Medical cannabis use by rheumatology patients in routine clinical care: results from The Ontario Best Practices Research Initiative

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Abstract Objective

Medical cannabis is often used to alleviate common symptoms in patients with chronic conditions. With cannabis legalisation in Canada and easier access, it is important that rheumatologists understand its potential impact on their practice. Among patients attending rheumatology clinics in Ontario we assessed: the prevalence of medical cannabis use; symptoms treated; rheumatologists' perceptions.

Methods

Eight rheumatology clinics recruited consecutive adult patients in a 3-part medical cannabis survey: the first completed by rheumatologists; the second by all patients; the third by medical cannabis users. Student's t-test and Chi-square test were used to compare medical cannabis users to never users.

Results

799 patients participated, 163 (20.4%) currently using medical cannabis or within <2 years and 636 never users; most had rheumatoid arthritis (37.8%) or osteoarthritis (34.0%). Compared to never users, current/past-users were younger; more likely to be taking opioids/anti-depressants, have psychiatric/gastrointestinal disorders, and have used recreational cannabis (p<0.05); had higher physician (2.9 vs. 2.1) and patient (6.0 vs. 4.2) global scores, and pain (6.2 vs. 4.7) (p<0.0001). Pain (95.5%), sleeping (82.3%) and anxiety (58.9%) were the most commonly treated symptoms; 78.2% of current/past-users reported medical cannabis was at least somewhat effective. Most rheumatologists reported being uncomfortable to authorise medical cannabis, primarily due to lack of evidence, knowledge, and product standardisation.

Conclusion

Medical cannabis use among rheumatology patients in Ontario was two-fold higher than that reported for the general population of similar age. Use was associated with more severe disease, pain, and prior recreational use. Reported lack of research, knowledge, and product standardisation were barriers for rheumatologist use authorisation.

Key words

rheumatic disease, medical cannabis, survey, prevalence, tetrahydrocannabinol, cannabidiol

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Introduction

Medical cannabis has been a legal treatment option in Canada since 2001 for rheumatic diseases, including rheumatoid arthritis (RA) (1). Cannabis is known to help with inflammation, anxiety, poor sleep, nausea, and low appetite (1), all of which are symptoms of rheumatoid arthritis (2-4) or unwanted effects of RA treatment (5, 6). The effects of cannabis therefore make it an enticing therapeutic option for RA patients. In the first known controlled trial of cannabis in RA patients, cannabis significantly improved pain, quality of sleep, and disease activity compared to placebo (7); however, the sample size of this study was small, with only 58 patients randomised. A recent metaanalysis of studies assessing cannabis use among patients with rheumatologic diseases demonstrated that 20% of rheumatology patients consume cannabis and do in fact show significant improvements in pain (8). Clinical research, especially data on long-term efficacy and safety of cannabis use is, however, still lacking with most of the efficacy claims based on animal models or in vitro studies (9).

Cannabis was legalised for recreational use in Canada in October 2018, and it is suspected to potentially increase medical use. Indeed, there has been an observed increase in the proportion of rheumatology patients reporting having used medical cannabis over the years, specifically from 4.3% in 2014 (10) to 12.6% in 2019 (11). Furthermore, a 2020 Canadian study assessing the impact recreational legalisation of cannabis had on medical users with cancer not only demonstrated that there was an increase in prevalence of use by 26%, but that most of these patients did not use the legal medical access system (12). These findings suggest that the recent legalisation of cannabis could have an impact on its use for other medical conditions, including the management/ treatment of rheumatology patients.

The Canadian Rheumatology Association (CRA) released a position statement in 2019 acknowledging that, despite the lack of evidence for the effect of medical cannabis in rheumatologic diseases, there is still a need for rheumatologists

to provide empathetic and competent guidance concerning its medical use, especially now with increasing access to cannabis (13). It is therefore paramount that rheumatologists understand how cannabis legalisation has affected patients in their practices.

The aim of this study was to determine the prevalence of medical cannabis use and the symptoms being treated in patients attending rheumatology clinics in Ontario as well as to assess the rheumatologists' perceptions and comfort of use.

Materials and methods

Study design

The Ontario Best Practice Research Initiative (OBRI) is a multicentre registry across Ontario, Canada, collecting data from both rheumatologists and patients with RA at enrolment and during follow-up. It incorporates rheumatologist assessments from approximately onethird of rheumatologists in the province of Ontario. For this study, eight rheumatology clinics who were participating in the OBRI each recruited 100 consecutive patients between June 2019 and February 2020 who were invited to participate in a medical cannabis survey. All English-speaking rheumatology patients 18 years of age and older were eligible to participate in the study, regardless of their specific diagnosis. Ethics approval for the current study was obtained by University Health Network (REB #: 19-5284). Written informed consent was provided by all patients prior to completing the survey.

Data collection

The medical cannabis survey consisted of 3 parts: the first part to be completed by the rheumatologist and collected information on the patient diagnosis, current medication use, comorbidities, and physician global assessment of patient disease activity; the second by all recruited patients and collected information on knowledge of medical cannabis, recreational cannabis use, symptoms for which medical cannabis was (or would be) used for, patient global assessment, and patient pain assessment; and the third only by medical cannabis users, either current users or past users who

had consumed within the past 2 years, and collected information on the cannabis type/format used, frequency of use, access to medical cannabis, symptoms treated, and symptom relief.

OBRI rheumatologists were also invited to participate in a separate survey aimed at assessing their perceptions on cannabis use among their patients.

