Contents lists available at ScienceDirect



# International Journal of Drug Policy



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

**Research Paper** 

# International differences in patterns of cannabis use among adult cigarette smokers: Findings from the 2018 ITC Four Country Smoking and Vaping Survey



Shannon Gravely<sup>a,\*</sup>, Pete Driezen<sup>a,f</sup>, Danielle M. Smith<sup>b</sup>, Ron Borland<sup>c,d</sup>, Eric N. Lindblom<sup>e</sup>, David Hammond<sup>f</sup>, Ann McNeill<sup>g,h</sup>, Andrew Hyland<sup>b</sup>, K. Michael Cummings<sup>i,j</sup>, Gary Chan<sup>k</sup>, Mary E. Thompson<sup>l</sup>, Christian Boudreau<sup>l</sup>, Nadia Martin<sup>a</sup>, Janine Ouimet<sup>a</sup>, Ruth Loewen<sup>a</sup>, Anne C.K. Quah<sup>a</sup>, Maciej L. Goniewicz<sup>b</sup>, James F. Thrasher<sup>m,n</sup>, Geoffrey T. Fong<sup>a,f,o</sup>

- <sup>n</sup> Tobacco Research Department, Center for Population Health Research, National Institute of Public Health, Cuernavaca, Mexico
- ° Ontario Institute for Cancer Research, Toronto, Canada

#### ARTICLE INFO

Keywords: Tobacco cigarettes Cannabis Co-use Policy Regulation Harm Perceptions

#### ABSTRACT

*Background:* Although evidence shows that co-use of cigarettes and cannabis is common, there is little research examining if co-use patterns vary depending on the regulatory environment for cannabis. This study examined patterns of co-use and perceptions of relative harm among cigarette smokers in four countries with different histories, and at different stages of cannabis legalization.

*Methods*: Data are from the 2018 International Tobacco Control 4CV Survey and included 10035 adult cigarette smokers from Canada, United States (US), Australia, and England. At the time of the survey, Canada and the US had relatively more permissive cannabis regulations compared to Australia and England.

*Results*: Among this sample of 10035 cigarette smokers, Canada had the highest rate of cannabis co-use in the last 12 months (36.3%), followed by the US (29.1%), England (21.6%), and Australia (21.4%). Among past 12 month co-users (n = 3134), the US (40.2%) and Canada (35.2%) had the highest rates of daily cannabis use, followed by smokers in England (26.3%) and Australia (21.7%); Australian co-users had the highest rate of infrequent (<monthly) cannabis use. The highest proportion of co-users who smoked daily and used cannabis daily was in the US (34.8%), followed by Canada (30.6%), England (25.8%), and Australia (22.7%). More co-users in the US (78.3%) and Canada (73.6%) perceived smoked cannabis to be less harmful than cigarettes than in Australia (65.5%) and England (60.8%). The majority of co-users who used cannabis in the last 30 days had smoked it (92.3%), with those in England more likely to smoke cannabis (95.7%) compared to Canada (88.6%); there were no other differences between countries (US: 92.0%, Australia: 93.0%). Co-users in Canada (38.5%) and the US (22.3%).

Conclusion: Patterns of tobacco and cannabis co-use differed between countries. Smokers in Canada and the US

\* Corresponding author.

E-mail address: shannon.gravely@uwaterloo.ca (S. Gravely).

https://doi.org/10.1016/j.drugpo.2020.102754

0955-3959/ © 2020 The Author(s). Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).

<sup>&</sup>lt;sup>a</sup> Department of Psychology, University of Waterloo, Waterloo, Canada

<sup>&</sup>lt;sup>b</sup> Department of Health Behavior, Roswell Park Comprehensive Cancer Center, Buffalo, United States

<sup>&</sup>lt;sup>c</sup> School of Psychological Sciences, University of Melbourne, Melbourne, VIC, Australia

<sup>&</sup>lt;sup>d</sup> Cancer Council Victoria, Melbourne, VIC, Australia

<sup>&</sup>lt;sup>e</sup> O'Neill Institute for National & Global Health Law, Georgetown University Law Center, Washington, DC United States

<sup>&</sup>lt;sup>f</sup> School of Public Health and Health Systems, University of Waterloo, Waterloo, Canada

<sup>&</sup>lt;sup>8</sup> King's College London, Addictions Department, Institute of Psychiatry, Psychology & Neuroscience, London, United Kingdom

<sup>&</sup>lt;sup>h</sup> UK Centre for Tobacco & Alcohol Studies, Nottingham, United Kingdom

<sup>&</sup>lt;sup>i</sup> Department of Psychiatry & Behavioral Sciences, Medical University of South Carolina, Charleston, United States

<sup>&</sup>lt;sup>j</sup> Hollings Cancer Center, Medical University of South Carolina, Charleston, South Carolina, United States

<sup>&</sup>lt;sup>k</sup> Centre for Youth Substance Abuse Research, The University of Queensland, Brisbane, QLD, Australia

<sup>&</sup>lt;sup>1</sup>Department of Statistics and Actuarial Science, University of Waterloo, Waterloo, Canada

<sup>&</sup>lt;sup>m</sup> Department of Health Promotion, Education & Behavior, Arnold School of Public Health, University of South Carolina, Columbia, United States

had higher rates of co-use, daily cannabis use, dual-daily use of both cannabis and cigarettes, and were more likely to perceive smoked cannabis as less harmful than cigarettes compared to England and Australia. Further attention as to how varying cannabis regulations may impact co-use patterns is warranted.

# Introduction

Cannabis (marijuana) is a psychoactive drug used for medical and/ or recreational purposes, and is the most widely used drug worldwide (UN, 2018). An estimated 3.8% of the global population (188 million people worldwide aged 15–64) used cannabis in 2017 (UN, 2019). The annual prevalence of cannabis use was highest in North America (13.8%), Oceania (10.9%), and West and Central Africa (10.0%).

Cannabis use is associated with potential short- and long-term risks, including functional impairment of normal daily activities, and adverse physiological and mental effects (CSUCH, 2018; NIDA, 2019; NASEM, 2017; Watson, Benson & Joy, 2000). While cannabis is not as addictive as other substances, such as tobacco (nicotine), heroin, or cocaine (Anthony, Warner & Kessler, 1994), continued frequent and heavy cannabis use may lead to cannabis use disorder (CUD) (Miller, Oberbarnscheidt & Gold, 2017b; Patel & Marwaha, 2020; Zehra et al., 2018). Global estimates suggest that the number of cannabis users has increased in many countries over the last decade (United Nations, 2018), as has treatment for CUD (WHO, 2016).

Country-specific data show the prevalence of cannabis use is increasing among adults in high income nations, including Canada and the US, where cannabis laws have been changing during the last several years (Mauro et al., 2018; Statistics Canada, 2018, 2019a; SAMHSA, 2018; UN, 2018).

Cannabis use is more frequently reported by cigarette smokers compared to former and never smokers (Agrawal, Budney & Lynskey, 2012; Fix et al., 2019; Goodwin et al., 2018; Lemyre, Poliakova & Belanger, 2019; Smith et al., 2019; Statistics Canada, 2017). Cigarette smokers who also use cannabis (co-users) constitute a unique subset of smokers who are at even greater risk for serious health problems (Agrawal et al., 2012; Miller, Rosenman & Cowan, 2017a; Rabin & George, 2015). For example, cigarette smoking has been found to mediate the relationship between cannabis use and dependence, suggesting that tobacco co-use could be a partial driver of cannabis dependence (Hindocha et al., 2015). Moreover, co-use of cannabis and cigarettes is associated with additive risks of toxicant exposure, poorer physical and mental functioning, more intensive tobacco and cannabis use and dependence, and high rates of relapse among those who

#### Table 1

Summary and Depiction of Federal (National) Medical and Recreational Cannabis Laws for the Growth, Distribution, Sale, and Possession at the Time of the ITC 4CV2 (2018) Survey.

