Canadian Association for Population Therapeutics/ Association Canadienne pour la Thérapeutique des Populations Annual Conference

CAPT ACTP

"Managing risk to improve health outcomes: how to move population health forward in an era of uncertainty"

Breakout # 2
Oral Presentations
Real-world Studies

October 27th 2020
Virtual Platform

Using Real-World Data to Determine Treatment Patterns, Survival and Costs for Canadians Diagnosed with Chronic Lymphocytic Leukemia (CLL)

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when it matters MOST

Disclaimers

- This study was funded by an unrestricted research grant from AstraZeneca Canada Inc. The opinions, results and conclusions reported are those of the authors.
- This study made use of de-identified data from the ICES Data Repository, which is managed by the Institute for Clinical Evaluative Sciences with support from its funders and partners: Canada's Strategy for Patient-Oriented Research (SPOR), the Ontario SPOR Support Unit, the Canadian Institutes of Health Research and the Government of Ontario.
- No endorsement by the Institute for Clinical Evaluative Sciences or any of its funders or partners is intended or should be inferred. Parts of this material are based on data and information compiled and provided by CIHI. However, the analyses, conclusions, opinions and statements expressed herein are those of the author, and not necessarily those of CIHI.
- Parts of this material are based on data and information provided by CCO. The opinions, results, view, and conclusions reported in this paper are those of the authors and do not necessarily reflect those of CCO. No endorsement by CCO is intended or should be inferred.

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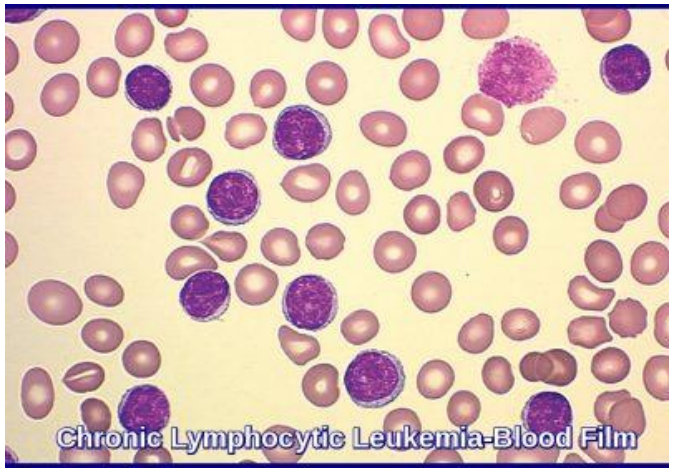
Background – Statistics

- Chronic lymphocytic leukemia (CLL) is the most common type of adult leukemia in Canada (44%).[1]
- In 2016/17, 1,745 Canadians were diagnosed with CLL, and 611 deaths were reported.[2] Median age at diagnosis = 71 years[1] and five-year net survival rate = 83%.[3]
- Majority of CLL patients (>80%) are diagnosed in early stages, thus, it is an indolent disease not requiring treatment until onset of symptoms.[4,5]



References
1. Leukemia & Lymphoma Society of Canada. Blood Cancer in Canada. Facts and Stats 2016. Available from: https://www.llscanada.org/sites/default/files/National/CANADA/Pdf/InfoBooklets/Blood_Cancer_in_Canada_Facts_%26_Stats_2016.pdf.
2. Canadian Cancer Society. Chronic lymphocytic leukemia. Available from: http://www.cancer.ca/en/cancer-information/cancer-type/leukemia-chronic-lymphocytic-cll/chronic-lymphocytic-leukemia/?region=on.
3. Canadian Cancer Statistics Advisory Committee. Canadian Cancer Statistics 2019. Toronto, ON: Canadian Cancer Society; 2019. Available at: www.cancer.ca/Canadian-Cancer-Statistics-2019-EN
4. Sagatys EM, Zhang L. Clinical and laboratory prognostic indicators in chronic lymphocytic leukemia. Cancer Control. 2012; 19: 18-25.
5. Van Bockstaele F, Verhasselt B, Philippe J. Prognostic markers in chronic lymphocytic leukemia: a comprehensive review. Blood Rev. 2009; 23: 25-47.

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Background – Treatments

- Current recommendations for first line (1L) treatment for fit, younger CLL patients without high-risk cytogenetics, is a combination of fludarabine, cyclophosphamide and rituximab (FCR).[6] For older, unfit patients, 1L chlorambucil (Chlo) in combination with obinutuzumab (C+O) is often used.
- Newer targeted therapies (e.g., ibrutinib) have proven effective in those considered FCR-ineligible, and have improved efficacy compared to C or C+O.[6,7]

References
6. Owen C, Gerrie AS, Banerji V, et al. Canadian evidence-based guideline for the first line treatment of chronic lymphocytic leukemia. Current Oncology. 2018; 25: e461-e74.
7. Moreno C, Greil R, Demirkan F, et al. Ibrutinib plus obinutuzumab versus chlorambucil plus obinutuzumab in first line treatment of chronic lymphocytic leukaemia (iLLUMINATE): a multicentre, randomised, open-label, phase 3 trial. The Lancet Oncology. 2019; 20: 43-56

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Study Objectives

- Determine treatment patterns, survival outcomes, resource utilization and costs for patients diagnosed with CLL using population-level administrative datasets in Ontario, Canada.
- For costs, CLL patients will be matched to controls to determine attributable costs.

Methods – Overall

- DESIGN: Longitudinal, population-level study of CLL patients diagnosed between 1-Jan-2010 and 31-Dec-2017 from the Ontario Cancer Registry (OCR), with follow-up until 31-Dec-2018.
- ETHICS: This study was approved by the Research Ethics Board at Sunnybrook Health Sciences.
- DATA SOURCES: Administrative data from the OCR and 11 other health databases.
  - For drug utilization, New Drug Funding Program (NDFP), Ontario Drug Benefit (ODB) Program and Activity Level Reporting (ALR) were all analyzed to identify lines of therapy.

Methods – Costing

- Total cohort, annual and mean per patient costs (CAD 2018) were determined using a costing methodology from ICES called GETCOST. The costs of short-term care episodes (e.g., hospitalization) were determined by multiplying the encounter's resource intensity weight by an annual cost per weighted case; long-term care episodes (e.g., complex continuing care) were determined by weighted days, and costs of visit-based encounters were determined at utilization.
- To estimate costs attributable with CLL ("cases"), a matched cohort arm ("controls") was included to account for non-CLL costs. Controls were non-CLL patients who met the following criteria: no CLL index date within 1 year (randomly generated for the controls to match the date at diagnosis of cases), age at diagnosis ± 1 year, sex, location of residence, Charlson score, comorbidities, prior cancer diagnosis and minimum 6-months follow-up. Cases and controls were matched 3:1.

Cohort Flowchart

N=10,008 CLL diagnosed

N=2,887 treated

N=7,121 never treated/watch+wait

N=1,782 1L “common” treatments

N=1,105 1L “other” treatments

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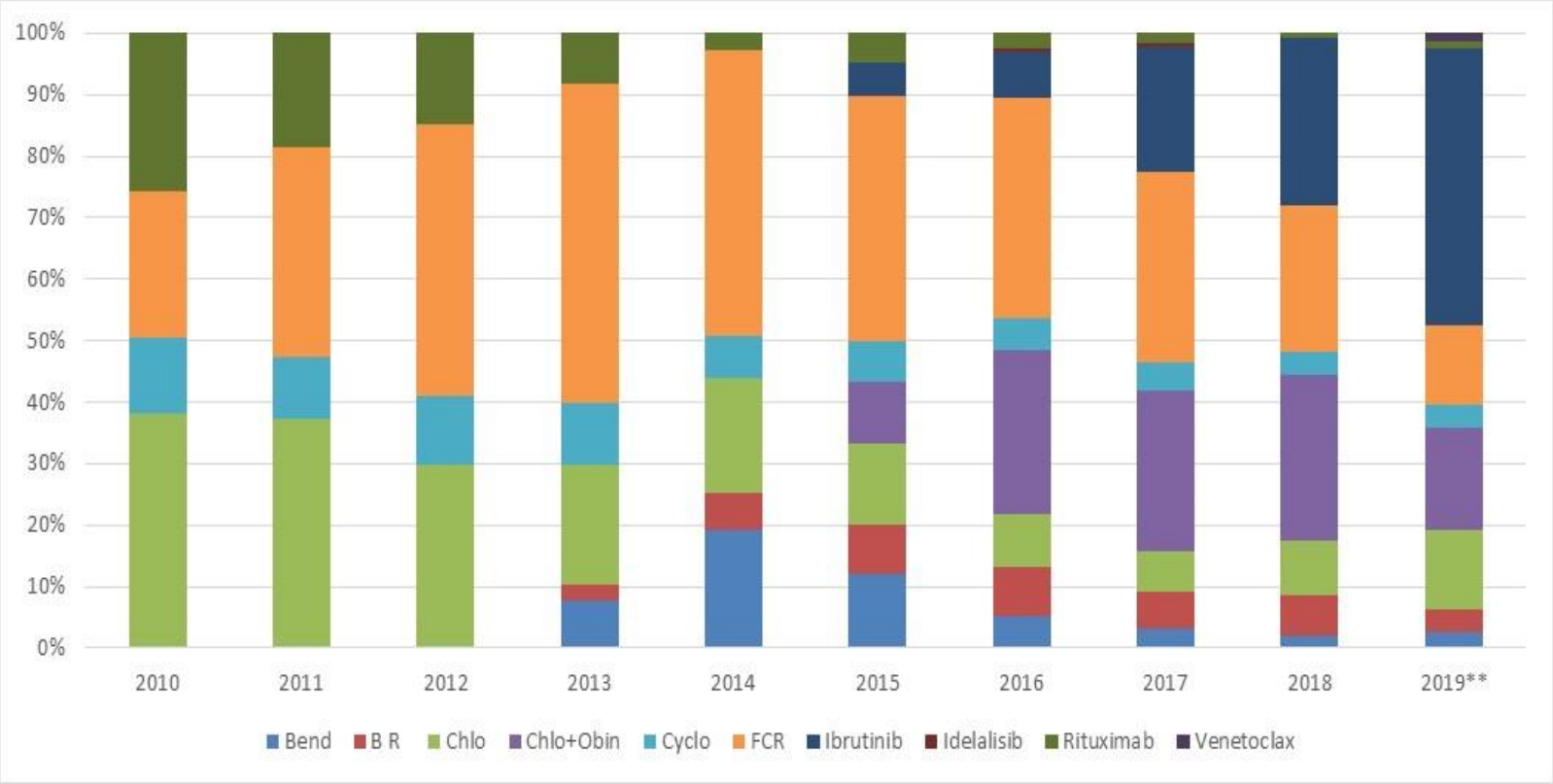
Results – Demographics

