

Characteristics of a population-based multiple sclerosis cohort treated with disease-modifying drugs in a universal healthcare setting

Huah Shin Ng¹, Feng Zhu¹, Elaine Kingwell¹, Yinshan Zhao¹, Shenzhen Yao^{2,3}, Okechukwu Ekuma⁴, Lawrence Svenson⁵, Charity Evans², John D. Fisk⁶, Ruth Ann Marrie⁴, Helen Tremlett¹

¹University of British Columbia, British Columbia, Canada; ²University of Saskatchewan, Saskatchewan, Canada; ³Health Quality Council, Saskatchewan, Canada; ⁴University of Manitoba, Manitoba, Canada; ⁵Alberta Health, University of Alberta and University of Calgary, Alberta, Canada; ⁶Nova Scotia Health Authority and Dalhousie University, Nova Scotia, Canada

Email: huahshin.ng@ubc.ca

Background

- The efficacy of a disease-modifying drug (DMD) is typically established via short, 2-3 year clinical trials in highly select and motivated groups of people with multiple sclerosis (MS).
- In clinical practice, DMDs are used for many years in a more diverse population of persons with MS.

Objective

To describe the characteristics of a population with MS exposed to their first DMD in the real-world setting.

Methods

- Linked, population-based health administrative data in **four Canadian provinces**: British Columbia, Saskatchewan, Manitoba and Nova Scotia (see [Data sources](#)).

➤ Population:



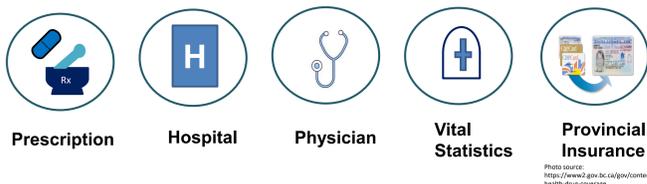
➤ Study follow-up:

- **Study entry:** most recent of their first MS or demyelinating event or 01/January/1996
- **Study end:** to the earliest of death, emigration, or 31/March/2018

➤ Characteristics captured:

- **Sex, age and DMD class:** at date of 1st prescription filled
- **Socioeconomic status** (based on neighbourhood income)
- **Comorbidity burden** (in the year pre-study entry, using the Charlson Comorbidity Index)
- **Calendar period** 1996-2012 and 2013-2017 (differentiating the time periods when <5 and ≥5 individual DMD classes were available)

Data sources:



Acknowledgements

This study was supported by Canadian Institutes of Health Research (CIHR) Project and Foundation grant (PJT-156363 and FDN-159934, PI: Tremlett). We are grateful to the Data Services Platform of the Saskatchewan Center for Patient-Oriented Research (SCPOR). We are also grateful to Yan Wang (Dalhousie University) for her support in performing data analyses in Nova Scotia. Access to, and use of, BC data was facilitated by Population Data BC, and approved by the BC Ministry of Health, BC PharmaNet, and the BC Vital Statistics Agency. The authors acknowledge the Manitoba Centre for Health Policy for use of the Population Research Data Repository under project #2018-023 (HIPC #2018/19-13). Some data used in this report were made available by Health Data Nova Scotia of Dalhousie University. All inferences, opinions, and conclusions drawn in this manuscript are those of the authors, and do not reflect the opinions or policies of the British Columbia Data Steward(s), Manitoba Centre for Health Policy or Manitoba Health, Health Data Nova Scotia or the Nova Scotia Department of Health and Wellness. This study is based, in part, on de-identified data provided by the Saskatchewan Ministry of Health and eHealth Saskatchewan. The interpretation and conclusions contained herein do not necessarily represent those of the Government of Saskatchewan, the Saskatchewan Ministry of Health, or eHealth Saskatchewan.

Disclosures

Huah Shin Ng receives funding from the MS Society of Canada's endMS Postdoctoral Fellowship and the Michael Smith Foundation for Health Research Trainee Award. During the past year, she has received funding from the Canadian Institutes of Health Research (CIHR) Drug Safety and Effectiveness Cross-Disciplinary Training Program. Feng Zhu has no disclosures. Elaine Kingwell is supported through research grants from the MS Society of Canada and the Canadian Institutes of Health Research. During the past 5 years, she has received travel expenses to attend conferences from ACTRIMS (2018, 2020) and ECTRIMS (2019). Yinshan Zhao, Shenzhen Yao, Okechukwu Ekuma and Lawrence Svenson have no disclosures. Charity Evans receives research funding from CIHR and the Saskatchewan Health Research Foundation. John Fisk receives research funding from CIHR, the MS Society of Canada, Crohn's and Colitis Canada, Nova Scotia Health Authority Research Fund, and licensing and distribution fees from MAPI Research Trust. Ruth Ann Marrie receives research funding from: CIHR, Research Manitoba, Multiple Sclerosis Society of Canada, Multiple Sclerosis Scientific Foundation, Crohn's and Colitis Canada, National Multiple Sclerosis Society, CMSC, and the US Department of Defense. She is supported by the Waugh Family Chair in Multiple Sclerosis. Helen Tremlett is the Canada Research Chair for Neuroepidemiology and Multiple Sclerosis. Current research support received from the National Multiple Sclerosis Society, the Canadian Institutes of Health Research, the Multiple Sclerosis Society of Canada and the Multiple Sclerosis Scientific Research Foundation. In addition, in the last five years, has received research support from the UK MS Trust; travel expenses to present at CME conferences from the Consortium of MS Centres (2018), the National MS Society (2016, 2018), ECTRIMS/ACTRIMS (2015, 2016, 2017, 2018, 2019, 2020), American Academy of Neurology (2015, 2016, 2019). Speaker honoraria are either declined or donated to an MS charity or to an unrestricted grant for use by HT's research group.

