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Risk of Dementia in Individuals With Emergency Department Visits or Hospitalizations Due to Cannabis

Daniel T. Myran, MD, MPH; Michael Pugliese, MSc; Lyndsay D. Harrison, MSc; Nathan M. Stall, MD, PhD; Colleen Webber, PhD

IMPORTANCE Cannabis use is associated with short-term memory impairment and long-term changes in brain structure; however, little is known about whether disordered cannabis use is associated with an increased risk of a dementia diagnosis.

OBJECTIVE To investigate the association between emergency department visits or hospitalizations (acute care encounters) due to cannabis and future dementia diagnosis.

DESIGN, SETTING, AND PARTICIPANTS Population-based, retrospective, matched cohort study using health administrative data from Ontario, Canada, between 2008 and 2021 (with follow-up until 2022) including all individuals aged 45 to 105 years living in Ontario who were eligible and did not have a diagnosis of dementia at cohort entry (2 620 083 individuals excluded).

EXPOSURE Individuals with incident acute care due to cannabis use, defined using *International Classification of Diseases and Related Health Problems, Tenth Revision* coding.

MAIN OUTCOMES AND MEASURES We used cause-specific adjusted hazard models to compare new diagnoses of dementia (from a validated algorithm) between individuals with acute care due to cannabis use with (1) individuals with all-cause acute care (excluding cannabis), (2) the general population, and (3) individuals with acute care due to alcohol use.

RESULTS The study included 6 086 794 individuals, of whom 16 275 (0.3%) had incident acute care due to cannabis use (mean age, 55.2 [SD, 8.3] years; 60.3% male). Annual rates of incident acute care due to cannabis use increased 5.0-fold in individuals aged 45 to 64 years (from 10.16 to 50.65 per 100 000) and 26.7-fold in individuals aged 65 years or older (from 0.65 to 16.99 per 100 000) between 2008 and 2021. Individuals with incident acute care due to cannabis use were at a 1.5-fold and 3.9-fold increased risk of dementia diagnosis within 5 years relative to individuals with all-cause acute care and the general population of the same age and sex, respectively (absolute rates of dementia diagnosis: 5.0% for cannabis-related acute care, 3.6% for all-cause acute care, and 1.3% in the general population). After adjustment for sociodemographics and chronic health conditions, individuals with acute care due to cannabis use remained at elevated risk relative to those with all-cause acute care (adjusted hazard ratio [aHR], 1.23; 95% CI, 1.09-1.39) and the general population (aHR, 1.72; 95% CI, 1.38-2.15). Individuals with acute care due to cannabis use were at lower risk than those with acute care due to alcohol use (aHR, 0.69; 95% CI, 0.62-0.76).

CONCLUSIONS AND RELEVANCE Individuals with cannabis use severe enough to require hospital-based care were at increased risk of a new dementia diagnosis compared with those with all-cause hospital-based care or the general population. These findings have important implications considering increasing cannabis use among older adults.

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Daniel T. Myran, MD, MPH, Ottawa Hospital Research Institute, 1053 Carling Ave, Box 693, Ottawa, ON K1Y 4E9, Canada (dmyran@ohri.ca).

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Cannabis is one of the most commonly used drugs, with an estimated 228 million individuals who use cannabis worldwide.[1] Cannabis use has increased over time in North America, with some of the largest increases occurring in older adults.[2,3] In Canada's most populous province of Ontario (15 million residents), past-year cannabis use in adults aged 50 years or older increased from 5.4% in 2010 to 21.8% in 2023.[3] Increasing use among older adults has occurred for a variety of reasons, including medical use for a myriad of conditions and symptoms and invigorated interest in nonmedical or recreational use in jurisdictions that have legalized cannabis.[4-6] Cannabis use is associated with structural brain changes and short-term memory problems.[7-11] In addition, cannabis use may increase the risk of several comorbidities (eg, hypertension, traumatic brain injury, depression) associated with dementia.[12] Consequently, there is concern that rising cannabis use in older adults could increase the risk of cognitive decline and dementia.[8] However, there is limited information about the long-term effects of heavy and regular cannabis use on cognition and the risk of Alzheimer disease in older adults.

The epidemiological literature studying the association between cannabis use and risk of dementia is limited, and the few existing studies have small sample sizes and often identified exposure to cannabis and cognitive outcomes at a single point in time.[13,14] A study of US veterans found that individuals with a diagnosis of cannabis use disorder had a greater risk of cognitive disorder than those without cannabis use disorder.[15] Brain imaging studies have shown functional, structural, and connectivity changes in the brains of individuals who regularly use cannabis.[9-11] Individuals with long-term heavy cannabis use, including those diagnosed with cannabis use disorder, also have lower performance on neurocognitive tests of memory, attention, learning, and executive function.[13] Whether cannabis use contributes to these symptoms and if they translate into a greater future incidence of dementia is uncertain.