	C+O	FCR-based	Ibrutinib	Other*	Total
	N=421	N=1,009	N=352	N=1,105	N=2,887
CLL diagnosis year					
2010	28 (6.7%)	119 (11.8%)	10 (2.8%)	185 (16.7%)	342 (11.8%)
2011	27 (6.4%)	137 (13.6%)	22 (6.3%)	172 (15.6%)	358 (12.4%)
2012	32 (7.6%)	145 (14.4%)	17 (4.8%)	145 (13.1%)	339 (11.7%)
2013	45 (10.7%)	151 (15.0%)	22 (6.3%)	170 (15.4%)	388 (13.4%)
2014	54 (12.8%)	148 (14.7%)	39 (11.1%)	125 (11.3%)	366 (12.7%)
2015	91 (21.6%)	125 (12.4%)	68 (19.3%)	120 (10.9%)	404 (14.0%)
2016	72 (17.1%)	89 (8.8%)	76 (21.6%)	101 (9.1%)	338 (11.7%)
2017	72 (17.1%)	95 (9.4%)	98 (27.8%)	87 (7.9%)	352 (12.2%)
Age at index					
Mean ± SD	73.55 ± 6.84	61.09 ± 9.39	67.92 ± 10.67	73.09 ± 10.82	68.33 ± 11.28
Median (IQR)	74 (69-78)	61 (55-67)	69 (62-76)	74 (66-82)	69 (61-77)
Age at treatment					
Mean ± SD	76.09 ± 6.38	62.63 ± 9.17	70.60 ± 10.33	74.47 ± 10.77	70.10 ± 11.17
Median (IQR)	76 (72-81)	63 (56-69)	71 (65-77)	76 (67-83)	71 (63-78)
Sex					
Female	131 (31.1%)	299 (29.6%)	105 (29.8%)	430 (38.9%)	965 (33.4%)
Male	290 (68.9%)	710 (70.4%)	247 (70.2%)	675 (61.1%)	1,922 (66.6%)
Charlson Comorbidity index					
Mean ± SD	1.06 ± 1.65	1.30 ± 1.59	0.95 ± 1.47	1.92 ± 2.03	1.46 ± 1.81
Median (IQR)	0 (0-2)	0 (0-2)	0 (0-2)	2 (0-3)	1 (0-2)

Results – 1L Treatments



- Mean time from diagnosis to 1L = 651 days.
- 1L treatment shift in 2015 = C+O and ibrutinib utilization increased, FCR and Chlor decreased.

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Results – 2L and 3L Treatments

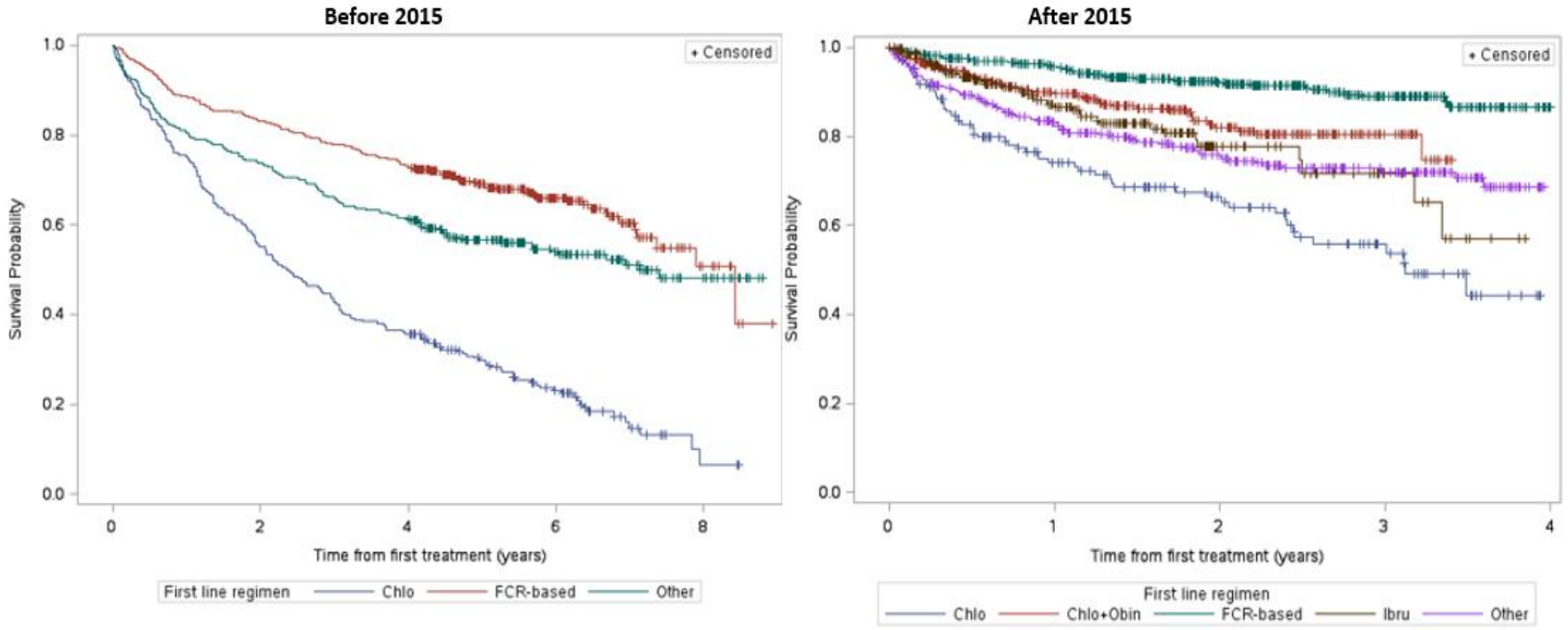
2L:

- Less then a third of 1L-treated CLL patients (N=827) received a 2L treatment, with ibrutinib as the most frequently (65%) 2L-administered treatment.
- Both 1L FCR-treated (78%) and C+O-treated (89%) patients went on to receive 2L-ibrutinib.

3L:

- 124 patients received 3L treatment and mean between treatment time was 0.98 years.

Results – Survival



- Median OS was 6.2 years for pre-2015 group; N/A for post-2015 group.
- Based on all 1L treatment initiation, 86% and 61% reached 1- and 5-year survival.
- FCR treated patients had better survival: 93% and 74% reached 1- and 5-year survival.

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Results – Attributable Costs

- Table 1 outlines attributable costs per year and by resource type.
- ***Overall mean attributable cost per CLL patient= $54,315.***
- The majority of costs were incurred in Year 1, with a steady decrease over subsequent years.
- The main cost drivers were oral medication, cost of intravenous medications and cancer clinic visits.

Results – 1L Costs by Treatment

Cost type	Ibrutinib	C+O	FCR	Other
First line treatment- N (patients)	***159***	***285***	***882***	***882***
Overall total costs	$57,739	$56,872	$48,934	*$31,658*
Cancer clinic visit total costs	$5,342	$16,461	$21,204	$9,800
Chemotherapy (NDFP) total costs	$197	$35,180	$19,931	$10,840
Emergency department visit total costs	$491	$217	$305	$425
Inpatient hospitalization admission total costs	$5,010	$1,440	$2,126	$3,476
Oral medications (ODB) total costs	$41,115	$1,138	$2,233	$2,636
Outpatient clinic visit total costs	$1,292	$529	$845	$1,383
Physician services (OHIP) total costs	$2,817	$1,626	$2,101	$2,244
Same day surgery admission total costs	$661	$76	$40	$129

- The overall mean cost per patient was highest with ibrutinib ($57,739) and lowest in the “other” group ($31,658).
- Cost drivers were drug costs (ODB in the ibrutinib group, chemotherapy in the C+O, FCR and other groups), followed by cancer clinic visits.

Conclusions

COHORT:

- Estimated 10,000 CLL patients identified in OCR, with almost 3,000 receiving 1L treatments.

TREATMENT:

- By 2015, 1L shift observed with increased utilization of C+O and ibrutinib and decreased utilization of FCR.

SURVIVAL:

- 1L FCR-treated patients had improved survival (1-year= 93% alive).

COSTS:

- $54,315 = Overall mean attributable cost per CLL patient.
- Amongst 1L treatments, ibrutinib had highest overall mean cost per patient ($57,739).

Take Away Message

Population-level results can support healthcare decision-makers by:

- Characterizing the size/demographics of CLL patient population.
- Identifying real-world treatment patterns (line, type, time).
- Calculating survival outcomes.
- Determining resource utilization and costs (attributable, drivers).

Questions and Thank You

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IMPACT OF THE COVID-19 PANDEMIC ON CHRONIC PAIN MANAGEMENT

Findings from the Chronic pain & COVID-19 Pan-Canadian Study

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Canadian Association for Population Therapeutics (CAPT) Virtual Conference

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UQAT

LABORATOIRE DE RECHERCHE EN ÉPIDÉMIOLOGIE DE LA DOULEUR CHRONIQUE

Disclosure

I have no conflict of interest related to the content of the presentation

Chronic pain & COVID-19 Pan-Canadian Study

Rationale

Rationale

Chronic pain (CP)

- Pain that persists beyond 3 months
- Affects approximately 1 in 5 adults
- Represents a major burden for society
- Despite decades of research on CP and its treatment, management of this condition unfortunately continues to be suboptimal

(Canadian Pain Task Force, 2019)

Rationale

- Multimodal treatment is recognized as the optimal paradigm for the management of CP *(Canadian Pain Task Force, 2019)*
- Careful balance between pharmacological and physical/psychological approaches is therefore desirable, but it can be hard to achieve and it is easily disrupted

  (Becker et al., 2017; CATH, 2018)

Why the COVID-19 pandemic would specifically affect CP treatment?

- Reduced access to prescribers
- Pandemic-related challenges regarding R_x used for pain treatment :
  - March 2020 – Uncertainty regarding use of nonsteroidal anti-inflammatory drugs (NSAIDs) *(INESSS, 2020a; Smart et al., 2020)*
  - March 2020 – Some patients were denied hydroxychloroquine or chloroquine (antimalarial drugs) *(INESSS, 2020b; Crosby et al., 2020; Pope, 2020)*
  - June 2020 – Opioids & sedatives shortages *(INESSS, 2020c)*
  - June 2020 – High demand for dexamethasone (corticosteroid) *(Mahase, 2020)*

Why the COVID-19 pandemic would specifically affect CP treatment?

