Drug Use 2

Public health implications of legalising the production and sale of cannabis for medicinal and recreational use

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This is the second in a Series of four papers about drug use

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We assess the current and describe possible future public health impacts of the legalisation of cannabis production, sale, and use in the Americas. First, we describe global patterns of cannabis use and their most probable adverse health effects. Second, we summarise evidence regarding the effectiveness of cannabinoids for medicinal use and describe approaches that have been used to regulate the use of medicinal cannabis and how these approaches might have affected medicinal and recreational use and harms (eg, road crashes). Third, we describe how jurisdictions that have legalised recreational use have regulated production and sale of cannabis. Fourth, we evaluate the effects of cannabis legalisation on cannabis use and harms and on the use of alcohol, tobacco, and other drugs. Fifth, we use alcohol and tobacco policy examples to identify possible long-term public health effects of cannabis legalisation. Finally, we outline policy approaches that could minimise harms to public health arising from the legalisation of a commercial cannabis industry.

Introduction

Cannabis has been an illicit drug in countries that signed the UN Single Convention for more than 50 years. Nevertheless, more than 192 million adults used cannabis globally in 2016.[1] The inclusion of cannabis in UN drug treaties has long been controversial because it causes much less harm than do illicit opioids and stimulants[2] or legal drugs such as alcohol and tobacco.[3] The comparatively high rates and modest harms of cannabis use have prompted calls for governments to legalise cannabis for medicinal and non-medicinal use since the late 1960s.[4] These calls have resulted in major changes in cannabis regulation in the Americas that might prompt similar policy changes in other countries in the future.

The first global wave of a cannabis policy change removed criminal penalties for possession of small amounts of the drug.[4] This occurred in the 1970s in the USA and in the Netherlands, and these countries also stopped enforcing criminal penalties on small retail cannabis sales in coffee shops. These reforms stopped short of legalising cannabis production.[4]

Two trends have transformed cannabis policy in North America since the 1990s. The first was the legalisation of medicinal cannabis use in some states in the USA and in Canada. Medicinal use was initially permitted for a short list of medical conditions, but in Canada and certain US states (eg, California, Colorado, Oregon, and Washington state) the conditions qualifying for medicinal use were progressively broadened, enabling almost any adult in those jurisdictions to obtain a medical recommendation and purchase cannabis from retail dispensaries.[5] Countries in Europe, Oceania, Africa, and Asia have since allowed use of medicinal cannabis.[5]

The second more radical change was the legalisation of large-scale commercial cannabis production and sale of cannabis for non-medicinal use, sometimes called recreational use.[6] This happened first by popular vote in the US states of Colorado and Washington State in 2012. Another eight US states and territories followed, and more are considering this change. However, cannabis remains illegal under US Federal law.[6]

The Government of Uruguay legalised cannabis in 2013, but cannabis supply only began in 2015 under more restrictive regulations than in the USA. In 2018, Canada legalised cannabis nationally, and Luxembourg and Mexico propose to legalise cannabis in the near future, perhaps within the next 5 years.[7]

In this section of the Series, we describe the regulation of legalised medical and recreational cannabis in the Americas. We focus on the Americas because these policies have been in place in this region for the longest time and their results are likely to prove influential for changes in global cannabis policies. We assess the public

Key messages

- Cannabis is the most widely used illicit drug globally
- Canada and ten US states have legalised the commercial production and sale of cannabis for medicinal and recreational use
- In Canada and certain US states, cannabis flower, oils, and concentrates are used to treat medical conditions in the absence of evidence of their effectiveness and safety
- Weakly regulated medicinal cannabis programmes in some US states and Canada have blurred the boundaries between medicinal and non-medicinal use
- Legalising cannabis production in the USA might have reduced the illicit market and allowed governments to regulate and tax cannabis, but cannabis potency is largely unregulated, and prices have fallen steeply within a few years of legalisation
- Legalisation has created a cannabis industry with an interest in promoting regular cannabis use, which has increased among adults in the USA since liberalisation
- True public health effects of cannabis legalisation cannot yet be assessed, because it has only been implemented within the past 5 years and cannabis remains illegal under US federal law
- The effect of legalising cannabis sales on use of alcohol, tobacco, opioids, and other drugs remains unknown

