Changes in cannabis involvement in emergency department visits for anxiety disorders after cannabis legalization: a repeated cross-sectional study

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Summary

Background An increasing number of countries have or are considering legalizing cannabis. One concern is that legalization of cannabis will result in increased cannabis use and in turn a higher prevalence of anxiety disorders. We examined changes in emergency department (ED) visits for anxiety disorders with cannabis involvement in Ontario, over a period that involved medical and non-medical cannabis legalization.

Methods This repeated cross-sectional population-based study identified all ED visits for anxiety disorders from residents of Ontario, Canada aged 10–105 between 2008 and 2022 (n = 15.7 million individuals). We used interrupted time series analyses to examine immediate and gradual changes in cannabis-involvement and alcohol-involvement (control condition) over four policy periods: medical cannabis legalization (January 2008–November 2015), expanded medical access (December 2015–September 2018), non-medical cannabis legalization with restrictions (October 2018–February 2020), and commercialization which overlapped with the COVID-19 pandemic (March 2020–December 2022). Poisson models were used to generate incidence rate ratios with 95% confidence intervals.

Findings Over the 14-year study, there were 438,700 individuals with one or more ED visits for anxiety disorders of which 3880 (0.89%) individuals had cannabis involvement and 6329 (1.45%) individuals had alcohol involvement. During the commercialization/COVID-19 period monthly rates of anxiety disorders with cannabis-involvement were 156% higher (0.11 vs 0.29 per 100,000 individuals) relative to the pre-legalization period, compared to a 27% increase for alcohol-involvement (0.27 vs 0.35 per 1100,000 individuals). Rates of anxiety ED visits with cannabis involvement per 100,000 individuals increased gradually over the study period with no immediate or gradual changes after expanded medical access, legalization with restrictions or commercialization/COVID-19. However, during the commercialization/COVID-19 period there were large declines in total anxiety disorder ED visits and anxiety disorder ED visits with alcohol-involvement. Consequently, during this period there was an immediate 31.4% relative increase in the proportion of anxiety visits with cannabis-involvement (incidence rate ratio [IRR], 1.31; 95% CI 1.05–1.65).

Interpretation We found large relative increases in anxiety disorder ED visits with cannabis involvement over a 14-year period involving medical and non-medical cannabis legalization. These findings may reflect increasing anxiety disorder problems from cannabis use, increasing self-medication of anxiety disorders with cannabis use, or both. The proportion of anxiety ED visits with cannabis involvement increased during the final period of the study but could have been the results of the market commercialization, COVID-19 or both and ongoing monitoring is indicated.

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Research in context

Evidence before this study

As a growing number of countries proceed with legalizing medical and non-medical cannabis, there is concern that these policy changes will cause increases in mental health conditions. While studies have assessed changes in some conditions (e.g., cannabis use disorders or cannabis-induced psychosis), few have examined changes in anxiety disorders. We searched PubMed with the search terms "anxiety", "anxiety disorders", "marijuana legalization", and "cannabis legalization" up to December 1, 2023 with no limits on publication dates or language. We identified two studies that examined the association between cannabis legalization and anxiety disorders. One study found that individuals with anxiety living in a state with legal recreational cannabis were more likely to report using cannabis that individuals living in states without legal recreational cannabis. Another study from three US states found no clear relationship between recreational cannabis legalization and changes in total hospitalizations for anxiety disorders. Importantly, prior studies examining the relationship between cannabis legalization and anxiety disorders have been limited by self-reporting, small samples sizes, and short time intervals that limit their certainty and generalizability.

Added value of this study

We studied all ED visits for anxiety disorders in individuals aged 10–105 years in Ontario, Canada between 2008 and 2022 during which time medical cannabis access was liberalized (2015) and non-medical cannabis was legalized with restrictions (2018) and commercialized (2020). Over our study period, the monthly rate per 100,000 individuals of ED visits for anxiety disorders with cannabis involvement increased by 156% relative to pre-legalization, compared to a 27% increase for alcohol involvement. Medical cannabis liberalization and non-medical cannabis legalization with market restrictions did not influence the general trend of increasing cannabis involvement in anxiety disorder ED visits over time. There was a 31% increase in the proportion of anxiety ED visits with cannabis-involvement during the market commercialization/COVID-19 period but this increase was largely driven by declines in overall anxiety ED visits. Throughout the study, cannabis involvement in ED visits for anxiety disorders was higher in younger individuals and men. However, women and older adults experienced the greatest increase in cannabis involvement over time, suggesting these gaps are narrowing.

Implications of all the available evidence

Cannabis use in individuals with anxiety disorders appears to be increasing in North America. Liberalization of medical or non-medical cannabis, specifically allowing widespread access to retail stores and a diversity of legal cannabis products, may be contributing to this trend. Ongoing work is needed to understand whether these changes reflect greater self-medication of anxiety symptoms using cannabis or the development of anxiety disorders subsequent to cannabis use.

Introduction

Studies consistently reveal an association between cannabis use and subsequent mental health problems, including anxiety disorders.[1–6] In contrast, there is growing interest in whether cannabis may reduce anxiety symptoms, although evidence for this effect is limited.[7] As an increasing number of countries have or are proceeding with the legalization of medical or non-medical cannabis, there is concern that consequent increases in cannabis use may exacerbate anxiety disorders or complicate the diagnosis or treatment of anxiety-related conditions.[8] The existing body of research on the relationship between cannabis legalization and anxiety disorders presents a mixed picture.[9,10] One study found that individuals with anxiety disorders living in a state with legal recreational cannabis were more likely to report using cannabis than individuals living in states without legal recreational cannabis.[10] Another study from three US states found no clear relationship between recreational cannabis legalization and changes in total hospitalizations for anxiety disorders.[9] Importantly, prior studies examining the relationship between cannabis legalization and anxiety disorders have been limited by self-reporting, small samples sizes, and short time intervals that limit their certainty and generalizability. Consequently, whether cannabis legalization is associated with an increase in anxiety disorders is unclear.[11]

