



What Have Been the Public Health Impacts of Cannabis Legalisation in the USA? A Review of Evidence on Adverse and Beneficial Effects

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Abstract

Purpose of Review To summarise empirical research on the adverse and beneficial public health impacts of cannabis legalisation in states in the USA.

Recent Findings The most consistent finding from surveys of drug use is that the legalisation of medical cannabis has so far not had an effect on rates of use or cannabis use disorders among youth, but it has increased the frequency of use among adult cannabis users. There are conflicting findings on the impact of legalisation of medical and recreational cannabis use on the following: cannabis use disorders in adults, rates of motor vehicle accidents in which the driver was impaired by cannabis, rates of suicide, and opioid-related harms. The legalisation of recreational cannabis use has increased emergency room attendances for cannabis-related medical conditions (acute adverse psychological effects, hyperemesis, and accidental poisoning of children). There is no evidence to date on the impact of medical or recreational legalisation on the prevalence of mental disorders such as psychoses, depression, and anxiety.

Summary There is suggestive evidence that cannabis legalisation is associated with a range of public health consequences. However, current evidence is limited in the capacity to confidently conclude that these changes are the result of cannabis legalisation. The impacts on public health may take some years to become apparent.

Keywords Cannabis · Marijuana · Legalisation · Public health · Medical marijuana laws · Legislation

Introduction

Since 2012, eleven states in the USA (details and map available in Supplement F) and the nations of Uruguay (2013) and

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Canada (2018) have legalised the production and sale of recreational cannabis for adult use [1–3]. Advocates of cannabis legalisation have argued that it will eliminate the adverse social effects of criminalisation on cannabis users and enable more effective public health responses to cannabis use, e.g., by regulating cannabis products to protect consumers, providing more accurate public education about the adverse effects of cannabis use, and treating persons who develop problems with cannabis use [4]. More recently, advocates have suggested that medical use of cannabis may reduce the substantial public health harms caused by alcohol and opioid use.

Opponents argue that cannabis legalisation will increase the prevalence of regular cannabis use because it will make cannabis more available at a lower price and in more potent forms and decrease public perceptions of the risks of cannabis use. Increased regular use, they claim, will increase cannabis-related harms, such as cannabis dependence and use disorders, motor vehicle crashes caused by cannabis-impaired drivers, emergency medical attendances, psychoses and depression, and cognitive impairment and poor educational outcomes in adolescent users [5].

The aim of this review is to summarise research on the impacts of cannabis legalisation in the USA on the major

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public health outcomes that advocates and opponents of legalisation claim will be affected [6, 7]. We also critically analyse the methods used in these studies and recommend more robust research to monitor the future public health impacts of cannabis legalisation. Our analysis draws on evidence from the USA where the legalisation of medical and recreational cannabis use has been in effect for the longest and where the most extensive research has been conducted to date.

Methods

We summarised systematic reviews of research, where available, and undertook our own reviews when they were not, using the step-wise method adopted by The National Academies of Sciences [8] (see supplementary material A). Firstly, we searched for reviews on the effects of cannabis legalisation in the USA on major contested public health outcomes. If a systematic review was available, our synthesis was based on the review and any original studies published thereafter. If no systematic reviews were found, we searched for original studies reporting on these outcomes. We included original prospective cohort studies, retrospective cohort studies, case–control studies, and cross-sectional studies that provided quantitative data. Qualitative studies; case study of individual patients; and commentaries, editorials, or opinion pieces without empirical data were excluded.

We carried out a series of searches from June to July 2019 in PubMed using MeSH terms and free text words (title, abstract, keywords), supplemented by additional articles from the authors' collections, hand searches, and secondary references. We ran separate searches for each public health outcome category (See Supplement B for the search terms). The outcomes of legalisation searched for included the following: impacts on cannabis use; motor vehicle road injuries; poisonings or emergency department presentations; hospital or treatment service use; psychosis; depression or self-harm; and tobacco, alcohol, or opioid use. References were screened chronologically (see Supplement C for PRISMA flowcharts). Characteristics and key findings of the included studies are tabulated in Supplement D. A list of acronyms and initialisms frequently used in this review is available in Supplement E.

Public Health Impacts of Cannabis Legalisation

Impacts on Cannabis Use

The impact of cannabis legalisation on prevalence of cannabis use and use disorders in major surveys in the USA has been reviewed [3, 9••] as has the prevalence of cannabis use and use disorders in adolescents [10, 11, 12••].

