The association between physical availability of cannabis retail outlets and frequent cannabis use and related health harms: a systematic review

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Summary

An increasing number of regions have or are considering legalising the sale of cannabis for adult use. Experience from tobacco and alcohol regulation has found that greater access to physical retail stores is positively associated with increased substance use and harm. Whether this association exists for cannabis is unclear. We completed a systematic review examining the association between cannabis retail store access and adverse health outcomes. We identified articles up until July 20, 2023 by searching four databases. We included studies examining the association between measures of cannabis store access and adverse outcomes: frequent or problematic cannabis use, healthcare encounters due to cannabis use (e.g., cannabis-induced psychosis), and healthcare encounters potentially related to cannabis (e.g., self-harm episodes). Results were compared by study design type, retail access measure, and by subgroups including: children, adolescents, young adults, adults, and pregnant individuals. This review was registered with PROSPERO (CRD42021281788). The search generated 5750 citations of which we included 32 studies containing 44 unique primary analyses (unique retail measure and outcome pairs). Studies come from 4 countries (United States, Canada, Netherlands and Uruguay). Among the included analyses, there were consistent positive associations between greater cannabis retail access and 1) increased healthcare service use or poison control calls directly due to cannabis (10/12 analyses; 83%) (2) increased cannabis use and cannabis-related hospitalization during pregnancy (4/4; 100%) and 3) frequent cannabis use in adults and young adults (7/11; 64%). There was no consistent positive association between greater cannabis retail and increased frequent cannabis use in adolescents (1/4; 25%), healthcare service use potentially related to cannabis (2/6; 33%) or increased adverse neonatal birth outcomes (2/7; 26.8%). There is a positive association between greater cannabis store access and increases in cannabis harm. In countries with legal cannabis, retail restrictions may reduce use and harm.

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Introduction

An increasing number of countries and US states have legalised or are considering legalising the sale of medical or non-medical (i.e., recreational) cannabis for adult use.^{1,2} Legalisation has potential benefits, including reducing social harms and inequities arising from criminal records³ and generating government revenue.⁴ In contrast, there are public health concerns that legalisation, particularly commercialisation (e.g., increasing retail store access, marketing and promotion, and increasing product type and potency), may result in increased problematic cannabis use and consequent



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health and social harms.5-7 Evidence from the alcohol and tobacco literature has found that greater access to physical retail stores is associated with increased substance use and harms.8-10 Increases in the number and hours of operation of alcohol outlets^{9,11} are associated with increased alcohol-related harms. Similarly, increased proximity to tobacco outlets has been associated with increased rates of youth smoking12 and reduced levels of smoking cessation.13 Consequently, regulating the density of alcohol retail outlets and restricting hours and days of sale are considered "best buys" for reducing population-level alcohol use and harms and is recommended by the World Health Organization.¹⁴ There are important differences between cannabis and alcohol and tobacco, which decrease the generalisability of these findings (e.g., large pre-existing illicit cannabis markets). Consequently, determining whether access to cannabis retail stores is associated with greater cannabis use and harms is a crucial research question to inform evidence-based policy in jurisdictions considering and proceeding with legalisation.

An increasing number of studies have examined the association between cannabis retail access and consequent health harms. A systematic review of US studies examining the association between cannabis store access and traffic-related outcomes (i.e., fatal collisions) found that 6/9 (66.7%) studies identified a positive association between greater retail access and harms.15 A systematic review examined the association between cannabis retail access and cannabis use, including a small number of cannabis harms such as psychosis, vomiting, or cannabis-involved pregnancies.¹⁶ Importantly, the review mainly focused on changes in pastyear or past-month cannabis use (7 or the 13 included studies), which has lower public health and clinical relevance than healthcare visits due to cannabis use or measures of frequent use such as cannabis use disorders.16 The review included only three small studies, all from Colorado state, examining the association between cannabis retail access and healthcare visits related to cannabis use. In addition, the number of studies in this area has expanded rapidly, including a growing number of studies from Canada, which recently legalised nonmedical cannabis. Consequently, the relationship between retail access and cannabis-related health harms (e.g., health care visits, cannabis use disorder, and daily cannabis use) has not been adequately appraised and synthesised.

To address this gap, we conducted a systematic review of studies examining the relationship between physical cannabis retail access, harmful cannabis use, and related health harms. To ensure clinical and public health relevance, we limited our outcomes to healthcare visits caused by cannabis, diagnoses of cannabis use disorders, harmful cannabis use (e.g., daily or near-daily use, use during pregnancy), or conditions potentially related to harmful cannabis use (e.g., episodes of selfharm, vomiting-related emergency department visits, adverse neonatal outcomes).

Methods

This study was registered on PROSPERO (CRD42021281788)¹⁷ and completed according to Preferred Reporting Items for Systematic Review and Meta-Analysis for Protocols (PRISMA-P) reporting guidelines. See Supplementary Fig. S1 for a completed PRSIMA checklist.

Search strategy and inclusion criteria

We searched the following databases for this review: Medline (OVID interface), EMBASE (OVID interface), CINAHL (EBSCO interface) and PsycINFO (OVID interface). The search included studies from database inception to July 20th 2023, including those in prepublication. Articles that were selected for inclusion following full-text screening had their reference lists inspected for any additional eligible studies. Additional articles were also identified by expert author opinion. Our search strategies were developed by a health science librarian with expertise in systematic reviews (LS) and peer-reviewed according to the Peer Review of Electronic Search Strategies (PRESS) Framework. See Supplementary Materials for our search strategy (Appendix A).

Eligibility criteria were defined *a priori*, and were framed according to criteria regarding population, exposure, outcomes, and study design as described below. Only English-language, published, peer-reviewed articles with full-texts available were included in this review. Conference proceedings and abstracts were excluded.

Population

Studies involving the general population and those involving key subpopulations (adolescents, paediatrics, young adults and pregnant individuals) were included.

