Impact evaluations of drug decriminalisation and legal regulation on drug use, health and social harms: a systematic review

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ABSTRACT

Objectives To review the metrics and findings of studies evaluating effects of drug decriminalisation or legal regulation on drug availability, use or related health and social harms globally.

Design Systematic review with narrative synthesis.

Data sources We searched MEDLINE, Embase, PsycINFO, Web of Science and six additional databases for publications from 1 January 1970 through 4 October 2018.

Inclusion criteria Peer-reviewed articles or published abstracts in any language with quantitative data on drug availability, use or related health and social harms collected before and after implementation of de jure drug decriminalisation or legal regulation.

Data extraction and synthesis Two independent reviewers screened titles, abstracts and articles for inclusion. Extraction and quality appraisal (modified Downs and Black checklist) were performed by one reviewer and checked by a second, with discrepancies resolved by a third. We coded study-level outcome measures into metric groupings and categorised the estimated direction of association between the legal change and outcomes of interest.

Results We screened 4860 titles and 221 full-texts and included 114 articles. Most (n=104, 91.2%) were from the USA, evaluated cannabis reform (n=109, 95.6%) and focussed on legal regulation (n=96, 84.2%). 224 study outcome measures were categorised into 32 metrics, most commonly prevalence (39.5% of studies), frequency (14.0%) or perceived harmfulness (10.5%) of use of the decriminalised or regulated drug; or use of tobacco, alcohol or other drugs (12.3%). Across all substance use metrics, legal reform was most often not associated with changes in use.

Conclusions Studies evaluating drug decriminalisation and legal regulation are concentrated in the USA and on cannabis legalisation. Despite the range of outcomes potentially impacted by drug law reform, extant research is narrowly focussed, with a particular emphasis on the prevalence of use. Metrics in drug law reform evaluations require improved alignment with relevant health and social outcomes.

INTRODUCTION

An estimated 271 million people used an internationally scheduled (‘illicit’) drug in 2017, corresponding to 5.5% of the global population aged 15 to 64.1 Despite decades of investment, policies aimed at reducing supply and demand have demonstrated limited effectiveness.2,3 Moreover, prohibitive and punitive drug policies have had counterproductive effects by contributing to HIV and hepatitis C transmission,4,5 fatal overdose,6 mass incarceration and other human rights violations7,8 and drug market violence.9 As a result, there have been growing calls for drug law reform10-12 and in 2019, the United Nations Chief Executives Board endorsed decriminalisation of drug use and possession.13 Against this backdrop, as of 2017 approximately 23 countries had implemented de jure decriminalisation or legal regulation of one or more previously illegal drugs.14-16

A wide range of health and social outcomes are affected by psychoactive drug production, sales and use, and thus are potentially impacted by drug law reform. Nutt and...
colleagues have categorised these as physical harms (eg, drug-related morbidity and mortality to users, injury to non-users), psychological harms (eg, dependence) and social harms (eg, loss of tangibles, environmental damage). Concomitantly, a diverse and sometimes competing set of goals motivate drug policy development, including ameliorating the poor health and social marginalisation experienced by people who use drugs problematically, shifting patterns of use to less harmful products or modes of administration, curtailing illegal markets and drug-related crime and reducing the economic burden of drug-related harms.

Given ongoing interest by states in drug law reform, as well as the recent position statement by the United Nations Chief Executives Board endorsing drug decriminalisation, a comprehensive understanding of their impacts to date is required. However, the scientific literature has not been well-characterised, and thus the state of the evidence related to these heterogeneous policy targets remains largely unclear. Systematic reviews, including two meta-analyses, are narrowly focussed on adolescent cannabis use. Diriwu et al found no conclusive evidence that cannabis legalisation for medical or recreational purposes increases cannabis use by young people. In the two meta-analyses, Sarvet et al found that the implementation of medical cannabis policies in the USA did not lead to increases in the prevalence of past-month cannabis use among adolescents and Melchior et al found a small increase in use following recreational legalisation that was reported only among lower-quality studies.

Given increasing interest in quantifying the impact of drug law reform, as well as a lack of systematic assessment of outcomes beyond adolescent cannabis use to date, we conducted a systematic review of original peer-reviewed research evaluating the impacts of (a) legal regulation and (b) drug decriminalisation on drug availability, use or related health and social harms. Our primary aim is to characterise studies with respect to metrics and indicators used. The secondary aim is to summarise the findings and methodological quality of studies to date.

**METHODS**

Consistent with our aim of synthesising evidence on the impacts of decriminalisation and legal regulation across the spectrum of potential health and social effects, we conducted a systematic review using narrative synthesis without meta-analysis. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in preparing this manuscript.

The review protocol was registered in PROSPERO (CRD42017079681) and can be found online at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=79681.