Most studies have examined the impacts of the legalisation of medical cannabis (LMC) because in the USA, and elsewhere, this policy was first enacted earlier and in many more jurisdictions than the legalisation of recreational cannabis (LRC). Many of these studies involve comparisons of trends in health outcomes (e.g. prevalence of cannabis use disorders and road crashes) between states that have and have not legalised medical and recreational cannabis use. The better controlled studies distinguish among states which have LMC using indicators of liberal regulations such as whether retail dispensaries are active. The limitations of these study designs are discussed below.

Trends Among Adults

Hasin and colleagues [9••] summarised trends in the epidemiology of cannabis use and cannabis use disorders among adults in the USA in surveys of nationally representative samples over the period 2002 to 2014. These included the following: the National Survey on Drug Use and Health (NSDUH; conducted annually beginning in 2002), the set of national surveys conducted by the National Institute on Alcohol Abuse and Alcoholism (the National Longitudinal Alcohol Epidemiologic Survey (NLAES, 1991–1992), the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC 2001–2002), the NESARC-III (a new sample, independent of the NESARC sample 2012–2013), and collectively, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) surveys), and the National Alcohol Surveys (NAS, conducted every 4–6 years from 1979 to 2015).

The prevalence of past-year cannabis use was relatively stable at around 4% before the millennium. The NSDUH surveys reported a significant increase overall between 2002 and 2014 in the prevalence of past-year cannabis use from 10.4 to 13.3%. There was also a significant increase between 2002 and 2014 in past-year prevalence of regular (daily or near daily) use and frequency of use. Analyses of this data have shown that significant increases in prevalence and other indicators during this period began in 2007. Similar trends were reported in other surveys (NIAAA surveys: from 4 to 9.5% between 2001–2002 and 2012–2013; NAS surveys: from 6.7 to 12.9% between 2004–2005 and 2014–2015). All three surveys showed that cannabis use increased in all population subgroups defined by gender, age (within adults; see below section for trends of adolescents), race/ethnicity, income, education, marital status, and geographical region.

In NSDUH surveys from 2002 to 2014, the annual prevalence of *cannabis use disorder* (CUD) remained stable at around 1.5%. By contrast, the NIAAA surveys reported significant increases in the prevalence of CUD, from 1.2% in 1991–1992 to 1.5% in 2001–2002, rising to 2.9% in 2012–2013. The inconsistent findings between NIAAA and

NSDUH prompted Hasin and colleagues to examine veterans' health administrative records, state, and national hospital inpatient records. They found consistent indicators of increased CUD in different population groups and argued that the increased prevalence of CUD in the NIAAA surveys was reliable.

We previously reviewed studies comparing trends in cannabis use and CUD in US states with and without medical cannabis programs [3]. We concluded that between 2004 and 2013, adults over the age of 26 who resided in states with LMC were more likely to have used cannabis in the past 30 days, to have used daily, and to have higher rates of CUD than adults who resided in states without LMC.

Trends in Cannabis Use Among Adolescents

Data collected on adolescent cannabis use include the National Survey on Drug Use and Health (NSDUH; conducted annually beginning 2002), Monitoring the Future (MTF; sampling 8th and 10th grade students annually beginning 1991; and 12th grade students beginning 1976), and the Youth Risk Behavior Survey (YRBS) (conducted biennially beginning 1991). These surveys show either an overall decrease or very little change in the prevalence of adolescent cannabis use in the USA since 2002.

In the NSDUH surveys, the prevalence of past-year cannabis use decreased among adolescents aged 12–17, from 15.8 to 13.1% between 2002 and 2014. There were decreases between 2002 and 2007 and then a slight increase. The prevalence of past-year use, past-30-day use, repeat use, and frequent use decreased in the YRBS surveys among 8th, 10th, and 12th graders between 1995 and 2015. Decreases occurred in boys and girls but were larger among boys reducing gender differences in the prevalence of use by 2013. The MTF surveys showed little change in past-year cannabis use among adolescents between 2005 and 2016. The prevalence of CUD also declined among adolescents. According to the NSDUH surveys, its prevalence decreased from 4.3 to 2.3% between 2002 and 2014. Meta-analyses of survey data to 2014 also do not find any indication that the legalisation of medical cannabis use had increased adolescent cannabis use [10].