Exposures

The primary exposure of interest was access to physical cannabis retailers. Given anticipated variability between studies, we included multiple measures of physical cannabis retail access. We used the United States Centres for Disease Control (CDC) guide for measuring alcohol outlet density¹⁸ to inform the creation of three exposure categories: 1) container-based measures (e.g., measuring the number of cannabis outlets in a specified area); 2) distance-based measures (e.g., measuring the distance between a reference point such as home address or zip code centre to surrounding cannabis outlets); and 3) spatial access-based measures (spatial access index between the reference point and a prespecified number of surrounding cannabis outlets

weighted by distance or travel time). A fourth exposure category was created after our systematic search to include studies with crude pre-post exposure variables (e.g., a categorical measure denoting periods of changing retail access, typically before and after opening at least one cannabis retailer or removal of limits on retail store density). Different types of cannabis (medical vs. non-medical) and legal store regulations (i.e., legal, illicit, delivery, or grey market) were eligible for inclusion. Studies assessing legalisation without an explicit retail store access measure were excluded from this review.

Comparator

The comparison group of interest consisted of exposure groups involving either no access or comparatively less physical access to retail cannabis outlets (relative to the exposure group) through measures such as proximity, outlet density, or degree of commercialisation.

Outcomes

Outcomes of interest were determined a priori to include those considered by the study team as most relevant to public health. Outcomes of interest included health harms related to cannabis use resulting in a healthcare encounter (such as emergency department visits or hospitalisations due to cannabis and/or unintentional poisonings from administrative databases), cannabis use during pregnancy and neonatal birth outcomes (i.e., admissions to NICU, pre-term births), and frequent or problematic cannabis use (measured via a validated screening instrument or self-report). We excluded studies that examined less clinically relevant measures of cannabis use (i.e., lifetime or any past-year use). We excluded studies examining the association between physical retail access to cannabis and drivingrelated outcomes (i.e., motor vehicle collisions), as a recent systematic review has previously examined this relationship.15 We excluded studies examining changes in other drugs or alcohol use, including polysubstance use or substitution effects of cannabis use on other drugs (i.e., reduction in opioid use, increases in emergency department visits for co-cannabis and alcohol use) given the importance of accounting for concurrent changes in drug and alcohol policy in such analyses, which would be out of scope of the current review.

Study design

Eligible study designs included cross-sectional, cohort studies, and randomised-controlled trials. We identified whether studies used quasi-experimental methods (i.e., interrupted time series, difference-in-difference designs) based on an accepted methodology.¹⁹

Study selection and data extraction

Article screening was conducted in Covidence Systematic Review Management.²⁰ All titles and abstracts included in the screening stage were reviewed by two independent screeners (NC and MS), and conflicts were resolved by a third author (DM). See Fig. 1 for a summary of the study selection process. Data from eligible articles was extracted into a standardized form; see details on data extraction in Appendix B.

Risk of bias

Risk of bias assessment was conducted using the JBI clinical appraisal tools by two reviewers (NC and MS).²¹ See Appendix C for details on the JBI tool Appendix D for a full completed checklist.

Data analysis

We completed a descriptive synthesis of study findings consistent with the PRISMA 2020 Statement and the Synthesis Without Meta-Analysis guidelines.²² Studies were organized according to study outcomes (health service use, problematic use, birth outcomes) and populations (adults, children, young adults, and pregnant individuals). As some studies used inconsistent age ranges to classify young adults, we classified studies as focusing on young adults if the mean age range was between 18 and 25 given that this is a critical period of neurodevelopment with potentially unique harms.²³ Similarly, for studies that included all ages, we grouped them into either adult (18+), adolescent (10-18), or paediatric (0-9) based on the mean age range as calculated from the baseline summary statistics. When studies reported multiple exposure-outcome measures (i.e., impact of retail outlets on various neonatal birth outcomes, multiple retail access measures' association with cannabis use), we included all stated primary analyses but excluded any sensitivity analyses. We considered statistical significance for primary analyses as p < 0.05. We also completed a sensitivity analysis considering statistical significance at p = 0.10. Given substantial study heterogeneity between exposures and outcomes, meta-analysis was not performed.

Results

Search outcomes

Database searches identified 5750 citations, of which 1233 duplicates were removed. Two investigators (NC and MS) completed title and abstract screening and excluded 4417 articles. Of the 100 articles assessed for eligibility, 24 met final inclusion criteria for this review (see Fig. 1 for PRISMA Flowchart and reasons for exclusion). Eight additional articles were identified from screening reference lists from primary papers or through expert opinion as meeting the inclusion criteria, and a total of 32 articles were included.

Overview of included studies

Of the 32 included studies, almost all (n = 25) were conducted in the United States, while the remaining were

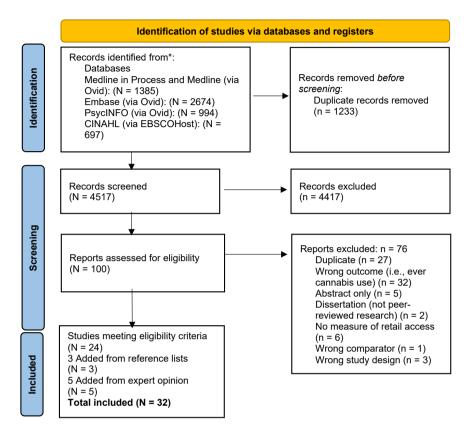


Fig. 1: PRISMA flowchart of included studies and reasons for exclusion.

from Canada (n = 4), the Netherlands (n = 1), and Uruguay (n = 2). Overall, study data came from 2003 to 2021, with 59% of studies including data between 2017 and 2021. Most studies assessed recreational cannabis dispensaries (n = 21), while a minority considered medical dispensaries (n = 5) or a combination of both (n = 6). See Table 1 for details on included studies and Supplementary Table S1 for detailed information on method of analyses and included results. We stratified cannabis retail access into the following pre-defined categories: 1) Crude pre-post exposure (i.e., categorical variables denoting periods of changing retail access, n = 16); 2) Container-based measures (i.e., cannabis outlet density per person or area, n = 11; and 3) Distance-based measures (i.e., proximity to cannabis outlets, n = 5); and 4) Spatial access-based measures (i.e., advanced geospatial methods, n = 4). 14 studies employed a cross-sectional design (single cross-sectional = 6, repeated crosssectional = 8), eight employed a cohort design, and ten reported using a quasi-experimental design (including difference-in-difference, interrupted time series, or lottery assignment of outlets). Analyses, including other retail measures (delivery service $[n = 1]^{24}$ or illicit storefronts $[n = 1]^{25}$), are not included in the main text or Fig. 2 but are reported for completeness in Supplementary Table S1.