- Reduced access to many types other types of treatments

  For example:
  - Multidisciplinary pain clinics / Infiltrations
  - Physical therapy
  - Massage therapy
  - Psychological counselling
  - Self-help groups

- Fear of going to healthcare appointments

- Self-medication/non-medical drug use

(Lynch et al., 2020; Dietze & Peacock, 2020; Clauw et al., 2020; Javed et al., 2020)

Rationale

- Major disruptions in the pharmacological and physical/psychological CP management were anticipated *(Lynch et al., 2020; Clauw et al., 2020; Cohen et al., 2020; Deer et al., 2020; Eccleston et al., 2020; El-Tallawy et al., 2020; Javed et al., 2020; Pope, 2020; Shanthanna et al., 2020; Webster et al., 2020)*

- But the impact of the pandemic among individuals living with CP had to be quantified

Objective

Documenting the impact of the COVID-19 pandemic on the pharmacological and physical/psychological treatment of CP

Chronic pain & COVID-19 Pan-Canadian Study

Methodology

Design & Population

- This study was part of a larger initiative, the *Chronic Pain & COVID-19 Pan-Canadian Study (Choinière, Pagé, Lacasse et al.)*, which used a web-based mixed-method design to answer various research questions surrounding how CP patients experienced the pandemic

- Population
  - ✓ Individuals aged ≥ 18 years
  - ✓ Living in Canada
  - ✓ Reporting pain for >3 months (defined as CP)
  - ✓ Able to complete a self-administered questionnaire in French or English
  - ✓ Had access to the Internet

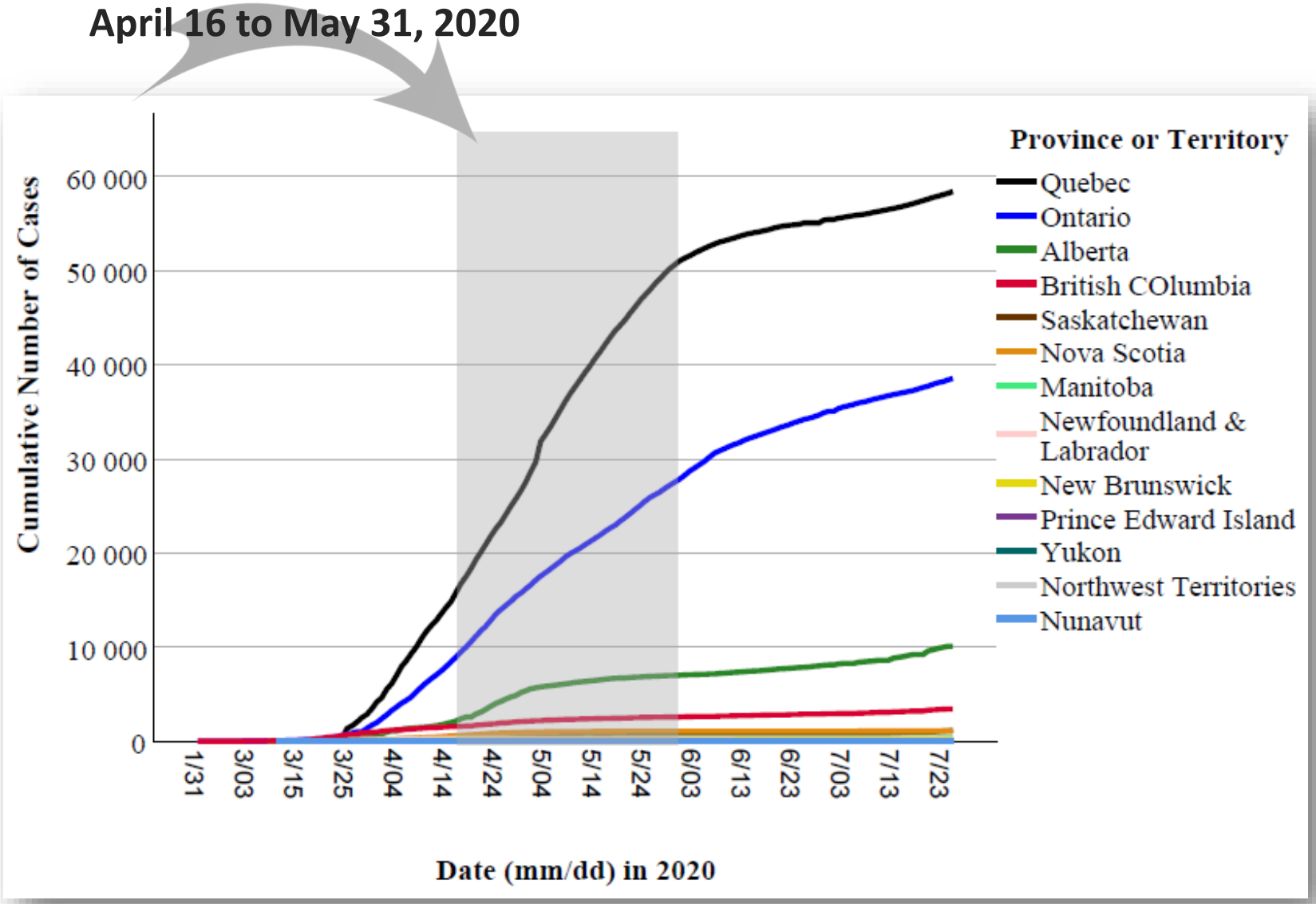
Recruitement

- Pre-tested web-based recruitment strategy:
  - ✓ Advertisement by national and provincial patient associations (e-newsletter, social media page and/or website)
  - ✓ Invitations shared among various Facebook® support groups
  - ✓ Email invitations and social media posts shared by colleagues and friends (snowballing technique)
  - ✓ Email invitations and social media posts shared by local, provincial, and national research networks
  - ✓ Intranets and press releases issued by the principal investigators' institutions → covered in various broadcasts and text interviews published on the web
- Draw to win one of ten $100 prepaid Visa® gift cards
- Approved by the Centre hospitalier de l'Université de Montréal (CHUM)'s Research Ethics Board
- Patient partners were involved in every step of the study

Recruitement

When the cumulative cases of the first COVID-19 pandemic wave were growing exponentially in some provinces and during the peak of daily reported new cases in Canada

(Government of Canada, 2020)



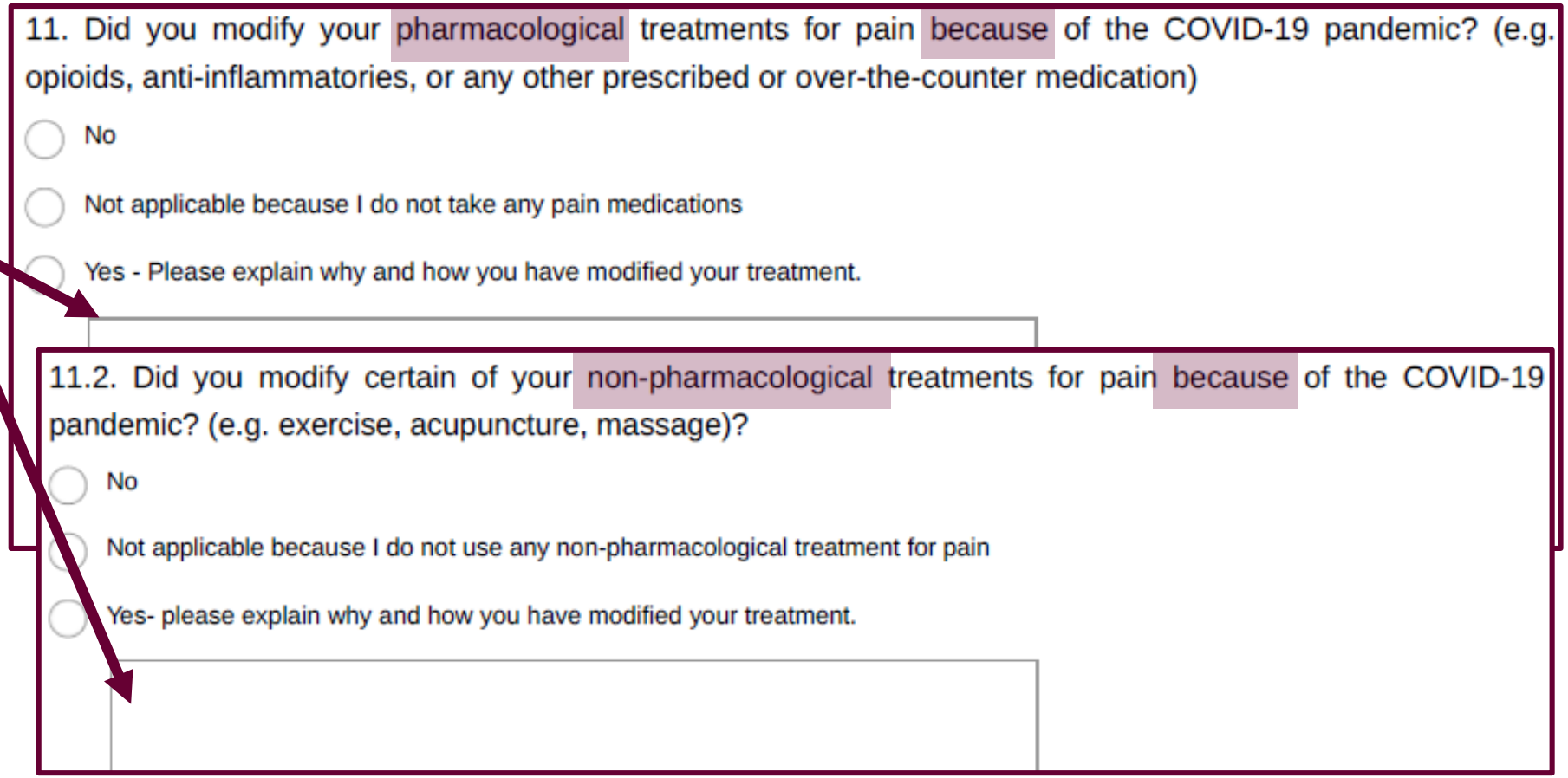
Data collection

Changes in pain treatment during the pandemic

Reasons collected using open-ended questions

- Exploratory nature of the study
- More insights and wide range of responses

Reviewed line by line to develop a standardized coding system / Coding achieved by two independent authors who reached consensus



Data analysis

Descriptive statistics

- % participants who reported changes in their pharmacological or physical/psychological pain treatment during the pandemic
- Reasons behind these changes