Cannabis policy in Canada has changed substantially over the past two decades. In 2001, Canadians became able to access medical cannabis for a limited list of severe or chronic conditions.[10] Starting in 2014, access to medical cannabis was expanded for any individual who received authorization from a physician or nurse practitioner who determined that the patient would benefit from medical cannabis.[11] Medical authorizations rapidly expanded starting in 2015. In December 2015 the Federal Government announced its intention to legalize non-medical cannabis, which went into effect in October 2018.[12] Initially there were restrictions on the legal market including limited stores and product types.[13] Starting in early 2020, the legal market in Ontario commercialized with a 916% increase in per-capita cannabis stores over a 14-month period and the

introduction of new higher potency products (e.g., vape pens, and concentrates) in January 2022.[14,15] This phase of expanded cannabis commercialization coincided with Ontario entering a state of emergency in response to the global COVID-19 pandemic in March 2020.[15] These four distinct phases of cannabis legalization create an opportunity to study the relationship between anxiety disorders and cannabis policy.[15]

This study aimed to examine the impacts of medical and non-medical cannabis liberalization and further commercial expansion on cannabis involvement during emergency department (ED) visits for anxiety disorders in Ontario, Canada. We used population-based health administrative data and interrupted time series (ITS) analysis of four key policy time-periods: medical cannabis legalization, pre-recreational cannabis legalization, recreational cannabis legalization, and expanded commercialization of cannabis which overlapped with the COVID-19 pandemic.

Methods

Personal health information data used in this cross-sectional 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. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for cross-sectional studies.[16]

Study design, population, and data sources

We conducted a repeated cross-sectional population-level study using health administrative databases for Ontario, Canada. The cohort included all Ontario residents aged 10–105 years between January 2008 and December 2022 who were eligible for the province's single-payer health insurance system. The Ontario Health Insurance Plan (OHIP) covers all ED visits, hospitalizations, and outpatient physician visits.[17] After excluding anyone not eligible for OHIP for a two-year period before study eligibility (n = 888,000), our cohort included 15.7 million people. We obtained data from six individual-level databases containing different types of healthcare visits and individual demographics. These databases captured 100% of ED visits in Ontario. Each individual in Ontario has a unique encoded identifier that allows linkage across datasets, which are completed and analyzed at IC/ES (formerly the Institute for Clinical Evaluative Science). We used the Interrupted Time Series (ITS) method with segmented regression analysis to assess immediate and gradual changes in anxiety disorder ED visits associated with cannabis legalization and commercialization.

Exposures

We divided our study into four time periods: medical cannabis legalization with restrictions (P1, January 2008–November 2015), medical cannabis liberalization and pre-non-medical legalization (P2, December 2015–September 2018), non-medical cannabis legalization with restrictions (P3, October 2018–February 2020), and expanded non-medical cannabis commercialization which coincided with the COVID-19 pandemic (P4, March 2020–December 2022, hereafter, *Commercialization/COVID-19*). We chose a start point for P4 as March 2020 to balance several competing interruptions – product expansion in January 2020, the onset of the pandemic in March 2020, and removal of store restrictions in April 2020. Data showing longitudinal changes in the cannabis retail market in Ontario are available online.

Outcomes

Our primary outcomes were ED visits for anxiety disorders with cannabis involvement. We examined our primary outcome either as a rate per 100,000 individuals, or expressed as a proportion per 1000 total anxiety disorders ED visits. We first identified all ED visits for anxiety disorders using the *International Classification of Diseases (ICD) 10th revision* codes for anxiety disorders (F40–F41, F48.8, F48.9). We then identified anxiety disorder ED visits with a documented diagnosis of cannabis involvement when an ICD-10 code for a mental and behavioural disorder due to cannabis use (F12.X) or for cannabis poisoning (T40.7) was listed as the main or contributing reason for the anxiety disorders ED visit.[18] As a secondary outcome, we identified all incident ED visits for an anxiety disorder with cannabis-involvement (defined as an individual with an ED visit for an anxiety disorder who has had no ED visits or hospitalizations for an anxiety disorder in the past two years). The control (tracer) condition was anxiety disorder ED visits that were positive for alcohol, identified with ICD-10 codes for a mental and behavioural disorder due to alcohol use (F10.X) or ethanol poisoning (T51.0). Alcohol use was included as a tracer condition to account for societal changes that may influence overall substance use (e.g., changes in substance use and health-seeking behaviour during the COVID-19 pandemic).

Covariates

At the time of each anxiety disorders ED visit, we obtained sociodemographic details including age, sex, rural residence, and neighbourhood income quintile using Statistics Canada census data.[19] We also obtained information on healthcare use in the preceding two years of the index ED visit, including outpatient or ED mental health (mood disorders, anxiety disorders, schizophrenia/psychosis, deliberate self-harm, and other) or substance use visits (cannabis, alcohol, opioids, and other) using diagnostic and billing codes.[20] Data at IC/ES is complete with no missing information, with the exception of neighbourhood income quintile and rural residence which is missing for 0.2% of individuals.

Statistical analyses

We identified the characteristics of individuals with anxiety disorder ED visits at the time of visit. For individuals with more than one anxiety disorder ED visit during the study, we captured characteristics at a randomly selected ED visit. We calculated the monthly rates per 100,000 individuals and per 1000 anxiety disorder ED visits of our primary and control outcomes over the four policy periods. We used segmented Poisson regression analysis to examine changes in anxiety disorder ED visits over time, and adjusted Poisson models to generated incidence rate ratios (IRRs) with 95% confidence intervals (CIs) to compare relative changes between subsequent policy periods. We offset our regressions by the population at risk for rates per capita and by the total anxiety disorder ED visits for rates per anxiety disorder visits. Immediate and gradual change in ED visits were analyzed by slope and level change at each policy interruption. We chose a priori to include a first-order autocorrelation term for all analyses as prior work has found that statistical tests for autocorrelation are underpowered.[21] We adjusted for seasonality using indicator variables.

