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# Journal of Affective Disorders



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

Research paper

# Cannabis-involvement in emergency department visits for self-harm following medical and non-medical cannabis legalization



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# ABSTRACT

Aims: Cannabis use may increase the risk of self-harm, but whether legalization of cannabis is associated with changes in self-harm is unknown. We examined changes in cannabis-involvement in emergency department (ED) visits for self-harm after the liberalization of medical and legalization of non-medical cannabis in Canada. *Methods*: This repeated cross-sectional study used health administrative data to identify all ED visits for self-harm in individuals aged ten and older between January 2010 and December 2021. We identified self-harm ED visits with a co-diagnosis of cannabis (main exposure) or alcohol (control condition) and examined changes in rates of visits over four distinct policy periods (pre-legalization, medical liberalization, non-medical legalization with restrictions, and non-medical commercialization/COVID-19) using Poisson models.

*Results*: The study included 158,912 individuals with one or more self-harm ED visits, of which 7810 (4.9 %) individuals had a co-diagnosis of cannabis use and 24,761 (15.6 %) had a co-diagnosis of alcohol use. Between 2010 and 2021, the annual rate of ED visits for self-harm injuries involving cannabis per 100,000 individuals increased by 90.1 % (3.6 in 2010 to 6.9 in 2021 per 100,000 individuals), while the annual rate of self-harm injuries involving alcohol decreased by 17.3 % (168.1 in 2010 to 153.1 in 2021 per 100,000 individuals). The entire increase in visits relative to pre-legalization occurred after medical liberalization (seasonally adjusted Risk Ratio [a<sub>5</sub>RR] 1.71 95 % CI 1.09–1.15) with no further increases during the legalization with restrictions (a<sub>5</sub>RR 1.77 95%CI 1.62–1.93) or commercialization/COVID-19 periods (a<sub>5</sub>RR 1.63 95%CI 1.50–176).

*Conclusions*: Cannabis-involvement in self-harm ED visits almost doubled over 12 years and may have accelerated after medical cannabis liberalization. While the results cannot determine whether cannabis is increasingly causing self-harm ED visits or whether cannabis is increasingly being used by individuals at high risk of self-harm, greater detection for cannabis use in this population and intervention may be indicated.

#### 1. Introduction

Regular use of cannabis has been linked to mental health problems, including psychosis, depression, and cannabis use disorders (Gobbi et al., 2019; Jefsen et al., 2023; Volkow et al., 2014). Cannabis use is increasing globally, and there is concern that the liberalization of cannabis policy may result in greater cannabis use with potential downstream adverse impacts on mental health (Centre for Addiction and Mental Health (CAMH), 2014; Hasin et al., 2019; Murray and Hall,

2020). Growing evidence also supports an association between regular cannabis use and self-harm and suicidality (Borges et al., 2016; Denissoff et al., 2022; Fontanella et al., 2021; Gobbi et al., 2019). A US study found that amongst adolescents with mood disorders, a concurrent cannabis use disorder was associated with an increased risk of nonfatal self-harm and dying by suicide (Fontanella et al., 2021). A study in Finland found that cannabis use during adolescence was associated with an increased risk of self-harm, irrespective of concurrent mental health disorders and other substance use (Denissoff et al., 2022). Data from the

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https://doi.org/10.1016/j.jad.2024.01.264

Received 10 November 2023; Received in revised form 26 January 2024; Accepted 29 January 2024 Available online 1 February 2024 0165-0327/© 2024 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/bync-nd/4.0/). US have found a large rise in cannabis involvement in calls to poison centers for attempted suicide over the past decade (Graves et al., 2023). However, there is little data about how the legalization of cannabis, including for both medical and non-medical use, may result in changes in self-harm behaviour and whether such changes disproportionately impact specific subpopulations.

In Canada, access to medical cannabis began in 2001 for individuals with a limited list of severe or chronic medical conditions. In 2014, access to medical cannabis was greatly expanded for any individual who received authorization from a physician that they would therapeutically benefit from medical cannabis (Fischer et al., 2015). In December 2015, the Federal government committed to legalizing non-medical cannabis, which went into effect in October 2018. (Cannabis Act, 2018; Task Force on Cannabis Legalization and Regulation, 2016). In Ontario, the setting of this study, the implementation of legalization took a multi-phased approach to introducing cannabis products and stores. For the first year and a half following non-medical cannabis legalization, there were tight restrictions on the number of cannabis stores in the province (maximum of 62 stores, 0.55 per 100,000 individuals aged 15+) and only the sale of dried cannabis flower, seeds and, oil products were permitted (Myran et al., 2022a,b). Starting in early 2020, the sale of new products with high THC content (concentrates, vapes, and commercially produced edibles) was allowed, and restrictions on the number of stores were removed, resulting in a 19.6-fold increase in stores between April 2020 and December 2021 (1342 stores, 10.78 stores per 100,000 individuals) (Myran et al., 2023a,c). Details of this timeline are in Supplementary Table 1. There is no age limit for medical cannabis in Canada, and in Ontario, the minimum legal age of non-medical cannabis purchase is 19 years.

This study aimed to investigate changes in cannabis-involvement in self-harm emergency department (ED) visits at the population level in Ontario, Canada, over time with a focus on changes following specific changes in cannabis policy (medical cannabis liberalization and nonmedical cannabis legalization). To control for trends over time in substance use and competing events, including the COVID-19 pandemic, we compared the changes in the proportion of self-harm events with documented cannabis involvement to self-harm events with documented alcohol involvement (control condition). In addition, we examined pre-specified age and sex subgroups to understand how legalization may result in differences between populations.

# 2. Methods

The data used in this study complied with section 45 of Ontario's Personal Health Information Protection Act (PHIPA), obviating the need for review by a research ethics board. This study adhered to the reporting guidelines outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) to ensure comprehensive and transparent reporting.

#### 2.1. Study design, population, and data sources

We conducted a population-level repeated cross-sectional study capturing all ED visits for self-harm from January 2010 to December 2021 in Ontario, Canada's most populous province (population 14.2 million in 2021). We used diagnostic codes from discharge records to identify ED visits for self-harm and co-diagnosis of cannabis or alcohol during self-harm ED visits. We then identified the count of self-harm ED visits and the population at risk each month over our study period. We excluded self-harm ED visits from individuals who, at the time of their ED visits, were younger than ten years, were not residents of the province of Ontario, or were not eligible for the province's universal health care coverage (Ontario Health Insurance Plan [OHIP]) at the time of visit, or in the prior two years. These analyses were completed using seven linked databases, which capture 100 % of ED visits in Ontario. These datasets were linked using unique encoded identifiers and analyzed at ICES (formerly the Institute for Clinical Evaluative Sciences). Additional details regarding the coding can be found in Appendix A.