	Medical Cannabis	Recreational Cannabis
	e Cannabis Regulatory Frameworks	
United States	• Cannabis is strictly prohibited by federal law but the federal government has followed a policy of tolerance regarding state-legalized cannabis.• Medical cannabis was first legalized in California in 1996, and then in 1998 in Colorado and Washington. Several other states proceeded with medical legalization in subsequent years (see timeline <sup>a</sup> ).• Although the specifics of the laws vary considerably, at the time of the 2018 survey, cannabis was legal for medical use in 28 states and the District of Columbia.• The Federal Drug Administration (FDA) has formally approved prescription drugs that contain synthetic THC and CBD, and in June 2018, containing cannabis-derived CBD for the treatment of two severe pediatric seizure disorders (Epidiolex).	• Illegal at the federal level to grow, distribute, sell, or possess.• Colorado and Washington became the first two states to legalize recreational cannabis in 2012. By 2018, 8 states and the District of Columbia had legalized cannabis for recreational use.• Some other US states have decriminalized recreational cannabis for personal use.
Canada	• July 2001: Medicinal use of cannabis was legalized nationwide under conditions outlined in the Marihuana Medical Access Regulations Act (MMAR <sup>b</sup> ). The MMAR allowed patients to possess dried flower/bud with a government issued license, signed off by a physician.• 2014: MMAR later superseded by the Marihuana for Medical Purposes Regulations (MMPR) <sup>c</sup> issued by Health Medical cannabis could be prescribed by a physician and a government license was no longer required, and allowed legal medical cannabis production by authorized licensed producers.• 2014–2015: Amendments were made to the MMPR which granted wider access to medical cannabis (e.g., health care providers had greater flexibility over diagnoses for which they were permitted to prescribe cannabis, a broader scope of cannabis products became legally available).• Registered patients allowed to grow cannabis in their residence.	• Illegal at the federal level to grow, distribute, sell, or possess.• Although recreational cannabis was not federally legal at the time of this survey, Canada was in a major transition period as a law to legalize recreational use (Cannabis Act, Bill C-45) was passed in June 2018. The federal Cannabis Act came into effect in October 2018.
Less Permissive Australia	<ul> <li>Cannabis Regulatory Frameworks</li> <li>February 2016: Australia's parliament passed the Narcotics Drugs Amendment</li> </ul>	• Illegal at the federal level to grow, distribute, sell, or possess.• Decriminalized
Ausudiid	Bill 2016, which set the framework for medicinal cannabis cultivation. Medical marijuana became legal on a federal level in November 2016. <sup>4</sup> Although cannabis use has been legal in all states for medicinal use (with a medical prescription) and for scientific purposes since February 2016, access to medical cannabis has been limited.• Qualifying conditions and other details vary by state.	for possession of small quantity in the Northern Territory, South Australia, and the Australian Capital Territory, but remains a criminal offence in the other states. <sup>e</sup>
England <sup>f</sup>	• Illegal at the federal level to grow, distribute, sell, or possess.• Note: Cannabis became legal for specific medical conditions in November 2018 (after survey collection). Prescriptions must be provided by a specialist physician.	• Illegal at the federal level to grow, distribute, sell, or possess.• It is a Class B drug under the Misuse of Drugs Act 1971, with penalties for unlicensed dealing, production and trafficking.• Cannabidiol (CBD) oil is legal for use and sale (with a maximum of 0.2% THC mg/ml).

 $^{a}\ https://www.fool.com/investing/timeline-for-marijuana-legalization-in-the-united.aspx$ 

<sup>b</sup> https://laws-lois.justice.gc.ca/eng/regulations/sor-2001-227/index.html

<sup>&</sup>lt;sup>c</sup> https://apollocannabis.ca/mmar-vs-mmpr-canadian-cannabis-regulation-simplified/

<sup>&</sup>lt;sup>d</sup> https://www.marijuanadoctors.com/international-patients/australia/.

<sup>&</sup>lt;sup>e</sup> https://www.loc.gov/law/help/decriminalization-of-narcotics/australia.php

 $<sup>^{\</sup>rm f}\ {\rm https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/119174/acmd-cannabis-report-2008.pdf$ 

attempt to quit either product (Agrawal et al., 2012; Meier et al., 2019; Peters, Budney & Carroll, 2012; Rabin et al., 2016; Smith et al., 2019; Tucker et al., 2019; Weinberger et al., 2018; Weinberger et al., 2019; Becker, Schaub, Gmel & Huag, 2015). Evidence suggests that tobacco and cannabis co-users have unique characteristics and experiences compared to single product users (Seaman, Howard, Green, Wang & Fryer, 2019), and there appears to be distinct processes that link cannabis and tobacco co-use, beyond what is observed between other drugs; likely owing to shared environmental and social factors, as well as both synergistic and/or attenuating physiological effects (Agrawal et al., 2012; Berg et al., 2018; Rabin et al., 2016; Van der Koov, Pomahacova & Verpoorte, 2009).

Cannabis is prohibited in most of the world's countries, therefore prevalence of use differs depending on the country and region as laws surrounding the sale and use of cannabis vary greatly. For example, some countries and regions have harsh penalties for the sale and use of cannabis (e.g., Saudi Arabia, Singapore, Indonesia, and United Arab Emirates), while others have decriminalized it (e.g., The Netherlands, and many South American and European countries). In recent years, an increasing number of countries and sub-jurisdictions have legalized cannabis for medical purposes, and some have legalized cannabis for recreational purposes. As of 2019, approximately 20 countries had passed laws permitting cannabis for medical use; however, policies are diverse, ranging from use allowed for only a limited number of qualifying conditions (e.g., Australia and the UK), to more expansive legal access (e.g., Canada and the US). Far fewer countries/jurisdictions have legalized recreational cannabis. As of December 2019, recreational cannabis had been legalized in four countries (Canada, Georgia, South Africa, and Uruguay) and several subnational jurisdictions (11 US states and the District of Columbia (DC), and the Australian Capital Territory).

Because of the higher propensity for smokers to use cannabis, the greater health risks among co-users, and the tendency toward increased cannabis use after legalization, it is important to consider how patterns of co-use may differ between countries with varying cannabis regulations. At the time of data collection for this study (February-July 2018), medical cannabis was not legal at the national level in England or the US. However in the US, cannabis was legal for medical use in 28 states and the District of Columbia, although the specifics of the laws varied considerably. Medical cannabis was legal and widely available in Canada. It was also legal in Australia, but narrow qualifying medical conditions meant that very few people were able to access it. In mid-2018, recreational cannabis was nationally illegal in all four countries. However, in the US, 8 states and DC had legalized cannabis for recreational use; Canada was in the process of implementing the Cannabis Act to legalize recreational cannabis (the law passed in June 2018, but not implemented until October 2018); and some Australian states had decriminalized possession in small quantities (policies are summarized in Table 1).

The main aim of this descriptive study was to examine cannabis use by cigarette smokers in countries with relatively more permissive cannabis policies (Canada and the US) versus (vs.) less permissive policies (Australia and England) based on laws that were in place at the time of the survey. For example, laws were more permissive in North America with regard to wide medical access in Canada and the US, as well as recreational cannabis legalization in some US states. With regard to tobacco smoking, all four countries had similar cigarette smoking rates (CDC, 2018; Greenhalgh, Bayly & Winstanley, 2019; ONS, 2018; Statistics Canada, 2019b). National tobacco control policies (e.g., excise taxes, health warnings, and marketing) were stronger in Canada, Australia, and England compared to the US, where tobacco control laws varied widely between states. This study also examined cross-country differences among co-users: frequency of cannabis use and of cigarette smoking, relative harm perceptions of smoked cannabis compared to cigarettes, and frequency of smoking cannabis mixed with tobacco among those who reported smoking cannabis.

#### Methods

#### Study design, sample and procedure

The ITC Four Country and Vaping Survey (ITC 4CV) is a cohort study that consists of four parallel online surveys conducted in Canada, US, England, and Australia. In addition to respondents retained from the Four Country Survey<sup>1</sup> (the predecessor of the ITC 4CV Survey), adults ( $\geq$ 18 years) were recruited by commercial panel firms in each country as cigarette smokers, former smokers, and/or at-least-weekly e-cigarette users. The sample in each country was designed to be as representative as possible of cigarette smokers (e.g., by age, sex and region). All data were collected online, and respondents were remunerated.

The current cross-sectional analysis used data from the 2018 (Wave 2) ITC 4CV Survey (conducted February to July 2018) which included 10284 adults (aged 18+) who smoked cigarettes at least monthly. Smokers were eligible if they completed the question that asked about marijuana/cannabis use in the last 12 months (n = 10035). The respondents analyzed in this study were either re-contact/cohort respondents (recruited in 2016 at Wave 1, n = 4107) or replenishment respondents who were newly recruited participants (n = 5928) to compensate for attrition and to maintain the total sample size.

The analyses examining cross-country differences among co-users included only those who reported "yes" to using cannabis in the last 12 months (n = 3134). Finally, those who reported their methods of cannabis use in the last 30 days (n = 2090) were included in the analysis of methods of consumption (smoked cannabis vs. used it in some other way). A study flow diagram is presented in **Supplemental Figure 1**. Further descriptions of the methods used in each country are presented in the ITC Wave 2 (2018) technical report (4CV2 2018) Technical Report) and in Thompson et al. (Thompson et al., 2018).

# Data weighting

Weighting survey data is one of the major components in survey sampling, and involves attaching a weight to each unit of the selected sample in order to obtain estimates of population parameters of interest. This process essentially incorporates a method of re-balancing the data, in order to more accurately reflect the population. This is especially important for complex survey designs (Lavallée & Beaumont, 2015).

In the current study, cross-sectional weights were computed for all respondents. A raking algorithm was used to calibrate the weights on smoking status, geographic region, and demographic measures (e.g., sex, age, ethnicity, and education). This calibration was done using benchmarks from national surveys from each of the respective countries. Finally, the weights were rescaled to sum to the sample size for each country to allow for cross-country comparisons.

#### Measures

All country-specific surveys are available at the ITC Project website (ITC Surveys). The following measures were used in the current study:

Sociodemographic variables: Sex (male or female), age group (18-24, 25-39, 40-54, or 55+ years), educational attainment (low, moderate, high), and annual household family income (low, moderate, high). Income and education categories are presented in **Supplemental Table 1**.

Smoking variables: Respondents were classified as a *daily smoker* or a *non-daily smoker* (smoked cigarettes weekly or monthly) at the time of completing the survey. The Heaviness of Smoking Index (HSI) was

<sup>&</sup>lt;sup>1</sup> https://itcproject.s3.amazonaws.com/uploads/documents/4c-w28-tech-report-sept.pdf

Respondent Characteristics Across Counties in 2018 (unweighted).