We ran stratified models of our primary outcome over the four time-periods for five stratifying variables: sex, age, neighborhood income, rurality and for incident anxiety disorder ED visits. For incident visits each month we identified all individuals with care for an anxiety disorder in the past two years. As a sensitivity analysis to account for immediate influences of the COVID-19 pandemic on ED visits for anxiety disorders, we censored the first five months of the pandemic (March 2020 to July 2020), which covers the start to the end of the first declaration of a state of emergency in Ontario. Statistical analyses were conducted using SAS Enterprise Guide version 7.1 (SAS Institute, Cary, NC) between July and August 2023.

Role of the funding source

The funders had no role in the study design, data collection or analysis, interpretation, writing of the report or the decision to submit for publication.

Results

Our study included 439,700 individuals who had one or more ED visits for anxiety disorders between January 2008 and July 2022. Of these individuals visits, 3880 (0.89%) had one or more anxiety disorder ED visits with cannabis involvement, 6329 (1.45%) had one or more anxiety disorder ED visits with alcohol involvement, and 416 (0.10%) had one or more anxiety disorder ED visits with both cannabis and alcohol involvement (Table 1). The mean (SD) age in years for anxiety disorder ED visits alone was 39.4 (19.2) and 25.7 (10.2) for anxiety disorder ED visits with cannabis involvement. Males account for 60.8% of anxiety disorder ED visits with cannabis involvement compared to 40.4% of anxiety disorder ED visits with no cannabis involvement. Those aged 10–18 or 19–24 were the majority of anxiety disorder ED visits with cannabis involvement (24.4% and 33.6%, respectively) when compared to anxiety disorder ED visits alone (12.2% and 15.8%, respectively). People living in the lowest-income quintile neighbourhoods incurred a greater number of anxiety disorder ED visits with cannabis involvement. Among those with an index anxiety disorder acute care visit with cannabis involvement, incidence of past mental health or substance use acute care visit in the last two years was 39.6% and 15.3%, respectively (Table 1).

Table 2 shows the total and mean monthly rates of anxiety disorder ED visits. Overall, there were 653,564 ED visits for anxiety disorders, 4048 ED visits for anxiety disorders with cannabis involvement, 7049 ED visits for anxiety disorders with alcohol involvement, and 425 ED visits for anxiety disorders with cannabis and alcohol involvement. Mean rates of overall ED visits for anxiety disorders were stable over the study period. In contrast, rates per 10,000 individuals of anxiety disorder ED visits with cannabis-involvement increased by 156% (RR 2.56; 95% CI, 2.29–2.86) between P1 and P4, compared with 27% rise in anxiety disorder ED visits with alcohol-involvement (RR 1.27; 95% CI, 1.18–1.36) and 121% in anxiety disorder ED visits with both alcohol and cannabis involvement (RR 2.21; 95% CI, 1.71–2.86). Normalizing rates per 1000 anxiety disorder ED visits also shows the proportion of ED visits due to anxiety disorders with cannabis involvement increased by 166% (RR 2.66; 95% CI, 2.40–2.95) between P1 and P4 compared to a 32% increase (RR 1.32; 95% CI, 1.23–1.41) in anxiety disorder ED visits with alcohol-involvement.

Fig. 1 shows the monthly change in rate of anxiety disorder ED visits per capita, anxiety disorder ED visits with cannabis involvement per capita and per all-cause anxiety, or anxiety disorder ED visits with alcohol involvement per capita and per all-cause anxiety between January 2008 and July 2022. During P1, all-cause anxiety disorder ED visits gradually increased over time by 0.13% each month (Incidence Rate Ratio [IRR], 1.0013; 95% CI, 1.0008–1.0019). P2 showed an immediate 6.2% level increase of monthly anxiety disorder ED visits (IRR, 1.062; 95% CI, 1.007–1.120). There were no significant slope or level changes in monthly anxiety disorder ED visits during P3. During P4, the monthly rate of all-cause anxiety disorder ED visits showed an 18.3% immediate level decrease (IRR, 0.817; 95% CI, 0.757–0.882), before gradually returning to the pre-pandemic rate.

The per capita rate of ED visits for anxiety with cannabis involvement increased gradually over time, and there were no significant level changes or slope changes following any of the cannabis policy changes. There were no significant level change or slope changes