Study objectives

The study objectives were to describe the prevalence of cannabis use among rheumatology patients, along with the patient profile of those who were current users, past users, or never users; the symptoms being treated; and rheumatologists' perceptions and comfort of cannabis use.

Statistical analyses

Baseline demographics and disease-related characteristics, cannabis information, and rheumatologists' perceptions were summarised using descriptive statistics, which included the mean and standard deviation for continuous variables and frequencies and proportions for categorical data. Patients were stratified by cannabis use and between group differences were assessed using the student's t-test for continuous data and the chi-square test for categorical data.

Results

A total of 799 rheumatology patients participated in the survey; 163 patients who were currently using or had used medical cannabis within the last 2 years (current/past-users) and 636 patients who had never used (never-users) medical cannabis.

Demographic and disease-related characteristics by use of medical cannabis (current/past-users *vs.* never-users) are summarised in Table I. Current/past-users were significantly (*p*=0.035) younger than never-users with a mean (SD) age of 56.7 (14.2) *vs.* 59.5 (15.3), respectively; gender, however, was comparable between groups (% female: 72.8% *vs.* 71.0%). Current/past-users more often had a diagnosis of osteoarthritis (40.5% *vs.* 32.4%; *p*=0.0515), fibromyalgia (10.4% *vs.* 4.9%; *p*=0.008), and other chronic pain syndromes (7.4% *vs.* 2.7%; *p*=0.0043) compared

Table I. Demographic and disease-related patient characteristics by use of medical cannabis.

	All patients		Medical Cannabis Use		
	(n:	=799)	Currently or within last 2 years (n=163)	Never (n=636)	<i>p</i> -value
Age, years, mean (SD) ¹	58.9	(15.1)	56.7 (14.2)	59.5 (15.3)	0.035
Female gender, n (%) ²	566	(71.4%)	118 (72.8%)	448 (71.0%)	0.64
Diagnosis, n (%)	202	(25.05)	(1 (07 10)	244 (25.0%)	0.01
Rheumatoid arthritis		(37.8%)	61 (37.4%)	241 (37.9%)	0.91
Psoriatic arthritis Spondyloarthritis		(9.9%) (6.6%)	17 (10.5%) 11 (6.8%)	62 (9.8%) 42 (6.6%)	0.80 0.95
Osteoarthritis		(34.0%)	66 (40.5%)	206 (32.4%)	0.0515
Fibromyalgia		(6.0%)	17 (10.4%)	31 (4.9%)	0.008
Other chronic pain syndromes		(3.6%)	12 (7.4%)	17 (2.7%)	0.0043
Polymyalgia rheumatic	38	(4.8%)	5 (3.1%)	33 (5.2%)	0.26
Systemic lupus erythematosus		(4.1%)	6 (3.7%)	27 (4.3%)	0.75
Gout		(3.9%)	1 (0.1%)	30 (4.7%)	0.0112
Osteoporosis Other		(2.5%)	1 (0.1%)	19 (3.0%)	0.10 0.39
Current medications, n (%)	1//	(22.2%)	35 (21.5%)	142 (22.3%)	0.39
Biologics	115	(14.4%)	27 (16.6%)	88 (13.8%)	0.38
DMARDs		(45.2%)	70 (42.9%)	291 (45.8%)	0.52
NSAIDs	283	(35.4%)	64 (39.3%)	219 (34.4%)	0.28
Opioids	72	(9.0%)	26 (16.0%)	46 (7.2%)	0.0005
Steroids		(21.5%)	32 (19.6%)	140 (22.0%)	0.51
Tranquilizers		(5.6%)	10 (6.1%)	35 (5.5%)	0.75
Anti-epileptics Anti-depressants		(3.4%)	8 (4.9%) 42 (25.8%)	19 (3.0%)	0.23 0.0001
Other		(16.0%) (42.6%)	63 (38.7%)	86 (13.5%) 277 (43.6%)	0.0001
Total number of current		(3.6)	6.2 (3.6)	5.1 (3.5)	0.0009
medications being taken, mean (SD) ³	5.0	(2.0)	0.2 (0.0)	211 (0.0)	0.0003
Comorbidities, n (%)					
Cardiovascular		(33.0%)	54 (33.1%)	210 (33.0%)	0.98
Kidney disease		(5.0%)	8 (4.9%)	32 (5.0%)	0.95
Liver disease Cancer		(2.3%)	2 (1.2%)	16 (2.5%)	0.32 0.51
Pulmonary		(6.3%) (10.5%)	12 (7.4%) 16 (9.8%)	38 (6.0%) 68 (10.7%)	0.31
Endocrine		(18.9%)	31 (19.0%)	120 (18.9%)	0.73
Osteoporosis		(13.9%)	21 (12.9%)	90 (14.2%)	0.68
Psychiatric disorder	108	(13.5%)	39 (23.9%)	69 (10.9%)	< 0.0001
Gastrointestinal	185	(23.2%)	50 (30.7%)	135 (21.2%)	0.01
Neurological		(5.9%)	13 (8.0%)	34 (5.4%)	0.20
Iritis		(4.9%)	3 (1.8%)	36 (5.7%)	0.0435
Psoriasis		(7.8%)	13 (8.0%) 46 (28.2%)	49 (7.7%)	0.91 0.17
Other Physician global (0-10), mean (SD) ⁴		(24.2%) (2.0)	2.9 (1.8)	147 (23.1%) 2.1 (2.0)	<0.0001
Pain intensity (0-10), mean (SD) ⁵		(2.9)	6.2 (2.5)	4.7 (3.0)	<0.0001
Patient global (0-10), mean (SD) ⁶		(3.0)	6.0 (2.6)	4.2 (3.0)	< 0.0001
Current cigarette smoker, n (%) ⁷		(12.0%)	25 (15.6%)	69 (11.1%)	0.11
Who should be prescribing medical	canna	bis, n (%)			
Primary care physicians		(72.9%)	116 (71.2%)	452 (71.1%)	0.98
Specialists	610	(76.3%)	119 (73.0%)	491 (77.2%)	0.26
Pharmacists		(19.8%)	49 (30.1%)	109 (17.1%)	0.0002
Medical cannabis clinic		(30.4%)	92 (56.4%)	161 (25.3%)	< 0.0001
Other		(3.0%)	10 (6.2%)	14 (2.2%)	0.009
Knowledge of medical cannabis, n					
Little or no knowledge		(34.1%)	5 (3.1%)	263 (42.2%)	< 0.0001
Minimal knowledge		(28.5%)	26 (16.0%)	198 (31.7%)	
Somewhat knowledgeable Knowledgeable		(24.8%) (10.6%)	72 (44.2%) 49 (30.1%)	123 (19.7%) 34 (5.5%)	
Very knowledgeable		(2.2%)	11 (6.8%)	6 (1.0%)	
Recreational cannabis use, n (%)	- /	(= -= /0)	(0.0.0)	- (1.070)	
Never	484	(60.6%)	59 (36.2%)	426 (67.0%)	< 0.0001
In the past, but not now		(24.9%)	53 (32.5%)	146 (23.0%)	10.0001
Currently		(12.8%)	46 (29.2%)	56 (8.8%)	
No answer	13	(1.6%)	5 (3.1%)	8 (1.3%)	

