Characteristics of a population exposed to a disease-modifying drug for multiple sclerosis in the real-world setting (1996-2017)

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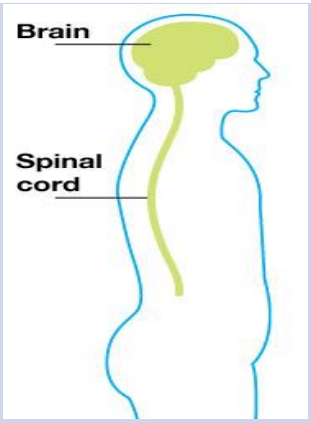
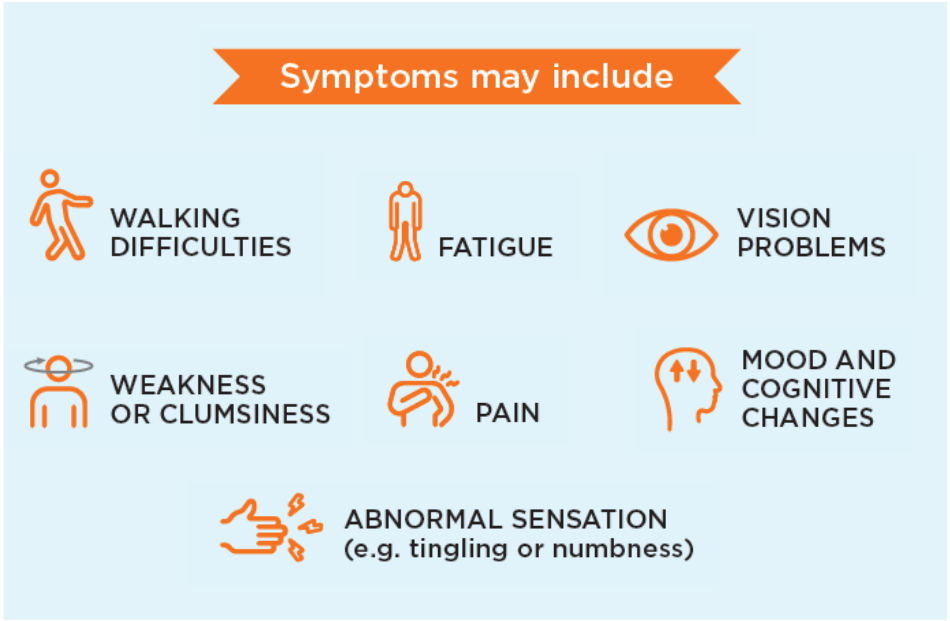
Background

Multiple sclerosis (MS)



Chronic disease affecting the central nervous system



has among the **world's highest prevalence** of MS.

Images sources:
https://www.mstrust.org.uk/a-z/central-nervous-system-cns
https://www.canada.ca/en/public-health/services/publications/diseases-conditions/multiple-sclerosis-infographic.html

Background

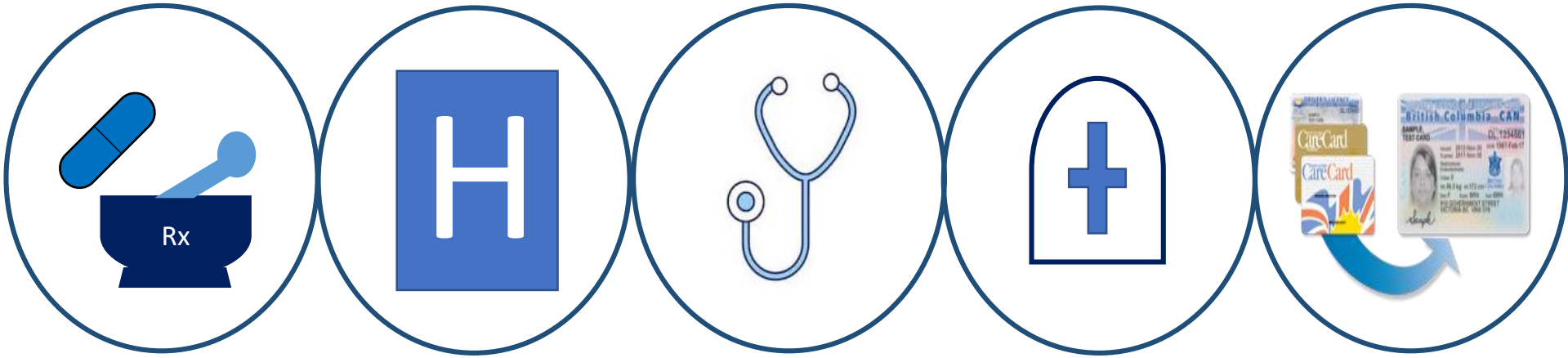
- In the last 2 decades, the **therapeutic options for MS have shifted** dramatically (from 0 disease-modifying drugs [DMDs] to >15).
- The **efficacy** of a DMD is typically established after **short clinical trials** in **highly selected groups** of patients.
- In **clinical practice**, DMDs are used in the **wider MS population** and require **long-term use**.