This study examined whether individuals with an acute care encounter, defined as an emergency department (ED) visit or a hospitalization, due to cannabis were at increased risk of a subsequent diagnosis of dementia. Our objective was to estimate the future risk of dementia diagnosis in individuals with acute care encounters due to cannabis relative to individuals with all-cause acute care encounters excluding cannabis (primary comparator), the general population (secondary comparator), and individuals with acute care encounters involving alcohol (secondary comparator).

Key Points

Question Are individuals who have an acute care encounter (an emergency department visit or hospitalization) due to cannabis use at increased risk of being diagnosed with dementia?

Findings In this cohort study of 6 million individuals aged 45 years or older with no history of dementia, those with acute care due to cannabis use were at 1.5-fold (absolute risk, 5.0% vs 3.6%) and 3.9-fold (absolute risk, 5.0% vs 1.3%) increased risk of a new dementia diagnosis within 5 years compared with individuals with an all-cause acute care encounter and the general population, respectively.

Meaning Individuals with cannabis use severe enough to require emergency department or hospital care may be at increased risk of being diagnosed with dementia.

Methods

This project was approved by the privacy office at ICES (formerly the Institute for Clinical Evaluative Science), which is authorized under section 45 of Ontario's Personal Health Information Protection Act to collect and analyze personal health information without patient consent for approved research projects. This study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Study Design and Population

We conducted a retrospective, population-level cohort study of all individuals aged 45 to 105 years in Ontario, Canada. We included all individuals who were alive and eligible for the province's public health insurance program (the Ontario Health Insurance Plan [OHIP]) between January 2008 and December 2021, with follow-up until December 2022 for dementia diagnosis. OHIP provides universal access to all hospital and medically necessary physician-based services for 97% of residents of Ontario.

To exclude prevalent dementia diagnoses, we required individuals to have been continuously eligible for OHIP for at least 5 years before study entry and excluded anyone with a diagnosis of dementia before study entry (minimum of 5-year look-back period, with look-back until database inception in 2003). We identified all individuals with an incident (no visit in the 3 years prior to index) acute care encounter due to cannabis and compared them with 3 comparator groups.

Data Sources

Eight linked health administrative data sources were used to create the study cohort, capture demographic characteristics, measure the use of health care services, identify comorbid conditions, and identify incident cases of dementia. These data sources were linked using unique encoded identifiers and analyzed at ICES. Basic demographic information and eligibility for government-funded health care was identified using the Registered Persons Database. Health service visits for ED visits, acute care hospitalizations, and mental health hospitalizations were obtained from the Discharge Abstract Database, the National Ambulatory Care Reporting System, and the Ontario Mental Health Reporting System (OMHRS). Outpatient visits were obtained from the OHIP databases, which include all covered physician primary and specialist visits. Prescriptions were obtained from the Ontario Drug Benefit databases, which included all claims for government-funded prescription medications. Information on recent immigrants was obtained from Immigration Refugees and Citizenship Canada's Permanent Resident Database. Rurality and income quintiles were obtained from the Postal Code Conversion File. All data sources are further described in eAppendix 1 in Supplement 1.

Exposure

Incident acute care due to cannabis use was defined as a first-time ED visit or hospitalization with *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*) code F12.X (mental and behavioral disorders due to use of cannabis) or T40.7 (poisoning by or adverse effects of cannabis, including derivatives) as the main or contributing reason for the visit. Prior to April 2019, the OMHRS, which captures adult admissions to designated mental health beds, used *International Classification of Diseases, Ninth Revision* and *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) codes. We used codes 304.30 (cannabis dependence) and 305.20 (cannabis abuse) to identify hospitalizations in the OMHRS prior to 2019.

Comparison Groups

We used 3 comparison groups: (1) matched individuals with incident acute care for a reason other than cannabis (all-cause acute care); (2) matched members of the general population with no acute care due to cannabis use; and (3) individuals with incident acute care due to alcohol use (see eAppendix 2 in Supplement 1 for details).[16] To create matched comparators, we used greedy matching in a 1:10 ratio, matching on age, sex, and index date of the acute care encounter for cannabis, and additionally on type of acute care ED visit, acute care hospitalization, and mental health hospitalization for the all-cause group.

Outcomes

The primary outcome was a diagnosis of dementia, including Alzheimer disease, which was identified using a previously chart-validated algorithm for residents of Ontario (sensitivity of 79.3% and specificity of 99.1%).[17] Individuals who met any of the following criteria had an incident dementia diagnosis: 1 or more hospitalization with a dementia diagnosis code on the discharge record; 3 or more outpatient physician visits with a dementia diagnosis code on the billing claim at least 30 days apart in a 2-year period (to rule out delirium, which might be short in duration); or a prescription dispensed for a dementia-specific medication (ie, a cholinesterase inhibitor).

