.7	2,974	[b]74.1	2,811	[b]73.4
Neurologist	7,577	61.4	6,517	*62.2	1,060	56.9	2,987	[a]66.4	2,357	[b]58.8	2,233	[b]58.3
General Practitioner	6,371	51.6	5,377	51.3	994	53.4	2,396	[a]53.3	1,964	[b]49.0	2,011	[a]52.5
Other type	2,395	19.4	2,104	*20.1	291	15.6	988	[a]22.0	786	[b]19.6	621	[c]16.2
MS tertiary clinic visit	7,164	58.1	6,200	*59.2	964	51.7	3,189	[a]70.9	1,965	[b]49.0	2,010	[c]52.5
Ambulatory visit	6,508	52.8	5,729	*54.7	779	41.8	3,145	[a]69.9	1,922	[b]47.9	1,441	[c]37.6
Emergency department	609	4.9	486	*4.6	123	6.6	177	[a]3.9	207	[b]5.2	225	[b]5.9
Hospitalization	269	2.2	215	*2.1	54	2.9	86	[a]1.9	85	[a]2.1	98	[b]2.6

*Significantly different between urban and rural.
[a,b,c]Significantly different between each of the geographical health zones of residence; zones sharing the same letter were not significantly different from each other. Statistical comparisons between groups were conducted using simple logistic regression; statistical significance was set at $p < 0.05$.

had a significantly higher proportion with a neurologist visit (all-cause: 70.7% versus 65.3% and 64.8%; MS-related: 66.4% versus 58.8% and 58.3%), non-neurologist specialist visit (MS-related: 22.0% versus 19.6% and 16.2%), ambulatory visit (MS-related: 69.9% versus 47.9% and 37.6%) and a MS tertiary clinic visit (70.9% versus 49.0% and 52.5%), along with a significantly lower proportion with an all-cause hospitalization (19.5% versus 21.3% and 21.9%) and MS-related ED visit (3.9% versus 5.2% and 5.9%).

Discussion

In this retrospective, observational, population based cohort study of 12,338 pwMS, DMT use and healthcare resource utilization was compared between those who resided in urban and rural areas, and across geographical health zones during a 2-year observation period between April 1, 2017 and March 31, 2019 in Alberta. A higher proportion of pwMS who resided in urban areas (versus rural) received a DMT; across the health zones, there were variations in the selection of specific therapies. Regarding healthcare resource utilization, pwMS who resided in urban areas (versus rural) had a higher proportion with an outpatient visit to a neurologist, non-neurologist specialist, ambulatory clinic for a MS-related purpose, and a MS tertiary clinic, along with a lower proportion who had an ED visit and hospitalization. Across the health zones, pwMS who resided in the Calgary health zone (versus the Edmonton and other zones) had a higher proportion with an outpatient visit to a neurologist and MS tertiary clinic, reflecting the management structure of MS care in the province - Calgary has the largest number of MS-clinic-based neurologists and the most extensive multi-disciplinary MS resources in the province compared to Edmonton and other zones; while a lower proportion had an all-cause hospitalization (1.8% lower than Edmonton; 2.4% lower than the other health zones) and MS-related ED visit (1.3% lower than Edmonton; 2.0% lower than the other health zones), this may not represent a clinically meaningful reduction.[24] Findings indicate that disparities in DMT use and healthcare resource utilization exist in pwMS who reside in rural areas in Alberta; this could have far-reaching impacts on the well-being of patients as well as provincial healthcare costs.

DMTs have a considerable influence on slowing disease course and disability progression in MS, and therefore equitable access is of great importance.[15] However, limited evidence exists regarding access to DMTs for pwMS by different geographical areas. Minden et al. (2008) reported that pwMS under the care of a neurologist were more likely to receive a DMT, but the probability of seeing a neurologist was lower for those who lived in rural areas compared with urban areas in the USA.[25] Similarly, Buchanan et al. (2006) found that a significantly smaller proportion of pwMS in rural areas reported having visited a neurologist in the past year than those in urban areas across the USA.[26] In these studies, rural

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residents reported greater difficulty in accessing MS-related care than those living in urban areas due to a lack of specialized care providers within their area and an inability to travel the distance needed to access care.[26,27] It is possible that these factors may have contributed to the observed inequality in DMT use in this study, as a lower proportion of pwMS who resided in rural areas (versus urban) received a DMT, as well as had an outpatient visit to a neurologist or MS tertiary clinic where access to DMTs is facilitated. Additionally, pwMS residing in rural areas in this study were more likely to have had a lower socioeconomic status than those living in urban areas. Previous studies have shown that pwMS who had a lower socioeconomic status visited specialists at a lower rate and were less likely to be prescribed a DMT.[28–31] Factors contributing to this inequality were found to be that pwMS from more deprived areas experienced barriers to services, were more likely to possess clinical characteristics that decreased their suitability for DMT use (including delayed diagnosis, older age and greater disease severity), and had less correspondence with their physicians that was suggestive of reduced advocation for treatment.[29–31] It is concerning that these underlying factors may exist within the Canadian and Alberta public healthcare system; a public healthcare system is designed to ensure equity in access for all. Other potential factors may have contributed to the observed disparity in DMT use such as individual and/or family choice, and drug coverage (status, type). Further research into elucidating the underlying factors (e.g., geographical, socioeconomic, personal choice and drug cost) driving these observed disparities will inform strategies to provide equitable access to DMTs and healthcare for all pwMS.

