

Hospital Admissions and MS: Temporal Trends and Patient Characteristics

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Multiple sclerosis (MS) is a chronic disease and the most common cause of non-traumatic neurological disability in young adults,^{1,2} placing a considerable burden on patients, families, and the healthcare system. In fact, MS patients are more than twice as likely to visit a medical professional or be hospitalized as individuals without MS.³

Hospital admissions are measured outcomes in both clinical trials and observational studies,⁴⁻⁸ and are often considered important surrogate measures for disease worsening and overall demand on healthcare resources.⁸ Thus, understanding hospitalization patterns is imperative to facilitate appropriate resource allocation, can aid in the evaluation of disease-management strategies, and can provide an indication of drug effectiveness. Despite this, few studies have specifically examined hospital admission patterns in MS.^{2,9,10} One American study evaluating admissions captured by a large inpatient care database found MS-related hospital stays average 5 days, remaining stable from 1998 to 2006.² However, much remains unknown; to date, few others have investigated hospital admission rates over time in MS, or done so in a setting where healthcare is universally covered for all residents. The purpose of this study was to examine patterns, temporal trends, and patient characteristics influencing hospital admissions in a large MS cohort in British Columbia, Canada, from 1986 to 2008.

METHODS

Data Source

Patients with definite MS (McDonald¹¹ or Poser¹² criteria) registered at one of the 4 British Columbia MS clinics by December 31, 2004, were identified through the British Columbia MS (BCMS) database. Established in 1980, the database contains prospectively collected clinical information on approximately 80% of the British Columbia MS population during the study period. We linked this clinical data with the British Columbia Ministry of Health's Discharge Abstract (hospital separations) database and Registry and Premium Billing Files (to confirm

residency in British Columbia¹³) at the individual level using unique health identification numbers. The latter linkage provided registration dates for all British Columbia

Objectives: Hospital admissions are important surrogate measures for disease worsening and increased demand on healthcare resources; few studies have examined hospitalizations in multiple sclerosis (MS). We examined hospital admission rates and patterns in a large Canadian MS cohort.

Study Design: Retrospective, observational study.

Methods: Data from the British Columbia MS database were linked with hospital separation and registry administrative data, 1986 to 2008. Main outcomes included all-cause hospital admission rates and length of stay. The influence of time and patient characteristics was examined using multivariable regression models.

Results: Overall rate of all-cause admissions was 32.4 per 100 MS patients. Rates decreased by 1.4% (adjusted incidence rate ratio [IRR] 0.986; 95% confidence interval [CI] 0.982-0.990) per year from 1986 onward. Higher admission rates were associated with older age (adjusted IRR 1.011; 95% CI 1.007-1.014), primary progressive MS (adjusted IRR 1.294; 95% CI 1.162-1.441), and a longer disease duration (adjusted IRR 1.030; 95% CI 1.027-1.034). Mean length of inpatient stay was 10.2 (standard deviation [SD] 24.8) days, and increased over time. Hospital stays were longer for older patients and those with a longer disease duration, but were not influenced by sex or disease course.

Conclusions: Admission rates for MS patients have decreased since 1986, but length of stay has increased. Patients with a longer disease duration and those with primary progressive MS had higher rates of admission and longer stays. Understanding the impact of time and patient characteristics on hospitalizations is important for resource allocation planning and designing future research studies examining interventions and treatments for MS.

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Take-Away Points

Patients with multiple sclerosis (MS) are relatively high users of the healthcare system, but little is known about one of the most financially burdensome elements of healthcare use—hospitalizations.

- Hospitalization rates have decreased over time, but length of stay has increased.
- Both patient (age) and disease (duration and course) characteristics were associated with the number or length of hospital stays.
- These study results will help aid in appropriate resource allocation planning, and are useful in planning future studies examining the impact of various MS interventions and treatments.

residents enrolled in the universal healthcare plan, providing confirmation of a patient's residence in British Columbia throughout the study period. These databases have served as the basis for many observational studies, and are considered to be of high quality.¹³⁻¹⁸

Data were extracted for all hospital admissions from 1986 (the first full year both hospital and registry data were available) to 2008 and included admission and discharge dates, length of stay, primary diagnostic classification (ie, reason for admission), and up to 24 additional diagnostic classifications (*International Classification of Disease [ICD]-9 or -10* codes). An ICD-9 code of 340 or ICD-10 code of G35 indicated an admission due to MS. Only admissions occurring after onset of MS symptoms (determined by the MS neurologist and recorded in the BCMS database) were included in the analyses.