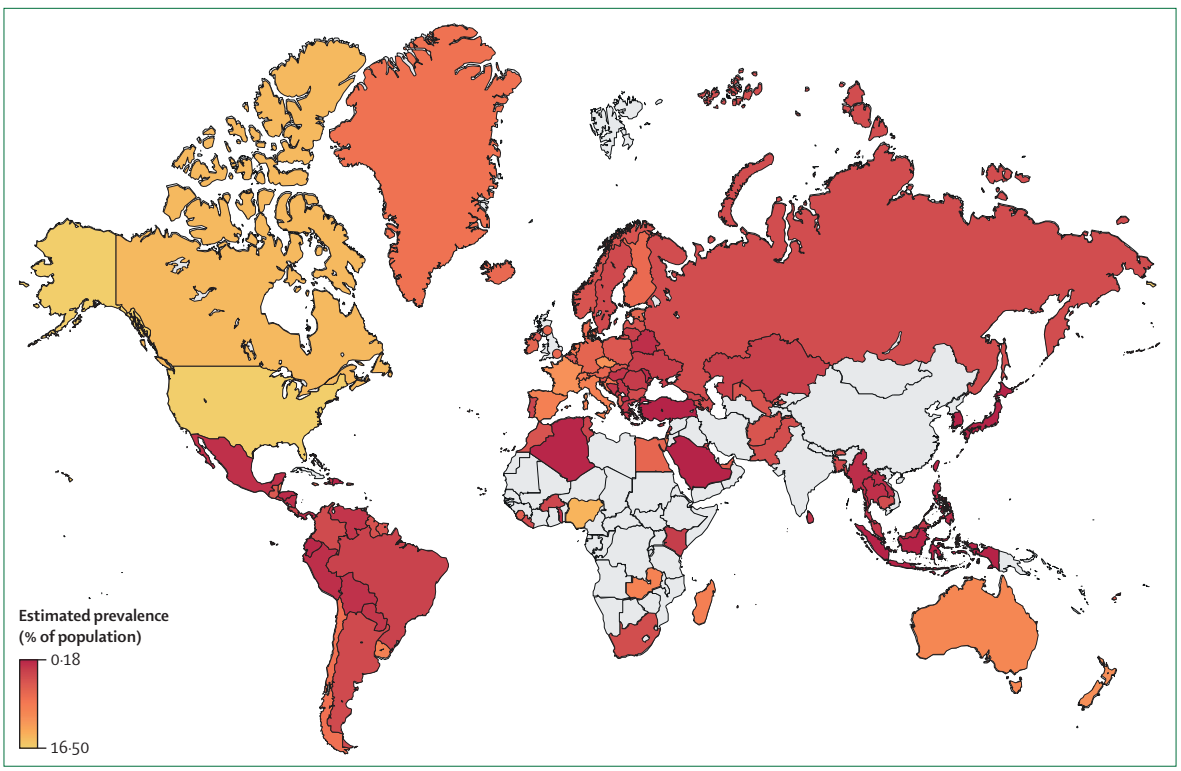

Figure: **Prevalence of cannabis use in 2016**
Data from UN Office on Drugs and Crime.[10]

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health effects of these changes to the degree that the evidence allows. We use historical examples of changing alcohol and tobacco policies to discuss possible future public health effects as the industry matures. We also outline approaches that could reduce future adverse public health effects that might arise from new legislation.

The global epidemiology of recreational cannabis use

Cannabis remains an illicit drug under international drug control treaties that have been ratified by most UN member states, including Canada and the USA. Despite this illegality, in 2015, an estimated 192 million adults (range 166–234 million) or 3·9% of the global adult population used cannabis.[1] Cannabis use is much more common in North America and high-income countries in Europe and Oceania than in low-income and middle-income countries.[8] Cannabis use has increased in low-income and middle-income countries,[9] but use in Asia remains low (figure; appendix p 5).

High school and household surveys in Australia, Canada, and the USA provide the most comprehensive data on long-term trends. In the USA, cannabis use peaked among young people in 1979 and declined until the early 1990s. Use again increased through the 1990s, but levelled off towards the end of the century[11] and has increased since 2006 but not reached the high proportion peak that was observed in 1979.[12] A substantial increase in the proportion of people who use cannabis who use daily or near daily has also been observed.[6,13]

In Canada, cannabis use increased between 1985 and 2000,[14] declined among adolescents in the early 2000s and increased among adults after 2002. Australia also reported an increase in cannabis use among young adults in the 1990s and a decline from the year 2000.[15] The prevalence of cannabis use and trends over time have varied substantially between EU countries.[16] Countries in western and southern Europe show a higher proportion of use than those in eastern and northern Europe, but generally use is lower than in countries in the Americas.[16]

Patterns of cannabis use during adulthood have changed in the USA. In the 1980s, cannabis use began in teenagers aged 15 or 16 years, prevalence of use was highest between age 20 years and 25 years, and steeply declined after age 28 years.[17] Since 2008, people in the USA continue to regularly use cannabis into their 30s.[18]

Tetrahydrocannabinol (THC) is the compound mainly responsible for the psychoactive effects of cannabis.[4] The THC content of herbal cannabis has increased markedly over the past several decades in the USA and Europe, from around 5% to more than 15%[19] (appendix pp 60–62). Cannabis users nowadays probably receive larger doses of THC, but we lack reliable data regarding average THC doses. In the absence of these data, epidemiological studies

