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# Journal of Substance Abuse Treatment

journal homepage: www.elsevier.com/locate/jsat



# Self-reported reductions in tobacco and nicotine use following medical cannabis initiation: Results from a cross-sectional survey of authorized medical cannabis patients in Canada

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ARTICLE INFO

Keywords: Cannabis Marijuana Tobacco Nicotine substitution Harm reduction

# ABSTRACT

*Background:* Despite decades of campaigns aimed at reducing tobacco/nicotine (T/N) use and the development of many different T/N reduction and cessation strategies, the impacts on international public health remain significant. Some studies have found an association between medical and non-medical cannabis use and T/N use, although the evidence on whether cannabis/cannabinoids increase or decrease the odds of reducing or ceasing T/N use remain contradictory. This paper explores the self-reported use of cannabis and associated changes in T/N use among a Canadian medical cannabis patient population.

*Methods*: This study examines the impact of medical cannabis on T/N use by comparing self-reported patterns of use before and after the initiation of medical cannabis. Participants completed an online cross-sectional survey examining demographics, patterns of medical cannabis use, and the impact of medical cannabis on the use of T/N and other substances. The survey also included novel measures examining whether patients intended to use medical cannabis to reduce T/N use or had experience with other pharmacological or psychobehavioral T/N cessation strategies. We conducted a series of descriptive analyses and univariate and multivariate logistic regressions to explore the potential association between primary variables of interest and T/N reduction and cessation.

*Results*: In total, the study recruited 2102 individuals, of whom 650 were current or former T/N users. Following initiation of medical cannabis use 320 (49%) T/N users self-reported reductions in use, with 160 (24.6%) reporting no T/N use in the 30 days prior to the survey. Odds of T/N cessation were greater among those who were age 55 or older (Adjusted Odds Ratio [AOR] = 2.56, 95% Confidence Interval [CI] 1.53–4.26), or those who reported >25 T/N uses per day in the pre-period (AOR = 2.11, 95% CI 1.14–3.92). Specific intent to use medical cannabis to quit resulted in significantly greater odds of reducing T/N use (AOR = 2.79, 95% CI 1.49–5.22); however, involvement with traditional T/N cessation treatments (pharmacological or psychobehavioral) was negatively associated with T/N cessation (AOR 0.39, 95% CI 0.18–0.86).

*Conclusions:* Results from this retrospective survey of medical cannabis users suggest that initiation of medical cannabis use was associated with self-reported reductions and/or cessation of T/N use in nearly half of study participants. In light of the significant morbidity, mortality, and health care costs related to T/N dependence, future research should further evaluate the potential of cannabis-based treatments to support efforts to reduce or cease T/N use.

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https://doi.org/10.1016/j.jsat.2021.108481

Received 23 September 2020; Received in revised form 18 February 2021; Accepted 11 May 2021 Available online 14 May 2021 0740-5472/© 2021 Elsevier Inc. All rights reserved.

# 1. Background

The past decade has witnessed a dramatic increase in popular and scientific interest in therapeutic applications of cannabis and cannabinoids for the treatment of a variety of conditions, including chronic pain, anxiety/depression, and treatment-resistance epilepsy (Lucas et al., 2019; MacCallum & Russo, 2018). The potential benefits of therapeutic cannabis use identified in observational studies include impacts on the use of more harmful substances (Boehnke et al., 2019; Lucas et al., 2019; Lucas & Walsh, 2017; Nutt et al., 2010). For example, a growing literature highlights the potential for cannabis to substitute for alcohol (Anderson et al., 2012; Sewell et al., 2009; Subbaraman, 2014), opioids (Lucas et al., 2019; Shi et al., 2019; Wen & Hockenberry, 2018), and cocaine (Labigalini et al., 1999; Socías et al., 2017). The public health benefits of cannabis substitution are suggested in publications noting reduced opioid overdose fatalities (Liang et al., 2018; Livingston et al., 2017), traffic accidents (Anderson et al., 2013; Santaella-Tenorio et al., 2017), and dispensation of pharmaceuticals (Bradford & Bradford, 2017; Shi et al., 2019; Wen & Hockenberry, 2018) in jurisdictions that have created licit access to medical or nonmedical cannabis. As this research is largely limited to observational cross-sectional surveys and population-level studies, we cannot conclude that a causal mechanism exists between cannabis use and reduced frequency of other substances. However, preliminary evidence suggests some people who use substances are intentionally employing cannabis to reduce the harms of other substances. Cross-sectional surveys of cannabis patients in the United States and Canada have found a high rate of self-reported deliberate substitution of cannabis for opioids and other pharmaceuticals, alcohol, tobacco, and illicit substances (Boehnke et al., 2019; Lake et al., 2020; Lucas et al., 2019). Additionally, a prospective study of people who use illicit drugs (PWUD) in Vancouver, Canada, found that intentional cannabis use to reduce crack use was associated with decreased frequency of crack use (Socías et al., 2017).

Canada was one of the first nations in the world to initiate a federal program to facilitate the legal use of medical cannabis through a physician's authorization (Belle-Isle et al., 2014; Lucas, 2008, 2009). The most recent iteration of the program—the Access to Cannabis for Medical Purposes Regulations (ACMPR)—resulted in the licensing of large-scale cultivators (known as licensed producers, or LPs) who provide medical cannabis products to authorized patients via mail. These products include dried flower cannabis, as well as extracts for oral consumption in the forms of oils and capsules (Capler et al., 2017; Lucas, 2017; Lucas & Walsh, 2017). As of June 2019, more than 360,000 Canadians were authorized to use medical cannabis under the ACMPR (Health Canada, 2019).

The World Health Organization estimates suggest there are approximately 1.1 billion adult smokers, and at least 367 million people using smokeless tobacco globally (WHO global report on trends in prevalence of tobacco smoking 2000-2025, second edition, 2018). Tobacco/nicotine (T/N) use is not only implicated in 12% of all deaths around the globe in adults aged 30 or older but is also a source of substantial health care-related costs (WHO, 2012). However, the topic of tobacco harm reduction has long posed challenges to tobacco scientists and policy experts, and remains a source of significant debate, especially the use of electronic cigarettes (Cobb et al., 2015; WHO Report on the Global Tobacco Epidemic, 2019, 2019; Zeller & Hatsukami, 2009), with some arguing that since research on the overall efficacy of e-cigarettes in tobacco cessation is inconclusive (Khoudigian et al., 2016; Lindson-Hawley et al., 2016; Malas et al., 2016), and that if the long-term harms of many smokeless tobacco products is unknown, treatment providers should consider only prevention and/or abstinence-based strategies. Data on the high rate of adoption of e-cigarettes/vaping by youth (Miech et al., 2019; WHO Report on the Global Tobacco Epidemic, 2019, 2019), and the 2019 health crisis that led to serious lung damage in thousands of people who use T/N and THC oil vapes in the United States have only heightened the debate around T/N harm reduction (Layden et al., 2020).

In light of the heavy burden of morbidity and mortality associated with T/N dependence, researchers have developed and evaluated a number of pharmacological, psychological/behavioral, and nicotine replacement therapies (NRT) for their potential impact on tobacco cessation. Overall, evidence suggests that combined pharmacotherapy (including NRTs) and behavioral treatment may assist with tobacco reduction/cessation (Cahill et al., 2013; Leyro et al., 2015; Lindson et al., 2019; Stead et al., 2016; Taylor et al., 2018; WHO Report on the Global Tobacco Epidemic, 2019, 2019). Unfortunately, the success rates of these treatments are low, highlighting the need for additional tools and strategies to address T/N use and associated harms.