#### 2.2. Exposures

We divided our study into four policy periods corresponding to the different phases of cannabis legalization in Canada (Supplemental Table 1). First, the period from January 2010 to November 2015 was defined as the "pre-legalization" period. Second, December 2015 to September 2018 was defined as "cannabis liberalization," during which time medical cannabis was liberalized, and the government officially announced that non-medical cannabis would be legalized. Third, October 2018 to February 2020 was defined as "restricted non-medical legalization" during which time there were restrictions on the number of stores permitted to operate and the types of products available. Fourth, March 2020 to December 2021, during which time restrictions on stores were lifted, and new products flooded the cannabis market. This period coincided with the COVID-19 pandemic and was defined as "non-medical cannabis commercialization/COVID-19".

#### 2.3. Outcomes

Emergency department visits for self-harm incidents were identified using the International Classification of Diseases (ICD) 10th revision codes for deliberate self-poisoning (Y10-Y19) and other forms of selfharm incidents (Y28, X60-X67, X670-X679, X68-X74, X7400, X7401, X7408, X7409, X75-X84). ICD-10 codes have been validated for injury intent using health administrative data and/or are used by injury surveillance organizations globally. (Annest et al., 2014; Gabella et al., 2022; Kipsaina et al., 2015; Swain et al., 2019). To identify episodes where cannabis and self-harm events co-occurred, we employed the relevant ICD-10 coding for cannabis use, including codes for a mental and behavioural disorder resulting from cannabis use (F12.X) or cannabis poisoning (T40.7). Self-harm visits were also considered to have cannabis involvement if a cannabis code was used during hospital admission or for transfer to another ED. For acute care hospitalizations, we used ICD-10 codes. For admissions to specialized mental health beds, we also identified cannabis-involvement when an ICD-9 code 304.30 (cannabis dependence) or 305.20 (cannabis abuse) was listed as the main or contributing reason for hospitalizations. We used the same approach to identify self-harm ED visits with alcohol involvement using ICD-10 codes related to mental and behavioural disorders caused by alcohol use (F10.X) and ethanol poisoning (T51.0), along with ICD-9 codes (291.0×, 303.00, 303.90, and 305.00).

As a secondary outcome we identified whether self-harm visits were incident visits (visit with no self-harm visits in past 2 years) or recurrent visits (visit with 1 or more self-harm visits in past 2 years).

#### 2.4. Covariates

At the time of each self-harm ED visit, we extracted individual characteristics including; age and sex, neighbourhood income quintile, and rurality (defined using Statistics Canada's definitions and census data) (Canadian Institute for Health Information, 2018; Statistics Canada, 2016) and outpatient visits, ED visits, and hospitalizations for mental health or substance use in the prior two years, defined using diagnostic and billing codes used in mental health system performance measurements across Canada (MHASEF Research Team, 2018). All data in ICES are complete except for rural residence or neighbourhood income quintile (<0.3 % missing).

# 2.5. Statistical analysis

We first described baseline sociodemographic and self-harm characteristics of individuals with self-harm ED visits during our study and compared the individuals with and without cannabis involvement using standardized differences. For individuals with multiple ED visits, characteristics were identified at a randomly selected ED visit. The cannabisinvolvement and alcohol-involvement groups were mutually exclusive from the no alcohol or cannabis-involvement but not from each other.

We then calculated the monthly rates of 1) overall self-harm ED visits along with 2) cannabis- and 3) alcohol-involved self-harm ED visits over the four policy periods. We examined rates per 100,000 individuals aged 10+ and per 1000 self-harm ED visits. We used seasonally adjusted quasi-Poisson models to generate rate ratios with 95 % CI confidence intervals (CIs) comparing the three legalization policy periods to the prelegalization rates.

We used segmented Poisson regression analysis to examine immediate and gradual changes in monthly ED visits over the four policy periods. We analyzed the monthly count of ED visits for our primary outcome and control conditions with the natural log of the population at risk (individuals aged 10+ years). or total ED visits for self-harm included as an offset. We identified the pre-legalization trend and included three sets of slope and level changes corresponding to a) cannabis liberalization, b) restricted legalization and c) commercialization/COVID-19. We included indicators representing the four seasons to account for seasonal variation, and all analyses included first-order autocorrelation. Each interruption's immediate and gradual changes were expressed as Incidence Rate Ratios (IRR) with 95 % Confidence Intervals. All statistical analyses were completed using SAS Enterprise Guide 7.1 (SAS Institute, Cary, NC).

#### 2.6. Sensitivity analysis

During our entire study period, data sets capturing ED visits and acute care hospitalizations used ICD-10 codes. In April 2019, specialized mental health hospitals transitioned from the ICD-9 to the ICD-10 coding system. As a sensitivity analysis, we excluded cannabis-involvement from specialized mental health hospitals.

# 2.7. Additional analysis

To understand the associations of sex and age and cannabis legalization, we performed the above analyses using pre-specified, clinically and policy relevant (minimum legal age of non-medical cannabis purchase is 19 in Ontario) sex and age groups (10 to 18 years [adolescents], 19 to 24 years [transition age youth],  $\geq$ 25 years [adults]).

### 2.8. Ethics and approvals

The use of the data in this study was authorized under section 45 of Ontario's Personal Health Information Protection Act (PHIPA) and did not require review by a research ethics board or informed consent.

#### 3. Results

Over our study period, a total of 158,912 individuals incurred 240,388 ED visits for self-harm. Of the 158,912 individuals, 7810 (4.9%) had a self-harm ED visit that involved cannabis, 24,761 (15.6%) had a self-harm ED visit that involved alcohol, and 1858 (1.2%) had a self-harm ED visits that involved both alcohol and cannabis. For individuals with self-harm ED visits that involved both alcohol and cannabis. For individuals with self-harm ED visits that involved cannabis, the mean age (SD) was 28.6 years (13.6), with 2524 individuals (32.3%) falling within the 22–44 age range, and 4170 individuals (53.4%) being male. Over twice the number of individuals lived in the lowest neighbourhood income quintile (2406 individuals, 30.8%) compared to the highest income quintile (1118, 14.3%). In the two years before the self-harm ED visit, 1830 (23.4%) and 3477 (44.5%) of individuals had one or more acute care visits for substance use or a mental health condition, respectively. Similarly, 5715 (73.2%) individuals had one or more outpatient mental health or addiction visits with a family physician, pediatrician, or

psychiatrist in the two years before the ED visit, **see** Table 1. Individuals with self-harm ED visits that involved cannabis were, on average, younger than individuals with self-harm ED visits without cannabis or alcohol (mean age 28.6 vs 33.4 years, SD 0.31), more likely to be male (53.4 % vs 41.2 %, SD 0.25), more likely to have prior substance-use related ED visits or hospitalizations (23.4 % vs 11.4 %, SD 0.32) and more likely to have previous mental health ED visits or hospitalizations (44.5 % vs 33.0 %, SD 0.24). There were no differences in urban residence, neighbourhood income quintile, or prior outpatient mental health services.