The 32 studies contained 44 primary analyses examining associations between increasing cannabis retail access and cannabis-related harms. 26 (60%) analyses found evidence of a statistically significant association between increasing retail access and increasing harms, while 16 (36%) found no statistically significant associations between increasing retail access and increasing harms. Two (5%) analyses found evidence of a statistically significant association between increased retail access and decreasing cannabis-related harms. See Fig. 2 for a visual summary of findings. In a sensitivity analysis using a p value of 0.10 to define statistical significance, an additional two primary analyses^{26,27} (64%, 28/44 primary analyses) reported a significant association between increased cannabis retail access and increased cannabis use and harms. See full results of sensitivity analysis in Supplementary Table S2.

Studies examined the following three outcomes categories: 1) Harms resulting in health care service use in children or adults (n = 16)^{28–36}; 2) Cannabis use during pregnancy or neonatal birth outcomes, such as admission to NICU and low birth weight (n = 5)^{27,37–40}; and 3) Frequent and/or problematic cannabis use, as assessed by a validated screener or self-report measure (n = 11).^{24,25,41–46} Complete study details can be found in Table 1 and Supplementary Table S1.

Stody and region	period	sample size	Study design and population details	Cannabis retail type	Exposure type	Specific exposure measured	Outcome(s)
Thomas et al. (2021) USA (WA)	2007-2016	N = 17	Single centre, retrospective cohort study of paediatric hospitalizations (Age = 0–9 years)	Non-medical	Pre-post introduction of retail outlets (binary variable)	2	
Thomas et al. (2019) USA (WA)	2010-2016	N = 161	State-wide, retrospective cohort study of paediatric poison control cases reported to the WA Poison Centre (Age = 0–9 years)	Non-medical	Pre-post introduction of retail outlets (categorical variable)		Unintentional paediatric cannabis exposures
Matthay et al. (2021) USA (All States)	2003–2017	N = 75 395 344	Population-level, retrospective cohort study of self-harm insurance claims in adults	Non-medical	Pre-post introduction of retail outlets (categorical variable)	States with RCL and outlets compared to those with varying cannabis polices but no outlets	Insurance claims of ICD-9 and -10 codes for self-harm
Shi and Liang (2020) ³⁶ USA (All States)	2010-2017	Not reported	Population-level, longitudinal cohort study of adult poison exposures reported to US National Poison Data System		Pre-post introduction of retail outlets (categorical variable)	States with RCL compared to states with and without MCL	
Mair et al. (2021) ³⁰ USA (CA)	2013-2016	N = 38 736 312	State-wide, longitudinal cohort study of cannabis- related adult hospitalizations	Medical	Geospatial access methods	cannabis outlets	Hospitalizations or emergency department visit due to cannabis abuse and dependence
Conyers and Ayres (2020) USA (AZ)	2010–2016	N = 2 087 880	State-level, retrospective cohort study of emergency department visits due to cannabis in adults	Medical	Container-based	least 1 medical cannabis outlet in a winning ZIP code	Emergency department visits due to cannabis abus and poisoning by psycho- dysleptics (ICD-9 and -10 codes)
Mair et al. (2015) USA (CA)	2012	Not reported	State-wide, single cross- sectional study of adults living in any ZIP code in CA with a medical cannabis outlet in 2012	Medical	Geospatial access methods	Local ZIP code outlet density (measured as one additional medical cannabis outlet per mile2)	cannabis dependence or
Wang et al. (2021) USA (CO)	2013-2018	Not reported	State-level, repeated cross- sectional study of emergency department visits due to vomiting in adults	Both	Container-based	 Baseline exposure to medical outlets (0, 1–9, >10) Growth in new 	Vomiting-involved emergency department visi (ICD-9 and -10 codes), eithe alone or co-occurring with cannabis-related ICD-9 and -10 codes
Myran et al. (2022) Canada (ON)	2016-2021	N = 13 853 396	Province-wide, multiple-ITS design study of emergency department visits due to cannabis in adults	Non-medical	Pre-post introduction of retail outlets (categorical variable)	legalization Period 1: Post-cannabis legalization with strict score restrictions	Cannabis-attributable emergency department visit (ICD-10 F12 for mental and behavioural disorders due t cannabis use and T40.7 for cannabis poisonings)
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	Study and region	Study period	Sample size	Study design and population details	Cannabis retail type	Exposure type	Specific exposure measured	Outcome(s)
(Continued from previous page	ge)							
	Myran et al. (2022) Canada (ON)	2014-2021	N = 12 866 emergency department visits (8140 individuals)	Province-wide, repeated cross-sectional ITS study of emergency department visits due to cannabis in adults	Non-medical	Pre-post introduction of retail outlets (categorical variable)	Period 0: Pre-cannabis legalization Period 1: Post-cannabis legalization with strict score restrictions Period 2: Post-cannabis legalization with no store restrictions	Monthly counts of emergency department visits for cannabis hyperemesis syndrome per capita (ICD-10 R11 was primary diagnosis and a cannabis harm i.e., ICD-10-CA code F12 or T40.7 was an additional diagnosis)
	Tolan et al. (2023) USA	2010-2019	Not reported	Multi-state, repeated cross- sectional study of monthly rates of cannabinoid immunoassay and cannabis- related emergency department visits across 15 different states		Pre-post introduction of retail outlets (categorical variable)	Stages of legalization: 1. No state laws 2. Decriminalized 3. Medical approval before dispensaries 4. Medical dispensaries available 5. Recreational approval before dispensaries 6. Recreational dispensaries available	Trends and monthly rates of cannabinoid immunoassay and cannabis-related emergency department visits (using ICD-9 and -10 codes for cannabis use, abuse and dependence, poisoning and adverse effects, and cannabinosis)
	Myran et al. (2023) Canada (ON)	2014-2021	N = 14 015 365 (6300 visits)	Province-wide, population level cohort ITS study of emergency department visits for cannabis-induced psychosis in adults (15+)	Non-medical	Pre-post introduction of retail outlets (categorical variable)	Period 1: Pre-cannabis legalization Period 2: Post-cannabis legalization with strict score restrictions Period 3: Post-cannabis legalization with no store restrictions	Monthly count of emergency department visits for cannabis-induced psychosis (ICD-10 code F12.5 or F12.7—psychotic disorders, or residual and late-onset psychotic disorder due to the use of cannabinoids) as main contributing reason for visit. Secondary outcome was first presentation emergency department visits for cannabis-induced psychosis
	Elser et al. (2023) USA	2003-2017	N = 63 680 589	National, retrospective cohort study of psychosis- related insurance claims (commercial and Medicare Advantage) in adults (16+)		Pre-post introduction of retail outlets (categorical variable)	were open and operational. 1. No medical or recreational policy 2. Medical only, no retail outlets 3. Medical only, retails outlets 4. Recreational, no retail outlets 5. Recreational, retail outlets	ICD-10 coding, subclassified as nonaffective psychoses, mood disorders with psychotic features, substance-related psychosis, and other psychosis