**Search strategy and selection criteria**

The review team developed, piloted and refined the search strategy in consultation with a research librarian and content experts. We searched MEDLINE, Embase, PsycINFO, Web of Science, Criminal Justice Abstracts, Applied Social Sciences Index & Abstracts, International Bibliography of the Social Sciences, PAIS Index, Policy File Index and Sociological Abstracts for publications from 1 January 1970 through 4 October 2018. We used MeSH (Medical Subject Headings) terms and keywords related to (a) scheduled psychoactive drugs, (b) legal regulation or decriminalisation policies and (c) quantitative study designs. Search terms specific to health and social outcomes were not employed so that the search would capture the broad range of outcomes of interest. See online supplemental appendix A for the final MEDLINE search strategy. For conference abstracts, we contacted authors for additional information on study methods and to identify subsequent relevant publications.

We included peer-reviewed journal articles or conference abstracts reporting on original quantitative studies that collected data both before and after the implementation of drug decriminalisation or legal regulation. We did not consider as original research studies that reproduced secondary data without conducting original statistical analyses of the data. We defined decriminalisation as the removal of criminal penalties for drug use and/or possession (allowing for civil or administrative sanctions) and legal regulation as the development of a legal regulatory framework for the use, production and sale of formerly illegal psychoactive drugs. Studies were excluded if they evaluated de facto (eg, changes in enforcement practices) rather than de jure decriminalisation or legal regulation (changes to the law). This exclusion applied to studies analysing changes in outcomes following the US Justice Department 2009 memo de-prioritising prosecution of cannabis-related offences legal under state medical cannabis laws. Eligible studies included outcome measures pertaining to drug availability, use or related health and social harms. We used the schema developed by Nutt and colleagues to conceptualise health and social harms, including those to users (physical, psychological and social) and to others (injury or social harm).

Both observational studies and randomised controlled trials were eligible in principle, but no trials were identified. There were no geographical or language restrictions; titles, abstracts and full-texts were translated on an as-needed basis for screening and data extraction. We excluded cross-sectional studies (unless they were repeated) and studies lacking pre-implementation and post-implementation data collection because such designs are inappropriate for evaluating intervention effects.

**Data analysis**

Screening and data extraction were conducted in DistillerSR (Evidence Partners, Ottawa, Ontario). We began with title-only screening to identify potentially relevant titles. Two reviewers screened each title. Unless both reviewers independently decided a title should be excluded, it was advanced to the next stage. Next, two reviewers independently screened each potentially eligible abstract. 

Inter-rater reliability was good (weighted Kappa at the question level=0.75). At this stage, we retrieved full-text copies of all remaining references, which were screened independently by two reviewers. Disagreements on inclusion were resolved through discussion with the first author. Finally, one reviewer extracted data from each included publication using a standardised, pre-piloted form and performed quality appraisal. A second reviewer double-checked data extraction and quality appraisal for every publication, and the first author resolved any discrepancies.

The data extraction form included information on study characteristics (author, title, year, geographical location), type of legal change studied and drug(s) impacted, details and timing of the legal change (eg, medical vs recreational cannabis regulation), study design, sampling approach, sample characteristics (size, age range, proportion female) and quantitative estimates of association. We coded each study-level outcome measure into one metric grouping, using 24 pre-specified categories and a free-text field (see figure 1 for full list). Examples of metrics include: prevalence of use of the decriminalised or regulated drug, overdose or poisoning and non-drug crime.

We also categorised the estimated direction of association of the legal change on outcome measure(s) of interest (beneficial, harmful, mixed or null). These associations were coded at the outcome (not study) level and classified as beneficial if a statistically significant increase in a positive outcome (eg, educational attainment) or decrease in a negative outcome (eg, substance use disorder) was attributed to implementation of decriminalisation or legal regulation, and vice versa for harmful associations. The association was categorised as mixed if associations were both harmful and beneficial across participant subgroups, exposure definitions (eg, loosely vs tightly regulated medical cannabis access) or timeframes. Although any use of cannabis and other psychoactive drugs need not be problematic at the individual level, we categorised drug use as a negative outcome given that population-level increases in use may correspond to increases in negative consequences; we thought that this cautious approach to categorisation was appropriate given that such increases are generally conceptualised as negative within the scientific literature. For outcomes that are not unambiguously negative or positive, the coding approach was predetermined taking a societal perspective. For example, increased healthcare utilisation (eg, hospital visits due to cannabis use) was coded as negative because of the increased burden placed on healthcare systems. The association was categorised as null if no statistically significant changes following implementation of drug decriminalisation or legal regulation were detected. We set statistical significance at \(a=0.05\), including in cases where authors used more liberal criteria.

Quality assessment at the study level was conducted for each full-length article using a modified version of the Downs and Black checklist for observational studies (online supplemental appendix B), which assesses internal validity (bias), external validity and reporting. Each study could receive up to 18 points, with higher scores indicating more methodologically rigorous studies. Conference abstracts were not subjected to quality assessment due to limited methodological details.
RESULTS
Study characteristics
As shown in the PRISMA flow diagram (figure 2), we screened 4860 titles and abstracts and 213 full-texts, with 114 articles meeting inclusion criteria (online supplemental appendix C). Key reasons for exclusion at the full-text screening stage were that the article did not report on original quantitative research (n=59) or did not evaluate decriminalisation or legal regulation as defined herein (n=23). Details of each included study are presented in online supplemental table 1. Included studies had final publication dates from 1976 to 2019; 44.7% (n=51) were first published in 2017 to 2018, 43.9% (n=50) were published in 2014 to 2016 and 11.4% (n=13) were published before 2014.