A more recent systematic review and meta-analysis of survey data covering the period 1975–2016 reported more mixed findings. Most surveys suggested that LMC had not increased youth cannabis use [12••]. There was suggestive evidence that cannabis use increased after LRC, but the effect was small and not statistically significant [12••]. A recent analysis of YRBS surveys to 2017 found that states that had LMC had a marginally lower prevalence of cannabis use (OR = 0.95 (0.89–1.01)) and frequent cannabis use (OR = 0.94 (0.87–1.03)) in adolescents [11]. The same was true for the small number of states with LRC (recent cannabis

use (OR = 0.92 (0.87–0.96), $p < 0.05$) and frequent cannabis use (OR = 0.91 (0.84–0.98), $p < 0.05$)).

Hasin and colleagues [9••] noted that trends in adolescent cannabis use paralleled trends in alcohol and tobacco use among adolescents. They suggested that this may be because adolescents have fewer opportunities to use alcohol, tobacco, and cannabis because they spend more time on social media and less time in face-to-face social activities.

Motor Vehicle Road Injuries

Cannabis use acutely produces dose-related impairments in cognitive and psychomotor performance that could adversely affect driving a motor vehicle (see Table 1). Case-control and culpability studies indicate a modest increase in the risk of accidents among cannabis users [13]. Many countries have introduced policies to discourage recreational cannabis users from driving, and these laws also apply in most states to patients who use cannabis for medical purposes.

The data series most often used to assess the effects of changing cannabis policy on cannabis impairment in road crashes in the USA is the Fatality Analysis Reporting System (FARS). This system comprises an annual census of all fatal motor vehicle accidents in the USA in which information is collected from police crash reports, driver licensing files, emergency medical services records, medical examiners' reports, toxicology reports, and death certificates. Data quality is limited by a lack of standardised definitions of cannabis-impaired driving in different states and a great deal of missing data (Sevigne, 2018). These limitations complicate the interpretation of differences in trends in cannabis-related accidents between states by LMC and LRC status. As with analyses of survey data, more studies have been done on the effects of medical cannabis laws than on recreational legalisation.

Santaella-Tenorio and colleagues analysed FARS data between 1985 and 2014 and found that states with LMC generally had lower traffic fatality rates than non-legalised states [14]. They reported an immediate reduction in fatalities after LRC, but the rate did not change after LMC. They reported significant long-term reductions in traffic fatality rates after legalisation in 7/19 LRC states among adults aged 25–44 years in states with medical cannabis dispensaries.

Anderson and colleagues used FARS data to estimate that there had been an 8–11% reduction in traffic fatalities in the first full year after medical cannabis was legalised [15]. There was also a 13.2% decrease in alcohol-impaired traffic fatalities (BAC > 0.08) and 15.5% decrease in fatalities resulting from significant alcohol impairment (BAC > 0.10). Anderson and colleagues argued that the reductions in rates of traffic fatalities might have been due to a reduction in alcohol-impaired driving if medical cannabis legalisation had encouraged some drinkers to use cannabis instead of alcohol.

Brady and Li found that cannabis-positive traffic fatalities increased after LMC from 4 to 12% while alcohol-positive fatalities remained stable in several states (including California, Hawaii, New Hampshire, Rhode Island, and West Virginia) between 1999 and 2010 [16].

Masten and Guenzburger compared trends in cannabis-positive traffic fatality rates in 14 medical cannabis legalised states and 34 non-legalised states [17]. They found that the passage of medical cannabis laws was associated with an *increase* in the annual cannabis-positive traffic fatality rate in California (315.2%), Hawaii (195.8%), and Washington (432.4%). Steinemann also reported a threefold increase in cannabis-positive traffic fatalities after LMC in Hawaii [18]. When medical cannabis became commercially more available in Colorado dispensaries after 2009, the trend in the prevalence of cannabis-positive traffic fatalities changed from a decrease to an increase. No change was observed in the 34 states that had not legalised cannabis.

Keric and colleagues [19] and Pollini and colleagues [20] assessed the impact of cannabis decriminalisation in California in 2010 on the rate of cannabis-positive traffic fatalities. They used Texas as their comparison states because it had not legalised medical cannabis and found that the use of cannabis detected was less often among patients treated for traumatic injuries from traffic accidents in Texas than in California (23% in California vs 4% in Texas positive cannabis blood test among total vehicular trauma 2006–2012) [19]. However, a comparison within California did not find any significant change in the trend in cannabis-positive traumatic injuries in California between 2006 and 2012 (varying between 18 and 26% with no apparent trend). The results were consistent with roadside surveys which found cannabis use remained stable among weekend nighttime drivers between 2010 and 2012 in California [20].