Chacteristics, n (%)		Australia $n = 1223$	Canadan = 2772	England $n = 4047$	$\mathrm{US}n=1993$	Overall N = 10,035
Wave (year) of study recruitment	Wave 1 (2016)	661 (54.1)	1328 (47.9)	1311 (32.4)	807 (40.5)	4107 (40.9)
	Wave 2 (2018)	562 (46.0)	1444 (52.1)	2736 (67.6)	1186 (59.5)	5928 (59.1)
Sex						
	Male	625 (51.1)	1320 (47.6)	2048 (50.6)	933 (46.8)	4926 (49.1)
	Female	598 (48.9)	1452 (52.4)	1999 (49.4)	1060 (53.2)	5109 (50.9)
Age, mean (SD)	Mean (SD)	52.5 (12.6)	41.3 (15.8)	41.2 (16.4)	45.1 (17.9)	43.4 (16.5)
Age group						
	18–24	19 (1.6)	646 (23.3)	1035 (25.6)	508 (25.5)	2208 (22.0)
	25–39	191 (15.6)	678 (24.5)	915 (22.6)	314 (15.8)	2098 (20.9)
	40–54	424 (34.7)	805 (29.0)	1037 (25.6)	394 (19.8)	2660 (26.5)
	55+	589 (48.2)	643 (23.2)	1060 (26.2)	777 (39.0)	3069 (30.6)
Education level						
	Low	429 (35.1)	823 (29.7)	1191 (29.4)	750 (37.6)	3193 (31.8)
	Medium	492 (40.2)	1205 (43.5)	1621 (40.1)	850 (42.7)	4168 (41.5)
	High	296 (24.2)	732 (26.4)	1170 (28.9)	392 (19.7)	2590 (25.8)
	Not reported	6 (0.5)	12 (0.4)	65 (1.6)	1 (0.1)	84 (0.8)
Income	-					
	Low	459 (37.5)	1096 (39.5)	963 (23.8)	744 (37.3)	3262 (32.5)
	Medium	266 (21.8)	701 (25.3)	1808 (44.7)	603 (30.3)	3378 (33.7)
	High	414 (33.9)	786 (28.4)	1020 (25.2)	635 (31.9)	2855 (28.5)
	Not reported	84 (6.9)	189 (6.8)	256 (6.3)	11 (0.6)	540 (5.4)
Cigarette Smoking status	-					
· · ·	Daily	1152 (94.2)	2149 (77.5)	3398 (84.0)	1624 (81.5)	8323 (82.9)
	Non-daily	71 (5.8)	623 (22.5)	649 (16.0)	369 (18.5)	1712 (17.1)
HSI†	Low	280 (24.3)	1069 (43.0)	1376 (37.5)	698 (39.0)	3423 (37.6)
	Medium	757 (65.6)	1268 (51.0)	2101 (57.3)	996 (55.6)	5122 (56.3)
	High	117 (10.1)	149 (6.0)	192 (5.2)	97 (5.4)	555 (6.1)
Used Cannabis in the last 12 months	0					
	Yes	215 (17.6)	1157 (41.7)	1070 (26.4)	692 (34.7)	3134 (31.2)
	Not at all	1008 (82.4)	1615 (58.3)	2977 (73.6)	1301 (65.3)	6901 (68.8)
Daily cigarette smokers and daily cannabis use	Yes (overall)	26 (2.1)	324 (11.7)	215 (5.3)	223 (11.2)	818 (8.2)
	Yes* (conditional)	26 (12.1)	324 (28.0)	215 (20.1)	223 (32.3)	818 (26.1)

HSI: Heaviness of smoking index; SD: Standard deviation; US: United States.

\* denominator is among those who have used cannabis in the last 12-months (n = 3134).

<sup>†</sup> Only 9100 respondents has complete data for the HSI measure.

included as a measure of nicotine dependence.<sup>2</sup> Smokers were categorized as 'low', 'medium' or 'high'. Because there were relatively few smokers in the high category, medium and high categories were combined for the country comparison analysis (low vs. medium/high).

Country of residence: Country of residence was used as a proxy measure for the cannabis regulatory environment. Canada and the US were considered to be relatively more permissive than Australia and England (see Table 1). The division between relatively 'more' and 'less' permissive cannabis policies was determined by the authors, and was based on the diversity of laws in Canada and the US compared to England and Australia. For example, supply and ease of access to cannabis were considered to be greater in the US and Canada. We did not consider the size of the illicit market in each country because it is too complex to conceptualize and compare illicit activity and the supply of cannabis for personal consumption.

Cannabis Use and Frequency: Cannabis use and frequency were determined with the following question: "In the last 12 months, how often, if at all, have you used marijuana/ cannabis in any way?" Response

options were: 'Not at all', 'less than once a month', 'at least once a month, but less than weekly', 'at least once a week, but less than daily', or 'daily'. The responses were categorized into 'yes, used cannabis in the last 12 months' vs. 'no, did not use cannabis in the last 12 months'. Those who responded 'yes' were classified as co-users. Those who used cannabis less than monthly were considered *infrequent users*. Respondents who reported 'don't know' (n = 141) or refused to provide a response (n = 108) were excluded from all analyses.

Daily use of cannabis and daily cigarette smoking: Using both cigarette smoking and cannabis use frequency variables, a variable was created to compare country differences between dual-daily cannabis users and cigarette smokers vs. co-users who did not use both products daily.

Perceptions of harmfulness: Compared to smoking cigarettes, how harmful do you think smoking marijuana/cannabis is? Here we mean only SMOKING marijuana/ cannabis, not other methods of consumption (coded as: 'less harmful', 'equally harmful', 'more harmful' and 'I don't know').

Smoked cannabis (with or without tobacco) vs. another method of consumption: Respondents who reported using cannabis in the last 30 days were asked: *Thinking just about the last 30 days... How did you use the marijuana/cannabis*? Six methods were listed, and respondents were categorized into two variables for anlayses: (i) Smoked cannabis (with or without tobacco) vs. some other method of consumption (vaped it in liquid or plant form, edibles, dabbed concentrates); and (ii) among co-users who reported smoking cannabis: smoked it with tobacco vs. smoked it without tobacco.

<sup>&</sup>lt;sup>2</sup> The HIS was developed as a test to measure nicotine dependence by using two questions from the Fagerström Tolerance Questionnaire and the Fagerström Test for Nicotine Dependence: time to first smoking in the morning and number of cigarettes per day. It uses a six-point scale calculated from the number of cigarettes smoked per day (1-10, 11-20, 21-30, 31 + ) and the time to first cigarette after waking (less than/equal to 5, 6-30, 31-60, and 61 + minutes). Nicotine dependence is then categorized into a three-category variable: low (0-1), medium (2-4), and high (5-6) (Heatherton, Kozlowski, Frecker, Rickert, & Robinson, 1989).

Model 1: Cannabis Use in the Last 12-months Among Cigarette Smokers in 2018 ( $n = 10,035^*$ ).

Variable		% Yes(Weighted)	P-value	OR	95% CI	
					Lower CI	Upper CI
Used cannabis in the last 12 months						
	Yes $(n = 3134)$	27.1				
Country			< 0.0001			
	Australia	21.4	< 0.0001	0.48	0.38	0.61
	England	21.6	< 0.0001	0.48	0.42	0.56
	United States	29.1	< 0.001	0.72	0.61	0.86
	Canada	36.3	Reference			
Gender			< 0.0001			
	Female	21.9		0.60	0.52	0.68
	Male	32.0	Reference			
Age			< 0.0001			
•	18–24	56.9	< 0.0001	8.85	7.30	10.72
	25–39	37.7	< 0.0001	4.06	3.40	4.86
	40–54	23.6	< 0.0001	2.07	1.75	2.44
	55 and up	13.0	Reference			
Income			< 0.0001			
	Low	33.1	< 0.0001	1.58	1.32	1.88
	Moderate	25.2	0.43	1.07	0.90	1.28
	Not reported	22.7	0.67	0.94	0.69	1.28
	High	23.9	Reference			
Education			0.22			
	Low	25.7	0.82	0.81	1.18	0.98
	Moderate	28.4	0.16	0.95	1.33	1.13
	Not reported	31.8	0.46	0.63	2.77	1.32
	High	26.1	Reference			
Smoking Status						
-	Daily	26.6	0.03	0.82	0.69	0.98
	Non-daily	30.6	Reference			

Overall Wald Test: 53.4, p < 0.0001; CI: Confidence Interval.

\* Note: Of the original 10,284 current smokers in the 2018 survey, 249 smokers did not answer the question about whether they had used cannabis in the last 12 months, and therefore were excluded.

#### Statistical analysis

Table 2 presents the unweighted descriptive statistics of the respondents by country.

Cannabis use in the last 12 months (outcome: yes vs. no) was estimated using a weighted multivariable logistic regression model (Model 1: Table 3). Country was the main independent variable; covariates were sex, age, income, education, and smoking frequency (daily vs. non-daily).

Regression models (Models 2–6, Table 4) were restricted to co-users only (n = 3134), and tested country differences for five outcomes: (1) daily vs. non-daily cigarette smoking; (2) heaviness of smoking/nicotine dependence (low vs. medium/high); (3) daily vs. non-daily cannabis use; (4) dual-daily co-use of both tobacco and cannabis vs. non dual-daily users; and (5) perceived harmfulness of smoked cannabis compared to cigarettes (less harmful, vs. equally harmful vs. more harmful vs. don't know). Covariates were: sex, age, income, education, and smoking frequency where applicable.