We had 2 secondary outcomes and a negative control outcome. First, we identified early-onset dementia, defined as dementia diagnosis before age 65 years. Second, we examined incident acute care for non-drug-induced delirium, identified when *ICD-10* code F05 (delirium not induced by alcohol or other psychoactive substances) was listed as the main or contributing reason for the acute care event.[18]

As a negative control (an outcome that should have no association with acute care due to cannabis use), we compared the risk of incident hearing loss, defined as 2 or more outpatient visits for hearing loss or an acute care visit in which hearing loss was a reason for care or a noted comorbidity. In these analyses, we further excluded individuals with the outcome (eg, delirium or hearing loss) in the 5 years before the index date (see eAppendix 2 in Supplement 1 for details).

Covariates

We obtained sociodemographic information for each individual, including age, sex, rural residence, neighborhood income quintile, and immigration status. We obtained information on mental health and substance use care in the 3 years prior to the index event, including outpatient physician mental health visits (primary care physicians or psychiatrists) and acute care for substance use (alcohol, opioids, cocaine, amphetamines, and other substances) and mental disorders (mood, anxiety, self-harm, and other disorders) using previously established coding.[19] We identified previous diagnoses of 13 chronic health conditions (head trauma, stroke, transient ischemic attack, diabetes, hypertension, acute myocardial infarction and congestive heart failure, chronic obstructive pulmonary disease, parkinsonism, epilepsy, asthma, chronic kidney failure, HIV, and multiple sclerosis) using established algorithms.[20] Selection of chronic health conditions was consistent with prior studies using health administrative data.[21] eAppendix 3 in Supplement 1 provides covariate definitions. Covariates in our study were complete except for rural residence and neighborhood income quintile (0.28% missing).

Statistical Analyses

We used the date of incident acute care due to cannabis use to track changes in annual rates by age group over the study period. We examined average annual changes separately before and after cannabis policy liberalization in 2015 (medical cannabis liberalization in 2014 and federal government commitment to legalize nonmedical cannabis in 2015).[22-24]

We compared the characteristics of individuals using descriptive statistics and standardized mean differences.[25] Characteristics were obtained at the time of incident acute care or matched index date for comparators. We compared the risk of incident dementia diagnosis between individuals with acute care due to cannabis use with comparators using cumulative incidence functions and cause-specific Cox proportional hazard models at 5 years. We ran models adjusted for age and sex and models further adjusted for prespecified variables including sociodemographics, comorbid mental health and substance use, and 13 chronic health conditions[21,26] (see eAppendix 4 in Supplement 1 for model covariate specifications).

Secondary and Sensitivity Analyses

We performed a sex-stratified analysis of the comparisons between cannabis-related acute care encounters and all-cause acute care encounters and the general population. We calculated an E-value for our primary outcome analysis, estimating the magnitude of effect for a hazard ratio that an unmeasured confounder would need to have with both exposure (acute care for cannabis use) and outcome (dementia) to explain any observed association of the point estimate.[27]

For the secondary outcomes (early-onset dementia diagnosis, delirium, and the control outcome, hearing loss), we compared individuals with an incident acute care encounter due to cannabis with matched individuals with all-cause acute care encounters and with the matched general population.

As a sensitivity analysis, we included only individuals with no outpatient or acute care encounters for mental or substance use disorders in the 3 years before their index data. As a second sensitivity analysis, to reduce misdiagnosis of delirium

as dementia, we ran models excluding patients with dementia diagnoses for which delirium codes were present during the dementia diagnosis encounter. Statistical analyses were conducted using SAS Enterprise Guide, version 8.3 (SAS Institute Inc).

Results

Our study included 6 086 794 individuals aged 45 years or older without a history of dementia diagnosis, of whom 16 275 (0.3%) had an incident acute care encounter due to cannabis (mean age, 55.2 [SD, 8.3] years; 60.3% male) (see the eFigure in Supplement 1 for cohort flow). We included 140 824 individuals in our primary matched analysis comparing individuals with cannabis-related acute care with individuals with all-cause acute care, with a median follow-up of 4 (IQR, 2-7) years. Characteristics of individuals are presented in **Table 1**. Of individuals with acute care involving cannabis, 76.4% received care in the ED and 23.6% in the hospital. Individuals with acute care due to cannabis use were more likely (standardized mean difference, >0.1) to have had care for mental health or substance use in the past 3 years, were more likely to have had head trauma, and were less likely to have been diagnosed with diabetes, hypertension, cancer, or heart disease than individuals with all-cause acute care. Characteristics of the general population and individuals with acute care for alcohol use are available in eTables 1 and 2 in Supplement 1.

Changes over time in the number and rates of individuals aged 45 to 64 years and 65 years or older with incident acute care due to cannabis use are shown in **Figure 1**. The annual rate of incident cannabis-related acute care increased by 5.4-fold in individuals aged 45 years or older between 2008 and 2021, with larger relative increases in individuals aged 65 years or older (26.7-fold increase) than in individuals aged 45 to 64 years (5.0-fold increase). Visits increased between 2008 and 2014 (average relative increase of 13.0% per year) and then accelerated between 2015 and 2021 (average relative increase of 23.0% per year).