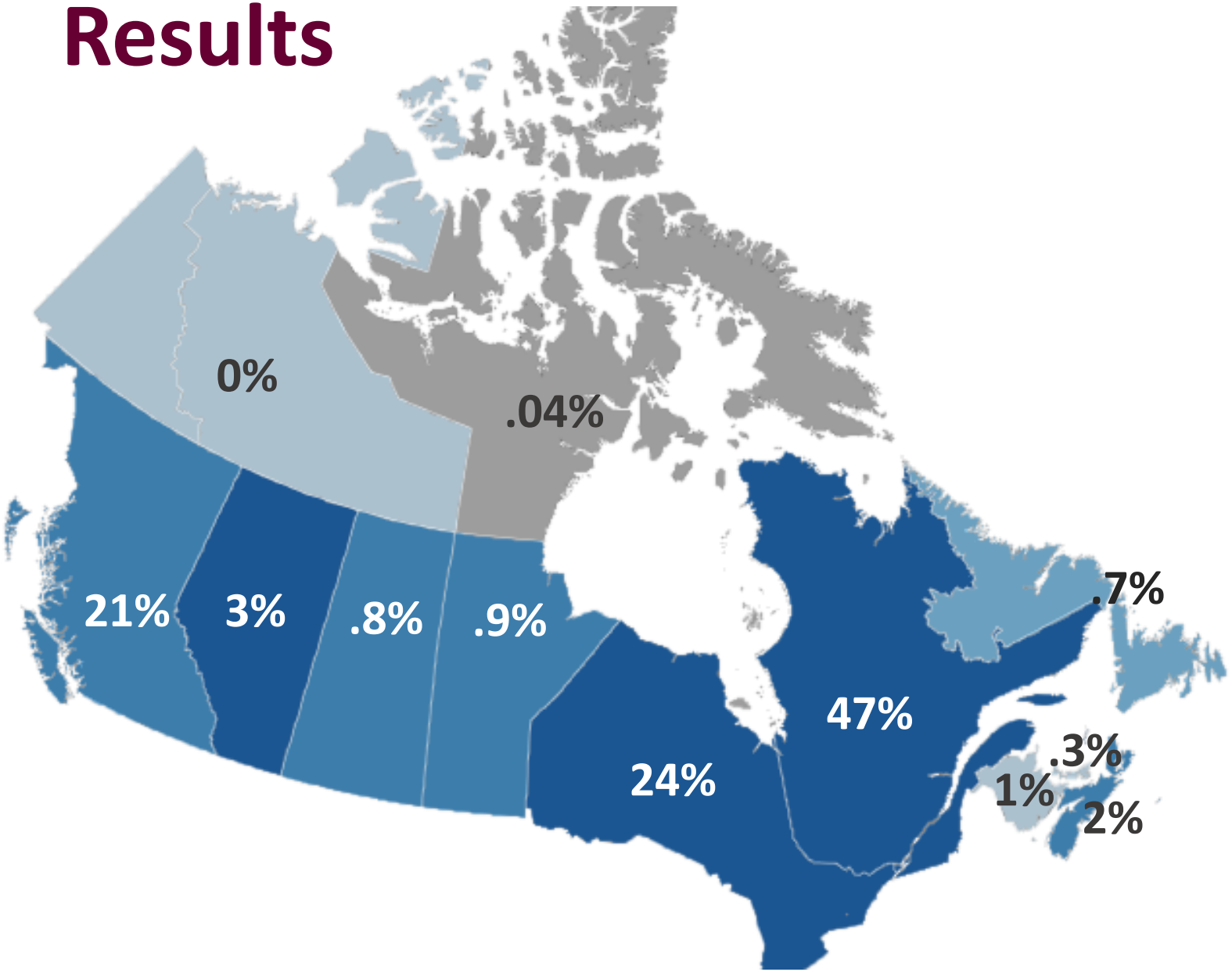
Multivariable logistic regression models

- Identify participants' characteristics associated with changes in pain treatment during the pandemic
  1) Among users of pain medications (n = 2533)
  2) Among users of physical/psychological approaches (n = 2467)

Chronic pain & COVID-19 Pan-Canadian Study

Results

Results

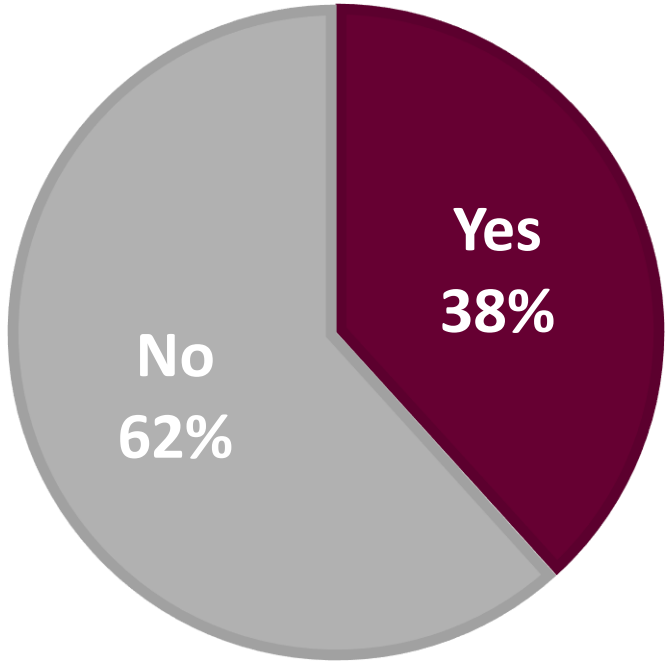


n = 2864 participants

- Females: 84%
- Age: 49.7 ± 13.7
- Change in pain symptoms since the beginning of the pandemic
  - ✓ Worsened: 69%
  - ✓ Unchanged: 26%
  - ✓ Improved: 5%

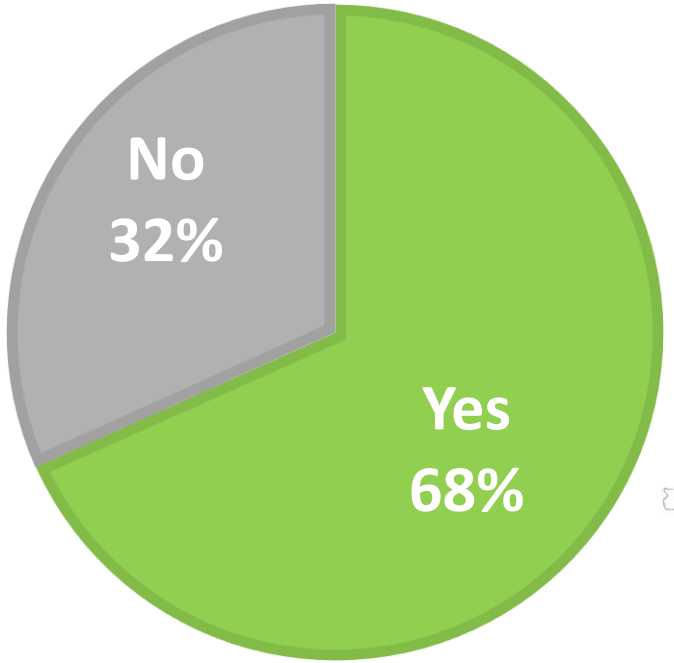
Changes in pain treatment during the pandemic

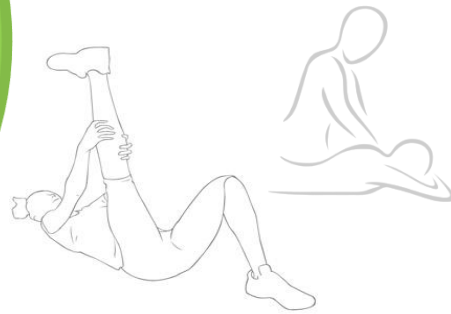
Users of pharmacological pain treatments (n = 2533)



- 40.5% reported COVID-related reasons
- 57.1% non-COVID-related reasons
- 2.4% no specific reason reported

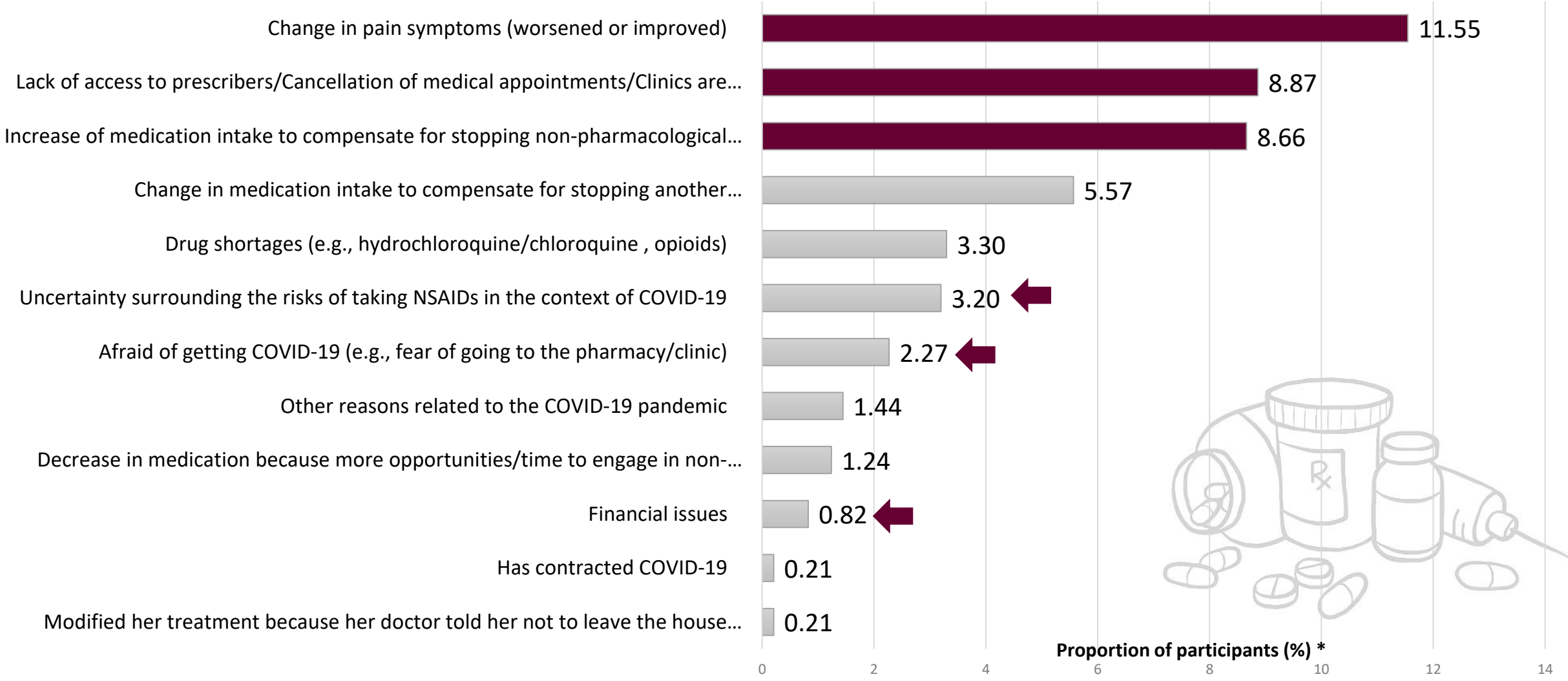
Users of physical/psychological pain treatments (n = 2467)