Two final regression models examined: (1) methods used to consume cannabis in the last 30 days (smoked it vs. used it in some other way, Model 7, Table 4), and (2) addition (mixing) of tobacco to smoked cannabis (yes vs. no) among those who reported smoking cannabis (Model 8, Table 4). The same covariates used in the other models were also included in these analyses.

Post-hoc comparisons were used to examine outcome differences between countries when the main omnibus test was significant (p < 0.05) (Table 5). All data were weighted unless otherwise specified.

All confidence intervals were computed at the 95% confidence level. Analyses were conducted using SAS version 9.4.

#### Results

Cross-country differences in cannabis use among current cigarette smokers

Among the 10035 smokers included in the main analysis (Model 1), the regression model showed that there were significant differences between countries in rates of cannabis use in the last 12 months (p < 0.0001). Specifically, smokers in Australia (21.4%) and England (21.6%) had similar rates of cannabis use in the last 12 months, which were both significantly lower than Canada (36.3%) and the US (29.1%), with Canadian rates also significantly higher than the US (p < 0.001).

Overall, cannabis use was greater among smokers who were male (p < 0.0001), younger (p < 0.0001), and had lower income (p < 0.0001). A slightly higher proportion of non-daily smokers reported using cannabis in the last 12 months (30.6%) than daily smokers (26.6%, p = 0.03). There were no significant interactions between country and any of the covariates included in the regression model (data not shown). Table 3 presents the overall regression model. Table 5 presents the post-hoc comparisons between countries (odds ratios and 95% confidence intervals).

# Cross-country differences among co-users

The next set of regression analyses (Models 2-6) included the 3134

Cross-country comparisons among smokers who reported co-using cannabis in the last 12 months (n = 3134).

Outcome*Weighted% (95% CI)	Canada <i>n</i> = 1157	United Statesn = 692	Australian = 215	England $n = 1070$	Cross–country DifferencesP-value\$
Model 2: Frequency of cigarette smoking					0.001
Daily smokers ( $n = 2387$ )	79.9 (76.8–82.8)	83.3 (78.6-87.1)	94.7 (89.0–97.5)	85.9 (82.3-88.8)	
Non-daily smokers ( $n = 747$ )	20.1 (17.2-23.2)	16.7 (12.9–21.4)	5.3 (2.5-11.0)	14.1 (11.2–17.7)	
Model 3: Heaviness of Smoking Index (HSI)					N/A
Low $(n = 1250)$	42.7 (38.6-46.8)	43.9 (37.5–50.3)	26.9 (18.1-35.8)	41.6 (36.4-46.8)	
Medium $(n = 1350)$	51.6 (47.5–55.7)	51.0 (44.7–57.3)	65.1 (55.9–74.3)	54.5 (49.3–59.6)	
High $(n = 136)$	5.8 (3.9–7.7)	5.1 (2.6-7.7)	8.0 (2.5-13.4)	3.9 (1.9–5.9)	
Low (n = 1250)	42.4 (38.4–46.5)	43.6 (37.4–50.0)	26.7 (18.9-36.3)	41.3 (36.2-46.5)	0.03
Medium/high (n = 1486)	57.6 (53.5–61.6)	56.4 (50.0-62.6)	73.3 (63.7–81.1)	58.7 (53.5–63.8)	
Model 4: Frequency of cannabis use (Model 4)					0.003
Daily $(n = 956)$	35.2 (31.5–38.8)	40.2 (34.2-46.2)	21.7 (14.5-28.8)	26.3 (22.0-30.5)	
Weekly $(n = 596)$	18.1 (15.1–21.0)	18.7 (14.1–23.4)	19.3 (11.8–26.9)	24.1 (19.9–28.4)	
Monthly $(n = 504)$	14.6 (11.9–17.4)	12.2 (8.7–15.7)	17.1 (9.3–24.9)	14.7 (11.3–18.2)	
Less than monthly $(n = 1078)$	32.2 (28.6-35.7)	28.9 (23.6–34.2)	41.9 (31.9–52.0)	34.9 (30.3–39.4)	
Model 5: Daily cannabis use and daily cigarette smoking					0.03
Yes $(n = 818)$	30.6 (27.2-34.2)	34.8 (29.5–40.6)	22.7 (16.2-30.9)	25.8 (21.7-30.3)	
Model 6: Compared to smoking cigarettes, how harmful do					< 0.0001
you think smoking marijuana/ cannabis is?					
More harmful ( $n = 270$ )	5.4 (3.8–7.0)	3.2 (1.1–5.3)	6.5 (1.9–11.0)	9.4 (6.8–11.9)	
Equally harmful $(n = 584)$	16.5 (13.7–19.3)	13.2 (9.1–17.3)	21.6 (13.6-29.5)	23.6 (19.5–27.7)	
Less harmful ( $n = 2105$ )	73.6 (70.3–76.9)	78.3 (73.4–83.1)	65.5 (56.1–74.9)	60.8 (56.1-65.4)	
Don't know ( $n = 161$ )	4.5 (3.1–5.9)	5.3 (3.0-7.6)	6.4 (0.8–12.1)	6.2 (3.9-8.6)	
Model 7: Smoked cannabis in the last 30 days (yes vs. used					
cannabis some other way)					
Yes, I smoked cannabis in the last 30 days ( $n = 1880$ )	88.6 (85.5–91.1)	92.0 (88.0–94.8)	93.0 (82.2–97.5)	95.7 (92.6–97.6)	0.009
Model 8: Mixing tobacco with smoked cannabis in the last					
30 days (yes vs no)					
Yes, smoked cannabis mixed with tobacco ( $n = 1014$ )	38.5 (34.1-43.0)	22.3 (17.3-28.3)	86.0 (78.2-91.3)	90.4 (86.1-93.5)	< 0.0001

Data are weighed and adjusted; CI: Confidence interval; N/A: Not applicable (not assessed); Percentages in the table reflect "yes" responses in the survey.

<sup>\$</sup> P-value is the main effect for 'country' in the regression model. Model 2, 4, and 5: n = 3134 (no missing cases); Model 3: n = 2736 (398 missing cases); Model 6: n = 3120 (14 missing cases); Model 7: n = 2090 (8 missing cases); Model 8: n = 1880.

cigarette smokers who reported co-using cannabis in the last 12 months Table 4 presents country-specific weighted estimates and Table 5 presents the post-hoc comparisons between countries.

# Frequency of cigarette smoking

*Daily cigarette smoking:* Among the 3134 co-users, the majority were daily smokers (84.8%). Australian co-users were significantly more likely to be daily cigarette smokers (94.7%) than those in Canada (79.9%, p < 0.001), the US (83.3%, p < 0.004), and England (85.9%, p = 0.01). Co-users in England were more likely to be daily smokers than co-users in Canada (p = 0.01). There were no differences between England and the US (p = 0.32) or Canada and the US (p = 0.21).

*Heaviness of Smoking/Nicotine Depedence:* Among co-users in this study, the majority were low (40.8%) or medium (54.0%) dependent smokers, with few being heavy smokers (5.2%). Co-users in Australia were more likely to be moderate to heavy smokers (higher nicotine dependence) compared to co-users in Canada (p = 0.004), the US (p = 0.005), and England (p = 0.01). No other differences were found between countries.

### Frequency of cannabis co-use

*Daily cannabis use:* Among this sample of co-users, about one-third were infrequent cannabis users (used cannabis less than monthly), with the largest proportion of these infrequent users being from Australia (41.9%). Australian co-users were more likely to be infrequent cannabis users compared to Canada (32.2%, p = 0.005), and the US (28.9%, p < 0.001), and co-users in England (34.9%, p = 0.02) were less frequent cannabis users than in Canada.

Co-users in the US (40.2%, p < 0.01) and Canada (35.2%, p < 0.01) were significantly more likely to use cannabis daily than co-users in England (26.3%). Daily cannabis use was lowest in Australia (21.7%), but only approached significance when compared to Canada (p = 0.07)

and the US (p = 0.06), possibly owing to the small Australian sample size. There were no other differences between the countries.

# Daily co-use of cannabis and cigarettes

Overall, 818 respondents (29.1%) reported co-using cannabis and cigarettes on a daily basis. The highest proportion of dual-daily use was in the US (34.8%), followed by Canada (30.6%), England (25.8%), and Australia (22.7%). The only significant differences found across countries were that more co-users in the US reported dual-daily use of both products than co-users in Australia (p = 0.02) and England (p = 0.01).

#### Perceptions of harm of smoked cannabis compared to cigarettes

Co-users in England were less likely than co-users in Canada (60.8% vs. 73.6%, p = 0.001) and the US (60.8% vs. 78.3%, p = 0.001) to believe that smoked cannabis is less harmful than smoking cigarettes. 'Less harmful' was the combination of more specific responses 'much less harmful' and 'somewhat less harmful'; the stronger 'much less harmful' response was also analyzed (**Supplemental Table 2**). More co-users in Canada (46.1%) and the US (53.5%) believed that smoked cannabis is much less harmful than cigarettes than co-users in Australia (37.5%) and England (33.9%), although significance was only found between Canada and England (p = 0.006), and England and the US (p = 0.002).

# Cross-country differences: smoking cannabis and mixing tobacco with cannabis in the last 30 days

Among those who reported co-using cannabis in the last 30 days (n = 2098, Model 7), 2090 reported methods used. Smoking cannabis was the most common mode of consumption in all four countries

Cross-country post-hoc comparisons.