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	Study and region	Study period	Sample size	Study design and population details	Cannabis retail type	Exposure type	Specific exposure measured	Outcome(s)
(Continued from previous pag	e)							
	Wang et al. (2022) USA (CO)	2013-2018	N = Not reported	State-level, repeated cross- sectional study of emergency department visits due to psychosis and schizophrenia	Medical and non-medical	Container-based	2 factors: 1) Baseline exposure to medical outlets (0, 1–9, >10) 2) Growth in new recreational outlets (number of recreational dispensaries per 10 000 residents), stratified by baseline exposure "Setting the high baseline medical exposure counties as the reference group, we interacted the categorical baseline exposure with the number of recreational dispensaries per 10,000 residents"	Emergency department visits for psychosis or schizophrenia using ICD-9 and -10 diagnosis codes
	Klein et al. (2022) USA	2016-2019	N = 7600	National, retrospective cohort study of synthetic cannabinoid exposures reported to the National Poison Data System (NPDS), including paediatric and general adult populations		Pre-post introduction of retail outlets (categorical variable)	Comparison of states with commercial retail markets to states with medical policies only over time	exposure reports,
	Kim et al. (2023) Canada (ON)	2015-2021	N = 12 079 699	Province-wide, retrospective cohort study of adult hospitalizations for cannabis in Ontario, Canada	Non-medical	Pre-post introduction of retail outlets (categorical variable)	Phase 0: Pre-legalization Phase 1: Flower and herb sales online and limited private retail storefronts Phase 2: Increased storefronts and availability of edibles	Rate of cannabis-related hospitalizations (ICD-10-CA: F12, T40.7) per 100 000
Maternal cannabis use and harms and neonatal outcomes	Lockwood et al. (2019) USA (CO)	2012-2016	N = 269 922	State-wide, retrospective cohort study of neonatal birth outcomes from Colorado Birth Dataset	Non-medical	Container-based	Counties with no, low (<17 recreational outlets per 100,000), and high (\geq 17 recreational outlets per 100,000) outlet densities	NICU admissions and SGA birth (<10th percentile)
	Gnofam et al. (2019) USA (CO)	2012-2015	N = 2392	Single-centre, retrospective cohort study of maternal cannabis use and perinatal outcomes	Non-medical	Pre-post introduction of retail outlets (binary variable)		Maternal cannabis use (self- report or biologically detected), fetal growth restriction, pre-term birth, SGA, NICU admission and length
	Straub et al. (2019) USA (WA)	2011–2016	N = 5343	Multi-centered, retrospective cohort of neonatal birth outcomes among mothers with positive UDS for cannabis	Non-medical	Pre-post introduction of retail outlets (categorical variable)	Period 1: Pre-legalization (2011–2012) Period 2: Post-legalization, prior to opening of retail outlets (2012–2014) Period 3: Post-introduction of retail outlets (2014–2016)	Low birth weight, SGA, pre- term birth

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	Study and region	Study period	Sample size	Study design and population details	Cannabis retail type	Exposure type	Specific exposure measured	Outcome(s)
(Continued from previous page	ge)							
	Young-Wolff et al. (2021) USA (CA)	2018	N = 35 195	State-wide, single cross- sectional study of cannabis use among pregnant individuals	Non-medical	Proximity-based Container-based	Additional 5-min drive time from recreational cannabis outlets, categorical-level variable of driving times Additional outlet within a 15-min drive	
	Wang et al. (2022) USA (CO)	2011-2018	N = 6229	State-wide, retrospective cohort study of pregnancy- related hospitalizations co- coded with cannabis diagnosis codes reported to Colorado Hospital Association	Both	Container-based	Period 1: Pre-introduction of retail outlets (2011-2014) Period 2: Post-introduction of retail cannabis outlets (2014-2018)	hospitalizations (ICD-9 or
Problematic or frequent cannabis use	Everson et al. (2019) USA (WA)	2009–2016	N = 85 135	State-wide, repeated cross- sectional cohort study of adult cannabis use from Washington Behavioural Risk Factor Surveillance System	Non-medical		Proximity: 3-level proximity variable (<0.8 mi, 0.8–1.1 mi, 1.2–18.4 mi, >18.4 mi) Geospatial density (distance to 5 nearest outlets). Density: Outlets per 100,000 population (county-level)	cannabis use (>20 occasions of cannabis use in last 30
	Pedersen et al. (2021) USA (CA)	2018–2019	N = 1097	State-wide, longitudinal cohort study of young adult (19–30 years) cannabis use		Container-based	Number of licensed and/or unlicensed recreational and medicinal cannabis outlets within a 4-mile circular buffer	used in last 30 days) self-
	Brooks-Russell et al. (2019) USA (CO)	2013-2015	N = 26 019 (2013) N = 15 970 (2015)	State-wide repeated cross- sectional study of high school students' cannabis use from the Youth Risk Behaviour Survey	Non-medical	Pre-post introduction of retail outlets (binary variable)	Period 1: Legal cannabis without introduction of retail outlets (2013) Period 2: Legal cannabis with introduction of retail outlets (2015) Comparison of schools located in counties permitting or not permitting retail outlet introduction	Frequent self-reported cannabis use (>20 occasions of cannabis in last 30 days)
	Laqueur et al. (2020) Uruguay	2007-2018	N = 35 854	Population-level, repeated cross-sectional study of high school students' cannabis use		Pre-post introduction of retail outlets	Period 1: Cannabis legalization without substantive retail access (2007–2014) Period 2: Post-introduction of retail outlets (2014–2018)	Frequent self-reported cannabis use (10 days or more in the past 30 days)
	Wouters et al. (2012) Netherlands	2008-2009	N = 2027	Population-level, single cross-sectional study of adult (15–35 year old) nightclub-goers geographically spread across Netherlands		Proximity-based	, ,	Dichotomous frequency of self-reported cannabis use: 0 = Seldom/Almost never 1 = More frequent
							(Tab	le 1 continues on next page)