See Online for appendix

	Size of effect (95% CI)	Level of evidence
Motor vehicle injuries*		
Use 1–3 h before driving	Small risk: RR 1·37 (1·2–1·5) to 2·7 (2·1–3·4)	B
Low birthweight†		
Maternal use in pregnancy	Small increase in risk: OR 1·8 (1·0–3·0)	B
Dependence syndrome†		
Lifetime use	Small to moderate risk: 7·2% (6·6–7·7) to 28·3% (22·0–34·6)	B
Daily use	Large risk: 40·9% (29·0–52·8)	B
Psychosis or schizophrenia*		
Ever used	Small increase: OR 1·4 (1·2–1·7)	B
Daily use	Doubling: OR 2·1 (1·5–2·8)	B
Depression*		
Ever used	Very small increase: OR 1·2 (1·1–1·3)	B
Daily use	Small increase: OR 1·6 (1·2–2·2)	
Bronchitis*		
Cannabis smoking	Large increase: RR 7·48 (no CIs)	D
Regular cannabis smoking	Large increase‡	B
Lung cancer		
Regular cannabis smoking	No significant increase: OR 0·95 (0·66–1·38)	B

OR=odds ratio. RR=relative risk. Evidence levels: B=findings in cohorts or representative population-based studies. D=findings in cross-sectional studies, representative population-based studies, or case-control studies. *References and details on supporting evidence are presented (appendix pp 11 –21). †References and details on supporting evidence are presented (appendix pp 11 –21). ‡Positive findings reported by multiple studies, but pooled effect size not reported.

Table 1: **Harms associated with non-medicinal cannabis use**

have focused on the adverse health effects of daily or near daily cannabis use.[20]

Harms related to recreational cannabis use

Systematic reviews of epidemiological studies have identified adverse effects of cannabis use (table 1; appendix pp 16–21).[20–22]

Overdoses of cannabis do not result in respiratory depression, which can occur with opioid use. However, a very small number of deaths from cardiovascular disease and stroke[23] and a hyperemesis syndrome[24] have been attributed to sustained, heavy use of cannabis.

Cannabis can produce adverse acute effects including anxiety, depression, psychotic symptoms, and adverse cardiovascular and gastrointestinal symptoms, which might prompt people who use cannabis to seek medical treatment.[20]

Cannabis produces acute dose-related impairment of cognitive and psychomotor performance[20] that could contribute to road crashes if individuals drive while cognitively impaired.[25,26] Measurement of cannabis-associated cognitive impairment in drivers is difficult because a complex relationship exists between THC concentration in the blood and cognitive impairment, with studies showing impairment is most marked after blood THC concentration has begun to decline.[26,27] Epidemiological studies find a modest association between markers of recent cannabis use and the risk of an accident (relative risk [RR] 1·3–2·0)[28,29] that is less than the risk for alcohol impairment (RR 5–10).[30]

Cannabis use during pregnancy might adversely affect fetal development.[20] Evidence suggests that it modestly reduces birthweight after controlling for tobacco use.[31]

People who use cannabis regularly can develop dependence on cannabis.[32] This is marked by difficulty in cutting down or ceasing use that is causing harm (appendix pp 11–12).[33] In Australia, Canada, the EU, and the USA, cannabis dependence is often treated with counselling, and is the most commonly treated type of drug dependence after alcohol and tobacco[32] (appendix pp 11–12).

In US surveys done in the 1990s, cannabis dependence was estimated to affect 1–2% of adults in the previous year and 4–8% of adults in their lifetime.[33] In these surveys, only 9% of those who ever tried cannabis developed dependence, compared with 32% for nicotine, 23% for heroin, 17% for cocaine, and 15% for alcohol.[34] The risk of dependence was 20–30% in people who used cannabis 100 times or more[6] and might be higher in those who use high potency products.[19] An Australian longitudinal study estimated the risk of cannabis dependence as 40·9% among those with a history of daily use in young adulthood (appendix pp 24–25). These studies probably underestimate the risk of cannabis dependence considering the increasing potency of cannabis products globally (appendix pp 60–62).

Adolescents who use cannabis are more likely than adults to develop dependence;[35] show cognitive impairment;[36] leave school early;[37,38] use other illicit drugs;[20] develop schizophrenia[39] and affective disorders;[40] and have suicidal thoughts.[41] Whether cannabis is a cause of these outcomes, or whether they reflect shared genetic risks, other drug use, or personal characteristics, is uncertain.[20]

Whether regular cannabis use over years adversely affects physical health also remains unclear. Very few people who use cannabis have used throughout adulthood and many who have used, have also smoked tobacco, and consumed alcohol.[10] Chronic bronchitis is the most consistently found adverse effect of cannabis smoking.[20] Cannabis smoke contains carcinogens at similar concentrations to cigarette smoke, but detecting any increased risk of lung cancer has been difficult,[20] probably because people who use cannabis typically smoke less often and inhale less smoke than tobacco smokers. Case series suggest that heavy cannabis smoking could increase risk of myocardial infarctions and strokes[20] and produce a hyperemesis syndrome (table 1).[42]

In the Global Burden of Disease project, regular cannabis use was found to produce much less harm than regular alcohol and tobacco use.[43] In Australia[2] and Canada,[44] two countries with a high prevalence of use, cannabis made a much smaller contribution to disease burden (largely through dependence) than did the opioids. The prevalence of cannabis dependence is much

lower in most other countries; therefore, cannabis makes a smaller contribution to disease burden (appendix pp 7–10).