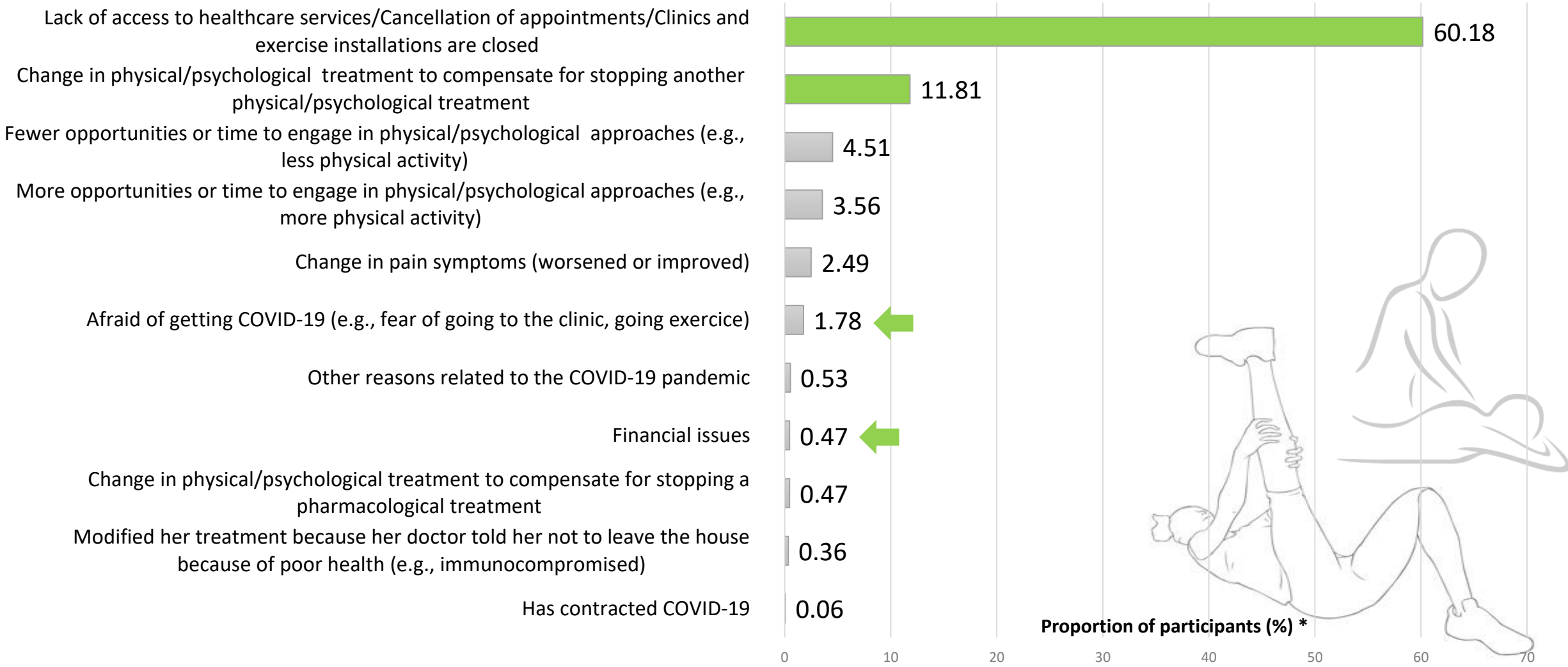
- 83.6% reported COVID-related reasons
- 15.6% non-COVID-related reasons
- 0.8% no specific reason reported

Reasons why participants changed their pharmacological treatment



** Categories are not mutually exclusive since participants could list various reasons; N.B. 577 of the 970 participants who reported changes in their treatment (59.48%) did not provide any specific reason (2.37%) or reasons not related to the COVID-19 pandemic (57.11%) –e.g., drug side effects, litigation with insurance company, (data not shown in the graph)*

Reasons why participants changed their physical/psychological treatment

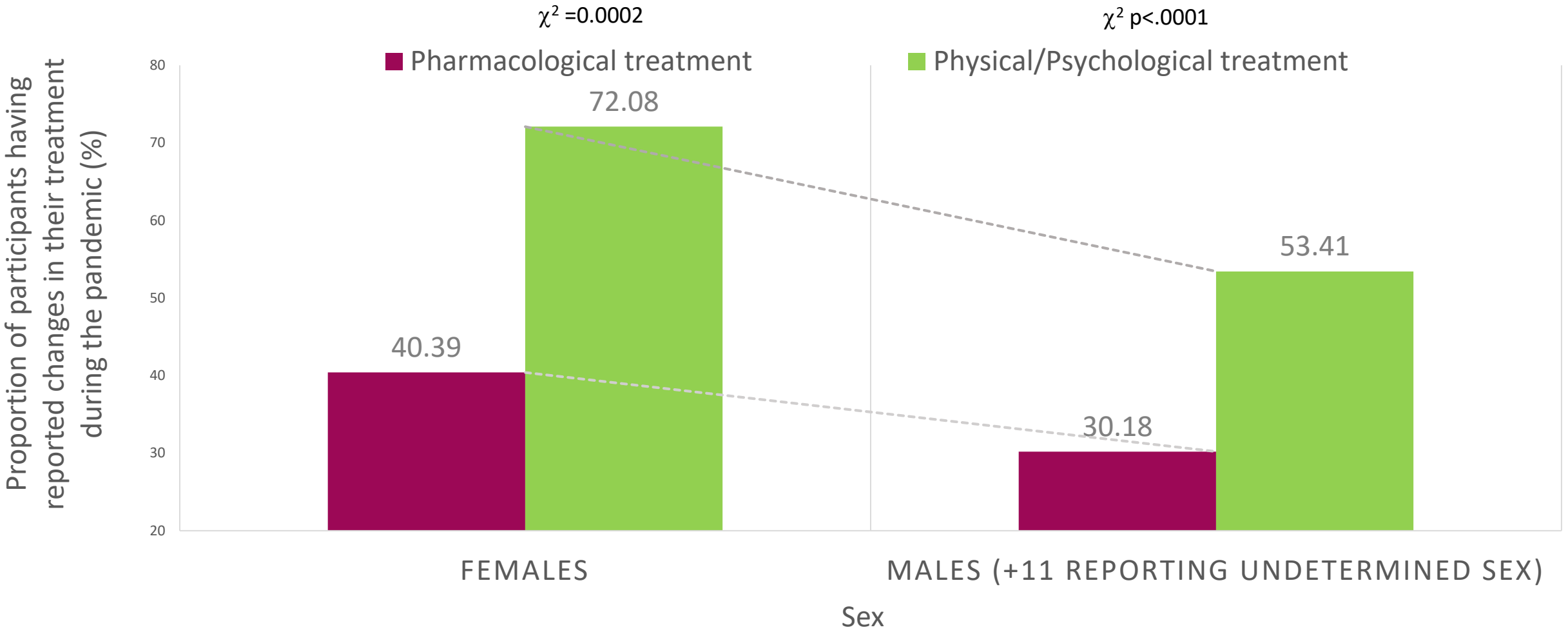


** Categories are not mutually exclusive since participants could list various reasons; N.B. 277 of the 1685 participants who reported changes in their treatment (16.44%) did not provide any specific reason (0.83%) or reasons not related to the COVID-19 pandemic (15.61%) (data not shown in the graph)*

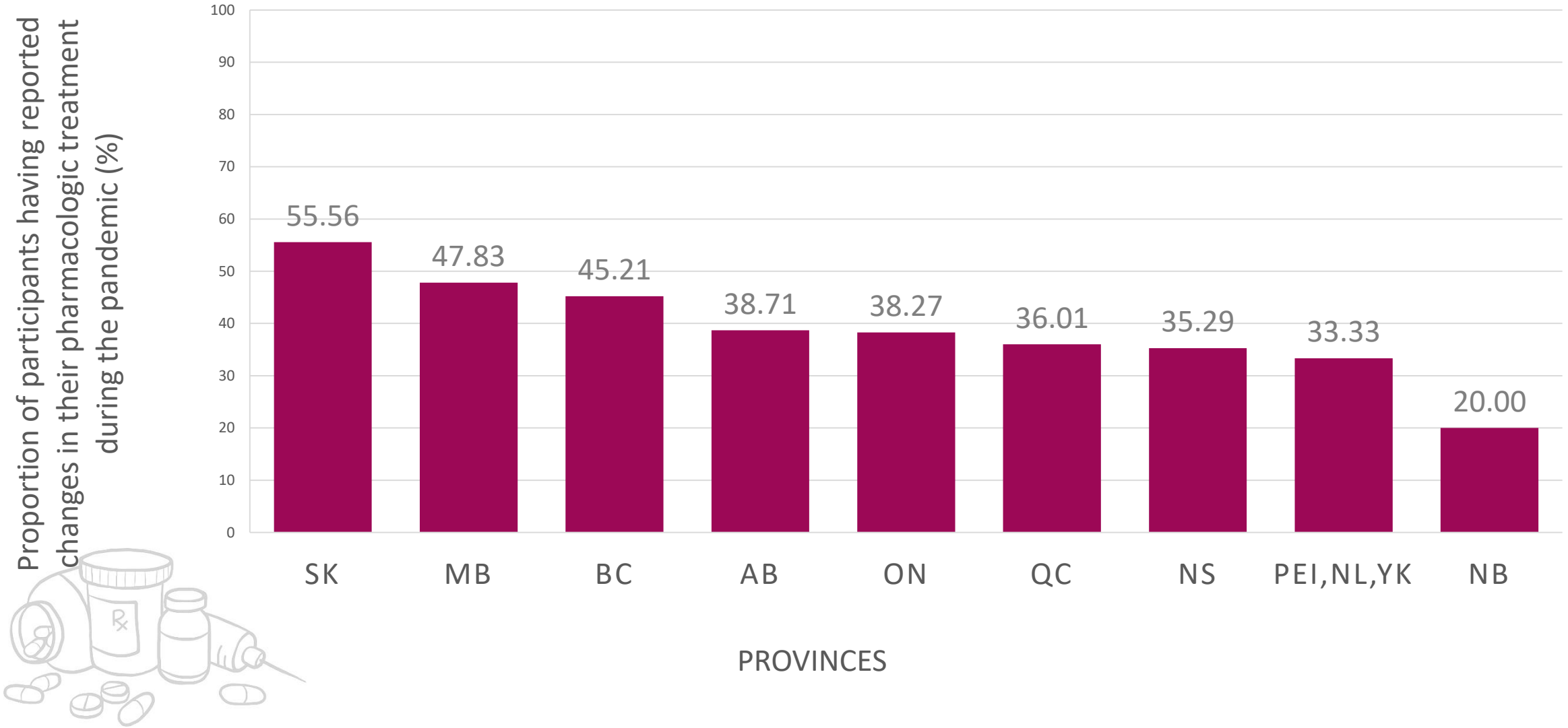
Results

- Incidental findings emerged from reading the high number of verbatim. For example, some participants:
    - Had to reintroduce or increase **opioids** in spite of tapering-off before the pandemic
    - Reported using more **cannabis** products (medical or not), or **alcohol** to ease their pain