Cumulative incidence functions for dementia diagnosis over time for individuals with acute care due to cannabis use and comparators are presented in **Figure 2**A. At 5 years, 5.0% of individuals with acute care due to cannabis use, 3.6% of matched individuals with all-cause acute care, and 1.3% of the matched general population were diagnosed with dementia. By 10 years, 18.6% of individuals with cannabis-related acute care were diagnosed with dementia. After adjustment for sociodemographics, prior substance use, mental health care, and chronic conditions, the risk of dementia diagnosis at 5 years in individuals with acute care due to cannabis use was 1.2-fold greater (adjusted hazard ratio [aHR], 1.23; 95% CI, 1.09-1.39; E-value = 1.76) and 1.7-fold greater (aHR, 1.72; 95% CI, 1.38-2.15; E-value = 2.84) than for individuals with all-cause acute care and the general population, respectively (**Table 2**). Similar increases in risk were observed in both males and females (eTable 3 in Supplement 1). Sensitivity analysis excluding individuals with prior outpatient or acute mental health or substance use care (eTable 4 in Supplement 1) or individuals with a diagnosis of delirium at the time of dementia diagnosis (eTable 5 in Supplement 1) showed consistent associations. Our analysis comparing individuals with cannabis-related vs alcohol-related acute care encounters found that cannabis-related acute care was associated with a lower risk of a new dementia diagnosis relative to alcohol-related acute care (aHR, 0.69; 95% CI, 0.62-0.76).

Individuals with acute care due to cannabis use were at elevated risk of delirium and early-onset dementia relative to matched individuals with all-cause acute care and the general population (Figure 2B-D). However, after adjustment for sociodemographics, prior substance use, prior mental health care, and chronic conditions, the risk was significant only relative to the general population for delirium (aHR, 2.26; 95% CI, 1.88-2.73) and early-onset dementia (aHR, 2.04; 95% CI, 1.50-2.79) (**Table 3**). There was no association between acute care due to cannabis use and the incidence of the control outcome of hearing loss relative to the matched general population (aHR, 0.93; 95% CI, 0.75-1.15), but individuals with cannabis-related acute care were at lower risk after adjustment relative to those with all-cause acute care (aHR, 0.74; 95% CI, 0.61-0.90).

Discussion

In this longitudinal, population-based study of 6 million people, we found that 5.0% and 18.6% of individuals aged 45 years or older with treatment for cannabis in the ED or the hospital were diagnosed with dementia within 5 and 10 years, respectively. Individuals with acute care due to cannabis use were at 1.2-fold and 1.7-fold higher risk than matched individuals with all-cause acute care and the general population, respectively, after accounting for differences in sociodemographics, mental health comorbidity, and diagnoses of 13 chronic health conditions. Increases in the risk of dementia diagnosis associated with acute care due to cannabis use were similar in males and females, although acute care for cannabis use was more common in males. Several secondary and sensitivity analyses continued to support a positive association between receiving care for cannabis use in the ED or hospital setting and a future diagnosis of dementia.

The limited available research on the epidemiological association between cannabis use and dementia has been mixed.[7,8] Importantly, prior research has been substantially limited by occurring in small, nonrepresentative samples, self-report of cannabis use, use of less clinically relevant exposures to cannabis, and lack of adjustment for confounding. Adding to the literature, we present the largest study to date, to our knowledge, on the longitudinal association between cannabis use leading to an ED visit or hospitalization and dementia diagnosis. We also observed large increases in the incidence of acute care for cannabis use in older adults over time, with most of the increases starting in 2015, coinciding with the liberalization of medical cannabis in 2014 and the Canadian federal government's commitment to the legalization of nonmedical cannabis in December 2015 (which was implemented in October 2018).[22-24]

Table 1. Characteristics of Individuals With Cannabis-Related and All-Cause Acute Care Encounters