Cannabis users and critics of cannabis prohibition have long argued that the modest adverse effects of cannabis compared with alcohol, tobacco, and illicit drugs, do not justify a prohibition on adults using cannabis for pleasure and relaxation.[45] Until 2010, this argument proved less successful in the USA than the notion that seriously ill patients should legally be able to use cannabis for medicinal purposes (panel 1).

The legalisation of medicinal cannabis use

Medicinal cannabis in the USA

In 1996, Californians voted to allow patients to use cannabis to treat nausea, weight loss, pain, muscle spasm, and serious medical conditions.[47] Following this, more than 30 jurisdictions in the USA have legalised medicinal cannabis use in some form (appendix pp 26, 36). States vary in the qualifying medical conditions, the type of cannabis products that can be used, and whether home cultivation or cannabis dispensaries are allowed.[48] Some states only allow use of cannabis low in THC and high in cannabidiol (CBD). In the states with the most liberal provisions, medical use is allowed for any condition approved by a doctor, and patients can purchase cannabis from retail dispensaries.[49]

Medicinal cannabis in other nations

In 2001, the Canadian federal government allowed access to cannabis for medicinal use in exceptional circumstances.[50] Since then, the qualifying medical conditions have progressively broadened in response to court decisions.[50] In March, 2014, the government licensed multiple cannabis producers, allowed any doctor to recommend cannabis, and permitted patients with a medical recommendation to buy cannabis from licensed producers, but not from dispensaries.[51]

Medically approved cannabinoids (eg, dronabinol and nabiximols) can be used in some European countries (appendix pp 26–28).[52] Only the Netherlands allows the use of cannabis flower for medicinal purposes and only Germany provides health insurance coverage for medicinal cannabis.[53,54] In Israel, doctors can prescribe herbal cannabis for medical use when recognised treatments have failed.[51]

Research evidence for medicinal cannabis use

Patients with multiple sclerosis in whom a standardised cannabis plant product with equal amounts of THC and CBD is added to other treatments report less muscle spasticity than those given placebo, but clinicians report only marginal reductions.[21,55] These standardised plant-based cannabis medicines produce modest but clinically significant reductions in chronic neuropathic pain in multiple sclerosis compared with placebo and in other types of chronic non-cancer pain.[56]

Panel 1*: Perspectives of North American cannabis consumers

Positive effects of cannabis use

"I have been a cannabis enthusiast since 1968. Like wine drinkers who have a glass or two daily, I enjoy some cannabis every day. I've led a productive, challenging, rewarding life", (man, age unspecified, Tucson, AZ, USA)

"I smoked marijuana regularly as I wrote an MA thesis and a PhD dissertation, and it helped me remain focused and engaged in my work for hours, sometimes even allowing for flashes of insight and serendipitous connections between ideas. I find it to be a mild enhancer of daily subjective experience", (man or woman, age unspecified, Montreal, ON, Canada)

"Marijuana isn't alcohol or an opioid. You can't die from an overdose. It doesn't really evince physical cravings',' (man, age unspecified, Austin, TX, USA)

"My husband, who quit drinking 32 years ago, replaced his alcohol addiction with pot. It worked for him for years, helping with his social anxiety and depression and saving his life", (man or woman, age unspecified, Portland, OR, USA)

Support for legalisation

"Prohibition of cannabis and its active ingredients has no scientific basis, and the many billions of taxpayers money used to criminalize cannabis users and maintain a public disinformation program to support its continued prohibition…could be used to research its optimal use and limitations, treat persons addicted to much more toxic substances, and educate people on the responsible use," (physician scientist, age unspecified, Chicago, IL, USA)

"…cannabis should be legal. The most dangerous thing about it, is being prosecuted by the state for possession of it" (man, age unspecified, Moscow, ID, USA)

"Reason to legalize marijuana is to keep people (kids, especially) from turning to the synthetic stuff instead—the stuff that isn't pot at all but is incredibly dangerous, laced with rat poison, formaldehyde, etc…" (man or woman, age unspecified, Philadelphia, PA, USA)

Problems with use since cannabis legalisation

"While I believe in legalization, it has only led to a massive increase in consumption. Prior to legalization I… could stretch out a bowl for days. But with such easy access and no scarcity issues, I'm smoking far too much and it's obvious even to me. Many of my pot-smoking friends have the same issues", (man, age unspecified, CO, USA)

"When marijuana was legalized…my husband began to smoke the much stronger weed. He looked like a crack head with stained teeth and a serious cough. He tried to quit on his own. Two days into detox he had a psychotic break", (man or woman, age unspecified, Seattle, CA, USA)