	All patients	Medical Cannabis Use			
	(n=799)	Currently or within last 2 years (n=163)	Never (n=636)	<i>p</i> -value	
Symptoms cannabis used for or w	ould consider usin	ng for, n (%) ⁹			
Pain	578 (94.8%)	151 (95.5%)	427 (94.5%)	0.59	
Depression	238 (39.0%)	77 (48.7%)	161 (35.6%)	0.0036	
Anxiety	281 (46.1%)	93 (58.9%)	188 (41.6%)	0.0002	
Difficulty sleeping	383 (62.8%)	130 (82.3%)	253 (26.0%)	< 0.0001	
Lack of appetite	140 (23.0%)	53 (33.5%)	87 (19.3%)	0.0002	
Fatigue	233 (38.2%)	68 (43.0%)	165 (36.5%)	0.15	
Nausea or vomiting	154 (25.2%)	54 (34.2%)	100 (22.1%)	0.0027	
Post-traumatic stress disorder	140 (23.0%)	51 (32.3%)	89 (19.7%)	0.0012	
Other	30 (4.9%)	11 (7.0%)	19 (4.2%)	0.27	

If medical cannabis was used anytime in the past but is no longer being used, reason for discontinuation¹⁰

Cost	29 (37.2%)
No effect	20 (25.6%)
Side effect	15 (19.2%)
No longer needed	4 (5.1%)
Accessibility issues	3 (3.8%)
Switched treatment	2 (2.6%)
Other	14 (17.9%)

¹ Information available for 796 patients. ² Information available for 793 patients. ³ Information available for 737 patients. ⁴ Information available for 718 patients. ⁵ Information available for 780 patients. ⁶ Information available for 787 patients. ⁸ Information available for 787 patients. ⁸ Information available for 787 patients. ⁹ Information available for 610 patients (158 users/past-users and 452 never-users). ¹⁰ Information available for 78 patients. Patients may have reported more than one reasons. Note: Statistically significant values (*p*<0.05) are highlighted in *italics*.

to never-users. A large proportion of patients were diagnosed with rheumatoid arthritis; however, this was comparable between groups (37.8% vs. 37.9%).

In terms of medication use, a higher proportion of current/past-users were taking opioids (16.0% vs. 7.2%; p=0.0005) and antidepressants (25.8% vs. 13.5%; p=0.0001). Although the mean (SD) number of current medications was significantly higher for patients with current/past cannabis use (6.2 [3.6] vs. 5.1 [3.5]; p=0.0009), a comparable (p>0.05) proportion of patients were taking DMARDs (42.9% vs. 45.8%), NSAIDs (39.3% vs. 34.4%), steroids (19.6% vs. 22.0%), and biologics (16.6% vs. 13.8%).

Overall, comorbidities were comparable between groups, except for psychiatric disorders (23.9% vs. 10.9%; p<0.0001) and gastrointestinal issues (30.7% vs. 21.2%; p=0.01), wherein a significantly higher proportion of current/past users reported these comorbidities compared to never-users; and iritis (1.8% vs. 5.7%; p=0.0435), which was experienced by a significantly lower proportion of current/past users. Regarding disease activity, current/past-

users had more severe disease as supported by higher mean (SD) scores for physician global (2.9 [1.8] vs. 2.1 [2.0]; p<0.0001), patient global (6.0 [2.6] vs. 4.2 [3.0]; p<0.0001), and patient pain (6.2 [2.5] vs. 4.7 [3.0]; p<0.0001).