#### 3.1. Characteristics and outcomes of self-harm ED visits

Our study included 8398 cannabis-involved self-harm ED visits. The most common cause of cannabis-involved self-harm ED visits was poisoning by cannabis (48.2 %) followed by harmful cannabis use (n = 28.9 %). Cannabis-involved self-harm was more likely to require admission to the hospital (57.7 % vs. 39.4 %) or admission to the ICU (15.8 % vs. 9.2 %) compared to self-harm injury ED visits without alcohol or cannabis involvement, see **STable 2** for detailed diagnostic codes and types of visits.

# 3.2. Overall trends

Changes in the monthly rate of overall self-harm ED visits and cannabis- and alcohol-involved self-harm ED visits are shown in Fig. 1. The annual rate of total ED visits for self-harm (with and without substance involvement) increased by 9.8 % over the 12-year study period (153.1 in 2010 to 168.1 in 2021 per 100,000 people). During the study the annual rate of cannabis-involved self-harm injury ED visits increased by 90.1 % (3.6 in 2010 to 6.9 in 2021 per 100,000 people), and the annual rate of alcohol-involved self-harm injury ED visits decreased by 17.3 % (22.2 in 2010 to 18.4 in 2021 per 100,000 people). The proportion of total self-harm ED visits that involved cannabis increased from 2.4 % in 2010 to 4.1 % in 2021, while the proportion that involved alcohol decreased from 14.5 % in 2010 to 10.9 % in 2021.

#### 3.3. Changes by legalization period

Total self-harm ED visits were relatively stable over the study period with small increases in the mean monthly rate of visits relative to the pre-legalization period during the cannabis liberalization (seasonally adjusted Risk Ratio [asRR] 1.12 95 % CI 1.09-1.15) and restricted legalization period (asRR 1.12 1.08-1.16) and no difference during the commercialization/COVID-19 period (asRR 1.03 1.00-1.07). Almost the entire increase in per capita cannabis-involved self-harm ED visits relative to pre-legalization occurred during the cannabis liberalization period (a<sub>s</sub>RR 1.71 95 % CI 1.59–1.83) with no further increases in rates of visits after non-medical cannabis legalization or during cannabis commercialization/COVID-19. In contrast, most of the decline in per capita alcohol-involved self-harm ED visits occurred during the cannabis commercialization/COVID-19 period (asRR 0.86 95 % CI 0.82-0.90) Mean monthly rates and relative risks comparing the four different policy periods can be found in Table 2. Similar but attenuated patterns were observed when examining rates of cannabis-involvement per total self-harm ED visits. Our sensitivity analysis excluding cannabis involvement in self-harm ED visits identified only hospitalizations to a specialized mental health bed (because of the migration coding from DSM 4 to 5 for the database capturing these hospitalizations) showed the same results see, STable 3.

The interrupted time series analysis of changes in the rate of cannabis-involved self-harm ED visits per 100,000 people aged 10+ years found that cannabis-involved self-harm ED visits were increasing by 1 % (IRR 1.01 95%CI 1.00–1.01) per month during the prelegalization period. Cannabis liberalization was associated with an immediate increase of 21 % (IRR, 1.21 95 % CI 1.08–1.35) and no gradual

#### Table 1

Characteristics of individuals with an ED visit for self-harm with and without cannabis or alcohol involvement between January 2010 and December 2021.

Number of individuals	Documented cannabis involvement	Documented alcohol involvement	Documented cannabis and alcohol involvement	No documented alcohol or cannabis involvement	Standardized difference (cannab vs no alcohol / cannabis)			
	N (%)							
	N = 7810	N = 24,761	N = 1858	N = 128,495				
Type of self-harm								
Poisoning	6901 (88.4)	20,735 (83.7)	1539 (82.8)	95, 750 (74.5)	0.36			
Other	1006 (12.9)	4330 (17.5)	349 (18.8)	33,719 (26.2)	0.34			
Sex								
Female	3640 (46.6)	13,186 (53.3)	891 (48.0)	75,598 (58.8)	0.25			
Male	4170 (53.4)	11,575 (46.7)	967 (52.0)	52,897 (41.2)	0.25			
4.00								
Age Maan   CD	00 E6 (10 C4)	07.00 (15.40)	29 (4 (12 05)	22.41 (17.96)	0.21			
Mean $\pm$ SD	28.56 (13.64)	37.80 (15.40)	28.64 (13.05)	33.41 (17.86)	0.31			
10–14 years	336 (4.3)	224 (0.9)	56 (3.0)	8610 (6.7)	0.11			
15–18 years	1897 (24.3)	1914 (7.7)	433 (23.3)	23,776 (18.5)	0.14			
19-24 years	1875 (24.0)	4366 (17.6)	463 (24.9)	23,156 (18.0)	0.15			
25–44 years	2524 (32.3)	9424 (38.1)	620 (33.4)	38,874 (30.3)	0.05			
45+ years	1178 (15.1)	8833 (35.7)	286 (15.4)	34,079 (26.5)	0.29			
Rurality								
Urban	6775 (86.7)	21,128 (85.3)	1615 (86.9)	111,414 (86.7)	0.00			
Rural	977 (12.5)	3505 (14.2)	229 (12.3)	16,353 (12.7)	0.00			
Neighbourhood income	quintile							
1 (poorest)	2406 (30.8)	7657 (30.9)	577 (31.1)	36,611 (28.5)	0.05			
2	1713 (21.9)	5176 (20.9)	388 (20.9)	27,159 (21.1)	0.02			
3	1274 (16.3)	4200 (17.0)	306 (16.5)	23,184 (18.0)	0.05			
4	1220 (15.6)	3823 (15.4)	284 (15.3)	21,270 (16.6)	0.02			
5 (Richest)	1118 (14.3)	3637 (14.7)	279 (15.0)	19,188 (14.9)	0.02			
Substance use acute care	visits in past 2 years							
Any	1830 (23.4)	8018 (32.4)	578 (31.1)	14,686 (11.4)	0.32			
Alcohol	793 (10.2)			6102 (4.7)	0.32			
	. ,	6550 (26.5) 564 (2.2)	403 (21.7)					
Opioids Connobio	262 (3.4)	564 (2.3)	40 (2.2)	3108 (2.4)	0.06			
Cannabis	366 (4.7)	238 (1.0)	62 (3.3)	1120 (0.9)	0.23			
Unspecified Other	225 (2.9) 940 (12.0)	993 (4.0) 2414 (9.7)	74 (4.0) 248 (13.3)	1376 (1.1) 7689 (6.0)	0.13 0.21			
Montal haalth aguta	visite in post 2							
Mental health acute care		10.061 (40.6)	012 (40 1)	42 412 (22 0)	0.34			
Any	3477 (44.5)	10,061 (40.6)	913 (49.1)	42,413 (33.0)	0.24			
Mood disorder	1792 (22.9)	5133 (20.7)	472 (25.4)	21,978 (17.1)	0.15			
Anxiety disorder Schizophrenia/	1895 (24.3)	5090 (20.6)	462 (24.9)	22,901 (17.8)	0.16			
psychosis	592 (7.6)	972 (3.9)	121 (6.5)	5922 (4.6)	0.12			
Deliberate self harm	1549 (19.8)	4Se,773 (19.3)	480 (25.8)	11,139 (8.7)	0.32			
Not classified	845 (10.8)	1715 (6.9)	227 (12.2)	8209 (6.4)	0.16			
Outpatient mental health	n and addiction visits in pa	st 2 years						
Any	5715 (73.2)	18,492 (74.7)	1399 (75.3)	89,168 (69.4)	0.08			
Family physician or	5290 (67.7)	17,267 (69.7)	1310 (70.5)	82,400 (64.1)	0.08			
pediatrician Developtrist								
Psychiatrist	3322 (42.5)	9251 (37.4)	825 (44.4)	45,867 (35.7)	0.14			