Used Cannabis in the last 12 months (yes)           AU vs EN         0.99         0.76         1.27           AU vs US         0.66         0.51         0.87           AU vs CA         0.48         0.38         0.61           EN vs US         0.67         0.56         0.81           EN vs CA         0.48         0.42         0.56           US vs CA         0.72         0.61         0.86           Daily cannabis use (yes)         0.72         0.61         0.86           AU vs EN         1.03         0.55         1.94           AU vs US         0.52         0.27         1.02           AU vs CA         0.58         0.32         1.05           EN vs US         0.51         0.33         0.79           EN vs CA         0.56         0.39         0.80           US vs CA         1.10         0.73         1.66           Dual-daily co-users of cannabis and         cigarettes (yes)         1.27         0.96         1.68           CA vs EN         1.27         0.96         1.68         Ch vs US         1.61
AU vs EN       0.99       0.76       1.27         AU vs US       0.66       0.51       0.87         AU vs CA       0.48       0.38       0.61         EN vs US       0.67       0.56       0.81         EN vs CA       0.48       0.42       0.56         US vs CA       0.72       0.61       0.86         Daily cannabis use (yes)       0.52       0.27       1.02         AU vs EN       1.03       0.55       1.94         AU vs US       0.52       0.27       1.02         AU vs CA       0.58       0.32       1.05         EN vs CA       0.56       0.39       0.80         US vs CA       0.56       0.39       0.80         US vs CA       1.10       0.73       1.66         Dual-daily co-users of cannabis and cigarettes (yes)       0.40       0.72       0.96
AU vs US       0.66       0.51       0.87         AU vs CA       0.48       0.38       0.61         EN vs US       0.67       0.56       0.81         EN vs CA       0.48       0.42       0.56         US vs CA       0.72       0.61       0.86         Daily canabis use (yes)       0.52       0.27       1.02         AU vs EN       1.03       0.55       1.94         AU vs US       0.52       0.27       1.02         AU vs CA       0.58       0.32       1.05         EN vs US       0.51       0.33       0.79         EN vs CA       0.56       0.39       0.80         US vs CA       1.10       0.73       1.66         Dual-daily co-users of cannabis and cigarettes (yes)       1.27       0.96       1.68
AU vs CA       0.48       0.38       0.61         EN vs US       0.67       0.56       0.81         EN vs CA       0.48       0.42       0.56         US vs CA       0.72       0.61       0.86         Daily cannabis use (yes)       0.52       0.27       1.02         AU vs US       0.52       0.27       1.02         AU vs US       0.58       0.32       1.05         EN vs US       0.51       0.33       0.79         EN vs CA       0.56       0.39       0.80         US vs CA       1.10       0.73       1.66         Dual-daily co-users of cannabis and cigarettes (yes)       1.27       0.96       1.68
EN vs CA       0.48       0.42       0.56         US vs CA       0.72       0.61       0.86         Daily cannabis use (yes)            AU vs EN       1.03       0.55       1.94         AU vs US       0.52       0.27       1.02         AU vs CA       0.58       0.32       1.05         EN vs US       0.51       0.33       0.79         EN vs CA       0.56       0.39       0.80         US vs CA       1.10       0.73       1.66         Dual-daily co-users of cannabis and cigarettes (yes)       I.27       0.96       1.68
US vs CA         0.72         0.61         0.86           Daily cannabis use (yes)              AU vs EN         1.03         0.55         1.94           AU vs US         0.52         0.27         1.02           AU vs CA         0.58         0.32         1.05           EN vs US         0.51         0.33         0.79           EN vs CA         0.56         0.39         0.80           US vs CA         1.10         0.73         1.66           Dual-daily co-users of cannabis and cigarettes (yes)         I.27         0.96         1.68
Daily cannabis use (yes)           AU vs EN         1.03         0.55         1.94           AU vs US         0.52         0.27         1.02           AU vs CA         0.58         0.32         1.05           EN vs US         0.51         0.33         0.79           EN vs CA         0.56         0.39         0.80           US vs CA         1.10         0.73         1.66           Dual-daily co-users of cannabis and cigarettes (yes)         I.27         0.96         1.68
AU vs EN       1.03       0.55       1.94         AU vs US       0.52       0.27       1.02         AU vs CA       0.58       0.32       1.05         EN vs US       0.51       0.33       0.79         EN vs CA       0.56       0.39       0.80         US vs CA       1.10       0.73       1.66         Dual-daily co-users of cannabis and cigarettes (yes)       1.27       0.96       1.68
AU vs US       0.52       0.27       1.02         AU vs CA       0.58       0.32       1.05         EN vs US       0.51       0.33       0.79         EN vs CA       0.56       0.39       0.80         US vs CA       1.10       0.73       1.66         Dual-daily co-users of cannabis and cigarettes (yes)       EX vs EN       1.27       0.96       1.68
AU vs CA       0.58       0.32       1.05         EN vs US       0.51       0.33       0.79         EN vs CA       0.56       0.39       0.80         US vs CA       1.10       0.73       1.66         Dual-daily co-users of cannabis and cigarettes (yes)
EN vs US         0.51         0.33         0.79           EN vs CA         0.56         0.39         0.80           US vs CA         1.10         0.73         1.66           Dual-daily co-users of cannabis and cigarettes (yes)
EN vs CA         0.56         0.39         0.80           US vs CA         1.10         0.73         1.66           Dual-daily co-users of cannabis and cigarettes (yes)         US         US <thus< th="">         US         US</thus<>
US vs CA 1.10 0.73 1.66 Dual-daily co-users of cannabis and cigarettes (yes) CA vs EN 1.27 0.96 1.68
Dual-daily co-users of cannabis and cigarettes (yes)         CA vs EN       1.27       0.96       1.68
cigarettes (yes) CA vs EN 1.27 0.96 1.68
CA vs EN 1.27 0.96 1.68
CA vs US 0.83 0.62 1.11
CA vs AU 1.50 0.95 2.36
EN vs US 0.65 0.47 0.91
EN vs AU 1.18 0.73 1.91
US vs AU 1.82 1.11 2.99
Nicotine dependence (HSI): moderate/
high vs. low
AU vs EN         1.93         1.17         3.18           AU vs US         2.12         1.25         3.59
EN vs CA         1.05         0.80         1.37           US vs CA         0.95         0.70         1.29
Perceive smoked cannabis to be less
harmful than cigarette smoking
among past 12-months cannabis users
AU vs EN 1.56 0.68 3.62
AU vs US 0.42 0.15 1.19
AU vs CA 0.74 0.32 1.71
EN vs US 0.27 0.13 0.54
EN vs CA 0.48 0.31 0.74
US vs CA 1.79 0.87 3.70
Smoked cannabis in the last 30 days (yes)
AU vs EN 0.60 0.17 2.10
AU vs US 1.16 0.35 3.82
AU vs CA 1.72 0.58 5.12
EN vs US 1.94 0.91 4.14
EN vs CA 2.88 1.50 5.56
US vs CA 1.49 0.89 2.49
Mixed tobacco with smoked cannabis in
the last 30 days (yes)
AU vs EN 0.65 0.33 1.29
AU vs US 21.34 11.34 40.15
AU vs CA 9.81 5.53 17.42
EN vs US 32.89 19.30 56.07
EN vs CA 15.13 9.46 24.20
US vs CA 0.46 0.32 0.66

CI: Confidence interval; AU: Australia; CA: Canada; EN: England; US: United States; HSI: Heaviness of Smoking Index.

(92.3%). The proportion of respondents who smoked cannabis was highest in England (95.7%), followed by Australia (93.0%), the US (92.0%) and Canada (88.6%). Co-users in Canada were less likely to report smoking cannabis than in England (p = 0.002). There were no other differences between countries.

Among those who smoked cannabis (n = 1880, Model 8), co-users in England (90.4%) and Australia (86.0%) were more likely to mix tobacco with their cannabis than in Canada (38.5% both p < 0.0001) or the US (22.3%, both p < 0.0001). Co-users from Canada were also more likely to mix tobacco with their cannabis (p < 0.0001) than those from the US. There was no difference between Australia and England (p = 0.21).

#### Discussion

This study found significant cross-country differences in patterns of cannabis co-use among cigarette smokers, where smokers from Canada and the US (the countries with more permissive cannabis laws) had higher rates of co-use, daily cannabis use, dual-daily co-use of cannabis and cigarettes, were more likely to smoke cannabis without tobacco, and believe that smoked cannabis is less harmful than cigarettes than co-users in England and Australia. These findings, obtained during a period of liberalization in many countries, introduce a number of important issues for future research on the impact of cannabis liberalization in general, and on tobacco-cannabis co-use.