Significant differences (p<0.0001) were also observed in terms of medical cannabis knowledge, with 19.1% of current/past-users reporting minimal to little/no knowledge compared to 73.9% of non-users. Recreational cannabis use was also significantly different between groups (p<0.0001) with a greater number of current/past-users versus non-users reporting past or current use (61.7% vs. 31.8%, respectively). Among current/past users who stopped using medical cannabis, the main reasons for discontinuation included cost (37.2%), no effect (25.6%), and side effects (19.2%). Demographic and disease-related characteristics by type of medical cannabis user (current vs. past-users) are summarised in Table II. This sub-population included a total of 85 patients who were currently using (current-users) and 78 patients who used cannabis within the last 2 years (past-users). Overall, characteristics were statistically comparable between currentand past-users, except for the belief whether specialists should be prescribing medical cannabis (p=0.0014) and the proportion reporting recreational cannabis use (p=0.0011). More specifically, 62.4% of current- vs. 84.6% of past-users (p=0.0014) believed that medical cannabis should be prescribed by specialists, while 31.8% vs. 41.0%, respectively, reported never having used cannabis recreationally.

Table III summarises medical cannabis information by current- versus pastusers (within last 2 years). Significant differences (p<0.05) were observed between current- versus past-users in terms of cannabis formats, frequency of use, perceived effectiveness in treating symptoms, and symptom relief. More specifically, use of dried flower (41.0% vs. 22.2%) and tincture (56.3% vs. 38.1%), the most common types used, was higher in current users compared to past-users. A total of 78.3% of current-users reported consuming cannabis daily compared to 60.3% of pastusers, while only 3.6% of current-users reported "rare" use compared to 17.5% of past-users. The perception of medical cannabis being effective was significantly more frequent among current-users, with 60.2% reporting it as effective or very effective at treating symptoms compared to 36.5% of past-users. No statistically significant between-group differences were observed in the type of cannabis used (i.e. tetrahydrocannabinol-THC, cannabidiol-CBD, and THC/CBD), changes to other medication use, cannabis prescriber, locations used to fill prescriptions, or experience of side effects.

Of the 66 rheumatologists invited to participate in the 'perceptions' survey, 29 (44%) provided responses to the questionnaire concerning their perceptions on cannabis use among their patients. The survey responders were fairly equally distributed across sexes (66% female) and community *versus* academic practices (45% community, 41% academic, 14% both), while, in terms of age, 41% were between the ages of 41–59 years, 31% were ≤40 years of age and 28% were ≥60 years of age. When asked which healthcare professional should

Table II. Demographic and disease-related characteristics of medical cannabis users by current use.

	Current Medical Cannabis Use		p-value
	Currently (n=85)	Within last 2 years (n=78)	
Age, years, mean (SD)	56.0 (13.4)	57.4 (15.2)	0.52
Gender female, n (%) ¹ Clinical diagnosis, n (%)	60 (71.4%)	58 (74.4%)	0.68
Rheumatoid arthritis	29 (34.1%)	32 (41.0%)	0.36
Psoriatic arthritis	6 (7.1%)	11 (14.1%)	0.14
Spondyloarthritis	6 (7.1%)	5 (6.4%)	0.87
Osteoarthritis Fibromyalgia	36 (42.4%) 11 (12.9%)	30 (38.5%) 6 (7.7%)	0.61 0.27
Other chronic pain syndromes	8 (9.4%)	4 (5.3%)	0.14
Other ²	31 (36.5%)	17 (21.8%)	0.04
Current medications, n (%)	13 (15.3%)	14 (18.0%)	0.65
Biologics DMARDs	34 (40.0%)	36 (46.2%)	0.03
NSAIDs	29 (34.1%)	35 (44.9%)	0.16
Opioids	12 (14.1%)	14 (17.9%)	0.50
Steroids	16 (18.8%) 5 (5.9%)	16 (20.5%)	0.79 0.89
Tranquilizers Anti-epileptics	6 (7.1%)	5 (6.4%) 2 (2.6%)	0.89
Anti-depressants	22 (25.9%)	20 (25.6%)	0.97
Other	36 (42.4%)	27 (34.6%)	0.31
Total number of current medications being	6.4 (4.0)	6.0 (3.1)	0.52
taken, mean (SD) Comorbidities, n (%)			
Cardiovascular	27 (31.8%)	27 (34.6%)	0.70
Kidney disease	3 (3.5%)	5 (6.4%)	0.20
Liver disease	1 (1.1%)	1 (1.3%)	0.50 0.06
Cancer Pulmonary	9 (10.6%) 10 (11.8%)	3 (3.9%) 6 (7.7%)	0.38
Endocrine	14 (16.5%)	17 (21.8%)	0.39
Osteoporosis	12 (14.1%)	9 (11.5%)	0.62
Psychiatric disorder	21 (24.7%) 31 (36.5%)	18 (23.1%)	0.81 0.09
Gastrointestinal Neurological	8 (9.4%)	19 (24.4%) 5 (6.4%)	0.09
Iritis	3 (3.5%)	0 (0%)	0.14
Psoriasis	6 (7.1%)	7 (9.0%)	0.65
Other Physician global (0-10), mean (SD)	25 (29.4%) 3.0 (1.9)	21 (26.9%) 2.7 (1.7)	0.72 0.35
Pain Intensity (0-10), mean (SD)	6.2 (2.5)	6.3 (2.6)	0.33
Patient global assessment (0-10), mean (SD)	6.1 (2.4)	5.8 (2.7)	0.49
Current cigarette smoker, n (%)1	12 (14.5%)	13 (16.9%)	0.67
Who should be prescribing medical cannabis,			
Primary care physicians	57 (67.1%)	59 (75.6%)	0.23 0.0014
Specialists Pharmacists	53 (62.4%) 26 (30.6%)	66 (84.6%) 23 (29.5%)	0.0014
Medical cannabis clinic	53 (62.4%)	39 (50.0%)	0.11
Other	7 (8.2%)	3 (3.9%)	0.14
Knowledge of medical cannabis, n (%) Little or no knowledge	2 (2.4%)	3 (23.1%)	0.43
Minimal knowledge	12 (14.1%)	14 (18.0%)	0.43
Somewhat knowledgeable	34 (40.0%)	38 (48.7%)	
Knowledgeable	31 (36.5%)	18 (23.1%)	
Very knowledgeable Recreational cannabis use, n (%)	6 (7.1%)	5 (6.4%)	
Never	27 (31.8%)	32 (41.0%)	0.0011
In the past, but not now	20 (23.5%)	33 (42.3%)	
Currently	35 (41.2%)	11 (14.1%)	
No answer	5 (3.1%)	8 (1.3%)	
Symptoms used/would consider using cannabi Pain	s for, n (%) ³ 80 (94.1%)	71 (97.3%)	0.34
Depression	40 (47.1%)	37 (50.7%)	0.65
Anxiety	52 (61.2%)	41 (56.2%)	0.52
Difficulty sleeping	76 (89.4%)	54 (74.0%)	0.0113
Lack of appetite	35 (41.2%)	18 (24.7%)	0.0283
Fatigue Nausea or vomiting	38 (44.7%) 34 (40.0%)	30 (41.1%) 20 (27.4%)	0.65 0.10
Post-traumatic stress disorder	32 (37.7%)	19 (26.0%)	0.12
Other	7 (8.2%)	4 (5.5%)	0.20