Characteristic	Anxiety disorder ED visit (no cannabis)	Anxiety disorder and cannabis ED visit[a]	Anxiety disorder and alcohol ED visit[a]	Anxiety disorder and cannabis and alcohol ED visit	Standardized mean difference[b]
	N (%)				
Total count of visits	N = 435,814	N = 3880	N = 6329	N = 415	
Sex					
Male	175,869 (40.4)	2359 (60.8)	3703 (58.5)	257 (61.8)	0.42
Female	259,945 (59.6)	1521 (39.2)	2626 (41.5)	159 (38.2)	0.42
Age					
Mean (±SD)	39.41 (19.2)	25.74 (10.23)	38.46 (14.76)	27.27 (10.67)	0.89
10–18 years	53,064 (12.2)	945 (24.4)	267 (4.2)	68 (16.3)	0.32
19–24 years	69,016 (15.8)	1304 (33.6)	997 (15.8)	150 (36.1)	0.42
25–44 years	156,744 (36.0)	1372 (35.4)	2947 (46.6)	160 (38.5)	0.01
45+ years	156,990 (36.0)	259 (6.7)	2118 (33.5)	38 (9.1)	0.77
Rurality					
Urban	358,506 (82.3)	3406 (87.8)	5181 (81.9)	363 (87.3)	0.16
Rural	75,907 (17.4)	453 (11.7)	1121 (17.7)	51 (12.3)	0.16
Neighbourhood income quintile					
1 (poorest)	112,753 (25.9)	1023 (26.4)	1911 (30.2)	113 (27.2)	0.01
2	91,799 (21.1)	835 (21.5)	1312 (20.7)	88 (21.2)	0.01
3	83,506 (19.2)	710 (18.3)	1081 (17.1)	74 (17.8)	0.02
4	76,839 (17.6)	669 (17.2)	1026 (16.2)	63 (15.1)	0.01
5 (richest)	68,332 (15.7)	615 (15.9)	935 (14.8)	74 (17.8)	0.00
Mental health ED visit in past 2 years					
Any	93,991 (21.6)	1537 (39.6)	2721 (43.0)	180 (43.3)	0.40
Mood disorders	35,652 (8.2)	596 (15.4)	1117 (17.6)	72 (17.3)	0.22
Anxiety disorders	43,295 (9.9)	850 (21.9)	1563 (24.7)	109 (26.2)	0.33
Schizophrenia/psychosis	12,922 (3.0)	249 (6.4)	269 (4.3)	21 (5.0)	0.16
Deliberate self-harm	11,177 (2.6)	199 (5.1)	557 (8.8)	26 (6.3)	0.13
Other	12,622 (2.9)	247 (6.4)	321 (5.1)	28 (6.7)	0.17
Substance use ED visit in past 2 years					
Any	24,924 (5.7)	592 (15.3)	2424 (38.3)	99 (23.8)	0.32
Cannabis	2641 (0.6)	226 (5.8)	75 (1.2)	9 (2.2)	0.30
Alcohol	12,299 (2.8)	190 (4.9)	2133 (33.7)	63 (15.1)	0.11
Opioids	3359 (0.8)	49 (1.3)	121 (1.9)	≤5	0.05
Other	10,975 (2.5)	256 (6.6)	617 (9.7)	41 (9.9)	0.20
Outpatient mental health and addiction visit in past 2 years					
Any	263,153 (60.4)	2724 (70.2)	4686 (74.0)	314 (75.5)	0.21
Family physician	249,029 (57.1)	2560 (66.0)	4457 (70.4)	302 (72.6)	0.18
Psychiatrist	91,970 (21.1)	1298 (33.5)	2095 (33.1)	141 (33.9)	0.28

ED = emergency department. [a]ED presentations for cannabis or alcohol use are not mutually exclusive. [b]Standard mean difference between cannabis involvement and no cannabis involvement.

Table 1: **Characteristics of individuals with ED visits for anxiety disorders with or without cannabis or alcohol use in Ontario, Canada.**

in the proportion of anxiety ED visits identified as cannabis-related following medical cannabis liberalization (P2) and non-medical legalization with restrictions (P3). There was a significant level increase of 31% (IRR 1.31, 95%CI 1.05–1.065) during cannabis commercialization/COVID-19 pandemic (P4). This change was the result of both a significant level change in the total number of anxiety ED visits at the onset of the COVID-19 pandemic (IRR, 0.82, 95%CI, 0.76–0.88) and a 9% non-significant increase in per capita anxiety ED visits with cannabis-involvement (IRR, 1.092; 95% CI, 0.868–1.373), see Supplementary Table S1 for full model coefficients. Our sensitivity analysis censoring the first five months of the pandemic showed similar results, with a significant 32.1% level increase during P4 in rates of anxiety disorders with cannabis involvement per all-cause anxiety disorder ED visits (IRR 1.321; 95% CI, 1.037–1.682). See Supplementary Fig. S1 and Table S2 for visualization and full model coefficients.

Subgroup analysis of monthly anxiety disorder ED visits with cannabis involvement per all-cause anxiety disorder ED visits is shown in Table 3. Women had a greater increase in monthly ED visit rates (RR P4 vs P1, 3.39; 95% CI, 2.92–3.94) compared with men (RR P4 vs

Denominator	Medical cannabis legalization with restrictions (Period 1)[a]	Medical cannabis liberalization and pre non-medical legalization (Period 2)[b]	Non-medical cannabis legalization with restrictions (Period 3)[c]	Commercial-ization/COVID-19 (Period 4)[d]	Period 2 vs Period 1	Period 3 vs Period 1	Period 4 vs Period 1
	No. or Mean monthly ED visit rate				Risk ratio[e] (95% CI)		
Number of visits							
Anxiety disorder ED visits	330,641	143,495	71,066	108,362			
Anxiety + cannabis ED visits	1297	1015	610	1126			
Anxiety + alcohol ED visits	3175	1631	871	1372			
Anxiety + cannabis + alcohol ED visits	145	112	60	108			
Per 100,000 people							
Anxiety disorder ED visits	28.59	32.41	31.33	27.62	1.13 (1.11–1.16)	1.10 (1.07–1.14)	0.96 (0.94–0.99)
Anxiety + cannabis ED visits	0.11	0.23	0.27	0.29	2.05 (1.83–2.29)	2.38 (2.08–2.72)	2.56 (2.29–2.86)
Anxiety + alcohol ED visits	0.27	0.37	0.38	0.35	1.34 (1.25–1.44)	1.42 (1.30–1.55)	1.27 (1.18–1.36)
Anxiety + cannabis + alcohol ED visits	0.01	0.03	0.03	0.03	2.04 (1.58–2.63)	2.11 (1.54–2.88)	2.21 (1.71–2.86)
Per 1000 anxiety disorder ED visits							
Anxiety + cannabis ED visits	3.85	7.07	8.57	10.40	1.80 (1.62–2.01)	2.16 (1.90–2.45)	2.66 (2.40–2.95)
Anxiety + alcohol ED visits	9.57	11.35	12.26	12.66	1.18 (1.11–1.26)	1.29 (1.19–1.39)	1.32 (1.23–1.41)
Anxiety + cannabis + alcohol ED visits	0.43	0.78	0.85	1.00	1.80 (1.29–2.32)	1.91 (1.40–2.60)	2.29 (1.77–2.96)

The medical cannabis legalization with restrictions (Period 1) is compared with the three following policy periods. ED = emergency department. [a]Period 1 defined as January 2008–November 2015 (95 months). [b]Period 2 defined as December 2015–September 2018 (34 months). [c]Period 3 defined as October 2018–February 2020 (17 months). [d]Period 4 defined as March 2020–July 2022 (29 months). [e]Risk Ratio adjusted for season.