Aydelotte applied difference-in-difference analytic methods (to control for underlying time trends, state-specific population, economic and traffic characteristics) to FARS data in states that had and had not LRC [21]. Difference-in-difference designs are commonly employed in studies investigating the impact of cannabis legalisation. As experimental designs are not possible, this method draws on observations from natural experiments. The states' cannabis legalisation status is operationalised as the 'treatment' or 'control' condition to compare changes over time in the outcomes. Aydelotte's study found that Washington State and Colorado did not show any significant changes in rates of traffic fatality after LRC compared with neighbouring states that had not legalised cannabis.

Sevigny used the FARS data set (1993–2014) to estimate trends in the number of fatal traffic accidents that had involved cannabis-impaired drivers [22•]. Unlike earlier studies, Sevigny used data imputation to address the large amount of missing data. He found, contrary to Anderson and colleagues,

that the prevalence of cannabis-positive driving did not change after LMC. He found that states with medical cannabis programs that allowed dispensaries showed a small increase in the prevalence of cannabis-positive drivers in fatalities. He also reported that LRC was followed by an 18% *reduction* in the prevalence of cannabis-positive driving.

Other studies have used data sets to study the impact of LRC on traffic accidents. For example, Chung and colleagues reported an overall increase in the rate of cannabis-positive patients admitted to Colorado hospitals for traumatic injury between 2012 and 2015 [23]. This increase did not occur in hospitals in neighbouring jurisdictions that had not legalised cannabis [23]. By contrast, Lane and colleagues [24] found that the commercialisation of recreational cannabis temporarily increased the monthly prevalence of *all* traffic fatalities in states that had legalised the commercial sale of cannabis (i.e. Colorado, Washington and Oregon). They found similar but smaller temporary increases in neighbouring jurisdictions between 2009 and 2016. Both studies only provided short-term assessments of the effects of LRC on traffic accidents immediately after commercialisation; studies of the longer-term effects remain to be done.

In summary, there is conflicting evidence on the impact of LMC on the prevalence of cannabis-positive traffic fatalities with different studies showing an increase, no change, or a decrease in the prevalence of these fatalities. Data on the prevalence of cannabis-positive traffic fatality and injuries post-commercialisation of cannabis legalisation (both medical and recreational) should be interpreted cautiously because of major data limitations and the possibility that increased detections of cannabis may reflect increased testing after LMC or LRC.

Cannabis-Related Emergency, Hospital Presentations, and Health Service Access

Cannabis-Related Hospital Presentations

The prevalence of cannabis-related hospital presentations in the USA increased nationally between 1993 and 2014, but trends have not been compared by jurisdiction [25]. Presentations in Colorado have been studied during the period of its liberal medical cannabis program starting 2009 and legalisation of recreational cannabis use in 2014. These policies in Colorado were associated with an increase in cannabis-related presentations to hospitals and emergency departments between 2000 and 2015 [26•]. Hospitalisations for cannabis abuse and dependence increased after LMC [27] while hospitalisations increased for motor vehicle accidents and injuries associated with cannabis abuse after LRC [28]. There was also an increase in cases of maxillary and skull base fracture after legalisation which was attributed to an increase in injuries from falls [29].

Cannabinoid Hyperemesis Syndrome

Cannabis hyperemesis syndrome (CHS) is a syndrome reported in chronic cannabis users that is characterised by cyclical vomiting that is unresponsive to standard emetic treatments but temporarily relieved by hot water bathing and by the cessation of cannabis use [30] (see Supplement G for additional information). Heard and colleagues (2019) reported an increased number of CHS presentations to emergency departments at a large hospital in Aurora, Colorado after the LMC in 2000 and LRC in 2012 (retail sales went into effect in 2014), with more than 100 patients admitted to the hospital annually with CHS.

Bhandari and colleagues analysed trends in hospitalisations for cyclic vomiting syndrome (CVS) in a Colorado State Inpatient Database 2010–2014 [31]. They found 806 cases of CVS from all causes in 2010 and a 46% increase in its incidence from 16 in 2010 to 22 per 100,000 population in 2014. The prevalence of cannabis use among CVS cases increased over time in both primary (14–25%) and all-listed diagnoses (9–19%). These trends could indicate increased cannabis use, an increase in the diagnosis of CHS, or more likely, both.

Kim and colleagues compared the prevalence of cyclic vomiting in emergency department visits in Colorado before (2008–2009) and after (2010–2011) medical cannabis legalisation [32]. Thirty-six patients with cyclic vomiting had 128 visits during this time and the prevalence ratio increased (OR = 1.92 (1.33, 2.79)). Cannabis use was more often mentioned in medical records after legalisation (OR = 3.59 (1.44, 9.00)), but it is not possible to determine how much of the increase was due to increased cannabis use and how much to increased reporting of cannabis use.