Currently there is mixed evidence about the effects of cannabis legislation on actual changes in cannabis use. and the majority of the available studies originate from the US (Melchior et al., 2019; Smart & Pacula, 2019). Reviews have shown that cannabis use may increase among adults in locations that have legalized medical (Smart & Pacula, 2019) or recreational (Melchior et al., 2019) cannabis, and a recent large cross-sectional study that examined the population-level impact of recreational cannabis legalization in Canada and across US states in 2018, found that both the prevalence and frequency of cannabis use were higher in US states that have legalized recreational cannabis compared to Canada (recreational cannabis was not yet legal at the time of the survey) and US 'illegal' states (Goodman, Wadsworth, Leos-Toro & Hammond, 2020). Recent national data from Canada (Leos-Toro et al., 2017; Statistics Canada, 2019a) and the US (Mauro et al., 2018; SAMHSA, 2017) have shown that adult cannabis use has been increasing where liberalization of cannabis laws has occurred. Some research has also shown that the prevalence of co-use is rising in the US (Schauer, Berg, Kegler, Donovan & Windle, 2015), with higher co-use rates in US states where medical cannabis has been legalized (Wang, Ramo, Lisha & Cataldo, 2016). It is currently unclear however if higher rates of cannabis use, co-use, and/or increases in use are attributable to policy changes, or if studies are detecting pre-existing trends that were in motion prior to liberalization, partly owing to the sophisticated illicit markets in Canada and the US. Moreover, while some studies have examined how cannabis use and co-use patterns may change during the period immediately following a policy change (Cerda et al., 2017; Schuermeyer et al., 2014; Wadsworth & Hammond, 2019), very little is known about how cannabis liberalization may impact longer-term patterns of tobacco and cannabis co-use. One public health implication to cannabis liberalization is the possibility that increased access to cannabis may weaken, or even reverse, longstanding downward trends in tobacco use. Ongoing, long-term research utilizing longitudinal study designs is critical to further explore the relationship between co-use and liberalization of medical and recreational cannabis.

With growing public support and social acceptibility of cannabis in many countries (MacLeans, 2017; GALLUP, 2019; Roy Morgan Single Source Australia, 2019; Subbaraman & Kerr, 2017), coupled with cannabis policy liberalization, harm perceptions of cannabis may be impacted. For example, some studies have shown that perceptions of absolute cannabis risks are lower, or have decreased, in jurisdictions that have legalized cannabis (Cerda et al., 2017; Schuermeyer et al., 2014; Wadsworth & Hammond, 2019), and lower harm perceptions are associated with use and appeal of drugs (Szalay, Inn, Strohl & Wilson, 1993), including cannabis (Salloum, Krauss, Agrawal, Bierut & Grucza, 2018). Not much is known about how product regulations may shape or change absolute perceptions about cannabis, and to our knowledge, there are no studies that have compared perceptions of relative risk between smoked cannabis and tobacco, particularily among co-users residing in different cannabis policy environments. A study by Popova et al. found that yong adults in Colorado (the first US state to legalize recreational cannabis in 2012) perceive combustion-smoking (including cannabis smoking) as more harmful than non-combustible products (e.g., e-cigarettes, vaporizers and edibles), but there was no

comparison between cigarettes and smoked cannabis (Popova et al., 2017). A qualitative study of young adults has suggested that co-users in Maryland (where recreational cannabis is decriminalized, and medical cannabis is legal) relate to their use of both substances in different ways, and may underestimate the harms of tobacco use in relation to their cannabis use, as well as underestimate the harms of cannabis use (Seaman et al., 2019). There is no evidence however if the underestimation of these risks varies between legal and illegal cannabis jusisdictions, as well as between single product users and co-users. While our study cannot determine this, our data do show that co-user's perceptions of lower relative risk of cannabis compared to cigarettes was substantially more common in Canada and the US. This is worrisome because tobacco smoke and cannabis smoke have been found to contain many of the same carcinogenic chemicals (Moir et al., 2008; Novotny et al., 2002), and some of these harmful constituents (e.g., tar, ammonia, carbon monoxide, nitrous oxide, and some aromatic amines) have been found in marijuana smoke at greater concentrations than in tobacco smoke (Moir et al., 2008; Wu, Tashkin, Djahed & Rose, 1988). However, regardless of the harmful constituents within each product, tobacco smoking is more deadly and addictive than cannabis. Tobacco smoking (mainly cigarettes) is attributed to 8 million global deaths each year, and the total annual global economic cost of smoking is estimated to be 1.4 trillion USD (WHO, 2019). Currently, there is much less evidence about the health effects of cannabis due to its status as a prohibited substance in most jurisdictions. Studies have shown that regular cannabis use is related to important adverse health outcomes including impaired decision making and memory deficits, increased risks of acute injuries, including impaired driving, dose-dependent risk of developing psychotic disorders, and high health care costs (Crean, Crane & Mason, 2011; Hasan et al., 2019; WHO, 2016; NASEM, 2017; CSUCH, 2018). However the scope and magnitude of these risks are substantially less than tobacco, which is a primary risk factor for a wide range of diseases including several non-communicable diseases, and more than a dozen forms of cancer (US HHS, 2014).

This study has demonstrated that the majority of co-users, regardless of the cannabis regulatory environment, are smoking cannabis alongside smoking cigarettes. One main difference was that fewer cousers from Canada and the US mixed tobacco with their cannabis compared to co-users in England and Australia. Research has consistently shown that co-use practices differ by country and region (Hindocha, Freeman, Ferris, Lynskey & Winstock, 2016), which our findings also support. Simultaneous use (mixing tobacco with cannabis) is more common in European countries (including England) and Australia, while sequential use (using tobacco and cannabis separately within the same use episode) is more common in North America (Belanger, Akre, Kuntsche, Gmel & Suris, 2011; Fix et al., 2019; Hindocha et al., 2016). However, in the US specifically, smoking 'blunts' (a cigar that has been hollowed out and filled with cannabis) is a common and increasing method of cannabis use (Fairman, 2015; Schauer, Rosenberry & Peters, 2017). Because tobacco is not directly mixed with cannabis, users may not consider this to be simultaneous use (Seaman et al., 2019), therefore this use pattern could have been underestimated by US co-users in this study.

Research suggests that simultaneous use (mixing) is associated with greater risk of problematic cannabis dependence, negative cannabisrelated outcomes, lower motivation to reduce tobacco consumption, and lower rates of smoking cessation (Agrawal et al., 2012; Hindocha et al., 2016). On the other hand, it has been found that sequential users use cannabis on more days per month, more cannabis per day, and found that not mixing tobacco with their cannabis to be more pleasurable in comparison to those who mix tobacco with their cannabis (Hindocha et al., 2016). Monitoring unique patterns of both simultaneous and sequential co-use occurring in different regions warrants significant public health attention. Notably however, regardless of couse patterns, nearly one-third of the sample in this study smoked cigarettes and used cannabis daily. While this study is not representative of cannabis-dependent people, there are several smokers who are at much higher risk of the additive effects of co-use. Physicians and other healthcare professionals should be vigilant in identifying co-users and offer tailored treatment, especially for co-users with cannabis dependence, as these users are significantly less likely to quit smoking and problematic cannabis use than those without cannabis dependency (Patel & Marwaha, 2020; Weinberger et al., 2019a).

Although this is a large study with representative smokers from four countries, there are some limitations to consider. First, comparing different policy environments is challenging, owing to the diversification of cannabis supply, possession, and use laws, both across and within countries, poor comparisons between national surveys, illicit cannabis markets, and because changing laws are in very early stages (Kilmer & Pacula, 2017). Future research is needed that tackles the difficult challenge of incorporating information about illicit cannabis into analyses of the legal market. Second, the countries included herein were treated as single jurisdictions (as the sample was not amenable to division at the sub-national level), which has the potential to mask important sub-national differences. Third, this is a cross-sectional study, therefore temporality issues exist, and causality cannot be determined. Fourth, the sample was limited to adult smokers, so observations may not apply to other populations of interest. Fifth, Canada had not yet officially legalized recreational cannabis at the time of data collection; therefore users would have purchased cannabis illegally or from a legal medical source (e.g., cannabis dispensary or a federally licensed seller). Sixth, cannabis use may be underestimated (particularly in jurisdictions where its use is prohibited) due to respondents' reluctance to admit to cannabis use. Finally, four high-income Western countries were included in the analyses presented in this paper; therefore, these results may not apply to other countries.

# Conclusion

As cannabis legalization proceeds across the globe, it will be important to understand the relationship between cannabis and cigarette smoking co-use and usage patterns. Given the high rate of cannabis use among cigarette smokers, there are public health concerns that legalizing cannabis may encourage problematic tobacco-cannabis smoking co-use, which could interfere with efforts to reduce tobacco smoking and its many harms. Overall, there is an urgent need for evidence to evaluate the short- and long-term impacts of different degrees of cannabis legalization on co-use of smoked tobacco and cannabis.

# **Conflict of Interest Statement**

KMC has received payment as a consultant to Pfizer, Inc., for service on an external advisory panel to assess ways to improve smoking cessation delivery in health care settings. KMC also has served as paid expert witness in litigation filed against the tobacco industry. GTF, DH, and JFT have served as expert witnesses on behalf of governments in litigation involving the tobacco industry. MLG has received a research grant from Pfizer and served as a member of scientific advisory board to Johnson & Johnson. AM is a UK National Institute for Health Research (NIHR) Senior Investigator. The views expressed in this article are those of the authors and not necessarily those of the NIHR, or the UK Department of Health and Social Care. All other authors have no conflicts of interest to declare.

#### Acknowledgments

The authors would like to acknowledge and thank all those that contributed to the International Tobacco Control Four Country Smoking and Vaping Survey (ITC 4CV) Survey: all study investigators and collaborators, and the project staff at their respective institutions.

# Funding

This study was supported by grants from the US National Cancer Institute (P01 CA200512), the Canadian Institutes of Health Research (FDN-148477), and by the National Health and Medical Research Council of Australia (APP 1106451). GTF was supported by a Senior Investigator Grant from the Ontario Institute for Cancer Research.