Table 2: **Mean monthly rate of ED visits per capita and per all-cause anxiety disorder ED visits in Ontario, Canada.**

P1, 2.26; 95% CI, 2.00–2.55, p interaction < 0.001). With increasing age, those older than 45 had a higher monthly anxiety and cannabis ED visit rate (RR P4 vs P1, 4.37; 95% CI, 3.10–6.17) compared with 19–24 year old's (RR P4 vs P1, 2.25; 95% CI, 1.94–2.62, p interaction < 0.001). There was also a 212% increase in the rate of anxiety and cannabis ED visits for those with no previous acute care anxiety ED visit in the last two years (RR P4 vs P1, 3.12; 95% CI, 2.60–3.75) compared to a 153% increase in the rate of those with a past acute care anxiety ED visit (RR P4 vs P1, 2.53; 95% CI, 2.28–2.81, p interaction < 0.05). There were no significant differences in change over time by neighbourhood income quintile (p interaction = 0.85) or rurality (p interaction = 0.91). See Supplementary Table S3 for comparisons with policy periods 2 and 3.

Discussion

In this population-based study, we found the per capita rate of ED visits for anxiety disorders with cannabis involvement increased by 156% during the period of legal cannabis commercialization/COVID-19 relative to the pre-legal period. In comparison over the same period, there were 27% increases in ED visits for anxiety disorders with alcohol-involvement. Per capita rates of ED visits for anxiety disorder with cannabis involvement increased gradually over time and were not influenced by the liberalization of medical cannabis, the legalization of non-medical cannabis with restrictions, or commercialization/COVID-19. During the cannabis commercialization/COVID-19 period, there was an immediate 31.4% increase in the proportion of cannabis involvement in anxiety disorder ED visits. The increase was driven by a large significant decline in overall anxiety visits and a small non-significant increase in anxiety visits with cannabis involvement, and during the same period there were significant decreases in anxiety ED visits with alcohol-involvement. The relative increase over time in cannabis involvement in anxiety ED visits was greater in women compared to men and older individuals compared to younger individuals.

Increasing cannabis-involvement in anxiety disorder ED visits findings are consistent with prior studies showing increases in cannabis use and cannabis-related health service visits over time in Ontario and other jurisdictions liberalizing cannabis policy.[22–26] While it is challenging to isolate out the effects of changing social norms towards cannabis use and policy changes, our findings suggest a steady increase in cannabis-involvement in anxiety disorder ED visits over time. During the final period of our study – market commercialization/COVID-19 per capita rates of anxiety ED visits with cannabis involvement were unchanged but the overall portion of anxiety ED visits with cannabis involvement increased. The pandemic has had well-documented influences on anxiety disorders, including declines in ED visits, along with changes in substance

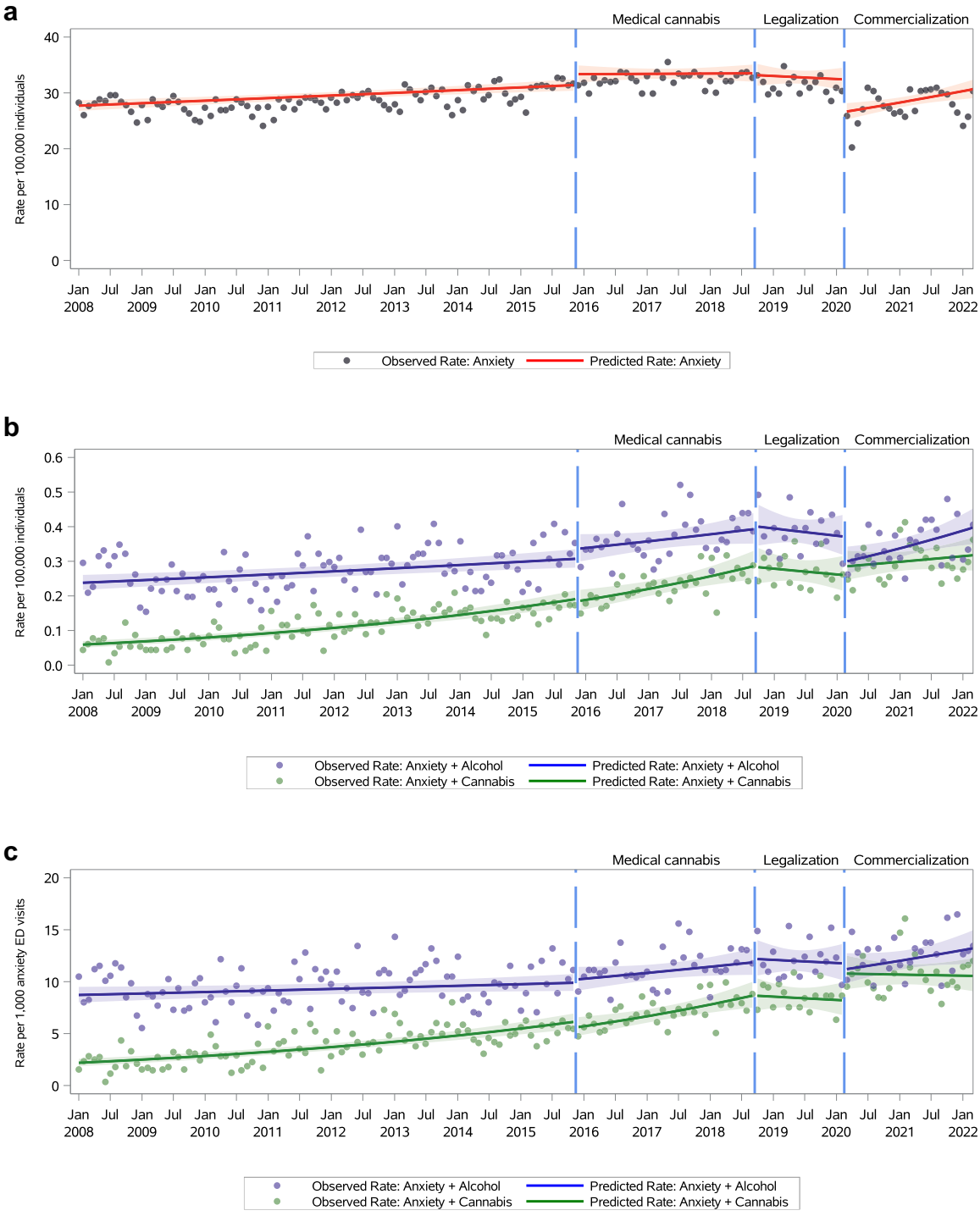
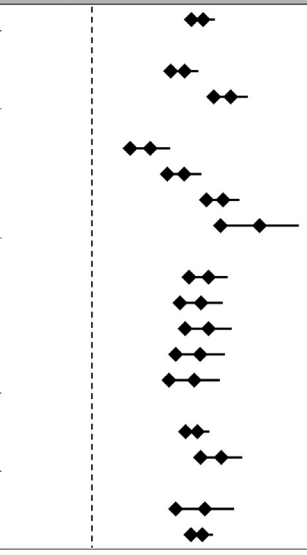