Outcomes

The main outcome in this descriptive study was annual all-cause hospital admission rates from 1986 to 2008. Hospital admissions were categorized as “inpatient” (acute admission requiring at least 1 overnight stay), “day care surgery” (admitted and discharged on the same day), and “all-cause” (all admissions [inpatient and day care surgery], regardless of reason, level of care, or length of stay). Day care surgery admissions typically involve a medical procedure, but do not include drug infusions (eg, intravenous corticosteroids or natalizumab). Secondary outcomes included admission rates attributed to MS (ie, with a primary or secondary diagnostic code for MS [ICD-9:340 or ICD-10:G35]), and the length of stay.

Statistical Analyses

Annual admission rates (all cause and MS specific) were estimated by dividing the total number of yearly hospital admissions by the number of MS cohort patients who were resident in British Columbia during that year, and reported per 100 patients with MS. Quasi Poisson regression, fitted using the method of generalized estimating equations (GEEs) with an exchangeable working correlation structure, was used to examine changes in all-cause admission rates over time. The following covariates were determined to be clinically relevant

or statistically important based on univariate analyses ($P < .1$) and were therefore included in the models: sex, age at observation year, disease course (relapsing-onset or primary progressive), disease duration, and calendar year. To account for differences in the British Columbia residency time between patients, the logarithm of time registered with the British Columbia Ministry of Health for each year was included as an offset in the model. No meaningful first-order interactions were detected ($P < .1$). Findings were reported as adjusted incidence rate ratios (IRRs), with 95% confidence intervals (CIs).

Admissions were further examined only in patients with at least 1 hospital admission during the study period to identify potential factors associated with admission with a primary diagnosis of MS. A multivariable logistic regression model fitted by the GEE method, with an exchangeable working correlation structure, was used, with the same covariates as above. An interaction between sex and age at observation year ($P < .001$) necessitated separate models for males and females. Findings were reported as adjusted odds ratios with corresponding 95% CIs.

The mean length of hospital stay was examined for inpatient admissions only; a separate mean was also estimated for inpatient admissions where the primary admission reason was MS. To identify factors associated with a longer hospital stay for all inpatient admissions, a negative binomial regression model¹⁹ fitted by the GEE method, with an exchangeable working correlation structure, with the same covariates as above, was used. No significant interactions were detected ($P < .1$). Findings were reported as adjusted IRRs with corresponding 95% CIs. Statistical analyses were carried out using SPSS version 18.0 (SPSS Inc, Chicago, Illinois) and R: A Language and Environment for Statistical Computing V.2.13.2 (R Foundation for Statistical Computing, Vienna, Austria; 2011). This study was approved by the University of British Columbia's Clinical Research Ethics board (study number: H08-01544).

RESULTS

A total of 6859 patients with a neurologist-confirmed diagnosis of definite MS were identified from the BCMS database, and 6601 (96.2%) were successfully linked to the British Columbia Ministry of Health's databases. Overall, 72.0% of patients were female and 90.7% had relapsing-onset MS. The mean age at symptom onset was 32.0 (standard deviation [SD] 10.2) years. Between January 1, 1986, and December 31, 2008, 5138 patients had 31,375 hospital admissions (**Table 1**).

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Table 1. Characteristics of MS Patients Identified From the British Columbia MS Database, 1986 to 2008

	Overall Cohort	All-Cause Admissions					
	N = 6601	All Years (1986-2008)	1986-1989	1990-1994	1995-1999	2000-2004	2005-2008
Number of patients with ≥ 1 hospital admission		n = 5138	n = 1655	n = 2330	n = 2572	n = 2855	n = 2532
Total number of hospitalizations	—	31,375	4365	6756	7116	7179	5959
Female (%)	4756 (72.0)	22,175 (70.7)	3096 (70.9)	4645 (68.8)	4998 (70.2)	5202 (72.5)	4234 (71.1)
Male (%)	1845 (28.0)	9200 (29.3)	1269 (29.1)	2111 (31.2)	2118 (29.8)	1977 (27.5)	1725 (28.9)
Mean age at MS symptom onset (SD)	32.0 (10.2)	31.4 (10.7)	30.2 (10.7)	30.6 (10.4)	31.3 (10.7)	32.3 (10.8)	32.5 (10.6)
Disease duration at observation year (years) (SD)	—	17.9 (12.2)	9.4 (9.3)	13.3 (10.9)	14.1 (11.2)	16.6 (12.5)	20.7 (11.7)
Relapsing-onset (%)	5989 (90.7)	27,447 (87.5)	3646 (83.5)	5800 (85.8)	6176 (86.8)	6496 (90.5)	5329 (89.4)
Primary progressive (%)	612 (9.3)	3928 (12.5)	719 (16.5)	956 (14.2)	940 (13.2)	683 (9.5)	630 (10.6)
Mean age at observation year (SD)	—	59.9 (12.9)	64.2 (12.5)	62.1 (12.7)	60.0 (12.7)	57.7 (12.8)	56.7 (12.3)