Objective:

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

Methods: Data source

Linked, population-based health administrative data in the province of British Columbia, Canada.



Prescription | Hospital | Physician | Vital statistics | Provincial insurance

Photo source: https://www2.gov.bc.ca/gov/content/health/health-drug-coverage

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1. BC Ministry of Health [creator] (2017): PharmaNet. V2. BC Ministry of Health [publisher]. Data Extract. Data Stewardship Committee (2017). http://www.popdata.bc.ca/data.
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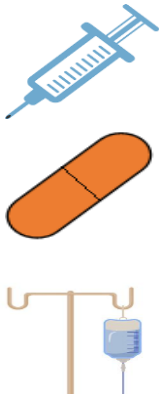
Methods: Population

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/December/2017

Methods: Characteristics captured

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



Route of administration	DMD class	Health Canada approval year
Injection	Beta-interferon	July 1995
Injection	Glatiramer acetate	October 1997
Infusion	Natalizumab	September 2006
Oral	Fingolimod	March 2011
Oral	Dimethyl fumarate	April 2013
Oral	Teriflunomide	November 2013
Infusion	Alemtuzumab	December 2013

1996-2012

2013-2017

Results: Characteristics of the multiple sclerosis cohort

Characteristics	Total N=4,732 n (%)
Sex	
Women	3,469 (73.3)
Men	1,263 (26.7)
Age group at first DMD	
< 30 years	815 (17.2)
30 to 39 years	1,547 (32.7)
40 to 49 years	1,560 (33.0)
50 to 59 years	686 (14.5)
≥ 60 years	124 (2.6)
Calendar period at first DMD	
1996-2012	3,477 (73.5)
2013-2017	1,255 (26.5)

Characteristics	Total N=4,732 n (%)
Socioeconomic status[a]	
1 (lowest income quintile)	914 (19.3)
2	870 (18.4)
3	992 (21.0)
4	1,006 (21.3)
5 (highest income quintile)	938 (19.8)
Unavailable	12 (0.3)
Comorbidity score[b]	
0	3,960 (83.7)
1	584 (12.3)
2	146 (3.1)
≥ 3	42 (0.9)

Key: DMD, disease-modifying drugs

[a]**Socioeconomic status** is represented by neighborhood income quintiles, based on the closest available measurement to the study entry date.
[b]**Comorbidity** 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.

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Most were **women**

Over **1 in 6** were **≥50 years old** at the time of their first DMD

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Distributed evenly across the income-based quintiles (neighborhood-level)

Almost **1 in 6 people** had at least **some comorbidity**

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Results:

Sex and age of the multiple sclerosis cohort *by individual DMD class*

Characteristics	Sex [female] n/Total N[a] (%)	Age at first DMD Mean (SD)
Overall cohort	3,469/4,732 (73.3)	39.7 (10.1)
By individual DMD class		
Beta-interferon	2,169/2,955 (73.4)	39.7 (10.0)
Glatiramer acetate	869/1,128 (77.0)	39.2 (10.1)
Natalizumab	45/68 (66.2)	40.0 (12.3)
Fingolimod	27/33 (81.8)	39.0 (11.5)
Dimethyl fumarate	202/313 (64.5)	39.7 (10.2)
Teriflunomide	132/196 (67.4)	43.1 (10.8)
Alemtuzumab	24/37 (64.9)	35.9 (10.3)

[a]**Total N** is the total number of people with that type (class) of first DMD.
Key: SD, standard deviation.

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Sex and age of the multiple sclerosis cohort *by individual DMD class*

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Glatiramer acetate	869/1,128 (77.0)
Natalizumab	45/68 (66.2)
Fingolimod	27/33 **(81.8)**
Dimethyl fumarate	202/313 **(64.5)**
Teriflunomide	132/196 (67.4)
Alemtuzumab	24/37 **(64.9)**

Ranged from **65%** for alemtuzumab and dimethyl fumarate to **82%** for fingolimod.

[a]**Total N** is the total number of people with that type (class) of first DMD.
Key: SD, standard deviation.