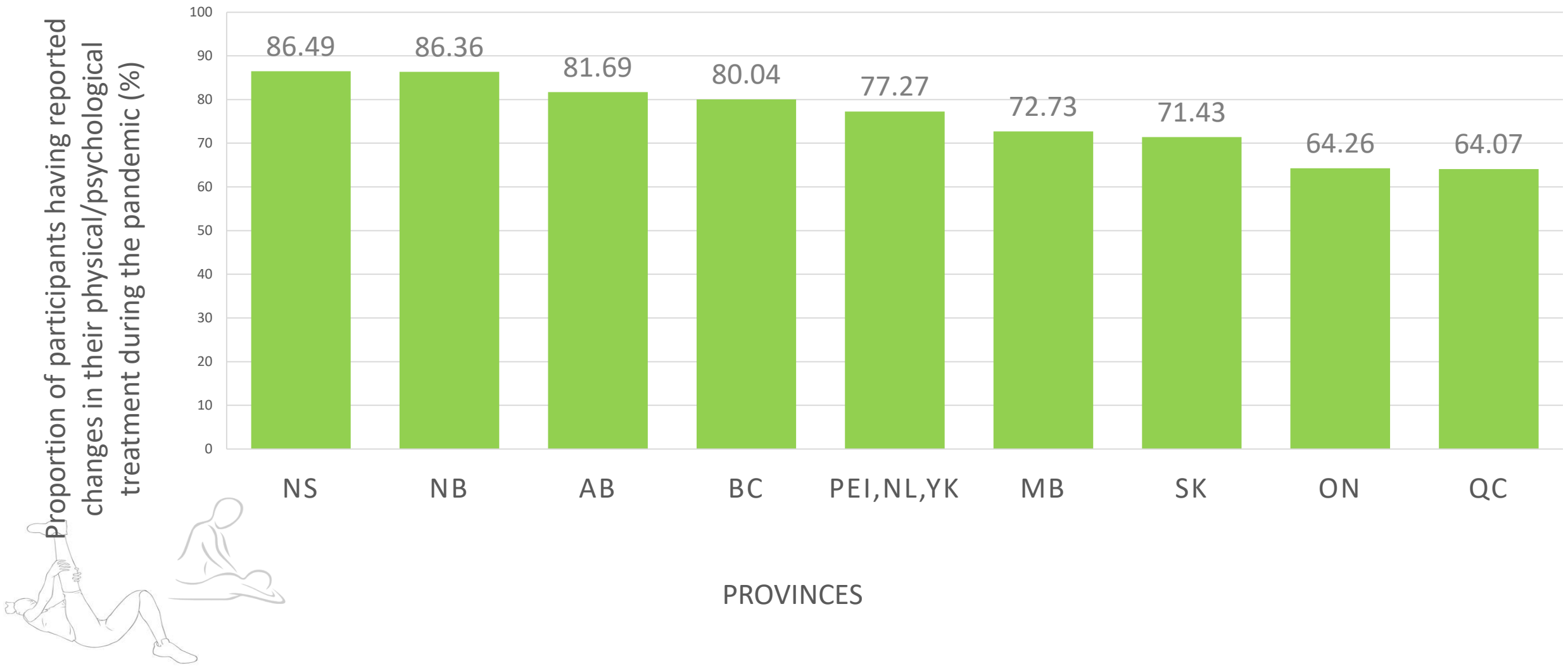
Changes in pain treatment during the pandemic



Changes in pain treatment during the pandemic



Changes in pain treatment during the pandemic



Multivariate exploration of factors associated with changes in pain treatment during the pandemic

	Pharmacological pain treatment	Physical/psychological pain treatment
Associated with an **increased** likelihood of changing : OR>1, 95%CI excludes 1	1) Change in pain symptoms since the beginning of the pandemic 2) Having needed to renew pain medication during the pandemic 3) Not being followed in a family medicine group (FMG) for pain treatment (vs other type of follow-up or no follow-up) 4) Employment status change during the pandemic 5) Change in physical/psychological treatment during the pandemic 6) Presence of anxiety and depressive symptoms in the past month 7) Having a post-secondary education 8) Being employed before the pandemic 9) Province of residence (OR British Columbia vs. Quebec)	1) Change in pain symptoms since the beginning of the pandemic 2) Change in pharmacological treatment during the pandemic 3) Being a female 4) Having a post-secondary education 5) Province of residence (OR British Columbia or Alberta vs. Quebec)
Associated with a **decreased** likelihood of changing : OR<1, 95%CI excludes 1	1) Reporting generalized pain 2) Week of questionnaire completion (week 6 vs week 1)	1) Higher average pain intensity in the past 7 days 2) Presence of anxiety and depressive symptoms in the past month 3) Older age 4) Being single, separated or divorced (vs. married)

Strengths

- Timing of the study with the peak of Canadian new COVID-19 cases
- Nationwide sample
- Substantial sample size
- Study sample comparable to previously described random surveys of individuals living with CP in terms of age, % of workers, % of participants living with pain >10 years, pain intensity

Limitations

- A good number of participants reported non-COVID-related reasons, even if they were asked about modifications made to their treatment *because* of the COVID-19 pandemic
- Cross-sectional study - Raises questions regarding temporal relationships between variables of interest
- Over-representation of females
- Under-representation of some provinces/territories (e.g., PEI, NL, YK)
- Data did not permit the assessment of associations between changes in pain treatment and ethnic minorities subgroups (too few representatives), income categories or gender constructs (variables not prioritized in comparison to COVID-related items for the benefit of a shorter questionnaire)

Conclusions

Conclusions

- Pain research community: Was urged to produce epidemiological data that could help characterize the impact of the pandemic among individuals living with CP and inform interventions to reduce its effects *(Clauw et al., 2020)*

- Health research community: Data collection that can inform risk and/or management of drug shortages and assessment of the impact of the COVID-19 crisis on healthcare utilization and outcomes for non-COVID-19 diseases were identified as research priorities *(Reagan-Udall Found.for the FDA & FCR, 2020)*

To our knowledge, the present pan-Canadian study is the **first of its kind** to quantify the impact of the COVID-19 pandemic on the pharmacological and physical/psychological treatment of CP

Conclusions

- Our study highlights the significant **negative** impact the COVID-19 pandemic had, and probably continue having, on access to pain relief
    - Especially non-pharmacological treatments (68% of participants) which are often hard to implement *(Becker et al., 2017; CADTH, 2018)*
    - The fact that fewer participants were impacted in terms of their pharmacological treatment suggests that relatively effective measures were put in place for many patients (e.g., deliveries from pharmacies, telemedicine, prescription prolongation, pharmacist extensions of controlled drug prescriptions, etc.)

Conclusions

- A priority: Maintain **continuity** of care for individuals living with CP despite the pandemic
    - Rapid introduction of virtual care options should supplement in-person care
- Our results justify resources allocation and can help inform and prioritize interventions to support persons living with CP. For example:
    - Short videos suggesting alternatives when the usual physical/psychological treatment is not feasible
        - ✓ Social media was identified as a useful tool to disseminate relevant information for patients and clinicians in situations of urgencies such as the COVID-19 pandemic *(Cuello-Garcia, 2020)*
        - ✓ Age and sex tailored-messages

Selected references (1)

- Andersen RM. (1995) Revisiting the behavioral model and access to medical care: does it matter? *J Health Soc Behav*, 36(1): 1-10.
- Becker et al. (2017). Barriers and facilitators to use of non-pharmacological treatments in chronic pain. *BMC family practice*, 18(1), 41.
- CADTH (2018). *Access to and availability of non-pharmacological treatments for chronic non-cancer pain in Canada: an environmental scan*. Ottawa: Canadian Agency for Drugs and Technologies in Health. (Environmental scan; no. 81)
- Canadian Pain Task Force. (2019). *Chronic Pain in Canada: Laying a Foundation for Action*. Ottawa: Health Canada.
- Cuello-Garcia et al. (2020) Social Media can have an impact on how we manage and investigate the COVID-19 pandemic. *Journal of Clinical Epidemiology*, *In Press*
- Clauw et al. (2020). Considering the potential for an increase in chronic pain after the COVID-19 pandemic. *Pain, 161*(8), 1694-1697.
- Cohen et al. (2020). Pain Management Best Practices from Multispecialty Organizations During the COVID-19 Pandemic and Public Health Crises. *Pain Med, 21*(7), 1331-1346.
- Cousins MJ, Lynch ME. The Declaration Montreal: access to pain management is a fundamental human right. *Pain*. 2011;152
- Deer et al. (2020). Emergence From the COVID-19 Pandemic and the Care of Chronic Pain: Guidance for the Interventionalist. *Anesth Analg, 131*(2), 387-394.

Selected references (2)

- Eccleston et al. (2020). Managing patients with chronic pain during the COVID-19 outbreak: considerations for the rapid introduction of remotely supported (eHealth) pain management services. *Pain, 161*(5), 889-893.
- El-Tallawy et al. (2020). Pain Management During the COVID-19 Pandemic. *Pain Ther, 2020, 1-14*.
- INESSS. (2020a). *COVID-19 et anti-inflammatoires non stéroïdiens*. Retrieved March 31st, 2020, from https://www.inesss.qc.ca/fileadmin/doc/INESSS/COVID-19/COVID-19_Anti-inflammatoires.pdf
- INESSS. (2020b). *COVID-19 et ruptures d'inventaire de chloroquine et d'hydroxychloroquine*. Retrieved April 1st, 2020, from https://www.inesss.qc.ca/fileadmin/doc/INESSS/COVID-19/COVID-19_INESSS_ruptures_inventaire_chloroquine_hydroxychloroquine.pdf
- INESSS. (2020c). *COVID-19 et pénurie de sédatifs, analgésiques et bloqueurs neuromusculaires*. Retrieved May 10th, 2020, from https://www.inesss.qc.ca/fileadmin/doc/INESSS/COVID-19/COVID-19_SedationSI_et_bloc.pdf
- Javed et al. (2020). Impact of COVID-19 on chronic pain patients: a pain physician's perspective. *Pain Manag, 10*(5), 275-277.
- Mahase, E. (2020). Covid-19: Demand for dexamethasone surges as RECOVERY trial publishes preprint. *BMJ*, 369, m2512.
- Pope, J. E. (2020). What Does the COVID-19 Pandemic Mean for Rheumatology Patients? *Curr Treatm Opt Rheumatol*, 1-4.
- Shanthanna et al. (2020). Caring for patients with pain during the COVID-19 pandemic: consensus recommendations from an international expert panel. *Anaesthesia, 75*(7), 935-944.
- Webster et al. (2020). Grappling with Chronic Pain and Poverty during the COVID-19 Pandemic. *Canadian Journal of Pain, 4*(1), 125-128.

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Sociodemographic, Disease, and Medication Profile of RA Patients under 65 years Compared with 65 Years or Older at Registry Enrollment: Results From The Ontario Best Practices Research Initiative (OBRI)

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BEST PRACTICES
RESEARCH INITIATIVE
Shaping the Future of Arthritis Care

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Disclosure

- No conflict of Interest

Background

- Age is an important factor that can affect disease course, physical function and treat to target strategy for patients with rheumatoid arthritis (RA).

Objectives

- To describe sociodemographic, disease and medication profile of patients with RA by their assigned age group at time of their enrollment in the Ontario Best Practices Research Initiative (OBRI); a clinical registry (OBRI-RA registry) (www.obri.ca)

Setting

- RA patients enrolled in the OBRI between 1st Jan 2008 and 31st Dec 2019 were included.