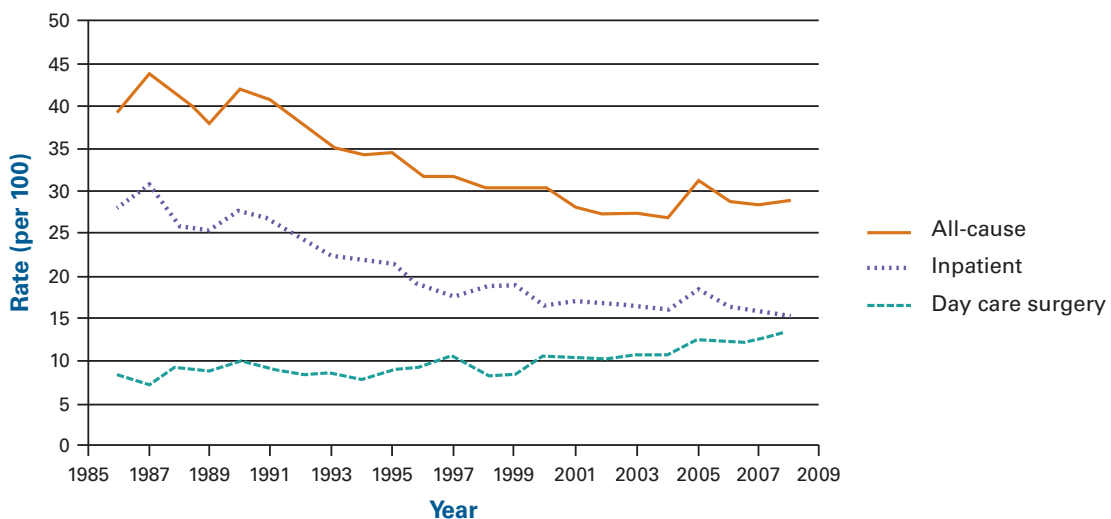
MS indicates multiple sclerosis; SD, standard deviation.

All-Cause Hospital Admissions

The overall rate of all-cause admissions was 32.4 admissions per 100 patients with MS, which decreased from an annual rate of 39.2 to 29.0 per 100 patients with MS between 1986 and 2008 (Figure 1). Admission rates, estimated using multivariable regression, decreased by 1.4% (adjusted IRR 0.986, 95% CI 0.982-0.990) per year from 1986 onward (Table 2). When examined separately, the rate of inpatient

admissions decreased over time while the rate of day care surgery admissions increased (Figure 1). Higher IRRs were associated with primary progressive MS (adjusted IRR 1.294, 95% CI 1.162-1.441), an older age at hospital admission (adjusted IRR per year 1.011, 95% CI 1.007-1.014), and a longer disease duration (adjusted IRR per year 1.030, 95% CI 1.027-1.034). Women had a lower rate of admission compared with men (adjusted IRR 0.875, 95% CI 0.811-0.945) (Table 2).

Figure 1. Annual All-Cause Admission Rates for Patients With MS (1986-2008)^a



MS indicates multiple sclerosis.

Inpatient and day care surgery were a subset of the overall all-cause admissions.

^aDenominator for each year was the number of MS cohort patients living in British Columbia for that year.

■ **Table 2.** Adjusted Incidence Rate Ratios for All-Cause Admissions for Patients With MS

Covariate	Adjusted Incidence Rate Ratio ^a	95% CI
Sex		
Male	—	
Female	0.875	0.811-0.945
Disease duration	1.030	1.027-1.034
Age at observation year	1.011	1.007-1.014
Disease course		
Relapsing-onset	—	
Primary progressive	1.294	1.162-1.441
Calendar year	0.986	0.982-0.990

CI indicates confidence interval; MS, multiple sclerosis.
^aAdjusted for all listed covariates.