# **Ethics** approval

Study questionnaires and materials were reviewed and provided clearance by Research Ethics Committees at the following institutions: University of Waterloo (Canada, ORE#20803/30570, ORE#21609/30878), King's College London, UK (RESCM-17/18-2240), Cancer Council Victoria, Australia (HREC1603), University of Queensland, Australia (2016000330/HREC1603); and Medical University of South Carolina (waived due to minimal risk);. All participants provided consent to participate.

#### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2020.102754.

#### References

- Agrawal, A., Budney, A. J., & Lynskey, M. T. (2012). The co-occurring use and misuse of cannabis and tobacco: A review. Addiction (Abingdon, England), 107(7), 1221–1233.
- Anthony, J. C., Warner, L. A., & Kessler, R. C. (1994). Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: Basic findings from the national comorbidity survey. *Experimental and Clinical Psychopharmacology*, 2(3), 244–268.
- Becker, J., Schaub, M. P., Gmel, G., & Haug, S. (2015). Cannabis use and other predictors of the onset of daily cigarette use in young men: What matters most? Results from a longitudinal study. *BMC Public Health*, 2(15), 843.
- Belanger, R. E., Akre, C., Kuntsche, E., Gmel, G., & Suris, J. C. (2011). Adding tobacco to cannabis–its frequency and likely implications. *Nicotine & Tobacco Research*, 13(8), 746–750.
- Berg, C. J., Payne, J., Henriksen, L., Cavazos-Rehg, P., Getachew, B., Schauer, G. L., et al. (2018). Reasons for marijuana and tobacco co-use among young adults: A mixed methods scale development study. *Substance Use & Misuse*, 53(3), 357–369.
- Canadian Center on Substance Use and Addiction (CSUCH)Canadian Substance Use Costs and Harms Scientific Working Group. (2018). Canadian substance use costs and harms (2007–2014). Ottawa, Ont.: Canadian Centre on Substance Use and Addiction Prepared by the Canadian Institute for Substance Use Research and the Canadian Centre on Substance Use and Addiction.
- Centers for Disease Control and Prevention (CDC). (2018). Current cigarette smoking among adults in the United States. Retrieved 7 December 2019 fromhttps://www. cdc.gov/tobacco/data\_statistics/fact\_sheets/adult\_data/cig\_smoking/index.htm.
- Cerda, M., Wall, M., Feng, T., Keyes, K. M., Sarvet, A., Schulenberg, J., et al. (2017). Association of state recreational marijuana laws with adolescent marijuana use. *The Journal of the American Medical Association Pediatrics*, 171(2), 142–149.
- Crean, R. D., Crane, N. A., & Mason, B. J. (2011). An evidence based review of acute and long-term effects of cannabis use on executive cognitive functions. *Journal of Addiction Medicine*, 5(1), 1–8.
- Fairman, B. J. (2015). Cannabis problem experiences among users of the tobacco-cannabis combination known as blunts. Drug and Alcohol Dependence, 150, 77–84.
- Fix, B. V., Smith, D., O'Connor, R., Heckman, B. W., Willemsen, M. C., Cummings, M., et al. (2019). Cannabis use among a nationally representative cross-sectional sample of smokers and non-smokers in the Netherlands: Results from the 2015 ITC Netherlands Gold Magic Survey. *BMJ open*, 9(3), E024497.
- GALLUP Poll. U.S. support for legal marijuana steady in past year. (October (2019)). Retrieved 7 December 2019https://news.gallup.com/poll/267698/support-legalmarijuana-steady-past-year.aspx.
- Goodman, S., Wadsworth, E., Leos-Toro, C., & Hammond, D. (2020). Prevalence and forms of cannabis use in legal vs. illegal recreational cannabis markets. *International Journal of Drug Policy*, 76, 102658.
- Goodwin, R. D., Pacek, L. R., Copeland, J., Moeller, S. J., Dierker, L., Weinberger, A., et al. (2018). Trends in daily cannabis use among cigarette smokers: United states, 2002-2014. American Journal of Public Health, 108(1), 137–142.
- Greenhalgh, E. M., Bayly, M., Winstanley, M. H., Scollo, M. M., & Winstanley, M. H. (2019). 1.3 Prevalence of smoking—Adults. Tobacco in australia: Facts and issues. Melbourne: Cancer Council Victoria. Retrieved 7 December 2019 from http://www. tobaccoinaustralia.org.au/chapter-1-prevalence/1-3-prevalence-of-smoking-adults.
- Hasan, A., von Keller, R., Friemel, C. M., Hall, W., Schneider, M., Koethe, D., et al. (2019). Cannabis use and psychosis: A review of reviews. *European Archives of Psychiatry and Clinical Neuroscience*. https://doi.org/10.1007/s00406-019-01068-z [Epub ahead of print].

- Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., Rickert, W., & Robinson, J. (1989). Measuring the heaviness of smoking: Using self-reported time to the first cigarette of the day and number of cigarettes smoked per day. *British Journal of Addiction*, 84(7), 791–799.
- Hindocha, C., Freeman, T. P., Ferris, J. A., Lynskey, M. T., & Winstock, A. R. (2016). No smoke without tobacco: A global overview of cannabis and tobacco routes of administration and their association with intention to quit. *Frontiers in psychiatry*, 5(7), 104.
- Hindocha, C., Shaban, N. D., Freeman, T. P., Das, R. K., Gale, G., Schafer, G., et al. (2015). Associations between cigarette smoking and cannabis dependence: A longitudinal study of young cannabis users in the United Kingdom. *Drug and Alcohol Dependence*, 148, 165–171.
- Kilmer, B., & Pacula, R. L. (2017). Understanding and learning from the diversification of cannabis supply laws. Addiction (Abingdon, England), 112(7), 1128–1135.
- Lavallée, P., & Beaumont, J.F. (.2015)., Why we should put some weight on weights. Survey Insights: Methods from the Field, Weighting: Practical Issues and 'How to' Approach, Invited article, Retrieved 18 February 2020 fromhttps://surveyinsights. org/?p=6255.
- Lemyre, A., Poliakova, N., & Belanger, R. E. (2019). The relationship between tobacco and cannabis use: A review. Substance use & Misuse, 54(1), 130–145.
- Leos-Toro, C., Reid, J. L., Madill, C. L., Rynard, V. L., Manske, S. R., & Hammond, D. (2017). Cannabis in Canada - Tobacco Use in Canada: Patterns and trends, 2017 edition, special supplement. Waterloo, ON: Propel Centre for Population Health Impact, University of Waterloo. Retrieved 7 December 2019 from https://uwaterloo.ca/ tobacco-use-canada/sites/ca.tobacco-use-canada/files/uploads/files/ cannabissupplement\_2017 final\_accessible.pdf.
- MacLeans. (Sep 26, (2017)). Majority of Canadians support marijuana legalization, says survey. Retrieved 7 December 2019 fromhttps://www.macleans.ca/society/ majority-of-canadians-support-marijuana-legalization-says-survey/.
- Mauro, P. M., Carliner, H., Brown, Q. L., Hasin, D. S., Shmulewitz, D., Rahim-Juwel, R., et al. (2018). Age differences in daily and nondaily cannabis use in the United States, 2002-2014. Journal of Studies on Alcohol and Drugs, 79(3), 423–431.
- Meier, E., Vandrey, R., Rubin, N., Pacek, L. R., Jensen, J. A., Donny, E. C., et al. (2019). Cigarette smokers vs. co-users of cannabis and cigarettes: Exposure to toxicants. *Nicotine & Tobacco Research* pii: Ntz199. [Epub ahead of print].
- Melchior, M., Nakamura, A., Bolze, C., Hausfater, F., El Khoury, F., Mary-Krause, M., et al. (2019). Does liberalisation of cannabis policy influence levels of use in adolescents and young adults? A systematic review and meta-analysis. *BMJ Open*, 9(7).
- Miller, A. M., Rosenman, R., & Cowan, B. W. (2017a). Recreational marijuana legalization and college student use: Early evidence. SSM - Population Health, 3, 649–657.
- Miller, N. S., Oberbarnscheidt, T., & Gold, M. S. (2017b). Marijuana addictive disorders: DSM-5 substance-related disorders. *Journal of Addiction Research and Therapy*, S11, 013.
- Moir, D., Rickert, W. S., Levasseur, G., Larose, Y., Maertens, R., White, P., et al. (2008). A comparison of mainstream and sidestream marijuana and tobacco cigarette smoke produced under two machine smoking conditions. *Chemical Research in Toxicology*, 21(2), 494–502.
- National Institute on Drug Abuse (NIDA). (2019). Marijuana. Retrieved 7 December 2019 fromhttps://www.drugabuse.gov/publications/drugfacts/marijuana.
- Novotny, M., Merli, F., Wiesler, D., Fencl, M., & Saeed, T. (2002). Fractionation and capillary gas chromatographic—Mass spectrometric characterization of the neutral components in marijuana and tobacco smoke condensates. *Journal of Chromatography*, 238(1982), 141–150.
- Patel, J., & Marwaha, R. (2020). Cannabis use disorder. Treasure Island (FL): StatPearls Publishing. Retrieved February 25 2020, from https://www.ncbi.nlm.nih.gov/books/ NBK538131/.
- Peters, E. N., Budney, A. J., & Carroll, K. M. (2012). Clinical correlates of co-occurring cannabis and tobacco use: A systematic review. *Addiction (Abingdon, England)*, 107(8), 1404–1417.
- Popova, L., McDonald, E. A., Sidhu, S., Barry, R., Richers Maruyama, T. A., Sheon, N. M., et al. (2017). Perceived harms and benefits of tobacco, marijuana, and electronic vaporizers among young adults in Colorado: Implications for health education and research. Addiction (Abingdon, England), 112(10), 1821–1829.
- Rabin, R. A., & George, T. P. (2015). A review of co-morbid tobacco and cannabis use disorders: Possible mechanisms to explain high rates of co-use. *The American Journal* on Addictions, 24(2), 105–116.
- Rabin, R. A., Ashare, R. L., Schnoll, R. A., Cinciripini, P. M., Hawk, L. W., Jr, Lerman, C., et al. (2016). Does cannabis use moderate smoking cessation outcomes in treatmentseeking tobacco smokers? Analysis from a large multi-center trial. *The American Journal on Addictions*, 25(4), 291–296.
- Roy Morgan Single Source Australia. (2019). A growing number of Australians want marijuana legalised. Retrieved 7 December 2019 fromhttp://www.roymorgan.com/ findings/8162-marijuana-acceptance-in-australia-june-2019-201910132241.
- Salloum, N. C., Krauss, M. J., Agrawal, A., Bierut, L. J., & Grucza, R. A. (2018). A reciprocal effects analysis of cannabis use and perceptions of risk. *Addiction (Abingdon, England)*, 113(6), 1077–1085.
- Schauer, G. L., Berg, C. J., Kegler, M. C., Donovan, D. M., & Windle, M. (2015). Assessing the overlap between tobacco and marijuana: Trends in patterns of co-use of tobacco and marijuana in adults from 2003 to 2012. Addictive Behaviors, 49, 26–32.
- Schauer, G. L., Rosenberry, Z. R., & Peters, E. N. (2017). Marijuana and tobacco co-administration in blunts, spliffs, and mulled cigarettes: A systematic literature review. *Addictive Behaviors*, 6(4), 200–211.
- Schuermeyer, J., Salomonsen-Sautel, S., Price, R. K., Balan, S., Thurstone, C., Min, S. J., et al. (2014). Temporal trends in marijuana attitudes, availability and use in colorado compared to non-medical marijuana states: 2003–11. *Drug and Alcohol Dependence*, 140, 145–155.