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	Study and region	Study period	Sample size	Study design and population details	Cannabis retail type	Exposure type	Specific exposure measured	Outcome(s)
Continued from previous pag	ge)			-		-		
	Rhew et al. (2022) USA (WA)	2015-2019	N = 10 009	State-wide, repeated cross- sectional study of young adults' (18-25 year old) cannabis use from Young Adult Health Survey	Non-medical	Proximity-based Container-based	Dichotomous measure of retail outlet availability within a 1 km road network buffer: 0 = no outlets 1 = any outlets Density of cannabis retail outlets per 1000 persons within one's census tract	Frequent self-reported cannabis use (at least daily)
	Shih et al. (2019) USA(CA)	2015-2017	N = 1887	LA county, cross-sectional study of young adults' (18–22) cannabis use from online survey	Medical	Proximity-based Density-based	Mean number of and proximity to medical cannabis outlets within 4- mile radius of respondent's home	Self-reported days using cannabis in the past 30 days
	Freisthler & Gruenewald (2014) USA (CA)	2009–2010	N = 8553	State-wide, cross-sectional study of adult cannabis use in 50 mid-sized CA cities from telephone interview	Medical	Container-based	Density of medical cannabis outlets and delivery services per roadway mile	
	Rogers et al. (2022) USA (CA)	2019–2020	N = 1573	State-wide, cross-sectional study of cannabis use in high school students across different jurisdictions in California	Non-medical	Proximity-based	Dichotomous proximity- based variable with a response for each participants city 0 = proximity to municipalities without recreational retail access 1 = proximity to municipalities with recreational retail access	Continuous measure of high school students' self- reported past 30 day cannabis use
	Rivera-Aguirre et al. (2021) Uruguay and Chile		N = 204 730	State-wide, difference-in- difference design repeated cross-sectional surveys of past month cannabis use in high school students		Pre-post introduction of retail outlets (categorical variable)	Varying levels of retail access (cannabis clubs, pharmacy access) over time in Uruguay are compared to a counter factual control country (Chile) with no retail access over the same period	Risky cannabis use, determined from the binary version of the Cannabis
	Ambrose et al. (2021) USA (WA)	2014-2016	N = 35 713	State-wide, repeated cross- sectional surveys of adults (18+) in Washington State	Non-medical	Geospatial Access Methods	information systems (GIS)	Any past-month use Heavy past-month use (≥20 days) Number of days used

Bold indicates quasi-experimental design. Abbreviations: AZ = Arizona state, CA = California state, CO = Colorado state, CUD = Cannabis use disorder, CUD-SF = Cannabis use disorder, ICD = International Classification of Diseases, ITS = Interrupted time series, MCL = Medical cannabis laws, NICU = Neonatal intensive care unit, NPDS = National Poison Data System, ON = Ontario province, RCC = Recreational cannabis commercialization, RCL = Recreational cannabis laws, RR = Risk ratio, SGA = small for gestational age, UDS = Urinary drug screen, WA = Washington state.

Table 1: Characteristics of included studies (n = 32).

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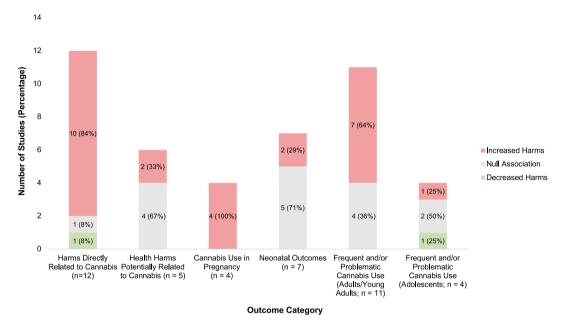


Fig. 2: Direction of association between increased cannabis retail access and adverse cannabis health outcomes by population and outcome.

Risk of bias appraisal

Overall, 69% (22/32) of studies satisfied all criteria on the JBI critical appraisal checklists for observational studies. Quasi-experimental (8/11) and cross-sectional studies (10/12) met more of the JBI criteria than the cohort studies (4/9). JBI scores of adult health service use were higher than other study outcome types. See Appendix D for a full breakdown of the JBI checklists stratified by study design and study outcome.

Healthcare service utilization

16 studies^{26,28-36,47-52} consisting of 18 unique primary analyses (16 in adults, 2 in paediatric population) assessed the relationship between any measure of cannabis retail access and a cannabis-related health harm resulting in a healthcare encounter. See Table 2 for a brief overview of exposure and outcome details and direction of association (see complete details in Supplementary Table S1). Nine analyses assessed healthcare use directly due to cannabis, three analyses assessed poison control calls due to cannabis, and six analyses measured healthcare use potentially associated with cannabis (i.e., any-psychosis presentation, vomiting). 12 of 18 (67%) analyses found evidence of a statistically significant association between greater retail access and increased harms. See Fig. 2 for a visual summary broken down harms directly and potentially associated with cannabis.