A consistent association between tobacco use and cannabis use exists. Current cigarette smokers report higher rates of cannabis use than nonsmokers, with more than 90% of Canadian students in grade 7–12 who are current cigarette smokers reporting that they have also tried cannabis on at least one occasion, while only 21.8% of grade 7–12 students overall report ever trying cannabis (Leos-Toro et al., 2017). Similarly, research has found that approximately 90% of people who use cannabis also report smoking tobacco (Agrawal et al., 2012). The concurrent and co-use of cannabis and tobacco is common due to a number of proposed behavioral, biological, sociocultural, and genetic mechanisms, including that some people who use cannabis combine it with tobacco when rolling joints/blunts (Agrawal et al., 2012; Schauer, Rosenberry, & Peters, 2017; Weinberger et al., 2019, 2020), which may increase both harms and dependence (Meier & Hatsukami, 2016; Tucker et al., 2019).

Nonetheless, reviews of the relative health impacts of widely used psychoactive substances rate the harms associated with tobacco as substantially higher than those associated with cannabis (Lachenmeier & Rehm, 2015; Nutt et al., 2010). Although cannabis use results in a comparatively low risk of dependence and harms to individuals and society compared to tobacco use, such dependence is not benign. Chronic use has been associated with potential cognitive deficits, and the psychoactive effects of use and associated impairment can lead to increased personal health and public safety risks (Fischer et al., 2011). Evidence also suggests that regular cannabis smoking may be associated with bronchial issues (Tashkin, 2013). However, while a large body of evidence (WHO, 2012) supports the association between tobacco use and cancer, the evidence of associations between cannabis smoking and cancer is inconclusive, with some research reporting a moderate increased risk of lung cancer among heavy users (Aldington et al., 2008; Callaghan et al., 2013), and others concluding no causal association (Hashibe et al., 2006; Huang et al., 2015; Ribeiro & Ind, 2016; Tashkin, 2013). Therefore, cannabis might play a harm reduction role by either reducing the use and/or associated harms of tobacco or nicotine use, either as a cessation aid or safer substitute.

However, population-level, cross-sectional, and prospective observational studies examining the relationship between cannabis and tobacco use and cessation have not resulted in consistent conclusions. A series of longitudinal, population-level studies focused on large U.S.based datasets such as the National Epidemiologic Survey on Alcohol and Related Conditions, the Population Assessment of Tobacco and Health Study, and the annual National Survey on Drug Use and Health, suggest that cannabis use may be associated with increased risk of cigarette smoking initiation, persistence and relapse, as well as reduced odds of quitting among some people who use cannabis, suggesting the two may be complements (Weinberger et al., 2018; Weinberger et al., 2019, 2020). While a cross-sectional study found that individuals who use cannabis had a higher prevalence of current tobacco use and a lower prevalence of sustained tobacco abstinence than those who never used cannabis (Schauer, King, & McAfee, 2017), a more recent cross-sectional survey of adult individuals who use cannabis and tobacco in the United States found a high rate (62%) of self-reported increases in tobacco use during cannabis quit attempts, as well as a self-reported 50% increase in rates of cannabis use during tobacco cessation (McClure et al., 2019), suggesting the two may be substitutes for one another. An Australian

prospective study of voluntary cannabis abstinence in a non-treatment seeking cannabis using population found an increase in both tobacco and alcohol use during cannabis abstinence, followed by a decrease in both once cannabis use resumed (Allsop et al., 2014), suggesting substitution, and leading us to consider the potential impact of alcohol cessation on T/N use in this analysis as well.

Qualitative, quantitative, and behavioral studies examining the relationship between tobacco and cannabis use have also yielded mixed results. A qualitative study of 48 young adult individuals 18–34 who use cannabis and tobacco in the United States found that these substances may both substitute for and complement one another under different circumstances and within different substance using populations, with the highest rates of tobacco use associated with the strongest corelationship between both substances (Schauer et al., 2016). A later quantitative study of 432 U.S. adults examining the interrelatedness of tobacco and cannabis in those who co-use both substances came to similar conclusions (Akbar et al., 2019). However, a behavioral economic evaluation found that cannabis and tobacco are neither complements nor substitutes, but rather that they were independent of each other (Peters et al., 2017).

Prospective studies specific to tobacco cessation have also come to contradictory conclusion. Whereas one study found that any pretreatment cannabis use led to decreased odds of tobacco smoking cessation (Gourlay et al., 1994), another study found that any illicit substance use in the pre-treatment phase reduced the likelihood of tobacco cessation. However, in the latter study, the tobacco abstinence rate among individuals who use only cannabis (40%) exceeded that of individuals who use other illicit substances (11%), though lagged behind that of nondrug users (55%) (Stapleton et al., 2009). Four other studies reported no statistical relationship between cannabis use and tobacco abstinence (Hendricks et al., 2012; Humfleet et al., 1999; Metrik et al., 2011; Rabin et al., 2016). In 2020 a large Canadian study of 35,246 patients enrolled in the Smoking Treatment for Ontario Patients (STOP) study found that cannabis use was associated with 15% lower odds of quitting. However, when cannabis use was broken down by intent (i.e., medical or recreational use) and the results were adjusted for confounders, recreational cannabis use was associated with lower odds of quitting (AOR 0.84, 95% CI 0.75-0.94, p = 0.002), but medical cannabis use was not (AOR 0.94, 95% CI 0.78–1.15, p = 0.561) (Voci et al., 2020) suggesting that reasons for cannabis use, be they medical or recreational, may play a role in the overall success of tobacco cessation attempts for those who use both substances.

Very little clinical research has been conducted in this area to date, but a 2013 examination of the use of cannabidiol (CBD), a nonintoxicating cannabinoid, as an adjunct to smoking cessation efforts reported that cigarette smokers randomized to a CBD inhaler evinced reductions in tobacco consumption without increased craving (Morgan et al., 2013). However, the small pilot study was limited by a relatively brief follow-up period. Further, the extent to which the effects of vaporized CBD might generalize to herbal cannabis use with various levels of different cannabinoids is not clear. A more recent study found that a single 800-mg oral dose of CBD reduced the salience and pleasantness of cigarette cues compared with placebo, but did not influence cravings or withdrawal (Hindocha et al., 2018).

In sum, despite contradictory findings, some evidence suggests a potential role for cannabis/cannabinoids in tobacco reduction/cessation, particularly among those using cannabis for medical purposes. However, to the best of our knowledge, to date no studies have evaluated the prevalence of changes in tobacco use following medical cannabis initiation, or assessed how potential correlates—such as intent to use medical cannabis to reduce/cease T/N use, primary method of use, involvement in other T/N treatment, and changes in alcohol use—may be associated with such changes. This analysis examines self-reported changes in T/N use among individuals participating in a large, national, cross-sectional survey of Canadian medical cannabis patients, with a focus on variables potentially associated with T/N reduction and/

or cessation.