Al-Shammari and colleagues conducted an interrupted time series analysis of presentations for persistent vomiting and cannabis dependence in a nationally representative sample of 7 million hospital discharges in the USA between 1993 and 2014 [25]. They compared national trends pre-legalisation (1993–2008), during legalisation (2009), and post-legalisation (2010–2014). Incidence rates of persistent vomiting (IRR = 1.08 (1.04, 1.28)) and cannabis dependence (IRR = 1.06 (1.02, 1.10)) increased after LMC. Similar elevated trends were observed for incidence of persistent vomiting during legalisation (IRR = 1.13 (0.98, 1.31)), although these were not statistically significant. A major limitation of this study was that it only examined national trends and did not compare trends between states that had and had not legalised medical cannabis use.

Cardiovascular Presentations

There are case reports of heart failure, hypertension, and cerebrovascular accidents [33, 34] and sudden cardiovascular

deaths in heavy cannabis users [35]. It is therefore important to examine trends in cardiovascular outcomes associated with LMC and LRC.

Patel and colleagues reported trends in the proportion of patients aged 18–50 years who were hospitalised with acute myocardial infarction (AMI) and who also had a diagnosis of cannabis use disorder between 2010 and 2014 [36]. Their data came from a database covering 4411 hospitals in 45 states comprising 20% of all hospitals in the USA. They found that the number of hospitalisations for AMI declined over the study period, but the proportion of these cases with a cannabis use disorder increased 32% and the severity of cases mentioning cannabis use, and the invasiveness of treatment required, also increased. They did not attempt to compare trends in states with and without medical cannabis programs.

Abouk and Adams used data from the National Vital Statistics System to examine changes in the rates of cardiac-related mortality after LMC. They also examined associations between mortality rates and state rules on cannabis dispensing [37]. Using difference-in-difference fixed-effects models, they compared cardiac-related mortality rates before and after the introduction of medical cannabis programs. Rates of cardiac deaths increased significantly after legalisation in both men (2.3% increase, $p < 0.001$) and women (1.3% increase, $p < 0.001$). There were larger increases in states with more lax medical regulations (Arizona, California, Colorado, Michigan, Montana, Nevada, Oregon, and Washington) than in those with stricter regulation. The study suggested that the impact of cannabis legalisation on cardiac health was greater for middle aged and older cannabis users.

Poisonings and Unintentional Consumption by Children

Wang and colleagues [26] reported an increase in paediatric visits for unintentional cannabis ingestion in Colorado from 2000 to 2015 in data on children's hospital visits and calls to regional poison centres after the LMC in 2010 (111.4% increase, $p < 0.001$) and LRC in 2014 (79.7% increase, $p < 0.001$). Interrupted time-series analysis of poison centre calls in Colorado and the Denver metropolitan area in 2007–2013 showed an increase of 0.8% per month (0.2–1.4; $p < 0.01$) [27]. A review of case reports from 1975 to 2015 found increasing numbers of unintentional cannabis ingestion cases by children in states that have legalised medical and recreational cannabis [38•].

The incidence of paediatric hospital visits and calls to poison centres for accidental cannabis ingestion has continued to increase since 2017, despite limits being set on package and serving sizes of the edible products [39]. Edibles were responsible for almost half of the paediatric cases in which young children ate these highly palatable products and unwittingly ingested doses of THC that produced severe intoxication requiring hospitalisation [40]. Richards and colleagues found

that the most common sources of paediatric exposure were cannabis resin (38%) and cannabis cookies (13%) [38•].

Other Health Service Use

Richmond and colleagues examined trends in the rates of patients screening positive for cannabis in Colorado's screening, brief intervention, and referral to treatment program [41]. This included data on 108,760 patients treated between 2008 and 2011 in hospitals, health centres, primary care clinics, urgent care clinics, trauma units, and one dental care clinic. The proportion screening positive for cannabis increased from 2009 and levels of self-reported cannabis use also increased. Cannabis use was more common in younger male patients, but there was a steeper increase in older patients, which may be because of increased medical use. The increase in cannabis-related health service presentations probably reflects a combination of increased adult use [9••] and the increased THC content in cannabis products [42, 43].