- Patients were allocated into two age groups, under 65 years and 65 years or older.

Methods

- Patients in two age group were compared for:

  - Sociodemographic characteristics (gender, ethnicity, spoken language, education, health insurance, and smoking status)

  - Disease activity [28 tender and swollen joint count (28SJC and 28TJC), physician global assessment (PhGA), clinical disease activity index (CDAI)]

  - Patient report outcomes (PROs) including patient global assessment (PtGA), fatigue score, global pain, and Health assessment questionnaire-disability index (HAQ-DI)

Methods…

- Patients in two age group were compared for:

  - Comorbidity profile including Hypertension, Cardiovascular disease, Diabetes Mellitus, and Depression

  - Antirheumatic medication profile [prior use of conventional synthetic disease modifying antirheumatic drugs (csDMARDs), prior use of biologic (b)DMARDs, using new bDMARDs or csDMARDs, and steroids)

Statistical analysis

- Descriptive cross sectional analysis was used to analysis the data.
- We calculated the standardized difference as the difference in means or proportions divided by the standard deviation.
- A significant difference between the two groups was defined as an absolute value ≥ 0.10.

Results

Sociodemographic profile by age group

	Total (N=3734)	<65 years (N=2562)	≥ 65 years (N=1172)	Standard difference	P Value
Gender, Female (%)	2902 (77.7)	2041 (79.7)	861 (73.5)	**0.15**	**<.001**
Age (years), Mean ± SD	57.9 ± 13.2	51.3 ± 10.0	72.4 ± 5.5	**0.26**	**<.001**
Ethnicity, Non-Caucasian (%)	416 (11.1)	337 (13.2)	79 (6.7)	**0.22**	**<.001**
Spoken language, English (%)	3222 (86.3)	2202 (85.9)	1020 (87.0)	**0.10**	**0.007**
Education, Post-secondary (%)	2020 (54.1)	1531 (59.8)	489 (41.7)	**0.40**	**<.001**
Health insurance coverage , OHIP+ private /ODB (%)	3044 (81.5)	1944 (75.9)	1100 (93.9)	**0.72**	**<.001**
Smoking , current (%)	563 (15.1)	461 (18.0)	102 (8.7)	**0.30**	**<.001**

OHIP: Ontario Health Insurance Plan; ODB: Ontario Drug Benefit

Disease activity profile by age group

	Total (N=3734)	<65 years (N=2562)	>= 65 years (N=1172)	Standard difference	P Value
Disease duration (years)	N=3730	N=2558	N= 1172		
Mean ± SD	8.2 ± 9.8	7.3 ± 8.6	10.2 ± 11.8	***0.30***	***<.001***
RF	N=3460	N=2375	N=1085		
Positive RF	2504 (72.4)	1748 (73.6)	756 (69.7)	*0.08*	*0.017*
ACPA	N=1591	N=1146	N=445		
Positive ACPA	978 (61.5)	722 (63.0)	256 (57.5)	***0.11***	***0.044***
PhGA	N=3065	N=2092	N=973		
Mean ± SD	4.2 ± 2.5	4.3 ± 2.5	4.1 ± 2.4	*0.09*	*0.025*
28SJC	N=3648	N=2505	N=1143		
Mean ± SD	5.4 ± 4.9	5.3 ± 4.9	5.5 ± 4.9	*0.04*	*0.231*
28TJC	N=3579	N=2458	N=1121		
Mean ± SD	5.9 ± 6.2	6.0 ± 6.3	5.6 ± 5.9	*0.07*	*0.069*
CDAI	N=3260	N=2242	N=1018		
Mean ± SD	20.4 ± 13.6	20.7 ± 13.8	19.7 ± 13.2	*0.07*	*0.074*

RF: Rheumatoid factor; ACPA: anti-citrullinated protein antibodies; SJC: Swollen Joint Count; TJC: Tender Joint Count; PhGA: Physician Global Assessment; CDAI: Clinical Disease Activity Index

Patient report outcomes by age group

	Total (N=3734)	<65 years (N=2562)	≥ 65 years (N=1172)	Standard difference	P Value
HAQ--DI					
N	3545	2447	1098		
Mean ± SD	1.2 ± 0.8	1.1 ± 0.8	1.2 ± 0.8	***0.15***	***<.001***
HAQ -Pain					
N	3544	2447	1097		
Mean ± SD	1.4 ± 0.9	1.5 ± 0.9	1.3 ± 0.9	***0.16***	***<.001***
PtGA					
N	3264	2237	1027		
Mean ± SD	4.7 ± 2.8	4.8 ± 2.8	4.5 ± 2.7	***0.13***	***<.001***
Patient pain feeling during past week					
N	3544	2447	1097		
Mean ± SD	4.7 ± 2.9	4.8 ± 2.9	4.4 ± 2.8	***0.16***	***<.001***
Fatigue					
N	3547	2448	1099		
Mean ± SD	4.9 ± 3.1	5.0 ± 3.1	4.6 ± 3.1	***0.15***	***<.001***

HAQ-DI: Health assessment questionnaire –Disability index; PtGA: patient global assessment

Comorbidity profile by age group

	Total (N=3734)	<65 years (N=2562)	≥ 65 years (N=1172)	Standard difference	P Value
Hypertension	1274 (34.1)	617 (24.1)	657 (56.1)	***0.69***	***<.001***
Cardiovascular disease	418 (11.2)	162 (6.3)	256 (21.8)	***0.46***	***<.001***
Diabetes Mellitus	322 (8.6)	184 (7.2)	138 (11.8)	***0.16***	***<.001***
Lung disease	498 (13.3)	286 (11.2)	212 (18.1)	***0.19***	***<.001***
Gastrointestinal disease	626 (16.8)	383 (14.9)	243 (20.7)	***0.15***	***<.001***
Cancer disease	277 (7.4)	128 (5.0)	149 (12.7)	***0.27***	***<.001***
Depression disease	611 (16.4)	455 (17.8)	156 (13.3)	***0.12***	***<.001***

Antirheumatic medication profile by age group

	Total (N=3734)	<65 years (N=2562)	≥ 65 years (N=1172)	Standard difference	P Value
Prior use of csDMARDs	3067 (82.1)	2099 (81.9)	968 (82.6)	*0.03*	*0.371*
Prior use of bDMARDs	1111 (29.8)	805 (31.4)	306 (26.1)	***0.12***	***<.001***
Starting a new csDMARDs	1407 (37.7)	990 (38.6)	417 (35.6)	*0.02*	*0.529*
Starting a new bDMARD	587 (15.7)	437 (17.1)	150 (12.8)	***0.12***	***0.005***
Use of MTX	2454 (65.7)	1716 (67.0)	738 (63.0)	*0.08*	***0.017***
Use of NSAIDs	817 (21.9)	612 (23.9)	205 (17.5)	***0.16***	***<.001***
Use of steroids	736 (19.7)	458 (17.9)	278 (23.7)	***0.14***	***<.001***

bDMARDs: biologic disease modifying antirheumatic drugs; csDMARDs: conventional synthetic disease modifying antirheumatic drugs.

Conclusions

- In this real world data descriptive study, we found that disease activity measures were similar in patients uder 65 years compared to those 65 years or older.

- Sociodemographics, PROs , comorbidities, and antirheumatic medication profiles were different between two groups.

- These differences should be taken into account for any clinical decision toward outcome improvement in patients.

CAPT Conference 2020

Time to Advanced Therapy Initiation or Switch in Response to Moderate-High RA Disease Activity Between Academic and Community Practice Settings: Data from the OBRI Registry

E. Hepworth, R. Mirza, M. Movahedi, S. Aydin, C. Bombardier and other OBRI Investigators

Time to Advanced Therapy Initiation or Switch in Response to Moderate-High RA Disease Activity Between Academic and Community Practice Settings: Data from the OBRI Registry

E. Hepworth, R. Mirza, M. Movahedi, S. Aydin, C. Bombardier and other OBRI Investigators

Overarching Question: Are there systematic differences between community and academic practice in the management of active rheumatoid arthritis?

Methods:

- Study period: OBRI Origin - Jan 2019. All patients were enrolled for 6 months with at least 2 visits.
- Population A: (n=135, Community 85, Academic 50)
  - Combined DMARD for at least 2 months (Lef/MTX or MTX/SSZ/Plq) + 1st DAS28CRP or CDAI mod-high dx = time 0
  - Adjusted Cox proportional hazards model - time to first advanced therapy between Comm/Academ
- Population B: (n=453, Community 272, Academic 181)
  - Advanced therapy + 1st DAS28CRP or CDAI mod-high dx activity = time 0
  - Adjusted Cox proportional hazards model - time to advanced therapy switch between Com/Academ

Time to Advanced Therapy Initiation or Switch in Response to Moderate-High RA Disease Activity Between Academic and Community Practice Settings: Data from the OBRI Registry

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Results

- Population A: n=135/278 (new start)
- Population B: n=453/1211 (switch)

Baseline Characteristics:

i) Two differences: SJC (Pop A&B), RA duration (Pop B)
Academic > Community

Primary Outcome(s):

i) No difference in unadjusted time-to-therapy alteration between community/academic

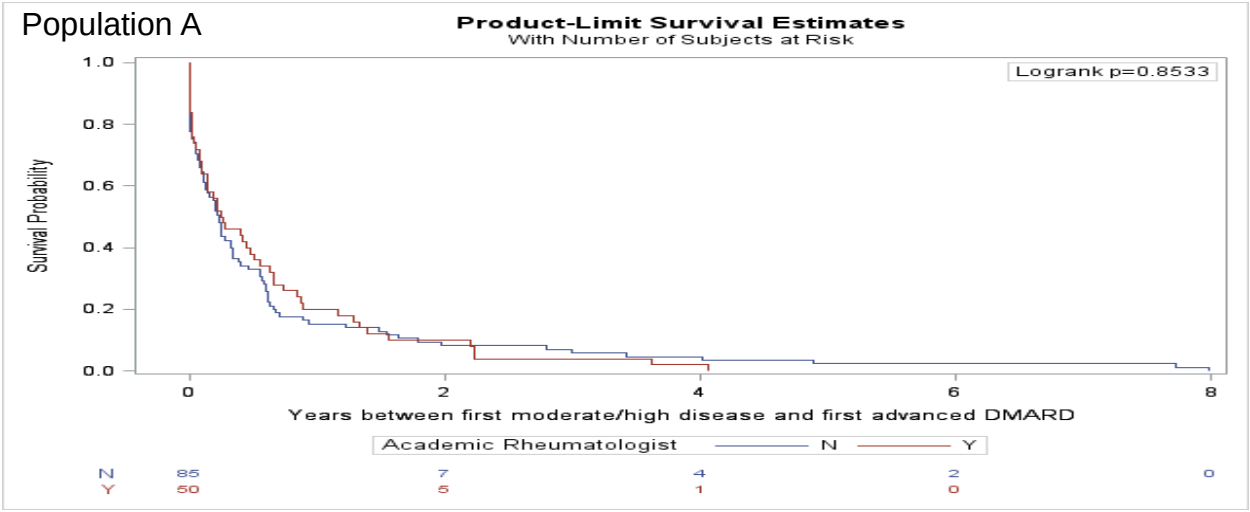
Concerning Incidental Finding:

i) Population A: mean time to advanced therapy was 241 days after 1st moderate/high disease activity - further exploratory analysis