Ten out of 16 (63%) analyses conducted in adult populations reported a statistically significant association between increasing physical retail access to cannabis and higher health care visits related or potentially related to cannabis use.^{26,28-30,34-36,47-49,51,52} Adult outcomes included: ED visits and hospitalisations directly related to cannabis use (e.g., ICD-10 codes for cannabis abuse and dependence, n = 8), cannabis exposures leading to poison control calls (n = 2), and healthcare service use potentially related to cannabis use (n = 6). Healthcare service use potentially related to cannabis included visits due to self-harm, general psychosis-related presentations, antipsychotic prescriptions, and vomiting. Seven out of eight (88%) analyses on healthcare service use directly due to cannabis (including cannabis abuse and dependence, cannabis hyperemesis syndrome, and cannabis-induced psychosis) in adults found evidence of increased harms.^{28-30,35,48,50-52} Poison control calls due to cannabis exposures increased,36 while those due to synthetic cannabis exposures decreased with greater retail access.49 One out of four analyses (25%) demonstrated statistically significant associations between increased cannabis retail access and increases in generalized psychiatric-related harms,^{26,47} one analysis found a statistically significantly increase in rates of emergency department presentations for vomiting following increased cannabis retail access,34 and there was no statistically significant association between greater cannabis retail access and Medicare claims due to selfharm.33 Both studies conducted in paediatric populations found that increased cannabis retail access in Washington State was statistically significantly associated with increased emergency department visits and poison control calls due to cannabis in children aged 0-9 years.31,32

Study	Population	Exposure Type	Outcome
		ervices Use (NAnalyses = 18)	
Conyers & Ayres (2020)	Adult	Container-Based**	ED/Hospital Visit due to Cannabis
Kim et al. 2023	Adult	Crude (Pre-Post)	Hospitalizations due to Cannabis
Mair et al. (2015)	Adult	Geospatial Access	ED/Hospital Visit due to Cannabis
Mair et al. (2021)	Adult	Geospatial Access	ED/Hospital Visit due to Cannabis
Myran et al. (2022)	Adult	Crude (Pre-Post)**	ED/Hospital Visit due to Cannabis
Myran et al. (2022)	Adult	Crude (Pre-Post)**	ED Visits due to Cannabis Hyperemesis Syndrome
Myran et al. (2023)	Adult	Crude (Pre-Post)**	ED visits due to Cannabis-Induced Psychosis
Tolan et al. (2023)	Adult	Crude (Pre-Post)	ED Visits due to Cannabis
Klein et al. 2022	Adult	Crude (Pre-Post)	Poison Control Calls - Synthetic Cannabis Exposures
Shi and Lang (2020)	Adult	Crude (Pre-Post)**	Poison Control Calls
Elson et al. (2022)	Adult	Crude (Dre Deat)	Psychosis-Related Diagnoses
Elser et al. (2023)	Adult	Crude (Pre-Post)	Antipsychotic Prescription
Matthay et al. (2021)	Adult	Crude (Pre-Post)	Self-Harm Health Care Visits
Wang et al. (2021)	Adult	Container-Based	ED Visits due to Vomiting
Wang at al. (2022)	۸ اورل ۱۴	Container Deced**	ED Visits due to Psychosis
Wang et al. (2022)	Adult	Container-Based**	ED visits due to Schizophrenia
Thomas et al. (2019)	Pediatric	Crude (Pre-Post)	Poison Control Calls
Thomas et al. (2021)	Pediatric	Crude (Pre-Post)	ED/Hospital Visit due to Cannabis
	Pregnancy and Neo	natal Outcomes (NAnalyses	
Gnofam et al. (2019)	Pregnancy	Crude (Pre-Post)	Cannabis Use During Pregnancy
· · · ·		Proximity	Cannabis Use During Pregnancy
Young-Wolff et al. (2021)	Pregnancy	Container-Based	Cannabis Use During Pregnancy
Wang et al. (2022)	Pregnancy	Container-Based**	ED Visits due to Cannabis during Pregnancy
e ()	5 1	Container-Dased	Small for Gestional Age
Straub et al. (2021)	Newborn	Crude (Pre-Post)	Low Birth Weight
			Pre-Term Birth
Gnofam (2019)	Newborn	Crude (Pre-Post)	NICU Admission
Gholani (2017)	Newbolli		Fetal Growth Restriction
			Small for Gestional Age
Lockwood (2019)	Newborn	Container Based**	NICU Admission
E	roquant and/or Proble	matic Cannabis Use (NA	
Ambrose et al. (2021)	Adults	Geospatial Access	Daily or Near Daily Cannabis Use
Friesthler & Gruenewald (2014)	Adults	Container-Based	Number of Days of Cannabis Use (Past-Year
Thestiner & Ordenewald (2014)	Adults	Container-Based	Daily or Near Daily Cannabis Use
Everson et al. (2019)	Adults	Proximity	Daily or Near Daily Cannabis Use
Everson et al. (2019)	Adults	Geospatial Access	Daily of Near Daily Cannabis Use
W	Adults	*	· ·
Wouters et al. (2012)	Adults	Proximity	More Frequent Cannabis Use (Not Specified)
Pedersen et al. (2021)	Young Adults	Container-Based	Cannabis Use Disorder (per CUDIT-SF)
Shih at al. (2010)		Container-Based	Daily or Near Daily Cannabis Use
Shih et al. (2019)	Young Adults		Days of Cannabis Use (Past-Month)
Rhew et al. (2022)	Young Adults	Container-Based	Daily or Near Daily Cannabis Use
• •		Proximity	Daily or Near Daily Cannabis Use Frequent Cannabis Use (> 10 days in Last
Rivera-Aguirre et al. (2022)	Adolescents	Crude (Pre-Post)**	Month)
Rogers et al. (2022)	Adolescents	Proximity	Days of Cannabis Use (Past-Month)
Laqueur et al. (2020)	Adolescents	Crude (Pre-Post)**	Frequent Cannabis Use (> 10 days in Last Month)
Brooks-Russell et al. (2019)	Adolescents	Crude (Pre-Post)	Daily or Near Daily Cannabis Use
Note: Asterisks (**) indicates a quas 'NICU' = Neonatal intensive care unit Identification Test – Short Form. Canr and/or positive urine screen.	; CUDIT-SF = Cannabi		Legend Decreased harms Null association Increased harms
ion of association between increased can	nahis retail access and ad	verse cannahis health outcon	nes by population, exposure type and outcome.