# 2. Methods

The research team designed a 392-question cross-sectional survey to gather information from Canadian federally authorized medical cannabis patients registered with Tilray, a Canadian licensed producer of medical cannabis. The survey included questions on participants' demographics; patterns of cannabis use; and self-reported changes in the use of prescription drugs, alcohol, tobacco, and illicit substances following medical cannabis initiation. The study entered all respondents who provided digital informed consent and completed the survey into a draw to receive one of five \$1000 credits applicable toward the purchase of medical cannabis. The study gathered data on REDCap (Vanderbilt University, Nashville, TN, USA). The inclusion criteria included being an authorized medical cannabis patient registered with Tilray, aged 18 years or older, capable of reading and understanding English, and of legally consenting age to participate in the study. For this particular analysis examining the impact of medical cannabis on tobacco use, the study included only those who identified previous/current tobacco/ nicotine use.

The survey received approval from the University of Victoria's Human Research Ethics Board on December 19, 2018. On January 11, 2019, the study team sent an invitation to participate in the survey to 16,664 federally authorized medical cannabis patients who provided email addresses to Tilray. Individuals could participate in the survey from January 11 to 18, 2019.

# 2.1. Measures

The primary outcome of interest was changes in T/N use prior to and post-medical cannabis initiation. The study assessed this by inquiring about typical T/N uses per day prior to using medical cannabis, and then comparing this with typical T/N uses per day in the 30 days prior to the survey, followed by varied analyses of demographic and other variables that may have affected rates of T/N use. The study gathered demographic data via multiple choice questions, and the data included gender, age, current relationship status, ethnicity, education levels, annual household income, and Canadian province/territory of residence.

To gather data on the medical reason for which participants used cannabis, participants could select one primary condition from a list of common conditions associated with medical cannabis use (Lucas et al., 2019; Lucas & Walsh, 2017; Reiman et al., 2017; Walsh et al., 2013) (Table 1). This question also included an option of clicking "other", which prompted a textual response to capture primary conditions that may not have appeared on the provided list.

The study initially assessed T/N use by inquiring if participants had ever regularly used tobacco/nicotine five or more times per day. A positive answer led to questions assessing the number of years of regular use (5 or more cigarettes/pipes/e-cig puffs per day), and typical rates of T/N per day use in the 30 days prior to initiating medical cannabis use, as well as in the 30 days prior to the survey, with the following response options: None; Less than one per day; 1 per day; 2-5 per day; 6-15 per day; 16-25 per day; 26-35 per day; More than 35 per day. The study defined reduction of use as lowering in the usage category in the "post" period, and a response of "none" in the 30 days prior to the survey was interpreted as complete cessation of use. Alcohol use was assessed in a similar manner, but with the addition of inquiring about the typical number of drinking days over a 30-day period prior to medical cannabis initiation, as well as in the 30 days prior to the survey. Once again, we interpreted no use of alcohol in the 30 days prior to the survey as complete cessation of use.

The study gathered cannabis use data via multiple choice questions and visual analogue scales (VAS). We assessed primary method of use by providing a list of common methods of use and limiting responses to a

### Table 1

Characteristics of 650 participants reporting tobacco/nicotine use pre-medical cannabis initiation.

Characteristics	n (%)
Gender, n (%)	
Unknown	32
Male	339 (54.9)
Female	278 (45.0)
Other	1 (0.1)
Age	
Unknown	94
Median (IQR)	45.0 (36.0,
	56.0)
Range	(21.0, 77.0)
Current relationship status, n (%)	
Unknown	1
Widowed/Single/Divorced/Single, never married	248 (38.2)
Married/In a domestic partnership or civil union/Single, but	401 (61.8)
cohabitating	
Ethnicity, n (%)	
Unknown	4
White	567 (87.8)
Hispanic Asian/South Asian	2 (0.3) 10 (1.5)
Black	4 (0.6)
Aboriginal/First Nation/Metis	20 (3.1)
Other	43 (6.7)
Highest degree completed, n (%)	43 (0.7)
Unknown	1
High school graduate or lower	198 (30.5)
College degree or higher	451 (69.5)
Annual household income, n (%)	
Unknown	10
Less than \$40,000	228 (35.7)
\$40,000-\$69,999	171 (26.7)
\$70,000–\$99,999	93 (14.5)
\$100,000-\$129,999	73 (11.4)
\$130,000 or more	75 (11.7)
Province/Territory, n (%)	
AB	298 (45.8)
BC	63 (9.7)
MB	33 (5.1)
NB/NS/PEI/NL	39 (6.0)
NWT/YT/NU	4 (0.6)
ON	191 (29.4)
QC	5 (0.8)
SK	17 (2.6)
Most prevalent primary conditions, n (%)	14 (0.0)
ADD/ADHD	14 (2.2)
Anxiety	75 (11.6)
Arthritis Chronic Dair	62 (9.6)
Chronic Pain	204 (31.4)
Depression	40 (6.2)
Fibromyalgia	31 (4.8)
Gastrointestinal Disorder	15 (2.3)
Headache/migraine Insomnia	19 (2.9)
Multiple Sclerosis	63 (9.7) 14 (2.2)
multiple belef0010	17 (2.2)

single answer. The study asked those who identified flower use about typical rates of use per day, ranging from "0.25 grams or less" to "4 grams or more". Participants also identified favorite flower types (indica; sativa; hybrid, 1:1 balanced CBD/THC; high CBD/low THC; or "I don't have a favorite"). Those who identified extract use (drops or capsules) answered questions specific to these products, including what type of Tilray extract formulations they used most via multiple choice options. The study assessed frequency of use for extracts by inquiring about "days per past week" use and "times per day" use (1 to 10 or more per day).

Additionally, the study team assessed level of deliberate intent to use cannabis as a T/N reduction/cessation strategy via single-answer multiple choice with the following options: I was surprised to find that my use of tobacco/nicotine changed after I began to use medical cannabis; I deliberately used medical cannabis with the goal of reducing my use of tobacco/nicotine; My MD recommended medical cannabis to reduce my use of tobacco/nicotine; My MD recommended medical cannabis and then worked with me to develop a specific tapering program to help reduce my use of tobacco/nicotine; None of the above. The survey also asked participants about their potential use of other T/N reduction strategies via multiple choice, which listed common treatment options for nicotine dependence.

The study then considered the following variables in the initial exploratory analysis and subsequent regression analyses to assess whether they were associated with changes in or cessation of T/N use following medical cannabis initiation. The study included primary patient characteristics such as gender (male vs. female) and age (>55 vs. <55), as were top three primary condition types (pain, mental health, and insomnia), daily cannabis use (yes vs. no), preferred type of cannabis (THC vs. CBD), and primary method of use (orally ingested vs. inhaled). The study included data on preferred type of cannabis and primary method of use to assess potential associations between pharmacological and/or behavioral aspects of cannabis use and changes in T/N use. Additionally, the study included T/N use characteristics potentially related to successful reduction and/or cessation such as number of T/N uses per day in the pre-period (>25 vs. <25) and years of T/N use ( $\leq 10$  vs. >10) in both the univariate and multivariate analysis, as were potential confounders such use of other tobacco reduction strategies (yes vs. no) and cessation of alcohol use in the postcannabis period (yes vs. no). While the study included in the initial analysis a single participant who reported a non-binary gender identity by clicking "other" rather than male or female, we excluded them from the multivariate analysis as it would be numerically unstable to include them.

Additionally, the study separated varied degrees of intent to quit that participants reported into two binary groups: those who reported deliberately using medical cannabis to reduce their use of T/N, and participants reporting their MD recommended the use of medical cannabis to reduce T/N or developed a tapering strategy to reduce the use of T/N into an "active intent" group, and compared them with a "no intent" group comprising those who reported either "no intent" or expressed surprise to find that they had changed their use of T/N following medical cannabis initiation.