"I too find that I become angrier faster—but only when I'm sober. I have allowed multi-decade relationships to end…there is also the very obvious cognitive effects. I used to have rules—not during the work day, not at events with family, etc. But those rules have faded", (man, age unspecified, CO, USA)

*Anonymous comments submitted in response to news article.[46]

Evidence that cannabinoids are better than placebo in improving appetite, nausea or vomiting, pain, or sleep in patients with cancer in palliative care is scarce.[57]

Adding CBD to other anti-epileptic drugs significantly reduces the frequency of epileptic seizures in children with Dravet and Lennox-Gestaut syndromes.[58]

Synthetic THC is more effective than placebo in reducing nausea and vomiting associated with cancer

	Effect (95% CI)	N of RCTs (n of participants)	Evidence level
Multiple sclerosis			
Pain (neuropathic)[56]	SMD −0·23 (−0·36 to −0·09)	7 (808)	High
Pain (chronic non-cancer pain)[56]	SMD −0·01 (−0·12 to 0·10)	6 (1363)	Very low
Spasticity[55]	SMD −0·76 (−1·38 to −0·14)	3 (698)	Low
Sleep[56]	SMD −0·38 (−0·69 to −0·06)	3 (159)	Low
Quality of life[56]	SMD 0·10 (−0·09 to 0·30)	2 (403)	High
Chronic non-cancer pain			
>50% reduction in pain (all pain)[56]	OR 1·43 (0·97 to 2·11)	5 (753)	Moderate
>30% reduction in pain (all pain)[56]	OR 1·46 (1·16 to 1·84)	9 (1734)	Moderate
Pain intensity (neuropathic pain)[56]	SMD −0·20 (−0·28 to −0·12)	22 (2226)	Moderate
Pain intensity (all pain)[56]	SMD −0·14 (−0·20 to −0·08)	34 (3869)	Moderate
Sleep[56]	SMD −0·29 (−0·40 to −0·19)	15 (1482)	Low
Quality of life[56]	SMD 0·08 (−0·02 to 0·19)	11 (1059)	Moderate
Cancer			
>30% reduction in pain[57]	RR 1·33 (0·95 to1·85)	2 (537)	Low
Nausea and vomiting[57]	SMD 0·21 (−0·10 to 0·52)	3 (441)	Very low
Quality of life[57]	SMD 0·09 (−0·13 to 0·33)	3 (441)	Very low
Epilepsy			
>50% reduction in seizure frequency[58]	Pooled RR 1·74 (1·24 to 2·3)	2 (291)	Low
Complete seizure freedom[58]	Pooled RR 6·17 (1·50 to 25·32)	3 (306)	Low
Quality of life[58]	Pooled RR 1·73 (1·33 to 2·26)	2 (274)	Low
HIV			
Nausea and vomiting[57]	SMD 0·20 (−0·15 to 0·54)	1 (139)	Very low
Quality of life[57]	SMD −0·24 (−0·58 to 0·11)	1 (139)	Very low
Mental health			
Depression[60]	−0·06 (−0·20 to 0·07)	13 (1700)	Very low
Anxiety[60]	−0·37 (−0·63 to −0·11)	10 (348)	Very Low

Quality of evidence was assessed by use of the grading of recommendations, assessment, development, and evaluation (GRADE) approach.[61] High quality indicates confidence that the true effect is similar to the estimated effect. Very low quality indicates that the true effect is likely to be substantially different to the estimated effect. RCT=randomised controlled trials. SMD=standard mean difference. OR=odds ratio. RR=relative risk.

Table 2: **Clinical trial evidence for use of the cannabis plant and cannabinoids for medicinal purposes**

chemotherapy.[21,55,59] Trials comparing THC with newer anti-emetic drugs are scarce (table 2).[21,55]

Systematic reviews have found weak evidence that synthetic THC stimulates appetite in people with AIDS-related wasting syndrome.[21,55]

Evidence suggests that cannibinoids might be effective in treating anxiety symptoms. Overall, there is reasonable evidence that medical quality cannabis preparations and cannabinoids modestly reduce the symptoms of chronic pain, epilepsy, and nausea and vomiting. In most cases, cannabinoids are superior to placebo but marginally so for chronic pain,[56] the most common reason for medicinal cannabis use.[21] Evidence on the effectiveness of the herbal cannabis products used for medicinal purposes in Canada and the USA is scarce.[21]

When used for short periods, the adverse effects of medicinal cannabinoids and standardised cannabis preparations are similar to those of many commonly used medicines.[21] However, very few studies have evaluated the safety of the herbal cannabis products sold in medical dispensaries in the USA and Canada, which might be used daily by some patients for considerable periods.[21]

The public health effects of medicinal cannabis programmes

In many US state programmes, patients are permitted to use cannabinoids to treat medical conditions for which evidence of efficacy is available—namely, nausea and vomiting, epilepsy, and neuropathic pain. More liberal US state programmes permit the use of herbal cannabis to treat medical conditions for which little evidence on efficacy or safety is available—for example, neurological disorders (other than multiple sclerosis), anxiety, and depression.[21] Many doctors in Canada and the USA have been reluctant to recommend medicinal cannabis use because of a scarcity of high-quality evidence and concerns about their legal liability for any adverse effects.[5] Data regarding the number of patients who use medicinal cannabis is scarce[62] and very little data exists on how many patients benefit from cannabis use or have adverse effects. Reasons for the absence of data might include a lack of incentive for medical cannabis retailers or governments to collect the information.