Mental Health

Presentations to Emergency Departments

In Colorado, the prevalence of mental illness among emergency department visits with cannabis-related codes was fivefold higher in 2015 than in 2000 (prevalence ratios = 5.07, 95% CI 5.0, 5.1) than the increase in the prevalence of mental illness presentations not related to cannabis [26•]. The highest ratios were for schizophrenia and other psychotic disorders (prevalence ratio = 9.18 (8.66, 9.75)), suicide and intentional self-harm (PR = 7.96 (7.49, 8.46)), and mood disorders (PR = 7.40 (7.12, 8.46)) [44].

Mental Disorders

Regular cannabis use has been associated with increased risks of psychosis and depression requiring specialist mental health treatment [13]. Our search did not find any studies of the effects of either LMC or LRC on the prevalence of these disorders in mental health services or in population surveys. Depression is a concern because medical cannabis advocates have promoted cannabis as a treatment for depression [45]. However, a recent review on medical cannabis use for depression found no significant benefits [8].

Self-Harm

Heavy cannabis use is associated with increased risks of suicidal ideation (OR = 2.53 (1.00–6.39)) and suicide attempts (OR = 3.20 (1.72–5.94)) [46]. There have been several studies of the impacts of LMC on suicide rates. Anderson and colleagues used state level data on suicide mortality from the

National Vital Statistics System and assessed the relationship between these deaths and state policies on medical cannabis [47]. They reported a steeper decline in suicide rates among males aged 20–30 in US states that had legalised medical cannabis than in states that had not [47]. This finding was not supported, however, by an independent analysis of the same data series whose authors controlled for differences between states in demographic variables and state policies that may be associated with rates of suicide [48••]. It found no association between state medical cannabis policies and trends in suicide. Another study by Rylander and colleagues [49] examined relationships between rates of completed suicides and the number of patients enrolled in medical cannabis programs in US states between 2004 and 2010. These authors also failed to find any association between patients in medical cannabis programs and state suicide rates [49].

Use of Other Substances

Alcohol and Tobacco Use

Cannabis legalisation advocates argue that alcohol and opioid use will decline after cannabis legalisation as users switch from these drugs to cannabis [50]. A survey of individuals from Colorado, Washington, Oregon, and New Mexico examined how often people use alcohol and cannabis together [51]. When using cannabis for recreational purposes only, 17% reported usually using alcohol at the same time, compared to 1–3% of those who used cannabis for medical reasons. Among those who self-identified as medical users, a large majority (86%) also reported recreational cannabis use, resulting in an overall level of 12% of cannabis users reporting using alcohol together with cannabis.

Reviews of evidence on whether alcohol is a substitute or a complement for cannabis have not produced clear conclusions [52, 53•]. Summaries of evidence from surveys and record-based studies up to 2016 among youth, general population, clinical, and community-based samples have reported mixed evidence for substitution (cannabis liberalisation associated with lower alcohol use), complementary (cannabis liberalisation associated with increases in both cannabis and alcohol use), and neither [52, 53•].

Subbaraman found that in longitudinal studies of young populations, some studies showed that cannabis decriminalisation was associated with higher alcohol use, while others suggested either that stricter alcohol policies were associated with lower cannabis use or that there was no association between LMC and alcohol use [53•]. Difference-in-difference analyses of large national population school surveys have also showed mixed results [54•, 55•]. Cerda and colleagues analysed data from the 1991–2015 MTF annual surveys of 8th-, 10th, and 12th graders to examine the relationship between state LMC and substance use [54•]. After

LMC, decreases in binge drinking and other drug use were observed only in 8th graders.

Johnson and colleagues analysed YRBS data for 9th–12th graders between 1991 and 2011 to assess associations between LMC and alcohol use [55]. They found that LMC was associated with lower odds of past 30-day adolescent alcohol use (OR = 0.92 (0.87–0.97)), but the effect was weak, and there was no change in binge drinking (OR = 0.95 (0.89–1.00)) or in alcohol use without cannabis use (OR = 0.96 (0.91–1.02)).

A study of trends in state-level alcohol sales data comparing states that have and have not legalised recreational cannabis use did not find any decreases in alcohol sales in states that have legalised cannabis [56]. The difference-in-difference analyses found that medical cannabis dispensaries were not associated with any change in alcohol consumption.

Opioid Prescribing and Fatal Opioid Overdoses

Advocates of medical cannabis have claimed that encouraging patients who use opioids for pain to switch to cannabis may reduce opioid overdose deaths [57]. This claim received widespread media attention when a study by Bachhuber and colleagues reported that rates of opioid overdose deaths had increased more slowly in US states with medical cannabis programs [58].