Fig. 1: Observed and mean monthly rates of anxiety disorder ED visits in Ontario, Canada during four policy time periods indicated by three vertical dashed lines. (a) Monthly anxiety disorder ED visits per capita. (b) Monthly anxiety + cannabis ED visits (green) or anxiety + alcohol ED visits (blue, tracer condition) per capita. (c) Monthly anxiety + cannabis ED visits or anxiety + alcohol ED visits per all-cause anxiety disorder ED visits.

use.[27–29] Consequently, separating the pandemic and cannabis policy effects is challenging. One possibility for our findings is that individuals with anxiety disorder who use cannabis are less likely to avoid presentations to the ED during a pandemic. Alternatively, market commercialization may have contributed to increased

Subgroup	Medical cannabis legalization with restrictions (Period 1) Monthly rate per 1,000 anxiety disorder ED visits	Commercialization /COVID-19 (Period 4) Monthly rate per 1,000 anxiety disorder ED visits	Risk Ratio[a] Period 4 vs Period 1 (95% CI)	p-value[b]
Overall	3.85	10.42	2.66 (2.40 - 2.95)	
Sex				<0.001
Male	6.20	14.07	2.26 (2.00 - 2.55)	
Female	2.23	7.80	3.39 (2.92 - 3.94)	
Age				<0.001
10-18 years	10.46	18.53	1.67 (1.40 - 1.99)	
19-24 years	8.65	20.17	2.25 (1.94 - 2.62)	
25-44 years	3.33	10.60	3.17 (2.74 - 3.66)	
45+ years	0.56	2.42	4.37 (3.10 - 6.17)	
Neighbourhood Income Quintile				0.85
1 (poorest)	3.59	10.27	2.79 (2.35 - 3.30)	
2	4.00	10.59	2.61 (2.17 - 3.16)	
3	3.72	10.60	2.79 (2.27 - 3.42)	
4	3.91	10.26	2.59 (2.09 - 3.22)	
5 (richest)	4.16	10.48	2.46 (1.97 - 3.08)	
Acute Care Anxiety Disorder ED Visit Last 2 Years				0.045
Yes	4.04	10.31	2.53 (2.28 - 2.81)	
No	3.30	10.72	3.12 (2.60 - 3.75)	
Rurality				0.91
Rural	2.58	6.99	2.70 (2.09 - 3.49)	
Urban	4.16	11.16	2.64 (2.39 - 2.90)	



Medical cannabis legalization (period 1) is compared with cannabis commercialization/COVID-19 (period 4). The other policy periods are in Supplementary Table S2. ED = emergency department. [a]Risk Ratio adjusted for season. [b]P-value is the interaction between the exposure and the subgroup.

Table 3: **Subgroup mean monthly rate of anxiety disorder + cannabis ED visits per 1000 anxiety disorder ED visits.**

cannabis use. Prior work has found that increased access to cannabis retail stores and higher-strength products are associated with greater cannabis use and related-harms.[30–32] Our sensitivity analysis, excluding the first five months of the COVID-19 pandemic, continued to show increases during this period, which supports some commercialization influence. In addition, during the commercialization/COVID-19 period there was a large decrease in anxiety disorder ED visits with alcohol-involvement suggesting that factors other than pandemic stressors and pandemic influenced-substance use might have been responsible for the observed increases in cannabis-involvement in anxiety disorder ED visits. Ultimately, both market expansion and pandemic influences may have contributed to changes during the final study period and ongoing monitoring is indicated.

Whether or not the relationship between cannabis use and anxiety disorders is causal continues to be unclear.[33] Individuals with anxiety disorders are more likely to self-report using cannabis to treat anxiety symptoms.[34] Cannabis may also cause the exacerbation and development of anxiety disorders.[35] In our study, we are unable to determine whether increasing cannabis involvement reflects an increase in ED visits for anxiety disorders caused by cannabis, self-treatment of anxiety disorders with cannabis, or both. We found that cannabis involvement in anxiety disorder ED visits increased more in individuals with no previous care for anxiety than in those who had previously received care. This finding suggests that cannabis use may be increasingly causing new anxiety disorders, or more individuals are trying to use cannabis to alleviate anxiety symptoms before seeking care from a physician. Clinically, there is limited evidence on the effectiveness of cannabis use for the management of anxiety disorders and cannabis use may complicate or delay other evidence-based treatments. The increases reported within our study emphasize the roles of clinicians in patient education and counselling. Our subgroup analyses suggest that women and older adults have experienced the largest increases over time in cannabis-involvement in anxiety disorder ED visits. This is consistent with survey data finding the relationship between problematic cannabis use and anxiety is moderated by gender, with females reporting a stronger effect.[34] While young men had the highest rates of cannabis-involvement in anxiety disorder ED visits, clinicians should be aware of changing demographics of harmful patterns of cannabis use. From a policy standpoint, our findings suggest these increases may be a harm of cannabis legalization. Further measures are indicated to prevent increases in cannabis use during anxiety episodes after cannabis legalization and subsequent market expansion.