In this study, the specific types of DMTs used by pwMS varied across the health zones; a number of different factors may have contributed to this variability. Cameron *et al.* (2019) conducted semi-structured interviews with consultant neurologists and MS specialist nurses from across the United Kingdom and found that a number of factors influenced DMT prescribing decisions, such as shared practices and organizational prescribing culture at the local peer level, prior experience with patient outcomes and familiarity with a drug (e.g., the number of patients a healthcare professional prescribed a drug);[32] it is possible that these factors may be contributing to the observed variability in specific types of DMTs across the health zones. To this end, DMT prescribing patterns were investigated among different groups of neurologists in Ontario, and those who were high-volume DMT prescribers (>100 prescriptions/year) showed a broader range of prescribing than those who were low-volume prescribers (≤100 prescriptions/year).[33] While neurology care for pwMS differs across the health zones in Alberta, with those residing in Calgary being managed by MS specialists, and other areas of the province delivering more varied neurologist care, this difference may not account for the variation in DMT selection observed in this study as no differences in DMT prescribing patterns between specialist and non-specialist neurologists has been found.[33,34] With that said, non-specialist neurologists have highlighted the importance of having access to a network of MS specialists to assist in DMT prescribing decisions;[32] this supports the growing need for specialized MS tertiary clinic teams for peer support in addition to optimizing patient care delivery, particularly for practitioners in non-urban areas.

Geographical variation in ED visits and hospitalizations among the general population of Alberta has been reported; the average number of ED visits was found to be twice as high and with typically lower acuity levels, and the rate of hospitalizations was 41% higher among those living in more rural health zones (North, Central and South) compared with those in the urban/population-dense health zones of Calgary and Edmonton.[35] In the current study, pwMS who resided in rural areas had a higher proportion with an acute care visit (ED visit and hospitalization) and a lower proportion with an outpatient visit (neurologist, non-neurologist specialist, ambulatory care clinic for a MS-related purpose and MS tertiary clinic) compared with those who resided in urban areas. These findings highlight the continued challenges in providing equitable access and care for pwMS to coordinated disease management. Improving timely telemedicine access by pwMS (video conferencing, telephone) to a MS specialist outpatient rapid response team for patient concerns, education and counseling may reduce the need for urgent care among pwMS in addition to utilizing other means of timely patient communication such as electronic medical record secure patient messaging systems, particularly for those who reside in rural areas. Based on medical record review of ED visits by pwMS, Abboud et al. (2017) proposed a telephone-based triaging system according to an established algorithm that provides appropriate care needs, facilitating the reduction of unnecessary acute care visits.[36] Leary et al. (2015) demonstrated that a rapid response team approach using proactive case management by primary care-based MS specialist nurses substantially reduced emergency presentation and hospital bed use among pwMS.[37,38] While a rapid response team could be incorporated into current multidisciplinary team-based MS clinics, results from a survey of healthcare professionals who work in MS tertiary clinics across Canada found that the majority of MS clinics are understaffed and do not currently have enough MS specialist healthcare providers to deliver adequate care or funding to provide a fully resourced and team-based approach for optimal MS care management.[39,40]

An important strength of this study is the large population based design. However, this study is also subject to several limitations that should be taken into consideration when interpreting results. Retrospective administrative claims-based studies use data as opposed to medical records, and therefore there is a potential for misclassification of the study cohorts or outcomes. To address this, a validated case definition was used to identify pwMS.[21] The PIN database only provides information on prescription medication dispensations and therefore may not represent actual medication uptake by individuals. Use of over-the-counter medications, prescription medications provided in a hospital or secondary care setting, and other non-pharmacotherapy management were not captured within the administrative data, and therefore not reported in this study.

Conclusions

Our study identified urban/rural disparities in MS care in Alberta - pwMS who resided in rural areas had a lower proportion with a dispensation for a DMT, and an outpatient visit to a neurologist, non-neurologist specialist, ambulatory clinic for a MS-related purpose, and a MS tertiary clinic, along with a higher proportion who had had an ED visit and hospitalization. These findings support the need for further investigation, assessing effect modifiers and confounding variables that if confirmed, underscores the need for investment in resources to increase access to DMTs and MS-related care, particularly for those pwMS residing in rural areas, and funding to provide a model of multidisciplinary team-based MS care to support non-specialist peers and pwMS. Before implementing any given strategy, further investigation into

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the identification of barriers to DMT use and equitable care management for pwMS is required.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/cjn.2024.54.

Data availability statement. The data that support the findings of this study are available from Alberta Health Services and Alberta Health, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

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Author contributions. KV, KM, HL, LR and SK contributed to the study concept and design. KV, SAH and HL conducted the analyses, and EB prepared the initial draft of the manuscript with assistance from KM. All authors contributed to the interpretation of the data and critical revision of the manuscript for intellectual content. SK provided study supervision.

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