\*Groups are not mutually exclusive, individuals can appear in both groups if they had a self-harm ED visit with alcohol involvement and a separate self-harm ED visit with cannabis involvement, or a self-harm ED visit with both alcohol and cannabis involvement.

\*Characteristics taken from a randomly selected ED visit not involving alcohol or cannabis.

change over time. Non-medical legalization with restrictions was associated with a significant monthly slope decrease of 3.0 % (IRR, 0.97 95 % CI 0.96–0.98) and no immediate change. Non-medical legalization with commercialization/COVID-19 was associated with a significant monthly slope increase of 2.0 % (IRR, 1.02 95 % CI 1.01–1.04) and no immediate change. Detailed immediate and gradual changes for each policy change for overall self-harm visits and for alcohol- and cannabisinvolved self-harm visits per 1000 self-harm visits can be found in Table 3.

# 3.4. Changes by age, sex and incident vs. recurrent visits

Changes in the annual rate of self-harm ED visits by age and sex subgroups and by incident or recurrent ED visits are Fig. 2. The smallest increases over time rates of visits per 100,000 individuals in cannabis-involved self-harm ED visits were in individuals aged 10–18 years ( $a_s$ RR in men 0.95 95 % CI 0.77–1.17,  $a_s$ RR in women 1.34 95 % CI 1.14–1.58, commercialization/ COVID-19 period relative to prelegalization). Individuals aged 19–24 and 25+ experienced larger increases. Increases in women were greater than for men in both 19–24 year-olds ( $a_s$ RR in women 2.75 95 % CI 2.26–3.34 vs.  $a_s$ RR in men 1.51

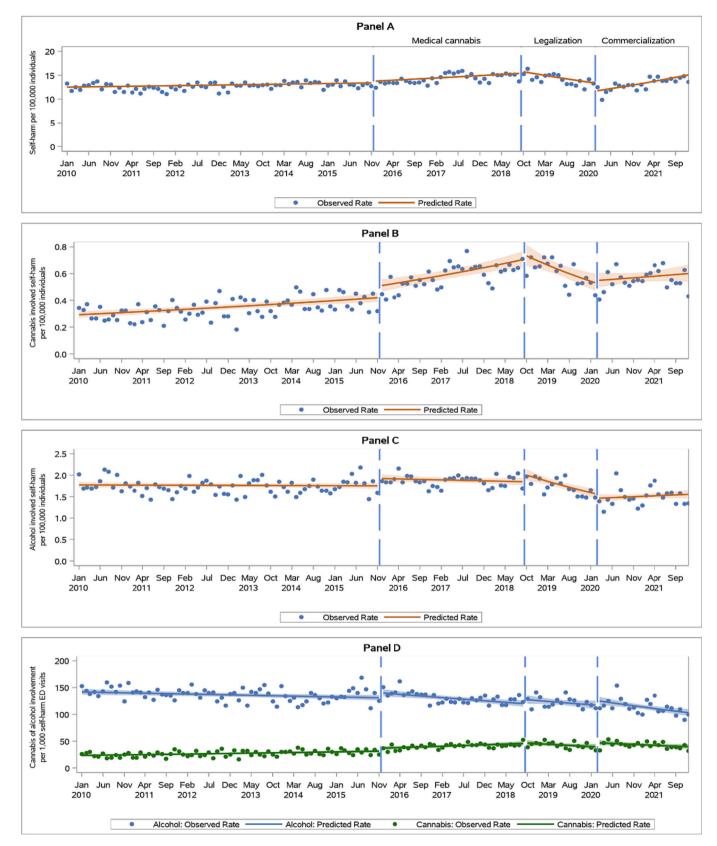


Fig. 1. Monthly time series showing rates of self-harm ED visits between 2010 and 2021. The dashed lines divides the four policy periods: before-legalization, prelegalization (P1), after legalization with restrictions (P2), and after legalization with commercialization/COVID-19 (P3). Panels A, B and C are self-harm visits per 100,000 individuals. Panel D is cannabis and alcohol involvement per 1000 self-harm ED visits.

#### Table 2

Changes in overall, cannabis-involved and alcohol-involved self-harm visits over the four periods of cannabis legalization in Canada.