The prevalence of regular cannabis use has increased among adults in US states with medicinal cannabis laws,[13] but cannabis use has not increased among those younger than age 21 years.[63–65] Some studies have reported fewer road crashes associated with alcohol and less deaths from opioid overdose in US states with medicinal cannabis programmes.[13] Many of these studies have not been able to test plausible alternative explanations for these changes (appendix pp 73–77).[66]

Liberal medicinal cannabis programmes might have facilitated the legalisation of recreational cannabis use by blurring distinctions between medicinal and non-medicinal use[67] and allowing the commercial retail sale of cannabis for medicinal use with minimal medical oversight.[67] They might also have reduced public perceptions of the harms and risks of cannabis use[13] and increased public support for legalising recreational cannabis use.[68]

The legalisation of cannabis supply for recreational use

Legalisation in the USA

Since 2012, ten US states have legalised commercial production of cannabis for recreational use (appendix pp 35–38).[69] The first legal sales began in Colorado and Washington in 2014, and in Oregon and Alaska in 2015. Vermont and the District of Columbia legalised possession and cultivation of cannabis for personal use but not for sale.

Several arguments appear to have attracted public support for cannabis legalisation.[70] The major one has been that cannabis use is widespread, does not harm

most people, and causes less harm than does alcohol. Another has been that criminalisation of use causes more harm than cannabis use — in particular, more arrests and criminal records, both of which disproportionately affect minority populations. Advocates suggest that legalisation would be a better policy, because it will eliminate the illicit cannabis market and enable cannabis to be better regulated to protect people—for example by controlling THC content and reducing contaminants (such as fungi and pesticides). Legalisation also promises to reduce the costs of policing cannabis prohibition and to allow state governments to raise tax revenue.[67]

The first US states to legalise commercial cannabis supply enacted laws modelled on those for alcohol.[6,71] Purchases were restricted to adults older than age 21 years.[72,73] States differed in how they licensed cannabis producers and retailers, but most imposed a tax on the retail sale price (appendix pp 35, 40–43).[48,49] Driving under the influence of cannabis was prohibited, but states differed in how the law was enforced.[71]

US Federal law still prohibits cannabis production, sale, and use.[6] There were no prosecutions under the Obama administration of state licensees who were following their state laws and so far there have been none under the Trump administration, but federal law has nonetheless constrained cannabis commercialisation.[6] It has created banking difficulties for cannabis businesses, deterred alcohol and tobacco companies from investing in US cannabis firms (as they have in Canadian firms), prevented cannabis businesses from deducting costs from their taxable income, and prevented legal interstate commerce in cannabis.[6,74]

Legalisation in Uruguay

Uruguay legalised cannabis for recreational use in 2013, but supply has increased slowly.[75] The policy aimed to remove organised crime from cannabis supply and to protect public health by restricting supply.[75] Uruguayans are only allowed to access cannabis if they register with the state. They then must choose only one of three ways of obtaining cannabis: growing their own; joining a cannabis growers' club that produces cannabis for its members; or purchasing cannabis from a small number of approved pharmacies.[75,76]

Legalisation in Canada

Canada legalised the commercial sale of cannabis for recreational use in October, 2018,[77] with the goals of eliminating the illicit cannabis market and regulating cannabis to protect public health and minimise youth uptake.[78] The federal government licenses and regulates cannabis producers. Advertising is not allowed, the minimum legal purchase age is 18 years (unless a province sets a higher one), and driving under the influence of cannabis is a legal offence. Provincial governments regulate wholesale and retail cannabis sales in a variety of ways (appendix pp 45–50). The sale of edibles and extracts taxed on THC content will begin in October, 2019.

The effects of cannabis legalisation

Legalisation is still in the early stages; therefore, evaluation of its public health effects is difficult.

Legalisation has probably produced a decline in arrests associated with cannabis for adults in US states that have legalised use and retail sales, but separating its effects from those of decriminalisation that preceded legalisation in many states remains a challenge.[79] The extent to which legalisation has reduced incarceration cannot yet be assessed, because few people have been imprisoned for cannabis possession in most US states that have since legalised cannabis.[6]

Legalisation has reduced the illicit cannabis market within US states that have legalised recreational use, but might have increased illicit cannabis trafficking between states that have legalised cannabis and those that have not (appendix pp 63–64). The effect of legalisation on the size of the illicit market is likely to have less of an effect in Uruguay than in Canada or the USA under Uruguay's restrictive policy because, at most, half of the estimated number people who use cannabis have registered for legal use and very few pharmacies supply cannabis.[80] Legalisation in Canada is too recent to evaluate its effects on the illicit market.