# 2.2. Analysis

Initial analysis summarized patient characteristics such as age and gender; alcohol use; involvement with traditional tobacco cessation strategies; frequency and type of cannabis use (CBD vs. THC; oral use vs. inhalation); and degree of self-reported intent to quit using median, inter-quartile range, and percentages (Table 1). The study included only the top three primary condition types cited by patients—pain, mental health and insomnia—in subsequent analysis, as these accounted for more than 83.2% of participants (n = 541), with the rest grouped as "other".

The study team examined change in T/N usage as a categorical variable based on the T/N uses per day categories presented in the Methods section, except that we grouped into a single category using <1 per day and 1–5 (<6), and we used the mid-point of each category to determine medians. The study defined change as moving from one category to another between the pre- and postperiod, and ultimately analyzed it as a binary variable as well (decreased - yes/no; quit - yes/ no) as these were the primary outcomes of interest. The study assessed significance of the change in number of T/N uses per day in the entire cohort using the sign test, and the study used the Kruskal-Wallis test to assess the significance of variables of interest in patterns of T/N use in the pre-period, as well as median changes in use post–medical cannabis between subgroups. The study used Chi-square or Fisher's exact test to assess the statistical significance of potential variables impacting rates of T/N reduction and/or cessation.

Then the study used univariate and multivariate logistic regression

analyses to estimate the relationship between each variable and the two primary outcomes of interest: decreased T/N use (yes/no), and ceased T/N use (yes/no). Effects measures were presented as Odds Ratios (OR) with 95% Confidence Intervals. Additionally, to ensure that the exclusion of participants in the multivariate analysis due to missing data did not affect the primary outcomes of interest, the study used a sensitivity analysis using Chi-square test to compare reductions in T/N use and rates of cessation post–medical cannabis initiation between those included in the multivariate analysis and those excluded due to missing data.

Finally, to assess for any potential bias or confounders associated with the increased period between the pre- and post-medical cannabis assessments, we conducted a multivariate analysis restricted to those patients who initiated medical cannabis within the past five years (n = 233) to see if there were any obvious differences in outcomes between those with more recent medical cannabis use compared to those reporting a longer history of use.

The research team conducted all analyses in SAS 9.4 (SAS Institute, Cary NC). All statistical tests were two-sided, with significance levels of 0.05. The study used no special statistical treatment to handle missing data, other than reporting it where relevant in the appropriate tables.

# 3. Results

The survey received 3768 responses, 2102 (55.8%) of which provided a verifiable Tilray patient number, thereby identifying participants as authorized medical cannabis patients. Of these 2102 respondents, 650 (30.9%) identified as individuals with previous or current T/N use and we, therefore, included them in this analysis. Table 1 reports the demographic, geographic, and health-related characteristics of the sample. This cohort was mostly male (339, 54.9%), with a median age of 45 (IQR = 36-56) years. A substantial percentage were married or equivalent (401; 61.8%), and the sample was largely white (567; 87.8%), and well educated, with 69.5% (451) reporting a college degree or higher. In terms of geography, Alberta and Ontario were over-represented in the sample, which is consistent with Health Canada data on medical cannabis patients in Canada (Health Canada, 2019). The top five primary conditions that patients cited were chronic pain (31.4%), anxiety (11.6%), insomnia (9.7%), arthritis (9.6%), and depression (6.2%); therefore, the majority of this population used medical cannabis to treat chronic pain, mental health conditions, and insomnia.

Table 2 reports the change in T/N use and proportion who reduced or ceased use by primary patient characteristics. Most respondents had used T/N for more than 10 years (75.7%; n = 491), with 15.4% citing 6–10 years of use (n = 110), and 8.9% having used for five years or fewer (n = 58). Gender was associated with greater median amounts of T/N use per day, with men reporting 20.5 (IQR 10.5–20.5) and women reporting a median of 10.5 (IQR 10.5–20.5) (p = 0.009). Years of T/N use were also associated with greater median amounts of T/N per day (20.5 for those who used tobacco >10 years vs. 10.5 for those who used tobacco <10 years, p < 0.001), as was alcohol use in the pre-period (20.5, IQR 10.5–20.5 vs. 10.5, IQR 10.5–20.5, p = 0.018).

When comparing self-reported T/N uses per day before medical cannabis initiation, and then again in the 30 days prior to completing the survey, 49.2% (n = 320) reported decreased use, 45.7% (n = 297) reported no change, and 5.1% (n = 33) reported increased use. Of those who reported decreased use, 50% (n = 160) reported complete cessation. The mean number of T/N uses per day prior to medical cannabis initiation was 17 (SD 10.3), while the mean number of T/N uses per day in the 30 days prior to the survey was 10.8 (SD 10.7), resulting in an average decline of 6.2 T/N uses per day (SD 10.8), or approximately 37.5%. Additionally, while a significant percentage of patients reported decline or cessation of T/N use following medical cannabis initiation, only six respondents reported initiating T/N after beginning to use medical cannabis.

A number of characteristics were associated with tobacco reduction and/or cessation. Reporting higher rates of daily T/N use prior to medical cannabis initiation resulted in greater overall reductions in use: 64.1% (n = 59) of those using T/N > 25 per day reported reducing use, with a median decline of 11.6 (IQR -30.5-0.0, p < 0.001). Intent to use cannabis specifically to quit T/N use was also associated greater reductions in use, with those citing this intent seeing both a higher percentage successfully reducing use (68.6%, n = 59) compared to those with no intent (46.4%, n = 261, p < 0.001), as well as a greater median reduction of T/N use (-10, IQR -17-0.0 vs. 0.0, IQR -10.0-0.0, p < 0.001).

More years of T/N use were also associated with greater median reductions. Those who reported more than 10 years of use saw reductions of 20.5 (IQR 10.5-20.5) compared to those reporting 6-10 years of use (10.5, IQR 10.5-20.5) or 5 or fewer years of use (10.5, IQR (3.5-10.5) (p < 0.001). However, the percentage who reported ceasing use was greatest in the middle tier (36%, n = 36 for those having used 6–10 years vs. 32.8%, n = 19 for those using 5 or fewer years and 21.4%, n = 105 for those using over 10 years). Reporting a complete cessation of alcohol use in the post-period was also strongly associated with greater T/N reductions per day, and higher rates of cessation. Stopping alcohol use resulted in an associated median -10 T/N uses per day (IQR -20.5 to -3.5), compared to -2.5 (IQR -10.5-0.0) for those using alcohol who did not quit, and was also associated with a far greater percentage reporting reductions in T/N use (78.6%, n = 33 vs. 51.3%, n = 139, p = 0.001) as well as complete cessation (42.9%, *n* = 18 vs. 26.6%, *n* = 72, *p* = 0.03).

Being older was also associated with a higher quit ratio (37%, n = 57 for those 55 or over, compared to 20.1%, n = 81 for those below 55, p < 0.001), but not with greater pre-medical cannabis T/N use, reductions in daily T/N use, or greater percent of those reporting reductions. Finally, reporting participation in past or present T/N reduction treatments was negatively associated with T/N cessation, with only 10.9% (n = 12) of those who used other treatments reporting cessation post-medical cannabis compared to 27.6% (n = 147) who did not (p < 0.001).