Policy period	P1: Pre-	P2: Medical Cannabis	P3: legalization with	P4: legalization with	P2 vs P1	P3 Vs P1	P4 vs P1
	legalization (Jan 2010 - Nov 2015)	liberalization (Dec 2015 - Sept 2018) <sup>a</sup>	restrictions (Oct 2018 - Feb 2020) <sup>b</sup>	commercialization/ COVID-19 (March 2020 - Dec 2021)	Risk ratio <sup>A</sup> (95%CI)		
Number of self-ha	arm ED visits						
Total	108,990	61,714	31,449	38,235			
Cannabis involvement	2927	2516	1335	1620			
Alcohol involvement	14,911	8051	3846	4342	NA		
Cannabis and alcohol- involvement	695	596	304	332			
Mean monthly se	lf-harm ED visits per 10	0,000 individuals					
Total	12.69	14.26	14.14	13.13	$1.12 (1.09-1.15) \\1.71 (1.59-1.83) \\1.07 (1.03-1.11)$	1.12 (1.08–1.16) 1.77 (1.62–1.93) 1.00 (0.95–1.05)	1.03 $(1.00-1.07)$ $1.63$ $(1.50-1.76)$ $0.86$ $(0.82-0.90)$
Cannabis involvement	0.34	0.58	0.60	0.56			
Alcohol involvement	1.74	1.86	1.73	1.49			
Cannabis and alcohol- involvement	0.08	0.14	0.14	0.11	1.70 (1.52–1.90)	1.71 (1.49–1.97)	1.41 (1.23–1.61)
Moon monthly w	site a set 1000 self herem	ED minito					
Cannabis involvement	sits per 1000 self-harm 1 26.77	40.62	42.43	42.58	1.52 (1.43–1.62) 0.95 (0.92–0.99)	1.58 (1.47–1.71) 0.90 (0.86–0.94)	1.57 (1.47–1.69) 0.83 (0.79–0.87)
Alcohol involvement	136.97	130.88	122.34	113.91			
Cannabis and alcohol- involvement	6.37	9.68	9.68	8.76	1.51     1.53       (1.35-1.69)     (1.46-1.73)		1.36 (1.19–1.56)

<sup>a</sup> Liberalization of medical cannabis under the Marihuana for Medical Purposes Regulations (MMPR) regime enacted on April 1, 2014, and announcement of Government that non-medical cannabis would be legalized in December 2015.

<sup>b</sup> Legalization of non-medical cannabis under the Cannabis Act on October 17, 2018.

# Table 3

Relative changes in monthly rates of overall self-harm ED visits, cannabis-involved and alcohol-involved self-harm ED visits over four policy periods in Ontario, Canada.

Sundan					
	Self-harm per capita	Self-harm with cannabis involvement per capita	Self-harm with alcohol involvement per capita	Self-harm with cannabis involvement per 1000 self harm	Self-harm with alcohol involvement per 1000 self harm
Incidence rate ra	atio (95 % CI)				
Period 1 slope	1.00 (1.00–1.00)	1.01 (1.00–1.01)	1.00 (1.00–1.00)	1.00 (1.00–1.01)	1.00 (1.00–1.00)
Period 2 level change	1.02 (1.00–1.05)	1.21 (1.08–1.35)	1.10 (1.04–1.16)	1.18 (1.05–1.31)	1.07 (1.01–1.13)
Period 2 slope change	1.00 (1.00–1.00)	1.00 (1.00–1.01)	1.00 (1.00–1.00)	1.00 (1.00–1.01)	1.00 (0.99–1.00)
Period 2 slope	1.00 (1.00–1.00)	1.01 (1.01–1.01)	1.00 (1.00–1.00)	1.01 (1.00–1.01)	1.00 (0.99–1.00)
Period 3 level change	1.03 (1.00–1.06)	1.06 (0.93–1.21)	1.10 (1.02–1.19)	1.02 (0.90–1.17)	1.07 (0.99–1.15)
Period 3 slope change	0.99 (0.98–0.99)	0.97 (0.96–0.98)	0.99 (0.98–0.99)	0.98 (0.97–1.00)	1.00 (0.99–1.01)
Period 3 slope	0.99 (0.99–0.99)	0.98 (0.97–0.99)	0.98 (0.98–0.99)	0.99 (0.98–1.00)	0.99 (0.99–1.00)
Period 4 level change	0.87 (0.84–0.89)	1.03 (0.88–1.20)	0.93 (0.85–1.02)	1.19 (1.02–1.39)	1.07 (0.98–1.18)
Period 4 slope change	1.02 (1.02–1.02)	1.02 (1.01–1.04)	1.02 (1.01–1.03)	1.00 (0.99–1.02)	1.00 (0.99–1.00)
Period 4 slope	1.01 (1.01–1.01)	1.00 (1.00–1.01)	1.00 (1.00–1.01)	0.99 (0.98–1.00)	0.99 (0.99–1.00)

Period 1: Pre-Legalization (Jan 2010-Nov 2015).

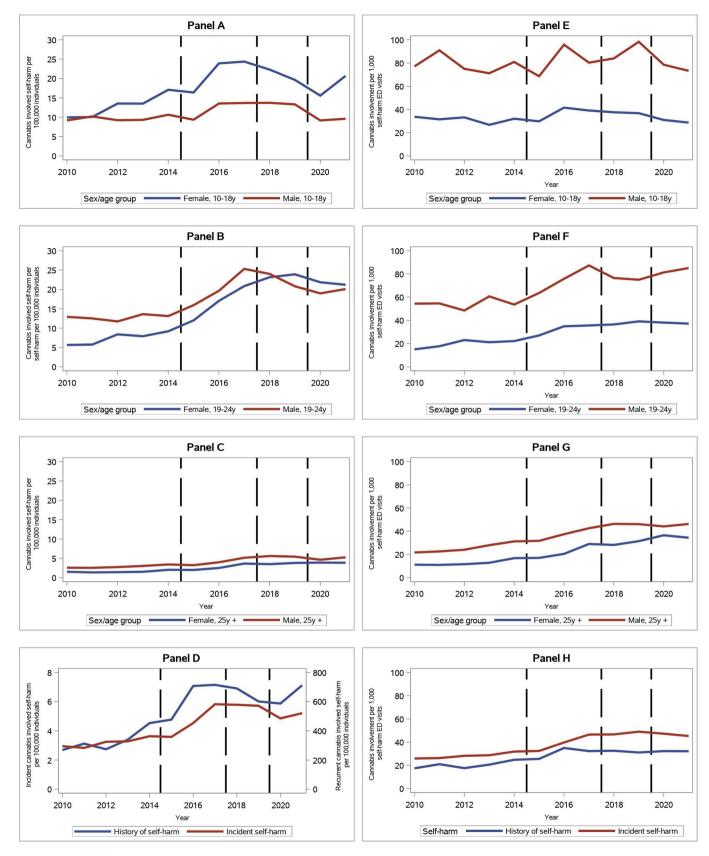
Period 2: Medical cannabis liberalization (Dec 2015-Sep 2018).