Multiple studies have since examined the effects of cannabis legalisation on opioid-related outcomes. Vyas and colleagues conducted a systematic review of the evidence on the association between state LMC policies and prescription opioid use and related harms [59]. They identified 10 studies published between 2010 and 2017 (4 cross-sectional surveys, 6 state-level secondary data analyses), which included data between 1999 and 2010 on opioids mortality, 2010–2013 on prescribing, and 1997–2014 on hospital discharges. They found that medical cannabis programs were associated with lower numbers of prescriptions for opioids filled by Medicaid beneficiaries, opioid-related presentations based on treatment facility and hospital admissions, and age-adjusted opioid-mortality rates in the population (13–25% reductions). They cautioned against concluding that medical cannabis programs were responsible for these changes because of major limitations in these studies, such as not accounting for policy, social, and demographic differences between states (further explained below).

Several recent studies that have extended the period of observation [60, 61, 62••, 63••] from 2010–2017 consistently reported that cannabis legalisation was associated with lower opioid prescribing rates, including for hydrocodone and morphine, especially in states with active cannabis dispensaries [60, 61, 63]. However, a recent study by Shover and colleagues [62••] that examined the association between medical cannabis laws and opioid overdose mortality of data through

to 2017 did not support the earlier findings of Bachhuber and colleagues. This study found that with the addition of 7 years of data the association between the presence or absence of LMC and age-adjusted opioid analgesic overdose death rates reversed direction from –21% (1999–2010) to +23% (1999–2017).

Discussion

There is suggestive evidence that legalisation of medical and recreational cannabis use has had both positive and negative effects on a range of health consequences. However, major methodological weaknesses in this research limit our capacity to confidently conclude that these changes are the result of legalisation. Randomisation is the gold standard for causal inference, but it is impossible to randomise states to legalise medical or recreational cannabis use or not. Many US states have legalised cannabis after referenda were passed, and these states are likely to differ from states that have not legalised cannabis in their patterns of cannabis and other drug use, their attitudes towards cannabis, in many sociodemographic characteristics and in public policies that may affect public health outcomes [64]. These facts make it unwise to conclude that differences between these states in health outcomes can be explained by their different cannabis policies.

Similarly, comparisons of health outcomes pre- and post-legalisation may be confounded by changing attitudes towards and use of cannabis in states where cannabis is legalised. Some studies have employed difference-in-difference methods to evaluate the impact of legalisation [21, 22••, 37, 54•, 55•, 56, 61, 63], but these analyses assume that measurement error is the same across the states and over time. This ignores the possibility that certain outcomes may be better detected and attributed to legalisation in states where cannabis has been legalised. For example, in the case of motor vehicle accidents, rates of testing for cannabis may differ between states [65]. This makes it uncertain whether changes in identification of cannabis-related accidents are due to legalisation or to an increased detection and attribution of these accidents to cannabis.

It is also too early to conclude that the apparent absence of short-term adverse effects of RCL mean that there will be no such effects in the longer term [66]. Some of the cannabis-related harms, such as psychosis and cannabis use disorder, develop after years of frequent use. RCL has only been recently introduced in some US states. The fact that cannabis also remains prohibited under Federal law in the USA has constrained the full commercialisation of the legal cannabis market in states that have legalised. In the case of the repeal of alcohol prohibition in the USA, it took four decades for alcohol consumption to return to pre-prohibition level after the repeal of national alcohol prohibition in 1932 [67].

Table 1 Summary of evidence on the impact of cannabis legalisation on motor vehicle accidents