Table 3 presents the results of the univariate and multivariate regression analyses of the primary covariates identified in earlier analyses. In examining baseline characteristics associated with changes in T/N use, univariate analysis reported that being over 55 was not associated with greater odds of reducing or ceasing use, but when adjusted for other variables such as gender, intent to quit, preferred type of cannabis, years of tobacco use, and other covariates, the study did find a strong association between being age 55 or older and ceasing T/N use altogether (AOR = 2.56, 95% CI 1.53-4.26). Greater number of T/N uses per day (>25) was positively associated with reduction in use in both univariate (OR 2.03, 95% CI 1.29-3.21) and multivariate analyses (AOR 2.83, 95% CI 1.14-3.92). Additionally, reporting 10 years of more of T/N use was associated with greater odds of cessation (AOR 2.00, 95% 1.20-3.33).

Other explanatory variables associated with tobacco reduction and/ or cessation were intent to quit T/N, involvement with other T/N treatments, and alcohol cessation. Active intent to use medical cannabis to quit resulted in significantly greater odds of reducing T/N use (OR = 2.52, 95% CI 1.55-4.09), even after adjustment for confounders (AOR = 2.79, 95% CI 1.49-5.22), but was not associated with increased odds of cessation. Involvement with traditional T/N cessation treatments (pharmacological or nicotine replacement) was negatively associated with T/N cessation (AOR 0.39, 95% CI 0.18-0.86). While this finding may appear counter-intuitive, it could suggest that previous/current (potentially unsuccessful) attempts to quit via other treatment modalities may be associated with a greater overall dependence to T/N, and therefore lower odds of cessation/reduction following medical cannabis initiation. To test this theory, we further examined the relationship between years of T/N use and participation in T/N cessation strategies,

# Table 2

Subgroup	Number o	of T/N per o	lay in the p	re-period, N	(%)	Number of day - pre*	. 1		Change in number of T/N per day*		Reduction in number of T/N per day		Complete cessation	
	<6	6–15	16–25	>25	Р	Median (IQR)	Р	Median (IQR)	Р	N (%)	Р	N (%)	Р	
Entire cohort £	84 (12.9)	229 (35.2)	245 (37.7)	92 (14.2)	-	20.5 (10.5,	-	0.0 (–10.5,	0.638	320/ 650	_	160/ 650	-	
Gender					0.035	20.5)	0.009	0.0)	0.107	(49.2)	0.223	(24.6)	0.214	
Male	42	104	136	57	0.035	20.5	0.009	-3.0	0.107	174/	0.225	89/339	0.214	
maie	(12.4)	(30.7)	(40.1)	(16.8)		(10.5,		(-10.5,		339		(26.3)		
						20.5)		0.0)		(51.3)				
Female	39	111	97	31		10.5		0.0		129/		61/278		
	(14.0)	(39.9)	(34.9)	(11.2)		(10.5,		(-10.0,		278		(21.9)		
Age					0.883	20.5)	0.589	0.0)	0.090	(46.4)	0.834		< 0.00	
<55	53	147	148	54	0.005	20.5	0.507	0.0	0.090	197/	0.004	81/402	<0.00	
	(13.2)	(36.6)	(36.8)	(13.4)		(10.5,		(-10.0,		402		(20.1)		
						20.5)		0.0)		(49.0)				
$\geq$ 55	19	52	62	21		20.5		-0.5		77/154		57/154		
	(12.3)	(33.8)	(40.3)	(13.6)		(10.5,		(-10.5,		(50.0)		(37.0)		
Primary condition					0.448	20.5)	0.524	0.0)	0.602		0.863		0.207	
Pain	33	122	123	38	0.770	20.5	0.024	0.0	0.002	154/	0.000	78/316	0.207	
	(10.4)	(38.6)	(38.9)	(12.0)		(10.5,		(-10.5,		316		(24.7)		
						20.5)		0.0)		(48.7)				
Mental health issues	31	53	58	23		10.5		0.0		76/165		36/165		
	(18.8)	(32.1)	(35.2)	(13.9)		(10.5,		(-10.0,		(46.1)		(21.8)		
Insomnia	9 (14.3)	19	26	9 (14.3)		20.5) 20.5		0.0) 0.0		31/63		23/63		
IIISOIIIIIIA	9 (14.3)	(30.2)	(41.3)	9 (14.3)		(10.5,		(-10.5,		(49.2)		(36.5)		
		(0012)	(1110)			20.5)		0.0)		(1)12)		(0010)		
GI	3 (12.5)	6	9	6 (25.0)		20.5		-3.3		13/24		6/24		
		(25.0)	(37.5)			(10.5,		(-20.3,		(54.2)		(25.0)		
	0 (11 1)	,	-	0 (1 ( 7)		25.5)		0.0)		11 (10		- (10)		
Movement Disorder	2 (11.1)	6 (33.3)	7 (38.9)	3 (16.7)		20.5 (10.5,		-7.0 (-10.5,		11/18 (61.1)		5/18 (27.8)		
		(33.3)	(36.9)			(10.3, 20.5)		(-10.3, 0.0)		(01.1)		(27.8)		
Preferred type of cannabis					0.332	ŗ	0.807	ŗ	0.463		0.409		0.887	
High THC	52	111	134	49		20.5		0.0		162/		83/346		
	(15.0)	(32.1)	(38.7)	(14.2)		(10.5,		(-10.5,		346		(24.0)		
Uish CDD	0(105)	26	20	10		20.5)		0.0)		(46.8)		20/06		
High CBD	9 (10.5)	36 (41.9)	29 (33.7)	12 (14.0)		10.5 (10.5,		0.0 (-10.0,		36/86 (41.9)		20/86 (23.3)		
		(41.))	(33.7)	(14.0)		20.5)		0.0)		(41.))		(20.0)		
Number of days per week used cannabis					0.091		0.396		0.263		0.530		0.590	
<7	21	39	35	20		10.5		0.0		54/115		26/115		
	(18.3)	(33.9)	(30.4)	(17.4)		(10.5,		(-10.0,		(47.0)		(22.6)		
7	60	100	204	60		20.5) 20.5		0.0)		257/		100/		
/	60 (11.7)	180 (35.2)	204 (39.8)	68 (13.3)		20.5 (10.5,		-1.8 (-10.5,		257/ 512		128/ 512		
	(110)	(0012)	(0).0)	(1010)		20.5)		0.0)		(50.2)		(25.0)		
Primary method of use					0.952		0.806		0.478	-	0.733	-	0.389	
Inhaled	64	168	182	69		20.5		0.0		237/		115/		
	(13.3)	(34.8)	(37.7)	(14.3)		(10.5,		(-10.5,		483		483		
Orally ingested	20	57	61	20		20.5) 20.5		0.0) -0.8		(49.1) 80/158		(23.8) 43/158		
Stany ingested	20 (12.7)	57 (36.1)	(38.6)	20 (12.7)		20.5 (10.5,		-0.8 (-10.5,		(50.6)		43/158 (27.2)		
						20.5)		0.0)						
Number of T/N uses per day in the pre-					-		-		<0.001		0.003		0.088	
period ≤5	84	0 (0.0)	0 (0.0)	0 (0.0)		3.5 (3.5,		0.0 (-3.5,		33/84		25/84		
<u>_</u> 3	84 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)		3.5 (3.5, 3.5)		0.0 (-3.5, 0.0)		33/84 (39.3)		25/84 (29.8)		
6 to 25	0 (0.0)	229	245	0 (0.0)		20.5		0.0		228/		106/		
		(48.3)	(51.7)			(10.5,		(-10.5,		474		474		
> 25	0.00.00	0.00.00	0.00	02		20.5) 20 5		0.0)		(48.1)		(22.4)		
>25	0 (0.0)	0 (0.0)	0 (0.0)	92 (100.0)		30.5 (30.5,		-11.6 (-30.5,		59/92 (64.1)		29/92 (31.5)		
						43.8)		0.0)						
Intent re. cannabis and T/N reduction None/Surprised					0.471		0.295		<0.001		<0.001		0.069	