Period 3: Legalization with restrictions (Oct 2018-Feb 2020).

Period 4: Legalization with commercialization/COVID-19 (Mar 2020-Dec 2021).

95 % CI 1.26–1.80 commercialization/ COVID-19 period relative to prelegalization) and 25+ (asRR in women 2.39 95 % CI 2.06–2.77 vs. asRR in men 1.69 95 % CI 1.49–1.92 commercialization/COVID-19 period

relative to pre-legalization). Increases over time in incident vs. recurrent visits were similar (a<sub>s</sub>RR for incident visits 1.56 CI 1.43–1.69, vs a<sub>s</sub>RR for recurrent visits1.92 CI 1.68–2.19, commercialization/COVID-19 period



**Fig. 2.** Annual rates of self-harm ED visits with cannabis involvement between 2010 and 2021 in Ontario. The dashed lines divide the four policy periods: before-legalization, pre-legalization (P1), after legalization with restrictions (P2), and after legalization with commercialization/COVID-19 (P3). Panels A, B, C and D are self-harm visits per capita. Panels E, F, G, and H are self-harm visits per 1000 self-harm ED visits. Panel A & E = age 10–18, Panel B & F = age 19–24, Panel C & G = age 25+, Panel D and H = incident (first time in at least 2 years) vs recurrent self-harm ED visits.

relative to pre-legalization). Similar but attenuated increases were observed for rates per 1000 self-harm ED visits. Detailed rates per 100,000 individuals and per 1000 self-harm events can be found in **STable4.** 

# 4. Discussion

During the 12-year study period, the annual rate of cannabisinvolved self-harm injury ED visits increased by 90.1 % between 2010 and 2021, and by the end of our study period, 4.2 % of self-harm ED visits had cannabis-involvement. Cannabis-involvement in self-harm injury ED visits increased substantially after the liberalization of medical cannabis but did not increase further during the non-medical cannabis legalization or subsequent commercialization/COVID-19 period. Attributing changes in cannabis-involvement in self-harm ED visits to specific policies is challenging. The findings may reflect a greater risk of self-harm episodes arising from increasing access to cannabis. In contrast, individuals at elevated risk of self-harm may be increasingly using cannabis to attempt to alleviate underlying mental health symptoms. Contextually, over the same study period, the annual rate of alcohol-involved self-harm injuries decreased by 17.3 %, demonstrating large shifts in patterns of substance use involvement in self-harm. Our findings also demonstrate important differences by subgroups with older adults and women experiencing the largest increase in cannabis-involved self-harm ED visits over time.

There is currently limited research on the potential impact of cannabis legalization on rates of self-harm. Studies from the US have found no significant association between state-level cannabis legalization and self-harm events overall but have found a modest increase in self-harm events in men younger than 40 years. However, these studies did not specifically examine cannabis involvement in self-harm events or deaths (Doucette et al., 2021; Matthay et al., 2021). A single Canadian study from New Brunswick found increased detection of cannabis in deceased individuals with toxicology screens after legalization, particularly for individuals who died by suicide (Jordan et al., 2022). Importantly, the study was not able to determine whether or not cannabis use contributed to deaths. A strength of our study was that we identified cannabis-involvement with self-harm ED visits when the treating clinical team felt that cannabis use was a main or contributing reason for the self-harm visit. Our findings are consistent with data from four population-representative surveys which have all found large increases in cannabis use over the course of our study period (Government of Canada, 2019). Similarly, ED visits and hospitalizations due to cannabis in Ontario have increased in the past 12 years (Myran et al., 2023a,b; Myran et al., 2022b). Our study suggests that there may have been corresponding increases in cannabis-involvement in self-harm ED visits.

Almost the entire observed increase in cannabis-involvement in selfharm ED visits occurred after the liberalization of medical cannabis in 2014 and the announcement by the Federal Government that they intended to legalize non-medical cannabis in 2015. During this time there was a proliferation of illicit, and gray market medical and nonmedical cannabis dispensaries and online vendors in Canada (Mahamad and Hammond, 2019). Between 2014-2015 and 2015-2016, the number of registered medical cannabis users in Canada increased by 189.5 %. The estimated proportion of the Canadian population using medical cannabis daily or near daily increased from 2.4 % in 2014 to 3.6 % in 2017 (Lucas, 2008; Shim et al., 2023). Cannabis-involvement in self-harm ED visits began declining after the legalization of non-medical cannabis in 2018, which involved strict restrictions on stores and products. This finding is consistent with other studies and may be the result of initial challenges to accessing legal cannabis due to legal product and store shortages and reductions in access to illicit sources (Armstrong, 2021; Myran et al., 2022c). Visits began to increase again during a period of cannabis commercialization/the COVID-19 pandemic, and as Canada's legal cannabis market continues to expand,

further monitoring is indicated.

Importantly, while the increase in cannabis-involved self-harm ED visits following medical cannabis liberalization suggests these events may be related, our study design is not causal. Increasing cannabis use may have made individuals more likely to engage in self-harm episodes, consistent with growing evidence of the link between cannabis use and self-harm (Fontanella et al., 2021; Gobbi et al., 2019). In contrast, individuals experiencing substantial emotional and mental distress, who are at high risk of self-harm, may have increased use of cannabis in patterns that may cause harm as it became more available, which was identified and documented by their treating teams (Coughenour et al., 2021; Romm et al., 2022). Regardless of direction, these findings suggest that greater efforts to identify cannabis use and offer appropriate counseling and treatment may be indicated in individuals presenting with self-harm to the ED. Of relevance to clinicians and policymakers, we observed substantial differences in changes over time in cannabisinvolvement in ED visits for self-harm by age and sex. Throughout the study cannabis-involvement in self-harm ED visits did not increase for vouth younger than 19 years of age. These findings may reflect the success of measures to prevent increases in access to cannabis sources for individuals below the minimal legal age of purchase and public messaging about potential adverse impacts of cannabis use in youth. In contrast, cannabis use appears to be increasingly associated with selfharm events in adults 19 and older, particularly women. Increased inquiry about cannabis use and counseling may be indicated in older adults with risk factors for self-harm.