¹ Information available for the following number of users vs. past-users: 84 vs. 78 for gender; 83 vs. 77 for current cigarette use.

Note: Statistically significant values (p<0.05) are highlighted in *italics*.

be responsible for authorising medical cannabis, 24 of the 29 rheumatologists reported cannabis clinics, 18 reported primary care physicians, 12 reported specialists, and 1 reported 'other'; no participant reported retail pharmacists (Fig. 1). In the scenario where a patient was to request medical cannabis, 22 (of 29) responded they would refer their patient to a medical cannabis clinic and only 3 indicated they would consider authorising. Nine of the surveyed rheumatologists had previously authorised use of medical cannabis, 22 reported routinely asking their patients if they are using cannabis, and osteoarthritis, rheumatoid arthritis, and fibromyalgia were quoted as the most common diagnoses of cannabis-users in their practices (Table IV). In terms of comfort level, 22 of the 29 rheumatologists reported being at least somewhat uncomfortable about authorising medical cannabis. The main reasons for their hesitation included lack of research/peer reviewed literature (n=20), lack of knowledge (n=18), and lack of product standardisation or prescription-related information (n=18); potential for misuse/abuse (n=14) and liability (n=13) were also listed as reasons for concern. On the other hand, few (n=3) rheumatologists reported being knowledgeable or very knowledgeable of the Canadian medical cannabis regulations and how patients can access medical cannabis. Despite this, 18 stated they would be interested in participating in a practice review to better understand how their patients were accessing medical cannabis and what symptoms they were treating with it. When asked if they would consider participating in a clinical trial looking at the effectiveness of medical cannabis in inflammatory arthritis patients, 11 rheumatologists would do so if they were required to authorise use while 17 would do so if they could refer patients to a cannabis clinic for authorisation.

Discussion

The aim of this study was to investigate the prevalence of medical cannabis use among patients attending rheumatology clinics in Ontario and the symptoms being treated, as well as how cannabis use is perceived by rheumatologists. We

Other diagnosis includes degenerative disc disease, ankylosing spondylosis, polymyalgia rheumatic, systemic lupus erythematosus, osteoporosis, and gout. ³Available n=158 (85 users and 73 past-users).

Table III. Cannabis information among patients using or having used cannabis within the past 2 years.