Limitations

Our study has limitations. First, as previously noted the close overlap of the COVID-19 pandemic with the commercialization of the cannabis market challenges the attribution of the observed changes during the final study period to either event. Findings during their period should be interpreted with caution and ongoing monitoring is indicated. Second, our method of detecting cannabis-involvement in anxiety disorder ED visits, which is based on the treating team documenting that cannabis use caused or contributed to the ED visit for anxiety disorders, likely only detects a small portion of ED visits for anxiety disorders in which the person used cannabis. We likely underestimate the proportion of individuals with anxiety disorder ED visits who use cannabis. Part of the increases over time in cannabis involvement may reflect better detection and documentation of cannabis use in anxiety presentations. Third, we lacked data on patterns of cannabis use and cannabis products. We have no information on patterns of use, source of the product (i.e., recreational, medical, or illicit) and product type (i.e., vapes, edibles, concentrates) and ongoing research is indicated to understand how different patterns of use and products may influence anxiety. Fourth, while we examined co-use of cannabis and alcohol, anxiety ED visits can involve additional substances. Future work can examine changes in other types of polysubstance use (e.g., cannabis and stimulant use). Fifth, changes over time and from the pandemic on our control condition, alcohol involvement in anxiety visits, may differ from cannabis. Nonetheless, larger increases in cannabis involvement than alcohol involvement over time in anxiety visits may suggest important shifts in co-morbid substance use in anxiety disorders. Finally, as previous mentioned we are unable to fully distinguish whether cannabis use is causing anxiety disorders, being used to self-medicate anxiety symptoms, or both.

Conclusions

Cannabis involvement in ED visits for anxiety disorders has increased substantially over the past 14 years, and neither medical cannabis liberalization nor non-medical cannabis legalization with restrictions was associated with a change in this trend. In contrast, cannabis-involvement in anxiety disorder ED visits may have accelerated during cannabis market commercialization and the COVID-19 pandemic. The bidirectionality of these findings may reflect increasing anxiety disorder problems from cannabis use, increasing self-medication of anxiety disorders with cannabis use, or both. Greater awareness and inquiry about cannabis use in individuals with anxiety disorders may be indicated, particularly in women and older adults who have seen the largest relative increases over time.

Contributors

DM and SM participated in the design and concept of the study. DM and MP had full access to all the data in the study, conducted statistical analysis, and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to the acquisition, analysis, and interpretation of the data. DM, SM, and JX wrote the first and revised drafts of the manuscript. All authors contributed to the critical revision of the manuscript. DM obtained funding and provided supervision. All authors approved the final version of the manuscript for publication.

Data sharing statement

The data set from this study is held securely at IC/ES. IC/ES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. While data-sharing agreements prohibit IC/ES 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.

Declaration of interests

The authors have no conflicts of interest relevant to this article to disclose.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2024.100815.

References

1 Onaemo VN, Fawehinmi TO, D'Arcy C. Comorbid cannabis use disorder with major depression and generalized anxiety disorder: a systematic review with meta-analysis of nationally representative epidemiological surveys. Elsevier B.V. *J Affect Disord*. 2021;281:467–475
2 Gage SH, Hickman M, Zammit S. Review association between cannabis and psychosis: epidemiologic evidence [cited 2024 Apr 8]; Available from: https://doi.org/10.1016/j.biopsych.2015.08.001.
3 Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E. Meta-analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr Bull*. 2016;42(5):1262–1269 [cited 2024 Apr 8]; Available from: https://academic.oup.com/schizophreniabulletin/article/42/5/1262/2413827.
4 Urits I, Gress K, Charipova K, et al. Cannabis use and its association with psychological disorders. *Psychopharmacol Bull*. 2020;50(2):56 [cited 2024 Apr 8]; Available from:/pmc/articles/PMC7255842/.
5 Cougle JR, Hakes JK, Macatee RJ, Chavarria J, Zvolensky MJ. Quality of life and risk of psychiatric disorders among regular users of alcohol, nicotine, and cannabis: an analysis of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) [cited 2024 Apr 8]; Available from: https://doi.org/10.1016/j.jpsychires.2015.05.004; 2015.
6 Myran DT, Harrison LD, Pugliese M, et al. Transition to schizophrenia spectrum disorder following emergency department visits due to substance use with and without psychosis. *JAMA Psychiatr*. 2023;80(11):1169–1174 [cited 2024 Feb 27]; Available from: https://