#### 4.1. Limitations

There are limitations to our study. First, part of the increase in cannabis-involvement in self-harm ED visits may reflect increasing awareness of health care providers about cannabis use and changing patterns of inquiry and documentation. Second, although our study outcome is likely specific for cannabis involvement in self-harm events, it is likely insensitive and does not fully capture all self-harm ED visits that involved cannabis use or intoxication. Third, while our codes indicate that a cannabis diagnosis contributed to the self-harm ED visit, we cannot determine whether cannabis caused the self-harm ED visit or was being used by a patient to attempt to mitigate the symptoms of underlying mental distress. Fourth, other competing events during the policy periods complicate the causal attribution of our findings. There was a large decline in overall self-harm ED visits in 2018 which is unlikely related to cannabis legalization and influenced our results for that period. In addition, the COVID-19 pandemic, which coincided with the commercialization of non-medical cannabis, may have led to important changes in emergency department visits for self-harm (Madigan et al., 2023). Further research is indicated post-pandemic to monitor changes in cannabis-involvement in self-harm ED visits as health service use returns to normal levels and pandemic-related stressors are diminished. Finally, the relationship between alcohol and cannabis use, specifically whether individuals will substitute one for another or use them together, is unclear (Gunn et al., 2022). Nonetheless, the declines in alcoholinvolvement in self-harm over time provide important context on shifting risk factors for self-harm events.

### 5. Conclusions

The findings of this repeated cross-sectional study suggest that cannabis-involvement with self-harm episodes has increased substantially over time and that the liberalization of medical cannabis may have contributed to this trend. Importantly, the study is unable to identify whether cannabis use lead to self-harm episodes or was increasingly being used in an attempt to alleviate symptoms in individuals at highrisk of self-harm. Our findings also suggest that older adults and women may be at an elevated risk of cannabis-involved self-harm. Given the potential implications of these findings, greater efforts to identify cannabis use and offer appropriate counseling and treatment may be indicated.

#### Funding

Dr. Myran was supported with a Research Fellow Salary Award from the Canadian Institutes of Health Research and the University of Ottawa Department of Family Medicine. Dr. Tanuseputro was supported by a PSI Graham Farquharson Knowledge Translation Fellowship. This study was supported by the University of Ottawa site of ICES, which is funded by an annual grant from the Ontario Ministry of Health and Ministry of Long-Term Care. This study also received funding from Canadian Institutes for Health Research (grant No 452360).

#### Analytic code and research material availability

We obtained study data from de-identified and linked health administrative databases housed at ICES. ICES is an independent, nonprofit research institute funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). As a prescribed entity under Ontario's privacy legislation, ICES is authorized to collect and use health care data for the purposes of health system analysis, evaluation and decision support. Secure access to these data is governed by policies and procedures that are approved by the Information and Privacy Commissioner of Ontario. In 2018, the institute formerly known as the Institute for Clinical Evaluative Sciences formally adopted the initialism ICES as its official name.

The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (e.g., healthcare organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

# CRediT authorship contribution statement

Daniel T. Myran: Conceptualization, Formal analysis, Funding acquisition, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. Adrienne Gaudreault: Project administration, Writing – original draft, Writing – review & editing. Michael Pugliese: Formal analysis, Software, Validation. Peter Tanuseputro: Funding acquisition, Supervision, Writing – review & editing. Natasha Saunders: Writing – review & editing.

# Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

# Data availability

The data set from this study is held securely at ICES. While datasharing agreements prohibit ICES from making the data set publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at https://www.ices.on.ca/DAS.

#### Acknowledgements

This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC).

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2024.01.264.

#### References

- Annest, J.L., Hedegaard, H., Chen, L.H., Warner, M., Smalls, E.A., 2014. Proposed Framework for Presenting Injury Data Using ICD-10-CM External Cause of Injury Codes.
- Armstrong, M., 2021. Legal cannabis market shares during Canada's first year of recreational legalisation. Int. J. Drug Policy 88, 103028. https://doi.org/10.1016/j. drugpo.2020.103028.
- Borges, G., Bagge, C.L., Orozco, R., 2016. A literature review and meta-analyses of cannabis use and suicidality. J. Affect. Disord. 195, 63–74.
- Canadian Institute for Health Information, 2018. Measuring Health Inequalities: A ToolkitArea-Level Equity Stratifiers Using PCCF and PCCF+.
- Cannabis Act, 2018. Pub. L. No. (S.C. 2018, c. 16), Parliament of Canada.
- Centre for Addiction and Mental Health (CAMH), 2014. Cannabis Policy Framework. htt ps://www.camh.ca/-/media/files/pdfs—public-policy-submissions/camhcannabis policyframework-pdf.pdf.
- Coughenour, P., Sadicario, J.S., Karjane, N., Parlier-Ahmad, A.B., Phipps, L., Svikis, D.S., 2021. Prevalence and social acceptability of cannabis, tobacco, and alcohol use in adult women. Women's Health Reports 2 (1), 452–458.
- Denissoff, A., Niemelä, S., Scott, J.G., Salom, C.L., Hielscher, E., Miettunen, J., Alakokkare, A., Mustonen, A., 2022. Does cannabis use in adolescence predict selfharm or suicide? Results from a Finnish Birth Cohort Study. Acta Psychiatr. Scand. 145 (3), 234–243.
- Doucette, M.L., Borrup, K.T., Lapidus, G., Whitehill, J.M., McCourt, A.D., Crifasi, C.K., 2021. Effect of Washington state and Colorado's cannabis legalization on death by suicides. Prev. Med. 148, 106548.
- Fischer, B., Kuganesan, S., Room, R., 2015. Medical Marijuana programs: implications for cannabis control policy—observations from Canada. Int. J. Drug Policy 26 (1), 15–19. https://doi.org/10.1016/J.DRUGPO.2014.09.007.
- Fontanella, C.A., Steelesmith, D.L., Brock, G., Bridge, J.A., Campo, J.V., Fristad, M.A., 2021. Association of cannabis use with self-harm and mortality risk among youths with mood disorders. JAMA Pediatr. 175 (4), 377–384.
- Gabella, B.A., Hume, B., Li, L., Mabida, M., Costich, J., 2022. Multi-site medical record review for validation of intentional self-harm coding in emergency departments. Inj. Epidemiol. 9 (1), 1–11.
- Gobbi, G., Atkin, T., Zytynski, T., Wang, S., Askari, S., Boruff, J., Ware, M., Marmorstein, N., Cipriani, A., Dendukuri, N., 2019. Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: a systematic review and meta-analysis. JAMA Psychiatry 76 (4), 426–434.
- Government of Canada, 2019. Canadian Alcohol and Drugs Survey (CADS): summary of results for 2019. https://www.canada.ca/en/health-canada/services/canadian -alcohol-drugs-survey/2019-summary.html.
- Graves, J.M., Dilley, J.A., Klein, T., Liebelt, E., 2023. Suspected suicidal cannabis exposures reported to US poison centers, 2009-2021. JAMA Netw. Open 6 (4), e239044.
- Gunn, R.L., Aston, E.R., Metrik, J., 2022. Patterns of cannabis and alcohol co-use: substitution versus complementary effects. Alcohol Res. 42 (1).
- Hasin, D.S., Shmulewitz, D., Sarvet, A.L., 2019. Time trends in US cannabis use and cannabis use disorders overall and by sociodemographic subgroups: a narrative review and new findings. Am. J. Drug Alcohol Abuse 45 (6), 623–643.
- Jefsen, O.H., Erlangsen, A., Nordentoft, M., Hjorthøj, C., 2023. Cannabis use disorder and subsequent risk of psychotic and nonpsychotic unipolar depression and bipolar disorder. JAMA Psychiatry. https://doi.org/10.1001/ JAMAPSYCHIATRY.2023.1256.
- Jordan, A., Sherazi, A., Flewelling, A.J., Northrup, V., Naseemuddin, A., Shea, J.L., 2022. Identification of cannabinoids in post-mortem blood samples from the province of New Brunswick before and after recreational cannabis legalization. Int. J. Drug Policy 103, 103629.
- Kipsaina, C., Ozanne-Smith, J., Routley, V., 2015. The WHO injury surveillance guidelines: a systematic review of the non-fatal guidelines' utilization, efficacy and effectiveness. Public Health 129 (10), 1406–1428.
- Lucas, P.G., 2008. Regulating compassion: an overview of Canada's federal medical cannabis policy and practice. Harm Reduct. J. 5 (1), 1–13.
- Madigan, S., Korczak, D.J., Vaillancourt, T., Racine, N., Hopkins, W.G., Pador, P., Hewitt, J.M.A., AlMousawi, B., McDonald, S., Neville, R.D., 2023. Comparison of paediatric emergency department visits for attempted suicide, self-harm, and suicidal ideation before and during the COVID-19 pandemic: a systematic review and meta-analysis. Lancet Psychiatry 10 (5), 342–351. https://doi.org/10.1016/ S2215-0366(23)00036-6.
- Mahamad, S., Hammond, D., 2019. Retail price and availability of illicit cannabis in Canada. Addict. Behav. 90, 402–408.
- Matthay, E.C., Kiang, M.V., Elser, H., Schmidt, L., Humphreys, K., 2021. Evaluation of state cannabis laws and rates of self-harm and assault. JAMA Netw. Open 4 (3), e211955.
- MHASEF Research Team, 2018. Mental health and addictions system performance in Ontario: a baseline scorecard. https://www.ices.on.ca/Publications/Atlases-and-Reports/2018/MHASEF.