Maternal cannabis use and harms and neonatal outcomes

Overall, five studies^{27,37–40} with 11 primary analyses measured the association between cannabis access and cannabis use and harms during pregnancy (n = 4) and/ or neonatal birth outcomes (n = 7). See details in

Supplementary Table S1. All four analyses examining cannabis retail access and cannabis use or harms during pregnancy found statistically significant associations between greater access and increased harms, while two out of seven analyses (28.6%) found statistically significant associations between greater retail access and increased adverse birth outcomes. See Fig. 2 for a visual summary of studies' direction of associations separated into cannabis use in pregnancy and birth outcomes.

Cannabis use and harms during pregnancy were assessed via self-report and/or positive urine toxicological screens (n = 3) and cannabis-involved hospitalization during pregnancy (n = 1). All four analyses found that cannabis use and cannabis-related emergency department visits or hospitalizations during pregnancy statistically significantly increased in a dose-dependent manner as the number of or proximity to cannabis retailers increased^{27,39,40} Three studies comprising seven analyses examined a variety of birth outcomes including small-for-gestational age (SGA), pre-term births, fetal growth restriction, and NICU admissions.27,37,38 Only two analyses found a statistically significant positive association between greater retail access and harms (fetal growth restriction and NICU admission). The remaining five analyses showed no evidence of statistically significant associations.

Problematic or frequent cannabis use

11 studies^{24,25,41–46,53–55} consisting of 15 primary analyses examined associations between increased physical access to retail cannabis and outcomes related to problematic cannabis use, including frequent use (i.e., >20 out of 30 most recent days) or cannabis use disorder (CUD) measured via a validated screening instrument. Eight of the 15 primary analyses (53%) demonstrated evidence of a statistically significant association between increasing retail access and harms. Studies were conducted in adult (n = 4), young adult (n = 3), and high school populations (n = 4). See Fig. 2 which presents studies separated by adolescent and adult/young adult. All 11 studies employed a survey design to assess changes in cannabis use, although study types varied. Two analyses examined the relationship between medical cannabis retail access and cannabis use; the remaining thirteen focused on non-medical cannabis retail access. See full study details in Supplementary Table S1.

There was wide variation in age-specific effects. Four of the six analyses conducted in adults24,41,54 and three of the five analyses conducted in young adults^{25,43-45} found statistically significant associations between greater retail access and increased problematic cannabis use. All five analyses of young adults used inconsistent definitions of young adults (e.g., ages 18-22, 18-25, 19-30), which greatly limited synthesis of findings. In non-adolescent analyses, problematic cannabis use outcomes were divided into either 1) daily or near-daily (>20 out of 30 days) cannabis use (n = 7) and cannabis use disorder (n = 1) or 2) other measures of frequent use (n = 3). There was evidence of a statistically significant association between greater retail access and frequent cannabis use (70% of analyses), but not for cannabis use disorder. Lastly, only one study (25%) of adolescents in high school found a statistically significant association between increased cannabis retail access measured by proximity to outlets and frequent cannabis use.⁵³ The remaining studies considering adolescents found no statistically significant associations between increased cannabis retail access (measured by the crude introduction of retail outlets) and increases in frequent or problematic cannabis, with one analysis reporting a statistically significant negative association between the introduction of outlets and daily or near-daily cannabis use.⁴⁶

Discussion

Overall, this systematic review of the literature suggests that greater cannabis retail store access is associated with increased cannabis-related health harms. Of the 44 unique exposure-outcome pairs, 59% (n = 26) found a statistically significant positive association between increased access and harm. The most consistent associations between greater access and harms were observed for emergency department visits, hospitalisations, or poison control calls directly due to cannabis (10/12 analyses; 83%), cannabis use or cannabis-related hospitalisations during pregnancy (4/4; 100%), and frequent or disordered cannabis use in adults and young adults (7/11; 64%). There was limited to no evidence to support a significant association between greater cannabis retail access and healthcare events potentially related to cannabis (total vomiting, total self-harm, total psychosis) and increased frequent cannabis use in adolescents or increases in adverse neonatal outcomes.

Our findings are consistent with two prior reviews suggesting that greater cannabis retail access is associated with increased traffic collisions and cannabis use prevalence (e.g., past-year use) and some adverse health outcomes.^{16,56} Adding to this literature, we found that greater cannabis retail access was associated with increases in adverse health outcomes, including daily and problematic cannabis use and cannabis-related emergency department visits and hospitalisations in a diversity of populations. Importantly, the causal nature of this association remains unclear. Prior research has found that cannabis stores are more likely to open in lower-income regions and areas with higher pre-existing cannabis use.57-59 Although most studies adjusted for available sociodemographic factors, there may be residual confounding, where part of the observed association is explained by store opening in regions of high demand rather than stores causing increasing cannabis use and harms. Second, studies using pre-post retail opening designs may be prone to ascertainment bias where part of the observed increase in events is caused by greater healthcare worker awareness of cannabisrelated harms over time, such as unintentional exposures in children and cannabis hyperemesis syndrome. Despite this uncertainty, several features support arguments for a causal component of the observed

associations. First, the more methodologically robust studies were more likely to support a relationship between increased retail access and harms with 73% (8/ 11) of the quasi-experimental analyses found evidence of a significant association between retail access and harms. Second, the associations showed a dose-response gradient where higher levels of access (either by closer proximity or increased store counts) were almost universally associated with increasing harm across studies. Third, aside from 6 single cross-sectional analyses, all studies established a temporal relationship between greater cannabis retail accessibility and harms. Fourth, several studies measuring health harms (i.e., hospital visits due to cannabis use) compare outcomes between three policy periods: pre-legalisation, periods of low or no cannabis retail access and periods with greater retail access. These studies35,50-52 found cannabis harms did not increase significantly during periods of non-medical cannabis legalisation with restrictive limits on outlets but then did increase when outlet limits were removed and store access increased. This observation reduces the likelihood that the changes were driven by ascertainment bias where healthcare workers became more aware of cannabis harms following legalisation. Finally, this evidence fits within the broader context of the drug control policy literature, which has shown that greater availability of tobacco and alcohol is associated with increased substance-related harms.8,11,12 Research supports that increasing retail cannabis availability can influence individuals' perceptions regarding substances and normalise their use.⁶⁰