	Current vs. past use of Medical Cannabis		p-value
	Currently (n=83)	Within last 2 years (n=63)	
Cannabis type, n (%)			
THC	23 (27.7%)	11 (17.5%)	0.15
CBD	43 (51.8%)	35 (55.6%)	0.65
THC and CBD	48 (57.8%)	28 (44.4%)	0.11
Unknown	5 (6.0%)	2 (3.2%)	0.42
Cannabis format, n (%)	24 (41 00)	14 (22 207)	0.02
Dried flower Milled product	34 (41.0%) 5 (6.0%)	14 (22.2%) 0 (0%)	0.02 0.07
Tinctures	47 (56.6%)	24 (38.1%)	0.03
Capsules	17 (20.5%)	14 (22.2%)	0.80
Topical cream	20 (24.1%)	11 (17.5%)	0.33
Edibles	20 (24.1%)	11 (17.5%)	0.33
Suppositories	1 (1.2%)	0 (0%)	0.57
Other	10 (12.0%)	15 (23.8%)	0.083
How often did/do you use medical cannabis,			
Daily	65 (78.3%)	38 (60.3%)	0.04
Weekly	10 (12.0%)	7 (11.1%)	0.04
Monthly Rarely	2 (2.4%) 3 (3.6%)	4 (6.4%) 11 (17.5%)	
Missing	3 (3.6%)	3 (4.8%)	
Made changes of medication use, n (%)	2 (21070)	2 (11070)	
Lowered use of other meds ¹	11 (13.3%)	4 (6.3%)	0.39
Completely stopped medications ²	6 (7.2%)	4 (6.3%)	0.25
Cannabis prescriber, n (%)			
Specialist	13 (15.7%)	7 (11.1%)	0.43
Family doctor Medical cannabis doctor	15 (18.1%)	8 (12.7)	0.38 0.49
Other	35 (42.2%) 21 (25.3%)	23 (36.5%) 25 (39.7%)	0.49
Where are prescriptions filled, n (%)	21 (23.370)	25 (57.170)	0.00
Licensed producer	59 (71.1%)	42 (66.7%)	0.57
Licensed to grow my own	4 (4.8%)	0 (0.0%)	0.10
Other ³	18 (21.7%)	17 (27.0%)	0.46
Overall, how affective is/was the medical ca	nnabis in treating you	r symptoms?	
Very effective	25 (30.1%)	12 (19.0%)	<.0001
Effective	25 (30.1%)	11 (17.5%)	
Somewhat effective	24 (28.9%)	11 (17.5%)	
Not effective	4 (4.8%)	26 (41.3%)	
Missing	5 (6.0%)	3 (4.8%)	
Symptoms treated, n (%) Pain ⁴	64 (80.0%)	55 (90.2%)	0.10
Depression	17 (20.5%)	13 (20.6%)	0.10
Anxiety	28 (34.6%) ⁵	19 (30.2%)	0.58
Difficulty sleeping	50 (64.1%)6	30 (47.6%)	0.0495
Lack of appetite	$17 (20.7\%)^7$	7 (11.1%)	0.13
Fatigue	$18 (22.0\%)^8$	12 (19.0%)	0.67
Nausea or vomiting Post-traumatic stress disorder	16 (19.3%)	7 (11.1%)	0.18
Other	9 (10.8%) 3 (3.6%)	4 (6.3%) 2 (3.2%)	0.15 0.35
	, ,	2 (3.270)	0.55
Symptom relief, mean (SD) 0-10, 0=no relie Pain	6.2 (2.4)	3.9 (2.3)	0.0001
Depression	7.4 (2.6)	6.0 (3.1)	0.21
Anxiety	7.0 (2.7)	6.7 (2.8)	0.70
Difficulty sleeping	7.3 (2.8)	6.1 (3.7)	0.10
Lack of appetite	7.3 (6.5)	6.1 (5.1)	0.35
Fatigue	4.8 (2.3)	3.1 (3.7)	0.12
Nausea or vomiting	6.8 (3.1)	3.9 (3.7)	0.67
Post-traumatic stress disorder	7.3 (3.1)	5.0 (4.1)	0.28
Experienced side effects, n (%) Yes	19 (22.9%)	18 (28.6%)	0.43
	17 (22.770)	10 (20.070)	0.75

¹ Medications that were lowered for current-users were Tylenol 3, prednisone, duloxetine, flexeril, DZ, Lyrica; and for past-users (missing n=2) were NSAIDs and percocet. ² Medications that were stopped for current-users (missing n=2) were zopiclone, ativan, morphine, hydromorphine, NSAIDs, T-3s, sleeping pills, and mood enhancers; and for past-users (missing n=2) were meloxicam and MTX. ³ Other places prescriptions were filled for current-users were: unlicensed clinic/store, unlicensed personal cultivation, street, farmer; and for past-users were unlicensed clinic, online, neighbor. ⁴ Information available for 80 current-users and 61 past-users. ⁵ Information available for 81 current-users.

THC: tetrahydrocannabinol; CBD: cannabidiol

Note: Statistically significant values (p<0.05) are highlighted in *italics*.

found that the prevalence of cannabis use was slightly lower among rheumatology patients in Ontario compared to that reported for the general Canadian population (≥25 years), specifically 20% vs. 21%-37%, respectively (14). Statistics Canada further stratified the age categories for cannabis use in 2019 (April to September) and reported that 6.6% of Canadians aged ≥65 years consumed cannabis compared to 10.3% of those aged 45–64 years (15). According to our findings, it appears as though the prevalence of current/past cannabis use among rheumatology patients in Ontario may be more than two-fold higher than that reported for age-matched general Canadian population. Furthermore, the prevalence we report here is comparable to that reported for fibromyalgia patients (23.9%) during a similar period in the province of Quebec, Canada, but higher than that for patients with other (non-fibromyalgia) rheumatic diseases (11.1%); this discrepancy could reflect differences in patient characteristics, patient management, access to cannabis, or other factors (16).

The results of our study demonstrated that, compared to non-users, patients who were currently or previously using cannabis were more likely to have psychiatric disorders. This is noteworthy, as psychosis is a well documented concern seemingly associated with frequent cannabis consumption and may become a long-term adverse complication (17, 18). In addition, current/past-users had higher disease activity and more pain, supported by both higher pain scores and more frequent use of opioids, along with more frequent comorbid chronic pain syndromes compared to non-users. These results are in agreement with those from an earlier study on cannabis use among rheumatology patients in Quebec (10). The more frequent use of opioids among medical cannabis users is likely an indicator of more severe pain but also raises the question as to whether a tendency towards addiction/ abuse is involved; additional studies are required to investigate this.

The primary symptoms current/pastusers in our study were trying to treat were pain, anxiety and sleep difficulties. Despite lack of concrete evidence

⁶ Information available for 78 current-users. ⁷ Information available for 82 current-users. ⁸ Information available for 82 current-users. ⁹ Information available for the following number of current-users *versus* past-users: 64 *vs*. 55 for pain; 17 *vs*. 13 for depression; 28 *vs*. 19 for anxiety; 50 *vs*. 30 for difficulty sleeping; 17 *vs*. 7 for lack of appetite; 18 *vs*. 12 for fatigue; 16 *vs*. 7 for nausea or vomiting; 9 *vs*. 4 for post-traumatic stress disorder.