jamanetwork-com.proxy1.lib.uwo.ca/journals/jamapsychiatry/fullarticle/2809870.
7 Solmi M, De Toffol M, Kim JY, et al. Balancing risks and benefits of cannabis use: umbrella review of meta-analyses of randomised controlled trials and observational studies. *BMJ*. 2023;382:44 [cited 2024 Feb 27]; Available from: https://www.bmj.com/content/382/bmj-2022-072348.
8 Shao H, Du H, Gan Q, et al. Trends of the global burden of disease attributable to cannabis use disorder in 204 countries and territories, 1990–2019: results from the disease burden study 2019. *Int J Ment Health Addict*. 2023. https://doi.org/10.1007/s11469-022-00999-4 [cited 2024 Apr 8]; 1. Available from:/pmc/articles/PMC9913032/.
9 Delling FN, Vittinghoff E, Dewland TA, et al. Does cannabis legalisation change healthcare utilisation? A population-based study using the healthcare cost and utilisation project in Colorado, USA. *BMJ Open*. 2019;9(5):e027432.
10 Weinberger AH, Zhu J, Levin J, et al. Cannabis use among US adults with anxiety from 2008 to 2017: the role of state-level cannabis legalization [cited 2024 Apr 8]; Available from: https://doi.org/10.1016/j.drugalcdep.2020.108163; 2020.
11 Shim M, Nguyen H, Grootendorst P. Lessons from 20 years of medical cannabis use in Canada. *PLoS One*. 2023;18(3):e0271079 [cited 2024 Feb 7]; Available from: https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0271079.
12 Task Force on Cannabis Legalization and Regulation. Health Canada. *A framework for the legalization and regulation of cannabis in Canada* 2016.
13 Parliament of Canada. *Bill C-45: the cannabis Act* 2018.
14 Myran DT, Friesen EL, Dickson S, Konikoff L, Arora G, Tanuseputro P. Access to legal cannabis market in Canada over the four years following non-medical cannabis legalisation. *Drug Alcohol Rev*. 2023;42(5):1114–1119 [cited 2023 Dec 6]; Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/dar.13650.
15 Myran DT, Pugliese M, Tanuseputro P, Cantor N, Rhodes E, Taljaard M. The association between recreational cannabis legalization, commercialization and cannabis-attributable emergency department visits in Ontario, Canada: an interrupted time–series analysis. *Addiction*. 2022;117(7):1952–1960.
16 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *BMJ*. 2007;335(7624):806 [cited 2024 Apr 8]; Available from:/pmc/articles/PMC2034723/.
17 Government of Ontario. What OHIP covers [cited 2024 Apr 8]. Available from: https://www.ontario.ca/page/what-ohip-covers.
18 Canadian Institute for Health Information. *Hospital stays for harm caused by substance use*; 2020 [cited 2023 Dec 6]. Available from: https://www.cihi.ca/en/indicators/hospital-stays-for-harm-caused-by-substance-use.
19 *Population centre and rural area classification*; 2016 [cited 2024 Jan 31]. Available from: https://www.statcan.gc.ca/en/subjects/standard/pcrac/2016/introduction.
20 ICES. Mental health and addictions system performance in ontario: a baseline scorecard [cited 2024 Apr 8]. Available from: https://www.ices.on.ca/publications/research-reports/mental-health-and-addictions-system-performance-in-ontario-a-baseline-scorecard/.
21 Turner SL, Forbes AB, Karahalios A, Taljaard M, McKenzie JE. Evaluation of statistical methods used in the analysis of interrupted time series studies: a simulation study. *BMC Med Res Methodol*. 2021;21(1):1–18 [cited 2024 May 6]; Available from: https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/s12874-021-01364-0.
22 Crocker CE, Carter AJE, Emsley JG, Magee K, Atkinson P, Tibbo PG. When cannabis use goes wrong: mental health side effects of cannabis use that present to emergency services. Frontiers Media S.A. *Front Psychiatry*. 2021;12:640222
23 Myran DT, Roberts R, Pugliese M, Taljaard M, Tanuseputro P, Pacula RL. Changes in emergency department visits for cannabis hyperemesis syndrome following recreational cannabis legalization and subsequent commercialization in Ontario, Canada. *JAMA Netw Open*. 2022;5(9):e2231937.
24 Imtiaz S, Nigatu YT, Ali F, et al. Cannabis legalization and cannabis use, daily cannabis use and cannabis-related problems among adults in Ontario, Canada (2001–2019). *Drug Alcohol Depend*. 2023;244:109765.
25 Myran DT, Pugliese M, Roberts RL, et al. Association between non-medical cannabis legalization and emergency department visits for cannabis-induced psychosis. *Mol Psychiatry*. 2023;28:4251–4260.
26 Myran DT, Gaudreault A, Konikoff L, Talarico R, Liccardo Pacula R. Changes in cannabis-attributable hospitalizations following nonmedical cannabis legalization in Canada key points. *JAMA Netw Open*. 2023;6(10):2336113.
27 Craig SG, Ames ME, Bondi BC, Pepler DJ. Canadian adolescents' mental health and substance use during the COVID-19 pandemic: associations with COVID-19 stressors. *Can J Behav Sci*. 2022;55(1):46–55.
28 Kim S, Rajack N, Mondoux SE, Tardelli VS, Kolla NJ, Le Foll B. The COVID-19 impact and characterization on substance use-related emergency department visits for adolescents and young adults in Canada: practical implications. *J Eval Clin Pract*. 2023;29(3):447–458.
29 Plett D, Pechlivanoglou P, Coyte PC. The impact of provincial lockdown policies and COVID-19 case and mortality rates on anxiety in Canada. *Psychiatry Clin Neurosci*. 2022;76(9):468–474.
30 Myran DT, Imtiaz S, Konikoff L, Douglas L, Elton-Marshall T. 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*. 2022;42:277–298 [cited 2022 Nov 7]; Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/dar.13546.
31 Cantor N, Silverman M, Gaudreault A, et al. The association between physical availability of cannabis retail outlets and frequent cannabis use and related health harms: a systematic review. *Lancet Reg Health Am*. 2024;32:100708 [cited 2024 Mar 6]; Available from: https://linkinghub.elsevier.com/retrieve/pii/S2667193X24000358.
32 Petrilli K, Ofori S, Hines L, Taylor G, Adams S, Freeman TP. Association of cannabis potency with mental ill health and addiction: a systematic review. *Lancet Psychiatr*. 2022;9(9):736–750 [cited 2022 Nov 15]; Available from: http://www.thelancet.com/article/S2215036622001614/fulltext.
33 Hall KE, Monte AA, Chang T, et al. Mental health–related emergency department visits associated with cannabis in Colorado. *Acad Emerg Med*. 2018;25(5):526–537.
34 Hellemans KGC, Wilcox J, Nino JN, Young M, McQuaid RJ. Cannabis use, anxiety, and perceptions of risk among Canadian undergraduates: the moderating role of gender. *Can J Addict*. 2019;10(3):22–29.
35 Myran DT, Harrison LD, Pugliese M, et al. Development of an anxiety disorder following an emergency department visit due to cannabis use: a population-based cohort study. *EClinicalMedicine*. 2024;69:102455 [cited 2024 Feb 15]; Available from: http://www.thelancet.com/article/S2589537024000348/fulltext.