#### D.T. Myran et al.

Murray, R.M., Hall, W., 2020. Will legalization and commercialization of cannabis use increase the incidence and prevalence of psychosis? JAMA Psychiatry 77 (8), 777–778.

- Myran, D.T., Imtiaz, S., Konikoff, L., Douglas, L., Elton-Marshall, T., 2022a. Changes in health harms due to cannabis following legalisation of non-medical cannabis in Canada in context of cannabis commercialisation: a scoping review. Drug Alcohol Rev. https://doi.org/10.1111/DAR.13546.
- Myran, D.T., Pugliese, M., Tanuseputro, P., Cantor, N., Rhodes, E., Taljaard, M., 2022b. The association between recreational cannabis legalization, commercialization and cannabis-attributable emergency department visits in Ontario, Canada: an interrupted time-series analysis. Addiction. https://doi.org/10.1111/ADD.15834.
- Myran, D.T., Staykov, E., Cantor, N., Taljaard, M., Quach, B.I., Hawken, S., Tanuseputro, P., 2022c. How has access to legal cannabis changed over time? An analysis of the cannabis retail market in Canada 2 years following the legalisation of
- analysis of the cannabis retain market in Canada 2 years following the regarisation of recreational cannabis. Drug Alcohol Rev. 41 (2), 377–385. https://doi.org/10.1111/ DAR.13351.
   Myran, D.T., Friesen, E.L., Dickson, S., Konikoff, L., Arora, G., Tanuseputro, P., 2023a.
- Access to legal canabis market in Canada over the four years following non-medical cannabis legalisation. Drug Alcohol Rev. https://doi.org/10.1111/DAR.13650.
- Myran, D.T., Gaudreault, A., Konikoff, L., Talarico, R., Pacula, R.L., 2023b. Changes in Cannabis-attributable hospitalizations following nonmedical Cannabis legalization

in Canada. JAMA Netw. Open 6 (10), e2336113. https://doi.org/10.1001/ JAMANETWORKOPEN.2023.36113.

- Myran, D.T., Imtiaz, S., Konikoff, L., Douglas, L., Elton-Marshall, T., 2023c. Changes in health harms due to cannabis following legalisation of non-medical cannabis in Canada in context of cannabis commercialisation: a scoping review. Drug Alcohol Rev. 42 (2), 277–298.
- Romm, K.F., Wang, Y., Ma, Y., Wysota, C.N., Blank, M.D., Huebner, D.M., Roche, K.M., Berg, C.J., 2022. The reciprocal relationships of social norms and risk perceptions to cigarette, e-cigarette, and cannabis use: cross-lagged panel analyses among US young adults in a longitudinal study. Drug Alcohol Depend. 238, 109570.
- Shim, M., Nguyen, H., Grootendorst, P., 2023. Lessons from 20 years of medical cannabis use in Canada. PloS One 18 (3), e0271079.
- Statistics Canada, 2016. Population Centre and Rural Area Classification 2016. htt ps://www.statcan.gc.ca/en/subjects/standard/pcrac/2016/introduction.
- Swain, R.S., Taylor, L.G., Braver, E.R., Liu, W., Pinheiro, S.P., Mosholder, A.D., 2019. A systematic review of validated suicide outcome classification in observational studies. Int. J. Epidemiol. 48 (5), 1636–1649.
- Task Force on Cannabis Legalization and Regulation, 2016. A Framework for the Legalization and Regulation of Cannabis in Canada.
- Volkow, N., Baler, R., Compton, W., Weiss, S., 2014. Adverse health effects of marijuana use. N. Engl. J. Med. 370 (23), 2219–2227.