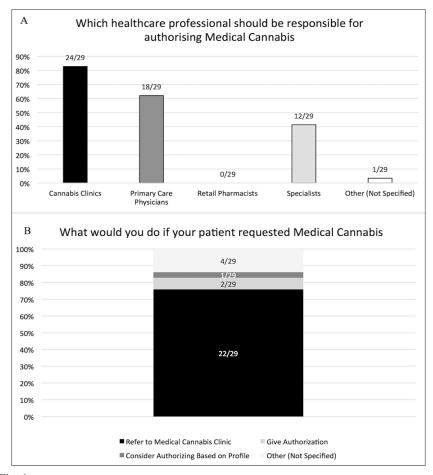


Fig. 1. Rheumatologist perceptions on authorisation of medical cannabis.

for its effectiveness (19) over half of current/past-users felt cannabis was successful at treating their symptoms. These results are in agreement with the findings of a recent single-arm observational showing some clinical benefits in patients with fibromyalgia, particularly in sleep (20). However, it is too early to speculate whether this effect is partially explained by a placebo effect or if cannabis truly has efficacy in treating rheumatic symptoms. Additional properly designed studies are required to reach conclusions regarding the efficacy of medical cannabis. Among patients discontinuing medical cannabis, approximately 20% did so due to side effects: however, unfortunately, details on the nature of these side effects were not collected during the study.

When assessing differences between current and past cannabis users, the type of cannabis product was significantly different between groups, whereby two-times the proportion of current-users reported using dried flower compared to past-users. In terms of perceived effectiveness, two-times the proportion of current-users also reported cannabis to be effective in treating their symptoms compared to past-users. Although this may be due to 'survival' bias by which only individuals perceiving benefits continue to be users, a recent study demonstrated that dried flower provided greater symptom relief, as reported by patients, suggesting that there may be an association between the type of cannabis product used and symptom relief (21).

Our results demonstrated that most rheumatologists felt somewhat to very uncomfortable authorising cannabis use and believed cannabis clinics or primary care physicians should be the healthcare professional responsible for authorising medical cannabis use. Very few rheumatologists declared being knowledgeable or very knowledgeable about the Canadian medical cannabis regulations and how patients obtain access. Earlier studies reflect this issue,

having concluded that rheumatologists were not entirely confident in their knowledge of cannabis or in their competency to prescribe for rheumatic conditions (22). It is therefore reasonable to suggest that rheumatologists may also benefit from medical education programs on the risk-benefit profile of medical cannabis and the potential benefits perceived by their patients.

There are several limitations to our study. As with all surveys, there is the potential for recall bias; although we have kept the recall period relatively short to minimise said bias, it is possible that certain details may not be accurately remembered. In addition, only a small sample of rheumatologists were surveyed, making it difficult to draw strong conclusions or speak of the generalisability of their perceptions. However, as previously mentioned, our results are in line with what has been found in the literature, supporting the external validity of our findings.

Conclusion

The prevalence of cannabis use among rheumatology patients in Ontario Canada appears to be two-fold higher than that reported for the general population of similar age in Canada. Medical cannabis use was associated with more severe disease, greater pain, and prior familiarity for recreational purposes. However, most rheumatologists felt uncomfortable authorising use and reported lack of research, knowledge, and product standardisation as the main barriers.

Key messages

- Cannabis use among rheumatology patients in Ontario was 2-fold higher than in the general population.
- Medical cannabis use was associated with more severe disease, pain, and prior recreational use.
- Reported lack of research, knowledge, and product standardisation were barriers for rheumatologist use authorisation.

References

- THE ARTHRITIS SOCIETY: Medical Cannabis 2021 [Available from: https://arthritis.ca/treatment/medication/medical-cannabis.
- CHOY EH, PANAYI GS: Cytokine pathways and joint inflammation in rheumatoid arthri-

Table IV. Rheumatologist perceptions on medical cannabis use.

	(n=29)
Have you ever authorised the use of medical cannabis? (Yes)	9
Oo you routinely ask your patients if they are using medical cannabis? (Yes)	22
Which diagnosis do the majority of your patients using medical cannabis fall under	?
Osteoarthritis	12
Rheumatoid arthritis	9
Chronic Pain	8
Fibromyalgia	7
Psoriatic arthritis	4
Spondyloarthropathy	4
Back pain	2
Other (mood / insomnia / neck pain)	3
How comfortable do you feel authorising patients to use medical cannabis?	
Very comfortable	2
Comfortable	3
Somewhat comfortable	2.
Somewhat uncomfortable	11
Not comfortable	8
Very uncomfortable	3
What concerns/barriers do you have with regards to authorising the use of med	_
cannabis?	• •
Lack of research / peer reviewed literature	20
Lack of knowledge	18
ack of product standardisation or prescription-related information (i.e., potency/dostrain, quality)	
Potential for misuse / abuse	14
Liability	13
Other (personal beliefs / lack of time)	2
None	1
Are you knowledgeable of the Canadian medical cannabis regulations, <i>i.e.</i> how patients can access medical cannabis?	
Little or no knowledge	6
Minimal knowledge	9
Somewhat knowledgeable	11
Knowledgeable	2
Very knowledgeable	1
Would you be interested in participating in a practice review to better understated how many of your patients are currently using medical cannabis and what symptoms the are treating with medical cannabis? (Yes)	
Would you consider participating in a clinical trial looking at the effectiveness nedical cannabis in inflammatory arthritis patients, if you were required as pa of this trial to:	
Authorise use of medical cannabis? (Yes)	11
Refer patients to a cannabis clinic for authorisation to use medical cannabis? (Ye	