Study's first author (year)	Motor vehicle road injury outcome assessed	Year of data collection	Setting	Cannabis legalization measure	Impact
Anderson 2013	Proportion of alcohol-involved fatal crashes over total traffic fatality per year	1990–2010	USA Fatality Analysis Reporting System (FARS)	Overtime across MML	↓
Aydelotte 2017	Compare year-over-year changes in motor vehicle crash fatality rates	2009–2015	Washington, Colorado, and 8 control states of motor vehicle crash fatalities	Before and after recreational cannabis legalization	↑
Brady 2014	Prevalence of drivers tested positive for cannabinal in blood, who were involved in fatal motor vehicle crash	1999–2010	Toxicological testing in California, Hawaii, Illinois, New Hampshire, Rhode Island, and West Virginia	Changes in rates over time	↑
Chung 2019	Rates of change in positive urine drug screen for cannabis and hospitals	2012–2015	Traumatic injury admissions in Colorado hospitals, compared with control states	Cannabis (pre or post) commercialization in Colorado in 2014	↑
Keric 2018	Cannabis-related vehicular trauma	2013	American Association for the Surgery of Trauma (AAST) survey	Cannabis decriminalization in California in 2010 vs Texas	–
Lane 2019	Monthly traffic fatalities rates	2006–2012	Trauma Center Registries	Changes in rates over time by legalization status	–
Masten 2014	Changes in prevalence of cannabinoid in blood/urine in fatal crashes	2009–2016	Legalized states relative to neighbouring non-legalized jurisdictions	MML of states	↑
Pollini 2015	Changes in prevalence of drivers tested positive for THC in oral fluid among weekend nighttime drivers	Survey: 2010 and 2012; FARS: 2008–2012	Roadside survey and FARS	Cannabis decriminalization in California in 2010	–
	Changes in prevalence of THC among drivers from roadside surveys				–
	Changes in cannabis-positive testing among fatally injured drivers				↑
Salomonsen-Sautel 2014	Changes in prevalence of drives tested positive for cannabinoid	1994–2011	Colorado vs 34 non-legalized states using FARS data	Commercialization of medical cannabis in Colorado in mid-2009	↑
Santaella-Tenorio 2017	Annual rate of traffic fatality	1985–2014	USA FARS	MMLs enactment and operational dispensaries by states	↓
Sevigny 2018	Cannabis positivity among fatally injured driver	1993–2014	USA FARS	MMLs in states	–
				State-licensed medical cannabis dispensaries	↑
Steinemann 2018	Cannabis positivity among fatally injured drivers	1993–2015	Hawaii FARS	Medical cannabis legalization in Hawaii in 2000	↑

Further details are available in Supplementary D

Impact: ↑ cannabis legalisation associated with an increase; ↓ cannabis legalisation associated with a decrease; – no evidence supporting increase or decrease. FARS: Fatality Analysis Reporting System; MML: Medical marijuana laws

Cannabis legalisation has stimulated innovation in a highly commercialised industry. Many novel high potency cannabis products, such as concentrates and vaping liquid, are now easily accessible and these products may increase the risks of negative outcomes, especially among regular users. The impacts of these innovations are yet to be clear, and their

effects on public health may take some years to become apparent.

Better future evaluations of the public health impacts of cannabis legalisation require monitoring of key outcomes (see Table 2) using improved data infrastructure [68]. This means that data on cannabis related outcomes need to be

Table 2 Key outcomes that future studies on the impacts of cannabis legalisation should monitor

- Changes in cannabis price and potency and the market share of different types of cannabis products, such as extracts, edibles, and beverages.
- Rates of daily and near daily cannabis use, and cannabis use disorders among adolescents and adults, including older adults.
- Cannabis use among pregnant women and their birth outcomes.
- Motor vehicle accidents involving cannabis related impairment.
- Possible medical consequences of regular cannabis use, such as cardiovascular disease among young and middle aged adults, hyperemesis syndromes, psychoses, depression, and suicide.

clearly defined prior to data collection and that similar data collection protocols and standards are used across states to ensure data comparability. We also need large-scale longitudinal population studies to evaluate the effects of legalisation over time on the health and well-being of adolescents and young adults, such as studies now underway in Canada [69].

Conclusions

The legalisation of adult cannabis use has increased access to cannabis, reduced its price, and increased the frequency of cannabis use among adult users. Cannabis impairs driving, and detections of cannabis in motor vehicle fatalities may have increased in some states after legalisation of recreational cannabis use, although there are conflicting findings and some of the increase may be attributable to increased testing for cannabis. There have been more presentations to emergency departments for acute outcomes of cannabis use (e.g. psychiatric, gastrointestinal, and cardiovascular effects) and cases of paediatric poisoning. Regular cannabis users, especially daily users, are the most susceptible to cannabis-related harms such as dependence, psychosis, depression, and self-harm. It is unclear whether the incidence or prevalence of these disorders has changed since cannabis legalisation. It is also unclear whether cannabis legalisation has reduced the use of alcohol and opioids.

Future research should examine trends in these health outcomes for a longer period after legalisation. Better studies will be needed in the USA if cannabis legalisation becomes national policy. Studies will also be needed to assess the extent to which states can implement public health policies to minimise the harmful patterns of cannabis use (e.g. taxes based on THC content). We also need better research on the extent to which any increases in cannabis use after legalisation may be offset by decreases in the use alcohol and opioids.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

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