Results:

Sex and age of the multiple sclerosis cohort *by individual DMD class*

Characteristics	Age at first DMD Mean (SD)
Overall cohort	39.7 (10.1)
By individual DMD class	
Beta-interferon	39.7 (10.0)
Glatiramer acetate	39.2 (10.1)
Natalizumab	40.0 (12.3)
Fingolimod	39.0 (11.5)
Dimethyl fumarate	39.7 (10.2)
Teriflunomide	**43.1** (10.8)
Alemtuzumab	**35.9** (10.3)

Overall mean age at first DMD= 39.7 years:

Ranged from **35.9** years for alemtuzumab to **43.1** years for teriflunomide.

[a]**Total N** is the total number of people with that type (class) of first DMD.
Key: SD, standard deviation.

Results:
Disease-modifying drug use in the multiple sclerosis cohort *by calendar period*

First DMD (drug class)	First DMD filled <u>1996-2012</u> n (%) of adults with MS	First DMD filled <u>2013-2017</u> n (%) of adults with MS
Beta-interferon	2,740 (78.8)	215 (17.1)
Glatiramer acetate	697 (20.1)	431 (34.3)
Natalizumab	31 (0.9)	37 (3.0)
Fingolimod	9 (0.3)	24 (1.9)
Dimethyl fumarate	*NA*	313 (24.9)
Teriflunomide	*NA*	196 (15.6)
Alemtuzumab	*NA*	37 (3.0)
Total	***3,477 (100)***	***1,253 (100)***

Key: NA, not applicable (as those individual DMDs were marketed in Canada after 2012).

Results:
Disease-modifying drug use in the multiple sclerosis cohort *by calendar period*

First DMD (drug class)	First DMD filled <u>1996-2012</u> n (%) of adults with MS	First DMD filled <u>2013-2017</u> n (%) of adults with MS	
Beta-interferon	2,740 (78.8)	215 (17.1)	3
Glatiramer acetate	697 (20.1)	431 (34.3)	1
Natalizumab	31 (0.9)	37 (3.0)	
Fingolimod	9 (0.3)	24 (1.9)	
Dimethyl fumarate	*NA*	313 (24.9)	2
Teriflunomide	*NA*	196 (15.6)	4
Alemtuzumab	*NA*	37 (3.0)	
Total	***3,477 (100)***	***1,253 (100)***	

Key: NA, not applicable (as those individual DMDs were marketed in Canada after 2012).

Discussion

Clinical trials	Real-world setting (British Columbia)
(a) Study population	
Typically excluded: ➢ Persons over 50 or 60 years of age ➢ Individuals with comorbidity	**Observed in our study:** ➢ About 17% of people were ≥50 years old ➢ Almost 17% of people had comorbidity
(b) Variations in the average age at first prescription fill across the different DMDs	
➢ 32.1-35.1 years for alemtuzumab ➢ 37.7 years for teriflunomide	➢ 35.9 years for alemtuzumab ➢ 43.1 years for teriflunomide
(c) Variations in sex distribution (i.e. proportion of women)	
➢ Alemtuzumab range: 64-66% ➢ Glatiramer acetate range: 68-72%	➢ Alemtuzumab: 65% ➢ Glatiramer acetate: 77%

Discussion

Clinical trials	Real-world setting (British Columbia)
(a) Study population	
Typically excluded: ➢ Persons over 50 or 60 years of age ➢ Individuals with comorbidity	Observed in our study: ➢ Nearly 20% of people were ≥50 years old ➢ Almost 17% of people had comorbidity
(b) Variations in the average age at first prescription fill across the different DMDs	
➢ 32.1-35.1 years for alemtuzumab ➢ 37.7 years for teriflunomide	➢ 35.9 years for alemtuzumab ➢ 43.1 years for teriflunomide
(c) Variations in sex distribution (i.e. proportion of women)	
➢ Alemtuzumab range: 64-66% ➢ Glatiramer acetate range: 68-72%	➢ Alemtuzumab: 65% ➢ Glatiramer acetate: 77%

Discussion

- **No large difference in socioeconomic status:**

  Likely a result of Canada's universal health care and the provincial government drug plan

- **Patterns of treatment:**
  - Changed considerably between 1996-2012 vs. 2013-2017
  - Increased uptake of the oral DMDs observed

  Likely reflects increased availability (choice) of DMDs to treat MS

Summary points

Overall....

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**.

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CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

MS Multiple Sclerosis Society of Canada / Société canadienne de la sclérose en plaques SP MD

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BC's health research funding agency