Characteristics	No. (%)		Standardized difference
	Acute care due to cannabis use (n = 15 120)	All-cause acute care (n = 125 704)	
Reason for acute care due to cannabis use			
Harmful use	5218 (34.5)		
Cannabis poisoning	2958 (19.6)		
Intoxication	2920 (19.3)		
Mental health bed	2019 (13.4)		
Dependence or withdrawal	1096 (7.2)		
Cannabis-induced psychosis	513 (3.4)		
Other, unspecified	576 (3.8)		
Sex			
Female	6117 (40.5)	52 942 (42.1)	0.03
Male	9003 (59.5)	72 762 (57.9)	0.03
Age, y			
Mean (SD)	55.32 (8.43)	55.96 (8.72)	0.07
45-54	8213 (54.3)	64 232 (51.1)	0.07
55-64	4794 (31.7)	41 290 (32.8)	0.02
65-74	1602 (10.6)	15 151 (12.1)	0.05
75-84	419 (2.8)	4136 (3.3)	0.03
≥85	92 (0.6)	895 (0.7)	0.01
Rurality			
Urban	13 036 (86.2)	102 952 (81.9)	0.12
Rural	2021 (13.4)	22 461 (17.9)	0.12
Neighborhood income quintile			
1 (Lowest)	4762 (31.5)	30 639 (24.4)	0.16
2	3255 (21.5)	26 223 (20.9)	0.02
3	2628 (17.4)	23 918 (19.0)	0.04
4	2265 (15.0)	22 842 (18.2)	0.09
5 (Highest)	2119 (14.0)	21 634 (17.2)	0.09
Long-standing resident of Canada			
Yes	13 892 (91.9)	106 806 (85.0)	0.22
No	1228 (8.1)	18 898 (15.0)	0.22
Substance use acute care visits in past 3 y			
Any	5950 (39.4)	10 467 (8.3)	0.78
Alcohol	3870 (25.6)	7784 (6.2)	0.55
Opioids	1714 (11.3)	2320 (1.8)	0.39
Cocaine	1405 (9.3)	918 (0.7)	0.40
Polysubstance	1326 (8.8)	2212 (1.8)	0.32
Amphetamines	680 (4.5)	599 (0.5)	0.26
Hallucinogens	50 (0.3)	46 (<0.1)	0.07
Other	340 (2.2)	386 (0.3)	0.17
Mental health acute care visits in past 3 y			
Any	5039 (33.3)	13 536 (10.8)	0.57
Mood disorder	2268 (15.0)	5604 (4.5)	0.36
Anxiety disorder	2012 (13.3)	7113 (5.7)	0.26
Deliberate self-harm	1555 (10.3)	2321 (1.8)	0.69
Schizophrenia	875 (5.8)	3032 (2.4)	0.17
Other	573 (3.8)	1827 (1.5)	0.15
Outpatient mental health and addiction visits in past 3 y			
Any	9933 (65.7)	54 200 (43.1)	0.47
Family physician	9214 (60.9)	50 928 (40.5)	0.42
Psychiatrist	4544 (30.1)	16 042 (12.8)	0.43

(continued)

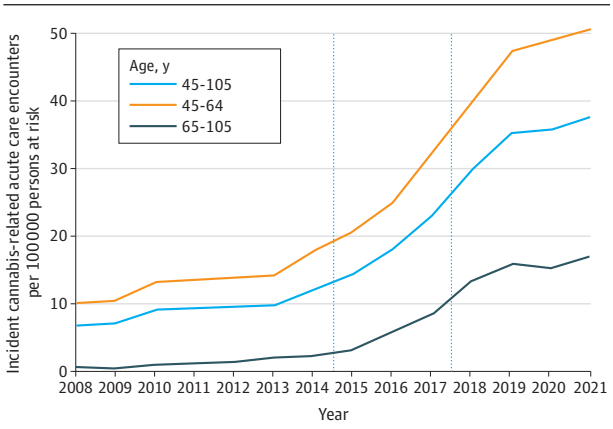
Table 1. Characteristics of Individuals With Cannabis-Related and All-Cause Acute Care Encounters (continued)

Characteristics	No. (%)		Standardized difference
	Acute care due to cannabis use (n = 15 120)	All-cause acute care (n = 125 704)	
Any acute or outpatient mental health and addiction visit in past 3 y			
Yes	11 587 (76.6)	57 663 (45.9)	0.67
No	3533 (23.4)	68 041 (54.1)	0.67
Chronic health conditions in past 3 y			
Hypertension	5464 (36.1)	53 764 (42.8)	0.14
Cancer	5259 (34.8)	49 842 (39.7)	0.101
Asthma	2931 (19.4)	22 670 (18.0)	0.035
Diabetes	2692 (17.8)	28 828 (22.9)	0.128
Chronic obstructive pulmonary disease	1413 (9.3)	9573 (7.6)	0.062
Head trauma	1232 (8.1)	7149 (5.7)	0.097
Chronic kidney disease	974 (6.4)	9045 (7.2)	0.03
Myocardial infarction/congestive heart failure	959 (6.3)	11 251 (9.0)	0.098
Transient ischemic stroke	517 (3.4)	5032 (4.0)	0.031
Stroke	460 (3.0)	4460 (3.5)	0.028
HIV	139 (0.9)	605 (0.5)	0.053
Multiple sclerosis	70 (0.5)	501 (0.4)	0.01
Parkinsonism	28 (0.2)	368 (0.3)	0.022