- Seaman, E. L., Howard, D. E., Green, K. M., Wang, M. Q., & Fryer, C. S. (2019). A sequential explanatory mixed methods study of young adult tobacco and marijuana couse. Substance Use & Misuse, 54(13), 2177–2190.
- Smart, R., & Pacula, R. L. (2019). Early evidence of the impact of cannabis legalization on cannabis use, cannabis use disorder, and the use of other substances: Findings from state policy evaluations. *The American Journal of Drug and Alcohol Abuse*, 45(6), 644–663.
- Smith, D. M., O'Connor, R. J., Wei, B., Travers, M., Hyland, A., & Goniewicz, M. L. (2019). Nicotine and toxicant exposure among concurrent users ("co-users") of tobacco and cannabis. *Nicotine & Tobacco Research, pii: Ntz*122 [Epub ahead of print].
- Statistics Canada. (2017). Canadian tobacco, alcohol and drugs survey (CTADS): Summary of results for 2017. Retrieved 7 December 2019 fromhttps://www.canada. ca/en/health-canada/services/canadian-tobacco-alcohol-drugs-survey/2017summary.html.
- Statistics Canada. (2018). Analysis of trends in the prevalence of cannabis use in Canada, 1985 to 2015. Retrieved 7 December 2019 fromhttps://www150.statcan.gc.ca/n1/ pub/82-003-x/2018002/article/54908-eng.htm.
- Statistics Canada. (2019a). Analysis of trends in the prevalence of cannabis use and related metrics in Canada. Retrieved fromhttps://www150.statcan.gc.ca/n1/pub/82-003-x/2019006/article/00001-eng.htm.
- Statistics Canada. (2019b). Smoking, 2018. Retrieved 7 December 2019 fromhttps:// www150.statcan.gc.ca/n1/pub/82-625-x/2019001/article/00006-eng.htm.
- Subbaraman, M. S., & Kerr, W. C. (2017). Support for marijuana legalization in the US state of Washington has continued to increase through 2016. *Drug and Alcohol Dependence*, 175, 205–209.
- Substance Abuse and Mental Health Services Administration (SAMHSA). (2017). Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health (HHS publication no. SMA 17-5044, NSDUH series H-52). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved 7 December 2019 from https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2016/ NSDUH-FFR1-2016.pdf.
- Substance Abuse and Mental Health Services Administration (SAMHSA). (2018). 2018 national survey on drug use and health (NSDUH). Retrieved 7 December 2019 fromhttps://www.samhsa.gov/data/.
- Szalay, L. B., Inn, A., Strohl, J. B., & Wilson, L. C. (1993). Perceived harm, age, and drug use: Perceptual and motivational dispositions affecting drug use. *Journal of Drug Education*, 23(4), 333–356.
- The National Academies of Sciences, Engineering and Medicine. (2017). The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research. Washington, DC: The National Academies Presshttps://doi.org/10.17226/ 24625 Retrieved 7 December 2019.
- Thompson, M. E., Fong, G. T., Boudreau, C., Driezen, P., Li, G., Gravely, S., et al. (2018). Methods of the ITC four country smoking and vaping survey, wave 1 (2016). Addiction (Abingdon, England), 114(Suppl 1), 6–14.
- Tucker, J. S., Pedersen, E. R., Seelam, R., Dunbar, M. S., Shih, R. A., & D'Amico, E. J. (2019). Types of cannabis and tobacco/nicotine co-use and associated outcomes in young adulthood. *Psychology of Addictive Behaviors*, 33(4), 401–411.

- U.S. Department of Health and Human Services (US HHS). (2014). The health consequences of smoking—50 years of progress: A report of the surgeon general. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health.
- United Nations (UN). (2018). Analysis of drug markets: Opiates, cocaine, cannabis, synthetic drugs. World drug report 2018. (United Nations publication, sales no. E.18.XI.9). Vienna: Division for Policy Analysis and Public Affairs United Nations Office on Drugs and Crime. Retrieved 7 December 2019 https://www.unodc.org/wdr2018/prelaunch/ WDR18 Booklet 3 DRUG MARKETS.pdf.
- United Nations (UN). (2019). World drug report 2019. United Nations publication, sales no. E.19.XI.8. Vienna: Division for Policy Analysis and Public Affairs United Nations Office on Drugs and Crime. Retrieved 13 February 2020 https://wdr.unodc.org/ wdr2019/prelaunch/WDR19\_Booklet\_2\_DRUG\_DEMAND.pdf.
- Van der Kooy, F., Pomahacova, B., & Verpoorte, R. (2009). Cannabis smoke condensate II: Influence of tobacco on tetrahydrocannabinol levels. *Inhalation Toxicology*, 21(2), 87–90.
- Wadsworth, E., & Hammond, D. (2019). International differences in patterns of cannabis use among youth: Prevalence, perceptions of harm, and driving under the influence in Canada, England & United States. Addictive Behaviors, 90, 171–175.
- Wang, J. B., Ramo, D. E., Lisha, N. E., & Cataldo, J. K. (2016). Medical marijuana legalization and cigarette and marijuana co-use in adolescents and adults. *Drug and Alcohol Dependence*, 166, 32–38.
- Watson, S. J., Benson, J. A., Jr, & Joy, J. E. (2000). Marijuana and medicine: Assessing the science base: A summary of the 1999 institute of medicine report. Archives of General Psychiatry, 57(6), 547–552.
- Weinberger, A. H., Delnevo, C. D., Wyka, K., et al. (2019). Cannabis use is associated with increased risk of cigarette smoking initiation, persistence, and relapse among adults in the US [published online ahead of print, 2019 May 21]. Nicotine & Tobacco Research. https://doi.org/10.1093/ntr/ntz085.
- Weinberger, A. H., Pacek, L. R., Wall, M. M., Zvolensky, M. J., Copeland, J., Galea, S., et al. (2018). Trends in cannabis use disorder by cigarette smoking status in the united states, 2002-2016. *Drug and Alcohol Dependence*, 191, 45–51.
- Weinberger, A. H., Pacek, L. R., Wall, M. M., Gbedemah, M., Lee, J., & Goodwin, R. D. (2019a). Cigarette smoking quit ratios among adults in the USA with cannabis use and cannabis use disorders, 2002–2016. *Tobacco Control*, 29(1), 74–80.
- World Health Organization (WHO). (2016). The health and social effects of nonmedical cannabis use. Geneva: WHO Press. Retrieved 25 February 2020 from https://www. who.int/substance\_abuse/publications/msbcannabis.pdf.
- World Health Organization (WHO). (2019). Tobacco. Retrieved 13 February fromhttps:// www.who.int/health-topics/tobacco.
- Wu, T. C., Tashkin, D. P., Djahed, B., & Rose, J. E. (1988). Pulmonary hazards of smoking marijuana as compared with tobacco. *The New England Journal of Medicine*, 318(6), 347–351.
- Zehra, A., Burns, J., Liu, C. K., Manza, P., Wiers, C. E., Volkow, N. D., et al. (2018). Cannabis addiction and the brain: A review. *Journal of Neuroimmune Pharmacology*, 13(4), 438–452.