Retail cannabis prices have decreased by up to 50%, and the average potency of cannabis flower has increased in the first US states to legalise cannabis.[81] An increase has also been noted in the variety of cannabis products available. These now include edibles, oils for vaporisation, and extracts and waxes with more than 60% THC that now comprise 21% of sales revenue in Washington state.[81]

Public health effects of legalisation

In household surveys, adults who use cannabis in the USA report using cannabis more often since cannabis liberalisation.[6] No increase in cannabis use has been observed among adolescents and adults younger than age 21 years,[82] despite declines in the perceived risks of cannabis use in this age group.[13]

The health effects of using cannabis products of increased potency are unknown, but of primary concern. In some surveys, people who use extracts report more symptoms of dependence and mental distress.[83] In the Netherlands, more people sought help to quit cannabis use as potency increased, and less people sought help when potency decreased.[84]

Detections of THC in road crash fatalities have increased after legalisation in some US states, but the amount of accident fatalities do not appear to differ between states that have and have not legalised cannabis.[85] The extent to which increased detections of THC reflect increased cannabis-impaired driving and increased testing for THC remains uncertain.[13,85]

Strategies for reducing cannabis-related harm after legalisation

After legalisation, governments can adopt policies that have been shown to mitigate alcohol-related and tobacco-related harm.[86] Governments can, for example, create a monopoly on cannabis production and sales, use taxes to discourage heavy use, decrease the number and location of retail cannabis outlets, restrict advertising and promotions, educate people about how to minimise the harms of cannabis, discourage adolescents from initiating use, treat so-called problem cannabis users, and deter people who use cannabis from driving while impaired. Strategies to reduce cannabis-related harm after legalisation could include increasing the CBD content of cannabis, targeting vulnerable populations for intervention (eg, individuals diagnosed with schizophrenia), and discouraging routes of administration that rely on combustion.[87]

One strategy to reduce cannabis-related harm could be taxation and regulation. State governments in the USA that have established retail cannabis markets have not taxed cannabis products according to potency, as is done for alcohol. Taxes have more often been set as a percentage of retail price, so tax revenue declines along with retail prices (appendix pp 55–59). No US jurisdiction has so far increased cannabis taxes enough to prevent price declines after legalisation.[6] Inherent tension exists between the policy goals of minimising taxes to reduce the illicit cannabis market and imposing high taxes to discourage heavy use. Taxing the potency of edibles and cannabis extracts has been proposed in Canada, but implementing these taxes might prove to be a challenge because of the costs and difficulties in testing the THC concentrations of cannabis products.[88] Illinois, USA, has passed legislation that would tax more potent cannabis products at a higher rate upon establishment of the retail market in 2020 (appendix p 41).

Programmes to prevent adolescent cannabis use might also be beneficial. Weak evidence exists that mass media campaigns reduce cannabis use and harms in young people.[89,90] More targeted family prevention strategies[91] and family-based prevention programmes might be more effective than media campaigns[92] and possibly have long term benefits.[93,94] School-based life skills programmes that combine social competence and social influence approaches reduce cannabis use at the 12-month follow-up.[95] Interventions that only increase participants' knowledge or attempt to increase self-esteem do not reduce use.[96]

Health education for people who use cannabis might also reduce harms associated with cannabis use.

After legalisation, people will need accurate information about cannabis products—for example, doses of THC, the risks and benefits of using more potent cannabis, and ways to minimise harm.[97] They will need to be informed about the scarcity of evidence for many of the putative medicinal uses of cannabis and CBD, risks of cannabis dependence, cannabis use during pregnancy, driving while impaired, and of exacerbating psychoses and other mental health disorders. The design of effective educational programmes will require research on the type of product labels, health warnings, and harm reduction advice most credible to people who use cannabis.

Major challenges exist in enforcing laws that prohibit cannabis-impaired driving.[98] Roadside behavioural tests of impairment are poor at detecting cannabis-related impairment.[99] Roadside testing of saliva to detect recent cannabis use and laboratory tests of THC in blood might seem useful, but they do not reliably measure cannabis-related impairment.[26] Whether roadside cannabis testing has reduced cannabis-impaired driving in countries that have introduced this procedure remains unclear.[98] Additionally, persuading people who have used cannabis that their driving is impaired after using cannabis will be difficult.[99]

Brief psychological interventions that use motivational enhancement, cognitive-behavioural therapy, and contingency management can increase cessation in people who use cannabis who are dependent, but only a minority remain abstinent after 6–12 months.[100] Antidepressants are not effective;[101] dronabinol and nabiximols reduce withdrawal symptoms but do not necessarily increase longer-term abstinence.[102]

The future of legal recreational cannabis markets

Major alcohol and tobacco firms have invested billions of dollars in Canadian cannabis (appendix pp 73–78). Similar investments will probably occur in the USA if cannabis legalisation becomes national policy. National legalisation in the USA would also provide strong constitutional protection for the promotion of cannabis products to adults.