Although the associations reported in our study should not be interpreted as causal, it is relevant to consider potential mechanisms in which regular cannabis use might increase the risk of dementia. Cannabis use may directly result in changes in brain structure and cognition in ways that increase the risk of dementia.[9-11,15] Long-term cannabis use has been associated with memory and attention problems in midlife along with declines in hippocampal volume,[8] which are both associated with dementia. In addition, cannabis use could indirectly increase the risk of dementia by increasing the prevalence of established risk factors. While the causal mechanisms that may lead to dementia continue to be investigated, 14 modifiable risk factors, including less education, hearing loss, high low-density lipoprotein cholesterol, depression, traumatic brain injury, physical inactivity, diabetes, smoking, hypertension, obesity, excessive alcohol use, social isolation, air pollution, and vision loss, have all been associated with dementia with strong evidence.[12] Cannabis use, particularly cannabis use disorders, is associated with greater prevalence of at least 5 of these risk factors, including reductions in educational attainment,[28,29] increased risk of hypertension, higher risk of head trauma via motor vehicle collisions[30] and other injuries, and greater risk of depression[31] and social isolation.[32]

Our findings raise caution that individuals with hospital-based treatment for cannabis use may be at increased risk of a subsequent diagnosis of dementia. In addition, the positive association between acute care for cannabis use and delirium highlights potential safety concerns in older individuals considering medical or nonmedical cannabis use. Our results should not be interpreted as showing that cannabis use in patterns sufficient to result in an ED visit or hospitalization due to cannabis cause dementia. However, regardless of causality, our findings have clinical implications highlighting a group at high risk of developing dementia who may benefit from close follow-up and intervention or preventive efforts.

Figure 1. Annual Rate of Incident Cannabis-Related Acute Care Encounters per 100 000 Persons at Risk by Age Group

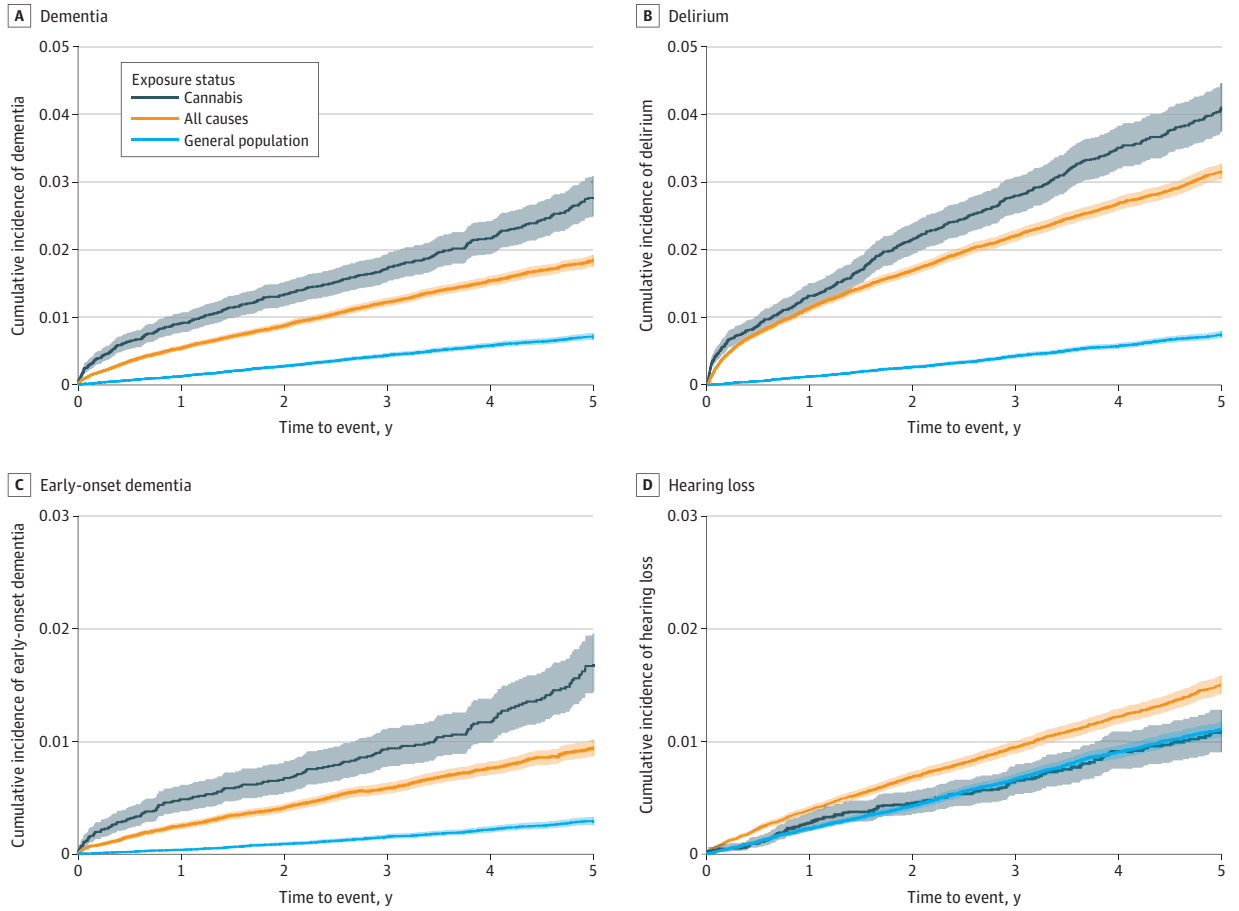


The first blue dotted line indicates the liberalization of medical cannabis and the Canadian federal government's announcement that nonmedical cannabis would be legalized; the second blue dotted line shows the date of nonmedical cannabis legalization in Canada.