Hospital Admissions Due to MS

Rates of admissions for MS decreased over time, although they differed considerably depending on whether MS was listed as the primary or as a secondary reason for admission. Where the primary reason for admission was MS, the overall rate per 100 MS patients was 5.9, decreasing from an annual rate of 14.1 in 1986 to 1.6 in 2008. When MS was listed as a secondary reason for admission, the overall rate was 10.7 per 100 patients with MS, decreasing from an annual rate of 12.1 in 1986 to 8.2 in 2008 (Figure 2). However, the odds of admission to hospital where MS was the primary reason have increased by approximately 9% per year when sex, age at observation, disease course, and disease duration are taken into account (Table

3). Older men were more likely to have a primary admission due to MS compared with younger men (adjusted odds ratio [OR] per year 1.026, 95% CI 1.016-1.036); this association with age was not significant for women (adjusted OR 0.995, 95% CI 0.988-1.001) (Table 3). Disease course and disease duration had no association when MS was the primary reason for admission (Table 3).

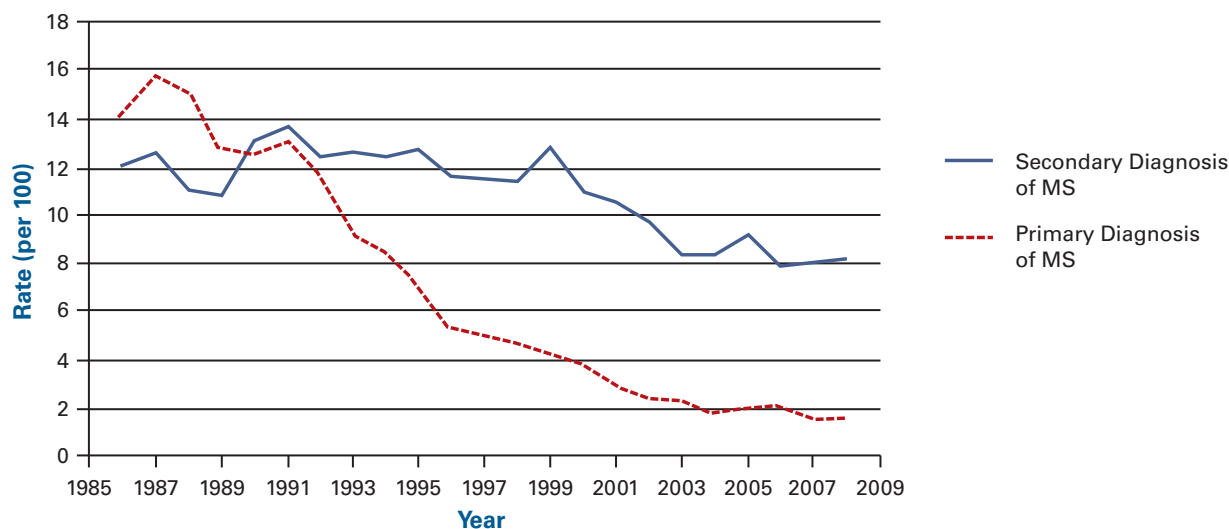
Length of Stay

The mean length of stay for all inpatient hospital admissions between 1986 and 2008 was 10.2 (SD 24.8) days, and 13.2 (SD 25.9) days when restricted to only inpatient admissions where the primary reason was MS (Figure 3). The length of hospital stay for MS patients increased with age (adjusted IRR per year 1.013, 95% CI 1.009-1.018). Patients with a longer disease duration had relatively longer hospital stays (adjusted IRR 1.010 per year, 95% CI 1.004-1.016). Sex or disease course were not associated with an extended hospital stay (Table 4).

DISCUSSION

In this retrospective British Columbian cohort study, 78% of the MS patients had at least 1 hospital admission between 1986 and 2008, with an overall admission rate of 32 per 100 patients. While admission rates have decreased over the last 2 decades, the mean length of stay has increased. MS-related clinical characteristics of the cohort appeared to influence our

■ **Figure 2.** Annual Admission Rates Where MS Was the Primary or Secondary Reason for Admission^a



MS indicates multiple sclerosis.