A major determinant of the public health effect of cannabis legalisation will be the effect that it has on alcohol use. The substitution of cannabis for alcohol would produce substantial public health gains, but any increase in the combined use of alcohol and cannabis could increase harm. The literature to date is unclear on which outcome is more probable (appendix pp 73–74). Similar uncertainties exist about the effects of cannabis legalisation on tobacco smoking. The claim that medical use of cannabis for pain relief has reduced deaths from opioid overdose is based on weak evidence (appendix pp 74–76).

An important source of uncertainty is the longer-term effect of legalisation and regulation on cannabis prices and potency. Prices have fallen steeply and potency increased in some US states, and both trends could be amplified if biotechnology companies are able to produce cheaper cannabinoids on a large scale using biosynthesis.

Legal recreational cannabis markets might not reach maturity for at least another 10 years.[6] Only then can an assessment be done to evaluate whether cannabis legalisation has increased cannabis use and harms; reduced or increased the use of alcohol, tobacco, and opioids; or resulted in other adverse social effects that

could offset the social benefits of eliminating criminal penalties to allow adults to use cannabis for pleasure.[6]

Alcohol regulation policies suggest that in the long term, commercialisation of cannabis will increase the frequency of use among people who use cannabis,[86] a trend already observed in the USA.[6,13] In the long term, the population prevalence and intensity of use will probably increase as cannabis becomes more socially acceptable, prices fall further, access increases, and new products are developed and marketed.[6] Promotion of more potent cannabis products could increase the risks of dependence and other harms.

Cannabis legalisation will make clinical trials of medicinal uses easier. It will also result in easier study of the adverse health effects of regular cannabis use (by increasing the number of people who regularly use and the duration of their use; panel 2). However, by the time information regarding costs and benefits of legislation becomes available, legalisation might be difficult to reverse because a profitable commercial cannabis industry will have been created that contributes substantial revenue to governments.

Implications of global cannabis policies

Cannabis liberalisation in the USA, Canada, and Uruguay will probably influence global policy in the long term. The USA has historically played a leading role in sustaining international cannabis prohibition; if cannabis legalisation becomes national US policy or most US states legalise cannabis, then this role will be difficult to maintain.

Medicinal cannabis programmes are expanding in Europe and Oceania and are being initiated in Asia, Africa, and South America. Medicinal cannabis producers in Canada and the Netherlands are exporting cannabis to these markets.[103] Observations from Canada and the USA suggest that liberally regulated medicinal cannabis programmes could facilitate the legalisation of recreational use.[67]

More nations are discussing cannabis legalisation—for example, Colombia, Luxembourg, Mexico, the Netherlands, New Zealand, and Switzerland. If more countries follow the examples of Canada and Uruguay the regulation of cannabis under international drug control treaties is uncertain.

Conclusions

The legalisation of commercial cannabis production for medicinal and recreational use in the Americas could transform global cannabis markets. Liberal medicinal cannabis programmes have facilitated the legalisation of supply for recreational use. Legalisation of recreational cannabis use has eliminated criminal penalties and allowed governments to raise tax revenue. It has also created a rapidly growing industry with an interest in promoting regular cannabis use and increasing the number of people who use cannabis.

***Panel 2*: Research priorities for assessing the effects of legalising non-medicinal cannabis use**

- How will use of more potent cannabis products affect cannabis use and harms?
- Will they increase acute harms—eg, psychological distress, psychotic symptoms, accidental poisonings in adults and children, and hyperemesis?
- Will they increase the risks of dependence, psychoses, and road crashes caused by impaired driving, or adversely affect school and job performance?
- How will the increased availability and promotion of cannabis, and accompanying changes in price and product variety, affect use among adolescents and adults?
- Will guidelines and social norms promote safer drug use by discouraging use by people who are at higher risk of being harmed, people who use heavily, and people who might drive while impaired?
- How effective will programmes be in preventing cannabis dependence among adolescents and adults?
- How can the treatment of cannabis dependence be improved?
- How will access to legal cannabis affect the use of alcohol, tobacco, and opioids?

Legalisation is likely to increase regular use among people who use cannabis and, in the long term, harms related to use, because it will make more potent cannabis products cheaper and more readily available. Cannabis legalisation is still at an early stage so there is considerable uncertainty regarding the extent to which cannabis use and harm might increase. It will depend, in part, on how the legal market is regulated and taxed. It will also crucially depend on whether a legal cannabis market is regulated in ways that increase or decrease harms caused by cannabis, alcohol, opioids, and other drugs. By the time we can confidently answer these questions, legalisation might have made cannabis the fourth major legal recreational drug after caffeine, alcohol, and tobacco.

Contributors

WH led the project, prepared drafts for comments by other authors, and produced the final document. DS, JL, and GC did the literature searches and reviews of the evidence summarised in the paper, wrote the appendix, and contributed to writing the manuscript. All authors contributed to, commented on, and approved the final draft.

Declaration of interests

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