None/Surprised

(continued on next page)

Table 2 (continued)

Subgroup	Number o	of T/N per o	day in the p	re-period, N	(%)	Number of T/N per day - pre*		Change in number of T/N per day*		Reduction in number of T/N per day		Complete cessation	
	<6	6–15	16–25	>25	Р	Median (IQR)	Р	Median (IQR)	Р	N (%)	Р	N (%)	Р
	76	197	212	77		20.5		0.0		261/		132/	
	(13.5)	(35.1)	(37.7)	(13.7)		(10.5, 20.5)		(-10.0, 0.0)		562 (46.4)		562 (23.5)	
Deliberately/MD recommended/MD developed	7 (8.1)	32 (37.2)	32 (37.2)	15 (17.4)		20.5 (10.5, 20.5)		-10.0 (-17.0, 0.0)		59/86 (68.6)		28/86 (32.6)	
Any T/N reduction treatments					0.270	20.0)	0.375	0.0)	0.173		0.510		< 0.001
No	74 (13.9)	182 (34.2)	202 (38.0)	74 (13.9)		20.5 (10.5, 20.5)		0.0 (-10.5, 0.0)		265/ 532 (49.8)		147/ 532 (27.6)	
Yes	8 (7.3)	43 (39.1)	42 (38.2)	17 (15.5)		20.5 (10.5, 20.5)		0.0 (-10.0, 0.0)		51/110 (46.4)		12/110 (10.9)	
Years of T/N use					< 0.001	,	< 0.001	,	0.260		0.056		0.003
$\leq$ 5	26 (44.8)	21 (36.2)	7 (12.1)	4 (6.9)		10.5 (3.5, 10.5)		-3.5 (-9.5, 0.0)		33/58 (56.9)		19/58 (32.8)	
6–10	23 (23.0)	42 (42.0)	25 (25.0)	10 (10.0)		10.5 (10.5, 20.5)		-7.0 (-10.5, 0.0)		58/100 (58.0)		36/100 (36.0)	
>10	35 (7.1)	165 (33.6)	213 (43.4)	78 (15.9)		20.5 (10.5, 20.5)		0.0 (-10.5, 0.0)		229/ 491 (46.6)		105/ 491 (21.4)	
Alcohol - complete cessation (among pre-users only)					0.003		0.018	-	<0.001	. ,	0.001	. ,	0.030
Yes	3 (7.1)	10 (23.8)	25 (59.5)	4 (9.5)		20.5 (10.5, 20.5)		-10.0 (-20.5, -3.5)		33/42 (78.6)		18/42 (42.9)	
No	48 (17.7)	104 (38.4)	83 (30.6)	36 (13.3)		10.5 (10.5, 20.5)		-2.5 (-10.5, 0.0)		139/ 271 (51.3)		72/271 (26.6)	

For comparison of median and percentages between subgroups, p value was based on Chi-square test, Fisher's exact test or Kruskal-Wallis test as appropriate.

finding a strong association between the two, with 19% (n = 92) of those who reported more than 10 years of T/N use also reporting experience with T/N cessation strategies, compared to 11.1% (n = 11) and 10.5% (n = 6) for those who reported 6–10 or 5 or fewer years of T/N use, respectively (see Appendix A). While the study found complete cessation of alcohol use to be associated with increased odds of reducing T/N uses per day (OR 3.48, 95% CI 1.60–7.55) and cessation of use (OR 2.07, 95% CI 1.06–4.04), the adjusted analysis did not reach a level of statistical significance.

Additionally, the study examined the following variables found them not to be associated with either T/N reduction or cessation: gender, primary condition type, THC vs. CBD preference, daily vs. non-daily cannabis use, and oral ingestion vs. inhalation. Furthermore, in noting the significant period of time between medical cannabis initiation and the 30 days prior to the survey reported by some participants (median 3 yrs., IQR 2.0-10.0), the team conducted a supplementary multivariate analysis to compare the primary outcomes in those who initiated medical cannabis within the past five years with the full study population, and the results remained largely the same (Appendix B). Finally, since missing data resulted in a smaller sample size (n = 460) in the multivariate analysis than the univariate analysis (n = 533-650), we conducted a sensitivity analysis comparing T/N reduction and cessation between those included and those excluded in the multivariate analysis, and we found no statistically significant difference in outcomes (Appendix C).

# 4. Discussion

Overall, 49.2% (n = 320) of participants who reported T/N use prior to initiating medical cannabis saw a reduction in use, and 24.6% (n =

160) reported complete cessation of use in the 30 days prior to the survey. Moreover, expressing a specific intent to use cannabis to reduce T/N use increased the rate of cessation to 32.6% (n = 28). Although this was a much smaller cohort and the observation period extended over a number of years following medical cannabis initiation, participants reporting an intent to use medical cannabis to reduce/cease T/N use actually reported a higher 30-day cessation rate than the 28.4% (n =4081) 30-day cessation rate reported in Smoking Treatment for Ontario Patients (STOP), a large-scale primary care-based smoking cessation program in Ontario that focused on a combination of counseling and pharmacotherapies such as the nicotine-replacement patch (Voci et al., 2020). Furthermore, unlike STOP, most participants in this survey did not report using NRT or other T/N cessation strategies, and those who did actually reported lower quit ratios compared to those who did not. Since studies assessing treatment outcomes for substance use disorders have consistently reported a relationship between motivation/intent to change and treatment success (Breda & Heflinger, 2007; McKay & Weiss, 2001; Shields et al., 2014), the significant association between the intention to use cannabis to reduce T/N use and greater subsequent rates of reduction in this study adds to these previous findings, and suggests a need to conduct more comprehensive assessments of intent/ motivation for cannabis use in polysubstance use research. Such investigations may be particularly relevant for those who have either had poor success with or are looking for alternatives to traditional pharmacologic or psychobehavioral treatments for T/N dependence. However, since only 13.2% (n = 86) of participants reported intentionally using cannabis as a T/N cessation strategy, we cannot draw firm conclusions, and further research should assess the association between intentional use of cannabis as a T/N reduction strategy and its impact on reduction and cessation.

### Table 3

Sociodemographic, behavioral, health, and cannabis use-related factors associated with changes in T/N usage among 650 participants.