^aDenominator for each year was the number of MS cohort patients living in British Columbia for that year.

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results. There are few other MS-specific studies with which to compare our findings, and although similar general patterns in hospitalizations are evident in the overall Canadian population,²⁰ we did observe some unanticipated differences.

Sex was associated with admissions in unexpected ways. Men with MS were more likely to have a hospital admission compared with women with MS, although length of stay was similar for men and women after adjusting for factors such as age and disease course. Findings were in contrast to those of a recent study evaluating the geography of hospital admissions for MS in England,¹⁰ as well as those typically found in the general population, where women tend to be higher users of the healthcare system,²¹⁻²³ including hospital admissions.²⁴ Possible explanations might include the more rapid disease progression (from MS onset) observed in men,²⁵⁻²⁷ or the higher odds of physical comorbidity reported in men with MS.²⁸

Age also had an impact on our findings; as expected,^{24,29} aging patients with MS had a greater rate of hospital admissions and longer hospital stays. When controlling for age, a longer disease duration was also associated with higher admission

rates and longer hospital stays. Essentially, if 2 individuals of the same age and sex were compared, the one who developed MS at a younger age would be more likely to have a higher rate of hospital admissions, and remain in hospital for longer. This finding appears to contradict the traditional belief that a younger age at MS onset is “favourable.”^{27,30-33} We were unable to find another study examining the impact of age or MS disease duration on hospital admissions with which to compare our results.

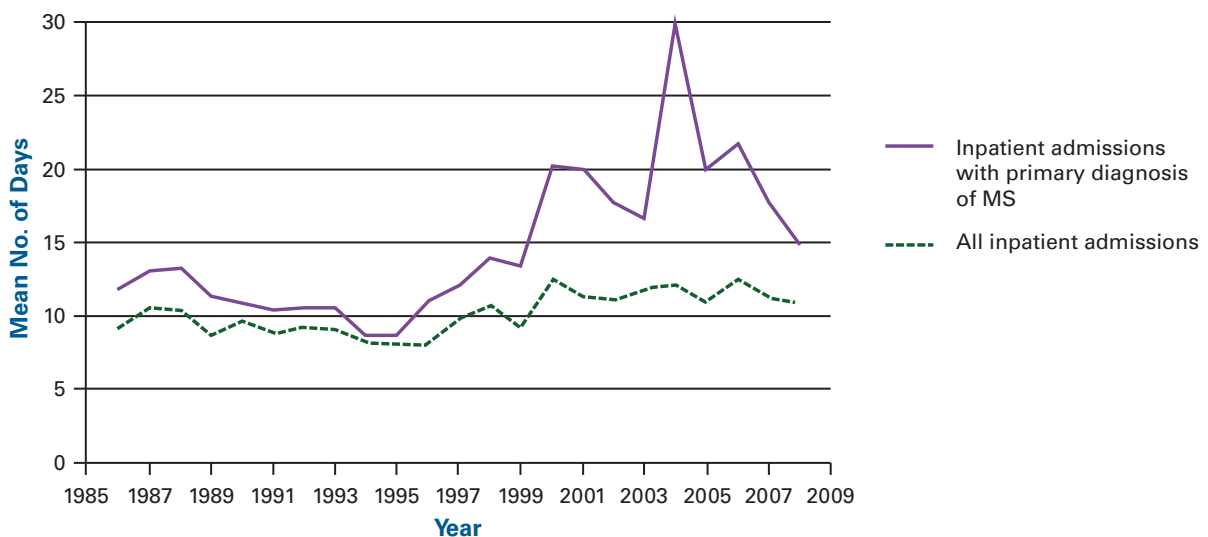
When compared with relapsing-onset, primary progressive MS was associated with higher all-cause admission rates. However, admissions specifically due to MS and the actual length of stay were unrelated to disease course. This increased rate in all-cause hospitalizations could be related to the more rapid disease progression observed in primary

■ **Table 3.** Factors Associated With Hospital Admissions When MS Was the Primary Reason (Primary Diagnostic Classification)^a

	Males		Females	
	Adjusted Odds Ratio ^b	95% CI	Adjusted Odds Ratio ^b	95% CI
Disease duration	1.003	0.991-1.014	1.008	1.000-1.016
Age at observation year	1.026	1.016-1.036	0.995	0.998-1.001
Disease course				
Relapsing-onset	—			
Primary progressive	1.072	0.835-1.377	1.136	0.908-1.421
Calendar year	1.089	1.073-1.105	1.090	1.080-1.101

CI indicates confidence interval; MS, multiple sclerosis.
^aOnly includes those patients with ≥1 hospital admission during follow-up.
^bAdjusted for all listed covariates.