Results

Table 1. Characteristics of the MS cohort

Characteristics	Total N=10,418 n (%)	Characteristics	Total N=10,418 n (%)
Sex		Socioeconomic status^a	
Women	7,693 (73.8)	1 (lowest income quintile)	1,800 (17.3)
Men	2,725 (26.2)	2	1,962 (18.8)
Age group at first DMD		3	2,175 (20.9)
< 30 years	1,860 (17.9)	4	2,179 (20.9)
30 to 39 years	3,359 (32.2)	5 (highest income quintile)	2,129 (20.4)
40 to 49 years	3,454 (33.2)	Unavailable	173 (1.7)
50 to 59 years	1,475 (14.2)	Comorbidity score^b	
≥ 60 years	270 (2.6)	0	8,673 (83.3)
Calendar period at first DMD		1	1,369 (13.1)
1996-2012	7,736 (74.3)	2	285 (2.7)
2013-2017	2,682 (25.7)	≥ 3	91 (0.9)

^aSocioeconomic status is represented by neighborhood income quintiles, based on the closest available measurement to the study entry date.
^bComorbidity is measured using the Charlson Comorbidity Index (modified to exclude hemiplegia/paraplegia to avoid misclassifying MS complications as comorbidity) during the one-year period prior to the study entry date.

Table 2. Sex and age of the MS population by individual DMD class

Characteristics	Sex [female] n/Total N ^a (%)	Age at first DMD Mean (SD)
Overall cohort	7,693/10,418 (73.8)	39.6 (10.1)
<i>By individual DMD class</i>		
Beta-interferon	4,531/6,171 (73.4)	39.7 (10.0)
Glatiramer acetate	2,289/2,967 (77.1)	39.3 (10.0)
Natalizumab	77/116 (66.4) ^b	39.6 (12.0)
Fingolimod	42/56 (75.0) ^b	41.0 (10.9)
Dimethyl fumarate	477/711 (67.1)	39.1 (10.4)
Teriflunomide	238/338 (70.4)	43.6 (10.9)
Alemtuzumab	24/37 (64.9) ^b	35.9 (10.0)

^aTotal N is the total number of people with that type (class) of first DMD. Key: SD, standard deviation.
^bAs per data privacy and access agreements, small cell size (<6 individuals within any group) in one or more provinces are suppressed and were not included in the total count (either the numerator or denominator).

Table 3. Disease-modifying drug use in the MS population by calendar period

First DMD (drug class)	First DMD filled 1996-2012 n (%) of adults with MS	First DMD filled 2013-2017 n (%) of adults with MS
Beta-interferon	5,569 (72.0)	602 (22.4)
Glatiramer acetate	2,084 (26.9)	883 (32.9)
Natalizumab	~49 (0.7) ^a	~67 (2.5) ^a
Fingolimod	21 (0.3)	~35 (1.4) ^a
Teriflunomide	6 (0.1)	332 (12.4)
Dimethyl fumarate	NA	711 (26.5)
Alemtuzumab	NA	~37 (1.4) ^a
Total	7,736 (100)	2,682 (100)

Key: NA, not applicable (as those individual DMDs were marketed in Canada after 2012).
^aAs per data privacy and access agreements, small cell size (<6 individuals within any group) in one or more provinces are suppressed and were not included in the total count (the denominator remains the same).

Summary points

Overall, 10,418 with MS filled a DMD prescription during the 22-year study period.

➤ Most were women:

- Variations in sex distribution observed.
- Ranged from 65% for alemtuzumab to 77% for glatiramer acetate.

➤ Mean (SD) age at first DMD:

- Variations in the average age at first prescription fill across the different DMDs observed.
- Ranged from 35.9 (SD 10.0) years for alemtuzumab to 43.6 (SD 10.9) years for teriflunomide.

➤ Socioeconomic status:

- The cohort was distributed evenly across the income-based quintiles (neighborhood-level).

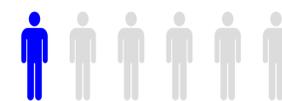
➤ Patterns of treatment:

- Changed considerably between 1996-2012 vs. 2013-2017
- Increased uptake of the oral DMDs.
- Likely reflects increased availability (choice) of DMDs to treat MS.

➤ Overall study population and implications:



people with MS had at least **some comorbidity**.



≥50 years old at the time of their first DMD.

Implications

Older individuals or individuals with comorbidity are typically excluded from clinical trials.

Findings illustrate the need to **understand the harms and benefits of DMD use in these understudied groups.**