Variable and comparison	Reduction in num	ber of T/N	uses per day	Complete cessation of T/N use				
	Univariate (n = 5	33–650)*	Multivariate (n =	460)*	Univariate (n = 533–650)*		Multivariate ( $n = 460$ )*	
	Odds ratio (95% CI)	Р	Odds ratio (95% CI)	Р	Odds ratio (95% CI)	Р	Odds ratio (95% CI)	Р
Level of intention to use cannabis to reduce T/N use								
Deliberately/MD recommended/MD developed vs.	2.52 (1.55,	< 0.001	2.79 (1.49,	0.001	1.57 (0.96,	0.071	1.54 (0.82,	0.184
None/Surprised	4.09)		5.22)		2.57)		2.89)	
Gender								
Female vs. Male	0.82 (0.60,	0.224	0.99 (0.66,	0.945	0.79 (0.54,	0.215	0.80 (0.50,	0.340
	1.13)		1.48)		1.15)		1.27)	
Age								
≥55 vs. <55	1.04 (0.72,	0.834	1.05 (0.66,	0.844	2.33 (1.55,	< 0.001	2.56 (1.53,	< 0.001
	1.51)		1.67)		3.50)		4.26)	
Primary condition type								
Pain – Y vs N	0.85 (0.59,	0.386	0.84 (0.51,	0.483	0.94 (0.62,	0.789	0.87 (0.51,	0.607
	1.23)		1.37)		1.43)		1.48)	
Mental health issues – Y vs N	0.75 (0.49,	0.177	0.66 (0.38,	0.139	0.78 (0.48,	0.332	0.69 (0.37,	0.224
	1.14)		1.14)		1.28)		1.26)	
Insomnia – Y vs N	0.87 (0.49,	0.631	0.79 (0.37,	0.540	1.87 (1.02,	0.042	1.30 (0.59,	0.515
	1.53)		1.68)		3.40)		2.86)	
Preferred type of cannabis								
THC vs. CBD	1.22 (0.76,	0.409	1.35 (0.68,	0.387	1.04 (0.60,	0.887	1.38 (0.59,	0.454
	1.97)		2.69)		1.82)		3.21)	
Used cannabis daily								
Yes vs. No	1.14 (0.76,	0.531	1.32 (0.79,	0.284	1.14 (0.71,	0.591	1.61 (0.87,	0.129
	1.71)		2.21)		1.84)		2.98)	
Primary method of use								
Orally ingested vs. Inhaled	1.06 (0.74,	0.733	1.43 (0.82,	0.205	1.20 (0.80,	0.389	1.35 (0.72,	0.350
	1.52)		2.49)		1.80)		2.52)	
Use of other T/N reduction strategies								
Yes vs. No	0.87 (0.58,	0.511	0.72 (0.41,	0.252	0.32 (0.17,	< 0.001	0.39 (0.18,	0.019
	1.31)		1.26)		0.60)		0.86)	
Number of T/N per day in the pre-cannabis period								
>25 vs. ≤25	2.03 (1.29,	0.002	2.83 (1.53,	< 0.001	1.50 (0.93,	0.098	2.11 (1.14,	0.018
-	3.21)		5.24)		2.43)		3.92)	
Years of T/N use							,	
<10 vs. >10	1.55 (1.08,	0.017	1.53 (0.96,	0.073	1.96 (1.33,	< 0.001	2.00 (1.20,	0.008
	2.23)		2.42)		2.91)		3.33)	
Complete cessation of alcohol	/		,					
Yes vs. No	3.48 (1.60,	0.002	2.04 (0.82,	0.127	2.07 (1.06,	0.032	2.36 (0.97,	0.058
	7.55)		5.08)		4.04)		5.74)	

\* Sample size in the univariate analysis varied across comparisons due to missing data. Multivariate analysis only included patients with no missing data for all variables.

Additionally, the association between alcohol and T/N use reinforces previous findings of complementarity between these substances (Room, 2004; Tauchmann et al., 2013), and could further inform cannabis-based harm reduction strategies aimed at reducing the use of both alcohol and T/N, while also providing a strong rationale for quitting alcohol use in those wishing to increase the odds of success in T/N cessation efforts. This finding may be of particular relevance to those affected by chronic physical and mental health conditions, since both are associated with an increased risk of problematic substance use, including dependence on alcohol and/or T/N (Hunt et al., 2016; Hunt et al., 2018; John & Wu, 2020; Walsh et al., 2017; Wu et al., 2018).

Our findings that the use of cannabis/cannabinoids may be associated with reductions or cessation of T/N use in those with an intent to quit are roughly consistent with research examining the use of CBD as aids to tobacco cessation (Hindocha et al., 2018; Morgan et al., 2013). However, those studies examined the use of isolated CBD, while our analyses indicate that T/N reduction/cessation was not associated with a specific preference for THC or CBD. This suggests that the mechanism proposed to underlie the effects observed in Morgan et al. (2013), such as reductions in T/N cravings associated with THC-related CB1 receptor activation and alterations of attentional processes that highlight tobacco-related cues, may contribute to these observed effects. However, more focused research should better specify the specific mechanisms that might underlie cannabis substitution for tobacco/nicotine, and how THC or CBD might play a part in these, both in isolation or when combined.

Limitations of this study include restricting the population to patients registered with Tilray as their provider of medical cannabis. Although this sample was a national one, it may have yielded data not representative of the broader population of medical cannabis patients in Canada. Furthermore, since we drew this sample from patients registered with a medical cannabis company, participants may be more likely to report positive effects related to the medical use of cannabis. Additionally, the study focused on the most prevalent forms of T/N use—cigarettes, e-cigs, and pipes—but did not inquire about the use of cigars/cigarillos, blunts (joints that include tobacco), or nonsmoked forms of T/N use such as snus or snuff, and not accounting for these may have confounded our results.

We also do not know whether results from a medical cannabis patient cohort are generalizable to a nonpatient population, as there may be characteristics inherent to a patient population—including an active intent to improve personal health outcomes—that may not be mirrored in a nonpatient cannabis use population. Despite the legalization of both medical and recreational adult cannabis use in Canada, many continue to find challenges in accessing the legal medical cannabis program (Belle-Isle et al., 2014; Capler et al., 2017; Valleriani et al., 2020), and a report from 2020 suggests that only 29.4% of Canadians who use cannabis obtain all of their cannabis products from legal sources (Rotermann, 2020). We do not know how this fact might further confound our outcomes, or the generalizability of our findings. Prospective studies examining changes in T/N use in nonmedical populations following cannabis initiation could better assess what role cannabis plays in T/N cravings, withdrawals, and reduction/cessation. Since all information regarding the use of cannabis or tobacco was selfreported and did not benefit from biological drug detection to verify substance use or nonuse, these data are vulnerable to recall bias, socially desirable responding, and other biases associated with self-report retrospective surveys. In particular, since the average duration of medical cannabis use in this population at the time of the survey was a mean/median of 7.2 years and 3 years, respectively, self-reported estimates of substance use frequency and pre-medical cannabis amounts may be particularly vulnerable to recall bias as well as other unobserved variables and confounders that may have impacted T/N use other than medical cannabis in the interim. However, a supplemental analysis comparing those who initiated medical cannabis use within the past five years with the entire cohort found largely similar results, suggesting that the time span between pre- and post-data points does not appear to have significantly impacted the primary outcomes of the study (Appendix B).

Additionally, these data may have been influenced by unobserved variables and confounders, and the lack of a control group suggests that we cannot assume causation. However, the large sample size, detailed measurement of tobacco use prior and post-medical cannabis initiation, and inclusion of potential variables such as "intent" and participation in other substance use treatment programs may address some of the limitations of previous cross-sectional surveys examining the impact of cannabis on the use of tobacco and other substances, and could inform future studies of this kind. In light of these limitations, it would be premature for us to promote cannabis-based therapies for T/N reduction/cessation, and these results should be interpreted with caution pending replication by research that employs systematic recruitment, longitudinal designs, control groups, and biological drug testing.