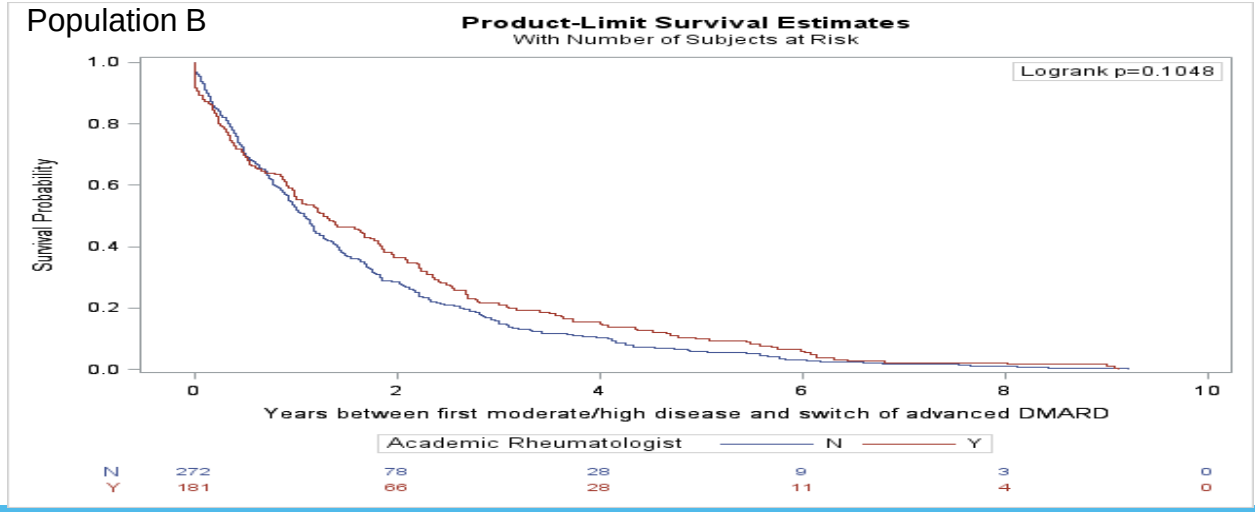
ii) Why are rheumatologists not following guidelines?

Time from first recorded moderate/high disease activity to advanced therapy initiation

Population A



Population B



Time to Advanced Therapy Initiation or Switch in Response to Moderate-High RA Disease Activity Between Academic and Community Practice Settings: Data from the OBRI Registry

E. Hepworth, R. Mirza, M. Movahedi, S. Aydin, C. Bombardier and other OBRI Investigators

Average disease activity during three visits prior to advanced therapy

	Any Therapy	**bDMARDs**	**tsDMARDs**
Population A (New start)	CDAI: 24 DAS28: 4.6 SJC 6.5	CDAI: 15.6 DAS28: 3.5 SJC: 4.3	CDAI: 5.9 DAS28: 3.1 SJC: 1.8
Population B (Switch)	CDAI: 24.1 DAS28: 4.6 SJC: 6.3	CDAI: 20.7 DAS28: 4.2 SJC: 5.2	CDAI: 18.7 DAS28: 3.9 SJC: 4.9

Time to Advanced Therapy Initiation or Switch in Response to Moderate-High RA Disease Activity Between Academic and Community Practice Settings: Data from the OBRI Registry

E. Hepworth, R. Mirza, M. Movahedi, S. Aydin, C. Bombardier and other OBRI Investigators

Time from first mod-high disease activity to initiation/switch in Advanced Therapy

	bDMARDs	tsDMARDs
Population A (New start)	0.6 year (SD=1.0)	3.0 year (SD=3.1)
Population B (Switch)	1.6 year (SD=1.7)	2.8 year (SD=2.4)

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

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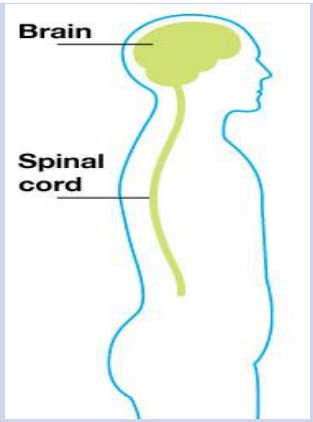
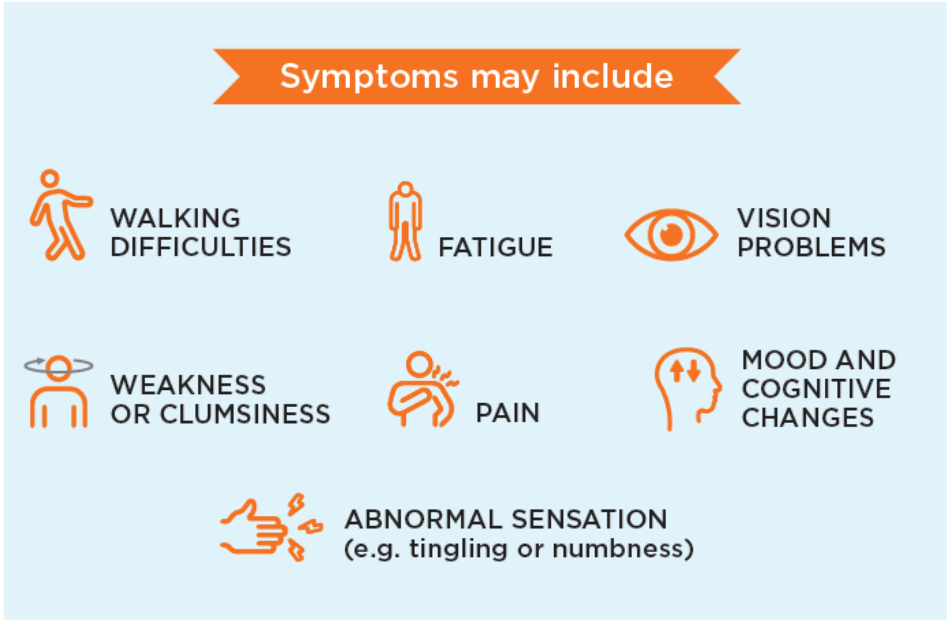
Background

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

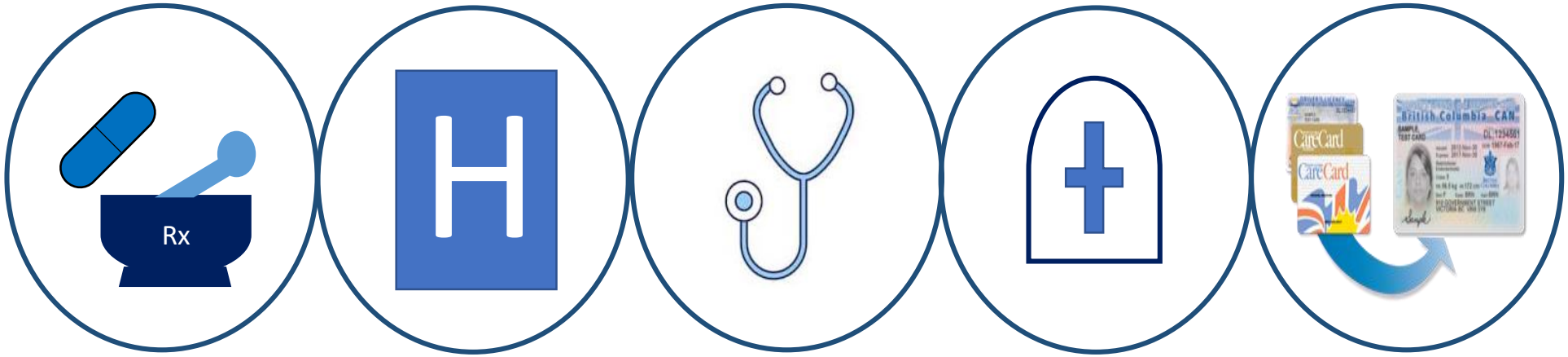
- In the last 2 decades, the **therapeutic options for MS have shifted** dramatically (from 0 disease-modifying drugs [DMDs] to >15).
- The **efficacy** of a DMD is typically established after **short clinical trials** in **highly selected groups** of patients.
- In **clinical practice**, DMDs are used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

References:
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.
2. Canadian Institute for Health Information [creator] (2017): Discharge Abstract Database (Hospital Separations). V2. Population Data BC [publisher]. Data Extract. MOH (2017). http://www.popdata.bc.ca/data.
3. British Columbia Ministry of Health [creator] (2017): Medical Services Plan (MSP) Payment Information File. V2. Population Data BC [publisher]. Data Extract. MOH (2017). http://www.popdata.bc.ca/data.
4. BC Vital Statistics Agency [creator] (2017): Vital Statistics Deaths. V2. Population Data BC [publisher]. Data Extract BC Vital Statistics Agency (2017). http://www.popdata.bc.ca/data.
5. British Columbia Ministry of Health [creator] (2017): Consolidation File (MSP Registration & Premium Billing). V2. Population Data BC [publisher]. Data Extract. MOH (2017). http://www.popdata.bc.ca/data.

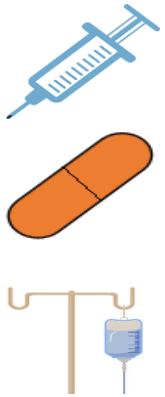
Methods: Population

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	1996-2012
Injection	Glatiramer acetate	October 1997	
Infusion	Natalizumab	September 2006	
Oral	Fingolimod	March 2011	
Oral	Dimethyl fumarate	April 2013	2013-2017
Oral	Teriflunomide	November 2013	
Infusion	Alemtuzumab	December 2013	

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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Calendar period at first DMD	
1996-2012	3,477 (73.5)
2013-2017	1,255 (26.5)

Most were **women**

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

Characteristics	Total N=4,732 n (%)
	(19.3)
	(18.4)
3	992 (21.0)
4	1,006 (21.3)
5 (highest income quintile)	938 (19.8)
	(0.3)
	(83.7)
	(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.

Results: Characteristics of the multiple sclerosis cohort

Characteristics	Total N=4,732 n (%)
Sex	
Women	[illegible]
Men	[illegible]
Age g	
< 30 y	[illegible]
30 to 39 years	1,547 (32.7)
40 to 49 years	1,560 (33.0)
50 to 59 [illegible]	[illegible]
≥ 60 y	[illegible]
Calen	
DMD	
1996-2	[illegible]
2013-2	[illegible]

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

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

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.

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

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Teriflunomide	132/196 (67.4)	**43.1** (10.8)
Alemtuzumab	24/37 (64.9)	**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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