Limitations

Our study has limitations. First, while our exposure objectively captured individuals with patterns of cannabis use severe enough to require acute care, we did not have detailed data on the duration (eg, number of years of use), frequency (eg, monthly vs daily), and type (smoked vs ingested) of cannabis use, which may be relevant to the relationship between cannabis use and dementia. The observed associations may not generalize to cannabis use

Figure 2. Cumulative Incidence of Risk of Dementia Diagnosis Over Time



The risks of dementia, delirium, early-onset dementia, and hearing loss (negative control condition) are shown for individuals with acute care encounters due to cannabis use compared with age- and sex-matched individuals with all-cause acute care encounters and the matched general population. Shaded regions represent 95% CIs.

that is less frequent or that does not come to medical attention. Second, while we observed a strong association between cannabis-related acute care and dementia, there is a possibility of residual confounding. For the general population comparison, the observed strength of association may be overestimated, as individuals with acute care for cannabis use have higher rates of risk factors for dementia (eg, alcohol and tobacco use) than the general population.[33-35] In contrast, for the all-cause acute care comparison, the observed association may be biased toward the null because individuals requiring acute care for non-cannabis-related reasons may, on average, have more medical comorbidities than those with acute care for cannabis use (as demonstrated by the higher rates of diagnosed hypertension and diabetes). Importantly, the E-value sensitivity analysis for the general population suggests that the observed associations between acute care for cannabis use and dementia diagnosis could only be explained by unmeasured confounders with an HR of 2.84. This value is much greater than the reported association between smoking and dementia (risk ratio of 1.30 for current vs never smoking)[36] and alcohol and dementia (risk ratio of 1.2 for consumption of >21 units of alcohol per week relative to ≤21 units).[37] In addition, the lack of association between acute care for cannabis use and the control condition (hearing loss) in the general population and the negative association in the all-cause acute care comparator support a potential independent association with dementia. Third, our fully adjusted models also included covariates that could be on a potential causal pathway between cannabis use and dementia (eg, diabetes, hypertension, head trauma). Finally, it is possible that reverse causation, in which individuals with symptoms of cognitive decline initiate cannabis use to try to control symptoms before ultimately being diagnosed with dementia, may explain part of the association observed in our study.

Conclusions

We found that individuals with acute care due to cannabis use were at an elevated risk of dementia diagnosis, early-onset

Table 2. Risk of Developing Dementia After Cannabis-Related Acute Care Compared With All-Cause Acute Care, the General Population, and Alcohol-Related Acute Care

Comparator	Population at risk, No.	Dementia, No.[a]	Dementia in 5 y, No. (%)[b]	Dementia in 10 y, No. (%)[b]	Crude dementia incidence[c]	Age- and sex-adjusted HR (95% CI)[c]	Fully adjusted HR (95% CI)[c,d]
All-cause acute care (excluding cannabis)							
Cannabis-related acute care	15 120	404	317 (4.95)	381 (18.81)	598.68	1.53 (1.36-1.72)	1.23 (1.08-1.39)
All-cause acute care	125 704	2256	1793 (3.63)	2164 (14.85)	417.36	1 [Reference]	1 [Reference]
General population							
Cannabis-related acute care	16 275	454	352 (4.97)	427 (18.56)	613.26	3.93 (3.47-4.45)	1.72 (1.38-2.15)
Matched general population	156 473	1120	826 (1.27)	1053 (5.47)	143.94	1 [Reference]	1 [Reference]
Alcohol-related acute care							
Cannabis-related acute care	16 275	454	352 (4.97)	427 (18.56)	613.26	0.76 (0.68-0.84)	0.69 (0.62-0.76)
Alcohol-related acute care	119 163	9733	6768 (7.96)	9143 (21.68)	1496.69	1 [Reference]	1 [Reference]

[a] Dementia diagnoses during the maximum follow-up period available.

[b] Denominator for percentages is number of individuals who could accrue at least 5 or 10 years of follow-up.

[c] Dementia diagnosis rates per 100 000 person-years and hazard ratios (HRs) at 5 years of follow-up.

[d] Adjusted for age; sex; neighborhood income quintile; rurality; immigration status; 3-year history of outpatient, emergency department, and hospital-based care for mental health (separately for self-harm, schizophrenia, anxiety, depression, and other disorders) and substance use (separately for alcohol, stimulants, cocaine, amphetamines, opioids, polysubstance use, and other substances); and presence or absence (separately for each condition) of 13 chronic health conditions (hypertension, asthma, chronic obstructive pulmonary disease, myocardial infarction or congestive heart failure, diabetes, cancer, chronic kidney disease, transient ischemic stroke, stroke, head trauma, parkinsonism, multiple sclerosis, and HIV).