Finally, the current results do not speak of the desirability of substituting cannabis for tobacco or nicotine. However, as noted earlier, significant evidence suggests that cannabis is a far safer substance than T/N, with much lower rates of morbidity and mortality, and fewer negative impacts on both individuals and society (Lachenmeier & Rehm, 2015; Nutt et al., 2010). Additionally, the risks associated with cannabis smoking can be further mitigated by using noninhaled forms of ingestion, which our study suggests result in similar rates of T/N reduction and cessation. Moreover, since tobacco use is particularly prevalent among individuals with chronic pain (Ditre et al., 2011) and mental health conditions (Aubin et al., 2012; Williams & Ziedonis, 2004), which are the most common conditions for which patients report using medical cannabis (Boehnke et al., 2019; Lucas et al., 2019; Reiman et al., 2017; Walsh et al., 2013), this intersection may present an opportunity for further investigations.

Ultimately, whether cannabis represents a viable T/N harm reduction strategy is beyond the scope of the current study, but certainly remains a pertinent question for future research. In light of the considerable health costs associated with tobacco and nicotine use, particularly in populations affected by chronic health conditions, these findings add a new dimension to the growing literature examining the impact of cannabis on the use of other substances, and perhaps suggest a previously unexplored avenue by which increased access to cannabis might benefit public health by subsequently reducing tobacco and nicotine use among medical cannabis patients.

# CRediT authorship contribution statement

Philippe Lucas: Conceptualization, Methodology, Funding acquisition, Investigation, Writing - Original draft preparation. Zach Walsh: Writing – Original draft preparation, Writing – Reviewing and Editing. Peter Hendricks: Writing – Original draft preparation, Writing – Reviewing and Editing. Susan Boyd: Writing – Reviewing and Editing. M-J Milloy: Writing – Reviewing and Editing.

# Source of funding

This study was funded by Tilray, a federally authorized Canadian medical cannabis production and research company.

# **Declaration of ethics**

This survey received ethics approval from the University of Victoria Human Research Ethics Board on December 19, 2018.

# Declaration of competing interest

Philippe Lucas is Vice-President, Global Patient Research and Access for Tilray, an authorized medical cannabis production and research company, and his compensation includes stock options in Tilray. Zach Walsh is the Primary Investigator in a Tilray-sponsored randomized clinical trial of medical cannabis and PTSD; and has also received research funding from DOJA licensed producer of cannabis; he receives no financial compensation from Tilray or DOJA. Zach Walsh is also a Director of Indigenous Bloom Corporation which works to establish opportunities for Canadian Indigenous groups to engage in the cannabis industry. He has been compensated for his work with shares in Indigenous Bloom. Peter Hendricks has no competing financial interest. Susan Boyd has no competing financial interests. M-J Milloy has no competing financial interests. He is supported by the United States National Institutes of Health (U01-DA0251525), a New Investigator Award from the Canadian Institutes of Health Research (CIHR) and a Scholar Award from the Michael Smith Foundation for Health Research (MSFHR). M-JM is the Canopy Growth professor of cannabis science at the University of British Columbia (UBC), a position created using unstructured arms' length gifts to the university from Canopy Growth Corporation, a licensed producer of cannabis, and the Government of British Columbia's Ministry of Mental Health and Addictions. UBC has also received unstructured funding from NG Biomed, Ltd., an applicant to the Canadian federal government for a license to produce cannabis, to support M-JM.

### Acknowledgements

The authors would like to thank the many patients who shared their thoughts and experiences through this survey, and Joel Singer and Terry Lee from the Centre for Health Evaluation Outcome Sciences (UBC) for assisting with the analysis of this data.

### Appendix A

### Appendix A

Association between years of T/N use and participation in T/N cessation strategies.

	Years of tobacco	use		P*
	≤5	6–10	>10	
Any substance use reduction strategies, n (%)				0.028

(continued on next page)

# Appendix A (continued)

	Years of tobacco us		P*	
	$\leq 5$	6–10	>10	
No	51 (89.5)	88 (88.9)	393 (81.0)	
Yes	6 (10.5)	11 (11.1)	92 (19.0)	
Pharmacological treatment, n (%)				0.16
No	55 (96.5)	97 (98.0)	456 (94.0)	
Yes	2 (3.5)	2 (2.0)	29 (6.0)	
Nicotine replacement therapy, n (%)				0.010
No	55 (96.5)	91 (91.9)	419 (86.4)	
Yes	2 (3.5)	8 (8.1)	66 (13.6)	

<sup>b</sup> *p* value based on Cochran-Armitage Trend Test.

# Appendix B

Multivariate analysis for change in T/N usage among those who initiated medical cannabis within the past five years.

Variable and comparison	Reduction in number of T	/N uses per day	Complete cessation of T/N use			
	Multivariate (n = 233)*		Multivariate ( $n = 233$ )*			
	Odds ratio (95% CI)	Р	Odds ratio (95% CI)	Р		
Level of intention to use cannabis to reduce T/N use						
Deliberately/MD recommended/MD developed vs. None/Surprised	1.79 (0.77, 4.17)	0.178	1.74 (0.70, 4.31)	0.233		
Gender						
Female vs. Male	0.90 (0.54, 1.50)	0.690	0.78 (0.43, 1.44)	0.430		
Age						
≥55 vs. <55	0.84 (0.46, 1.53)	0.570	1.88 (0.97, 3.67)	0.062		
Primary condition						
Pain – Y vs N	0.49 (0.22, 1.11)	0.086	0.68 (0.34, 1.35)	0.265		
Mental health issues – Y vs N	0.48 (0.20, 1.14)	0.094	0.44 (0.20, 0.99)	0.046		
Insomnia – Y vs N	0.27 (0.09, 0.86)	0.026	0.99 (0.34, 2.86)	0.978		
Preferred type of cannabis						
THC vs. CBD	1.41 (0.59, 3.34)	0.435	1.58 (0.54, 4.58)	0.404		
Used cannabis daily						
Yes vs. No	1.47 (0.81, 2.68)	0.203	1.51 (0.74, 3.08)	0.257		
Primary method of use						
Orally ingested vs. Inhaled	1.55 (0.76, 3.18)	0.231	1.93 (0.85, 4.40)	0.119		
Use of other T/N reduction strategies:						
Yes vs. No	0.80 (0.39, 1.63)	0.539	0.39 (0.14, 1.07)	0.068		
Number of T/N per day in the pre-cannabis period						
>25 vs. ≤25	2.65 (1.17, 6.03)	0.020	1.91 (0.82, 4.48)	0.136		
Years of T/N use						
≤10 vs. >10	1.60 (0.91, 2.82)	0.099	2.16 (1.13, 4.13)	0.019		
Complete cessation of alcohol						
Yes vs. No	1.69 (0.51, 5.60)	0.394	2.53 (0.73, 8.75)	0.142		

\* Sample size in the univariate analysis varied across comparisons due to missing data. Multivariate analysis only included patients with no missing data for all variables.

### Appendix C

Comparison of primary outcomes between those included and those excluded due to missing data in the multivariate analysis.

Outcome	Included	Excluded	P*
Tobacco analysis			
Reduction in number of T/N uses per day	229/460 (49.8)	91/190 (47.9)	0.661
Complete cessation of T/N use	116/460 (25.2)	44/190 (23.2)	0.579

\* p value based on Chi-square test.

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