■ **Figure 3.** Mean Length of Inpatient Hospital Stays for Patients With MS^a



MS indicates multiple sclerosis.

^aOnly includes those admissions with ≥1 overnight stay.

■ **Table 4.** Factors Associated With the Length of Hospital Stay for Patients With MS^a

	Adjusted Incidence Rate Ratio ^b	95% CI
Sex		
Male	—	
Female	0.977	0.886-1.078
Disease duration	1.010	1.004-1.016
Age at observation year	1.013	1.009-1.018
Disease course		
Relapsing-onset	—	
Primary progressive	1.098	0.981-1.230
Calendar year	1.002	0.996-1.009

CI indicates confidence interval; MS, multiple sclerosis.
^aOnly includes inpatient admissions.
^bAdjusted for all listed covariates.

progressive MS.^{34,35} Factors driving length of hospital stay are complex, and the absence of difference between the disease courses is unclear.

While there appeared to be a dramatic decrease in the overall admission rates and for admissions specific for MS over time, the odds of having a primary diagnostic classification of MS on admission were found to have increased in recent years once sex, age, and disease duration were taken into account. This might indicate that although fewer MS patients are being admitted, when they are, it is more likely to be MS related. However, it is difficult to differentiate whether this observation is due to clinical factors, or if the disease is now being recognized and recorded more often.

The mean length of stay increased over the study period, averaging 10 days for all inpatient admissions, and 13 days if the admission was MS-related. Although the length of hospital stays in the general Canadian population has also increased (by 5.6% from 1995-1996 and 2008-2009²⁰), we observed a more substantial increase of 25% in the MS cohort over the same time period. So although MS patients are now being hospitalized less, they tend to be hospitalized for longer durations, suggesting that those MS patients now being hospitalized are “sicker” or are admitted for more complex reasons. Our mean length of stay was over twice that reported in a recent American study.² However, differences in the healthcare system (universal coverage in Canada vs a mix of private and public insurance in the United States³⁶), study design, and possibly cohort structure (the US MS patients were not population based) could have influenced results.

Additional findings from our study included a shift from inpatient admissions to day care surgeries over time. This is likely a reflection of both the Canadian healthcare system

reorganization (initiated in the 1990s) that resulted in a reduction in the number of hospital beds available for inpatient admissions,³⁷ and advances in technology that now allow many services to be performed on an outpatient level.^{37,38}

Over the past 2 decades, there have been a number of changes in the management of MS which may have influenced hospital admission patterns, including advancements in the recognition and earlier diagnosis of the disease,³⁹ and the introduction of pharmacotherapies aimed at reducing relapses and slowing disease progression. The first disease-modifying drugs (DMDs) became available in Canada during the study period. While the decline in hospital admissions was apparent before the introduction of the first DMD

in 1995, a proper evaluation of their impact is beyond the scope of the current study and requires an entirely different study design and analysis.

Limitations

This study examined hospital admissions in a cohort of patients with MS in British Columbia, Canada, which may limit the generalizability of the findings. Although we have no reason to believe the demographic characteristics of the BC MS cohort would differ systematically from other MS cohorts, there is the potential for differences in hospital use due to variations in practice patterns and healthcare funding structures. Although our use of administrative data offers a population-based view, it inherently lacks information on some potentially important confounders that might influence hospital admissions, including smoking status, family history, socioeconomic status, and comorbidities. However, by linking to the British Columbia MS database, we were able to consider clinical factors such as disease course and disease duration, which is often not possible when using only administrative data sources. Despite these limitations, this is still one of the first population-based studies to examine temporal trends and the impact of patient characteristics on hospital admissions over an extended period of time, and to do so in a Canadian setting.

Despite the fact that patients with MS are relatively high users of the healthcare system, surprisingly few details are known about one of the most financially burdensome elements of healthcare use—hospitalizations. Our findings provide much-needed information to fill the knowledge gap in hospital services utilization by patients with MS, and the influence of clinical and demographic characteristics and time.

This information is needed for appropriate resource allocation planning and future studies examining the impact of various MS interventions and treatments.

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