Limitations

Our analysis faces several important limitations. First, the substantial heterogeneity between studies across all design elements (populations, exposures, outcome) prevents quantitative synthesis and meta-analysis. For example, included studies capturing youth and paediatric populations used inconsistent definitions of age ranges that challenge disentangling age-specific effects (i.e., cannabis poisonings in infants/toddlers vs. intentional cannabis use in high schoolers). Future research studies should use standardized definitions for population, outcomes and retail access measures to facilitate synthesis of findings. Second, the majority of the evidence reviewed (25/32; 78%) came from the US, of which over half (18/32; 56%) was further limited to three states (Washington, Colorado, and California). These findings may not be as generalizable to other countries or states currently contemplating legalisation of cannabis (i.e., Germany, Switzerland) which differ from the US with respect to sociocultural factors and the presence of pre-existing medical cannabis markets. Ongoing evidence from additional regions and policy contexts is needed to increase confidence in the generalizability of findings. Third, studies often lacked

sufficient detail on pre-legalisation or pre-retail access policies (e.g., pre-existing access to medical cannabis outlets). Future studies should include additional policy details to assist with policy synthesis. Fourth, studies often presented multiple outcome and exposure combinations without evidence of these combinations being pre-specified or adequately powered, which increases the possibility of false positives and negatives. This is particularly important as some studies concluded that there was no evidence of increased harms with greater access based off statistical significance which may have been underpowered. For example, a study of the association between the introduction of non-medical cannabis retail stores in the US and changes in healthcare visits for psychosis reported no increase in visits but the effect estimate found a 39% increase in visits and the confidence intervals approach significance (RR 1.39, 95%CI 0.98-1.97).26 Fifth, studies have focused on a limited set of priority populations (e.g., age and pregnancy). Further research is needed for a wider variety of priority populations, including race, socioeconomic status, and individuals with pre-existing mental health disorders. Finally, longer surveillance periods may be required to identify the full health impacts of legalisation as some included studies examined very short durations of exposure to cannabis retail stores and legal retail markets have taken time to develop and mature.56,61-63 These study design limitations prevent casual attribution of these findings and limit the specificity of recommendations that can be generated for policymakers. Consequently, there is a need for further studies using high-quality designs and standardized outcomes and exposures to generate evidence which can inform regulatory decisions in the increasing number of jurisdictions with legal cannabis. These gaps could be addressed using a variety of study designs, including individual-level cohort studies that include relevant geospatial data on individuals' access to cannabis retail stores and patterns of cannabis use and health outcomes and cohort studies leveraging variation in cannabis retail access and policies over time with aggregate outcomes (e.g., population-level cannabis use or health harms). See Box 1 for key recommendations to inform future research.

Despite current limitations, our findings may offer several important policy implications. First, our findings suggest that jurisdictions that legalize cannabis with widespread retail access may experience increases in harmful cannabis use and consequent health outcomes. Second, policies that limit cannabis retail stores may help reduce harmful patterns of cannabis use and health service use in regions with legal cannabis. Such policies may have important implications for health equity as prior research has shown that without regulatory oversight cannabis retail store tend to congregate in lowerincome regions.

Box 1.

Recommendations for Future Research

- Studies should describe in greater detail the retail environment (e.g., medical, and gray market) before and after the introduction of legal cannabis stores to help contextualize the findings and improve generalizability.
- 2. Studies should use standardized measures of cannabis retail access we propose aligning them according to CDC guidelines for measures alcohol outlet access. $^{\rm 18}$
- 3. Studies assessing health harms related to cannabis should use clinically relevant and standardized outcomes. We propose studies use similar ICD-10 diagnostic codes (any F12.x or T40.7) as these have been validated to detect healthcare visits potentially related to cannabis.⁶⁴ For harmful cannabis use, the same measures of self-reported cannabis use (daily), or validated assessment tools for cannabis use disorder (i.e., CUDIT⁶⁵-R or SDS) should be used between studies to facilitate comparisons.
- 4. Studies that examine multiple outcomes and exposures combinations should preregister these questions and indicate when combinations are primary analyses or exploratory in addition to providing power analyses.
- 5. Studies should standardize a definition for youth and young adults: we propose < 25 years of age given the recognition of this age as critical for neurodevelopment.
- 6. Studies should specifically examine changes for individuals above and below the minimum legal age of purchase.
- 7. Studies should report on changes by priority populations when data is available including by sex, gender, race, ethnicity, socioeconomic status and preexisting mental health.
- 8. Further studies with longitudinal and/or quasi-experimental designs are needed to increase certainty of evidence and better understand the causal relationship between retail access and cannabis use and harm.

Conclusion

Overall, this systematic review finds evidence of significantly increased associations between greater physical cannabis retail access and increased cannabis use and harms, including healthcare utilization related to cannabis and harmful patterns of cannabis use in a variety of populations (adults, young adults, pregnant individuals). These findings caution that allowing greater retail availability following legalisation may increase cannabis-related harms.

Contributors

The authors confirm contribution to the paper as follows: study conception and design: DM, NC. Article screening and data extraction: NC, MS, and AG. Developed search strategy: LS, NC, DM. Supervision: PT, DM. Draft manuscript preparation: NC, MS, DM. All authors reviewed the results and approved the final version of the manuscript.

Declaration of interests

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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.2024.100708.

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