- tis. *N Engl J Med* 2001; 344: 907-16. https://doi.org/10.1056/nejm200103223441207
- VANDYKE MM, PARKER JC, SMARR KL et al.: Anxiety in rheumatoid arthritis. Arthritis Rheum 2004; 51: 408-12. https://doi.org/10.1002/art.20474
- WOLFE F, MICHAUD K, LI T: Sleep disturbance in patients with rheumatoid arthritis: evaluation by medical outcomes study and visual analog sleep scales. *J Rheumatol* 2006; 33: 1942-51.
- FEELY MG, O'DELL JR: Update on the use of conventional disease-modifying antirheumatic drugs in the management of rheumatoid arthritis. *Curr Opin Rheumatol* 2010; 22: 316-20. https:// doi.org/10.1097/bor.0b013e3283383f87
- LAINE L: Gastrointestinal effects of NSAIDs and coxibs. J Pain Symptom Manage 2003; 25 (2 Suppl.): S32-40. https:// doi.org/10.1016/s0885-3924(02)00629-2

- BLAKE DR, ROBSON P, HO M, JUBB RW, MC-CABE CS: Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis. *Rheumatology* (Oxford) 2006; 45: 50-2.
- 8. GUILLOUARD M, AUTHIER N, PEREIRA B, SOUBRIER M, MATHIEU S: Cannabis use assessment and its impact on pain in rheumatologic diseases: a systematic review and meta-analysis. *Rheumatology* (Oxford) 2021; 60: 549-56. https://
 - doi.org/10.1093/rheumatology/keaa534
- 9. GONEN T, AMITAL H: Cannabis and cannabinoids in the treatment of rheumatic diseases. Rambam Maimonides Med J 2020; 11. https://doi.org/10.5041/rmmj.10389
- 10. STE-MARIE PA, SHIR Y, RAMPAKAKIS E et al.: Survey of herbal cannabis (marijuana) use in rheumatology clinic attenders with a rheumatologist confirmed diagnosis. Pain

- 2016; 157: 2792-7. https://doi.org/10.1097/j.pain.000000000000000706
- FITZCHARLES MA, RAMPAKAKIS E, SAMPA-LIS J et al.: Medical cannabis use by rheumatology patients following recreational legalization: a prospective observational study of 1000 patients in Canada. ACR Open Rheumatol 2020; 2: 286-93.
- HAWLEY P, GOBBO M, AFGHARI N: The impact of legalization of access to recreational Cannabis on Canadian medical users with Cancer. *BMC Health Serv Res* 2020; 20: 977. https://doi.org/10.1186/s12913-020-05756-8
- 13. FITZCHARLES MA, NIAKI OZ, HAUSER W, HAZLEWOOD G; CANADIAN RHEUMATOL-OGY ASSOCIATION: Position statement: A pragmatic approach for medical cannabis and patients with rheumatic diseases. *J Rheumatol* 2019; 46: 532-8.
 - https://doi.org/10.3899/jrheum.181120
- 14. Government of Canada. Canadian Cannabis Survey 2020: Summary [Available from: https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/researchdata/canadian-cannabis-survey-2020-summary.html.
- Statistics Canada. National Cannabis Survey, third quarter 2019 2019 [Available from: https://www150.statcan.gc.ca/n1/daily-quotidien/191030/dq191030a-eng.htm.
- 16. FITZCHARLES MA, RAMPAKAKIS E, SAMPALIS J et al.: Use of medical cannabis by patients with fibromyalgia in Canada after cannabis legalisation: a cross-sectional study. Clin Exp Rheumatol 2021; 39 (Suppl. 130): S115-9. https://doi.org/10.55563/clinexprheumatol/qcyet7
- GAGE SH, HICKMAN M, ZAMMIT S: Association between cannabis and psychosis: epidemiologic evidence. *Biol Psychiatry* 2016; 79: 549-56. https://
 - doi.org/10.1016/j.biopsych.2015.08.001
- 18. SEMPLE DM, McINTOSH AM, LAWRIE SM: Cannabis as a risk factor for psychosis: systematic review. *J Psychopharmacol* 2005; 19: 187-94.
 - https://doi.org/10.1177/0269881105049040
- 19. FITZCHARLES MA, BAERWALD C, ABLIN J, HAUSER W: Efficacy, tolerability and safety of cannabinoids in chronic pain associated with rheumatic diseases (fibromyalgia syndrome, back pain, osteoarthritis, rheumatoid arthritis): A systematic review of randomized controlled trials. Schmerz 2016; 30: 47-61. https://doi.org/10.1007/s00482-015-0084-3
- 20. GIORGI V, BONGIOVANNI S, ATZENI F, MAROTTO D, SALAFFI F, SARZI-PUTTINI P: Adding medical cannabis to standard analgesic treatment for fibromyalgia: a prospective observational study. Clin Exp Rheumatol 2020; 38 (Suppl. 123): S53-9.
- STITH SS, VIGIL JM, BROCKELMAN F, KEEL-ING K, HALL B: The association between cannabis product characteristics and symptom relief. Sci Rep 2019; 9: 2712. https://doi.org/10.1038/s41598-019-39462-1
- 22. FITZCHARLES MA, STE-MARIE PA, CLAUW DJ et al.: Rheumatologists lack confidence in their knowledge of cannabinoids pertaining to the management of rheumatic complaints. BMC Musculoskelet Disord 2014; 15: 258. https://doi.org/10.1186/1471-2474-15-258