Table 3. Risk of Secondary and Control Outcomes After Cannabis-Related Acute Care Compared With All-Cause Acute Care and the General Population

Outcomes	Population at risk, No.	Outcome, No.[a]	Outcome in 5 y, No. (%)[b]	Outcome in 10 y, No. (%)[b]	Crude outcome incidence[c]	Age- and sex-adjusted HR (95% CI)[c]	Fully adjusted HR (95% CI)[c,d]
All-cause acute care comparator							
Early-onset dementia							
Cannabis-related acute care	12 745	174	142 (2.46)	167 (8.70)	317.00	1.60 (1.34-1.92)	1.07 (0.88-1.30)
Matched all-cause acute care	103 093	931	725 (1.67)	895 (6.58)	203.55	1 [Reference]	1 [Reference]
Delirium							
Cannabis-related acute care	14 636	621	474 (7.63)	577 (29.32)	925.56	1.30 (1.18-1.43)	0.93 (0.84-1.04)
Matched all-cause acute care	123 215	3869	3119 (6.41)	3724 (25.83)	737.43	1 [Reference]	1 [Reference]
Hearing loss (negative control outcome)							
Cannabis-related acute care	14 959	147	121 (1.91)	142 (7.10)	229.22	0.70 (0.58-0.84)	0.74 (0.61-0.90)
Matched all-cause acute care	123 800	1836	1415 (2.91)	1749 (12.18)	333.99	1 [Reference]	1 [Reference]
General population comparator							
Early-onset dementia							
Cannabis-related acute care	13 798	249	175 (2.73)	227 (10.39)	349.00	6.38 (5.28-7.71)	2.04 (1.5-2.79)
Matched general population	133 607	474	278 (0.46)	427 (2.30)	55.43	1 [Reference]	1 [Reference]
Delirium							
Cannabis-related acute care	15 762	686	519 (7.54)	640 (28.56)	934.42	6.09 (5.46-6.79)	2.26 (1.88-2.73)
Matched general population	156 083	1234	850 (1.31)	1165 (6.06)	148.32	1 [Reference]	1 [Reference]
Hearing loss (negative control outcome)							
Cannabis-related acute care	16 101	163	133 (1.90)	157 (6.91)	232.36	1.03 (0.86-1.23)	0.93 (0.75-1.15)
Matched general population	154 848	1793	1278 (1.98)	1675 (8.80)	225.48	1 [Reference]	1 [Reference]

[a] Secondary outcome diagnoses during the maximum follow-up period available.

[b] Denominator for percentages is number of individuals who could accrue at least 5 or 10 years of follow-up.

[c] Secondary outcome diagnosis rates per 100 000 person-years and hazard ratios (HRs) at 5 years of follow-up.

[d] Adjusted for age; sex; neighborhood income quintile; rurality; immigration status; 3-year history of outpatient, emergency department, and hospital-based care for mental health (separately for self-harm, schizophrenia, anxiety, depression, and other disorders) and substance use (separately for alcohol, stimulants, cocaine, amphetamines, opioids, polysubstance use, and other substances); and presence or absence (separately for each condition) of 13 chronic health conditions (hypertension, asthma, chronic obstructive pulmonary disease, myocardial infarction or congestive heart failure, diabetes, cancer, chronic kidney disease, transient ischemic stroke, stroke, head trauma, parkinsonism, multiple sclerosis, and HIV).

dementia, and delirium. Individuals with acute care for cannabis use were at lower risk of a dementia diagnosis than individuals with acute care for alcohol use but were at higher risk than individuals with acute care for reasons other than cannabis. Large increases in regular cannabis use and related acute care visits in older adults highlight the potential importance of heavy cannabis use as an emerging risk factor for dementia in older adults.

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Author Affiliations: Department of Family Medicine, University of Ottawa, Ottawa, Ontario, Canada (Myran); Ottawa Hospital Research Institute, Ottawa, Ontario, Canada (Myran, Harrison, Webber); ICES Ottawa, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada (Myran, Pugliese); Bruyère Health Research Institute, Ottawa, Ontario, Canada (Myran, Harrison, Webber); School of Epidemiology and Public Health, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada (Myran); Division of General Internal Medicine and Geriatrics, Sinai Health and the University Health Network, Toronto, Ontario, Canada (Stall); Women's Age Lab and Women's College Research Institute, Women's College Hospital, Toronto, Ontario, Canada (Stall); Department of Medicine, University of Toronto, Toronto, Ontario, Canada (Stall).

Author Contributions: Drs Myran and Pugliese had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Stall and Webber are co–senior authors.
Concept and design: Myran, Stall, Webber.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Myran, Harrison.
Critical review of the manuscript for important intellectual content: All authors.
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