Characteristics of included studies are described in table 1, both overall and stratified by whether they evaluated decriminalisation (n=19) or legalisation (n=96) policies (one study evaluated both policies). Most studies (n=104, 91.2%) were from the USA and examined impacts of liberalising cannabis laws (n=109, 95.6%). Countries represented in non-US studies included Australia, Belgium, China, Czech Republic, Mexico and Portugal. The most common study designs were repeated cross-sectional (n=74, 64.9%) or controlled before-and-after (n=26, 22.8%) studies and the majority of studies (n=87, 76.3%) used population-based sampling methods. Figure 3 illustrates the geographical distribution of studies among countries where national or subnational governments had decriminalised or legally regulated one or more drugs by 2017.

Study quality
Quality assessment was performed for the 93 full-length articles included in the review, excluding 21 conference abstracts (online supplemental table 1). Scores ranged from 7 to 18 of 18 possible points, with a mean of 14.4 (SD=2.56). Quality scores were similar comparing US to non-US-based studies (X=14.4 and 13.7, respectively, p=0.386) but higher for studies evaluating legal regulation (X=14.8) versus decriminalisation (X=12.8) (p=0.003). Study quality differed significantly (p<0.001) by the direction of the association with the outcome of interest, with higher quality scores among studies estimating mixed (X=15.4) or beneficial (X=15.2) versus null (X=14.2) or harmful (X=13.1) effects of legal change on the outcome of interest. Study quality did not appear to increase over time (eg, X=14.0 in 2014 and 14.4 in 2018).
Study outcome measures and metrics

Across 114 studies we extracted 224 outcome measures, which were coded into 32 metrics (figure 1). The most common metric employed by studies was the prevalence of use of the decriminalised or legally regulated drug, which was examined in 39.5% of studies (n=45) and represented 22.3% of outcome measures (n=50). Of these studies, 13 (28.9%; 8 full-length articles and 5 abstracts) did not report any other metric26–38 and an additional 6 studies (13.3%) reported on the prevalence of use in addition to a single drug-related perception metric (either harmfulness or availability).39–44 The second most common metric was the frequency of use of the decriminalised or legally regulated drug (14.0% of studies, n=16) and the third was the prevalence or frequency of use of tobacco, alcohol or drugs that remained illegal (12.3% of studies, n=14). The fourth most commonly employed metric was any change in the perceived health harmfulness of using the decriminalised or regulated drug (10.5% of studies, n=12), which was assessed among adolescents or young adults in all studies except for one that assessed this metric among parents.45

All other metrics were assessed in <10% of included studies. Health service utilisation was evaluated in 7.9% of studies (n=9) using 12 outcome measures, primarily related to emergency department visits and/or hospitalisations. Prescribed (primarily opioid) drug use and perceived availability of the decriminalised or legally regulated drug were reported in 7.0% of studies each (n=8). Overdose or poisoning by the decriminalised or regulated drug, and by other drugs (predominantly opioids), were examined in 5.3% (n=6) and 6.1% of studies (n=7), respectively. Driving while under the influence or with detectable concentrations of the decriminalised or regulated drug (cannabis) was examined in seven studies (6.1%) inclusive of eight outcome measures.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (%) N (%) (n=114)</th>
<th>Decriminalisation* N (%) (n=19)</th>
<th>Legal regulation* N (%) (n=96)</th>
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<tbody>
<tr>
<td>Country</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>104 (91.2)</td>
<td>10 (52.6)</td>
<td>95 (99.0)</td>
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<tr>
<td>Australia</td>
<td>3 (2.6)</td>
<td>3 (15.8)</td>
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<td>2 (10.5)</td>
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<td>China</td>
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<td>0 (0.0)</td>
<td>1 (1.0)</td>
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<tr>
<td>Czech Republic</td>
<td>1 (0.9)</td>
<td>1 (5.3)</td>
<td>0 (0.0)</td>
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<tr>
<td>Mexico</td>
<td>1 (0.9)</td>
<td>1 (5.3)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Multi-country†</td>
<td>2 (1.8)</td>
<td>2 (10.5)</td>
<td>0 (0.0)</td>
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<td>Focus of drug law reform</td>
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<tr>
<td>Cannabis</td>
<td>109 (95.6)</td>
<td>15 (78.9)</td>
<td>95 (99.0)</td>
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<td>Opium</td>
<td>1 (0.9)</td>
<td>0 (0.0)</td>
<td>1 (1.0)</td>
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<td>1 (0.9)</td>
<td>1 (5.3)</td>
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<td>Multiple/all drugs</td>
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<td>3 (15.8)</td>
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<td>Cohort</td>
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<tr>
<td>Controlled before-and-after</td>
<td>26 (22.8)</td>
<td>6 (31.6)</td>
<td>20 (20.8)</td>
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<td>Interrupted time series</td>
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<td>6 (6.3)</td>
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<tr>
<td>Repeated cross-sectional</td>
<td>74 (64.9)</td>
<td>11 (57.9)</td>
<td>64 (66.7)</td>
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<tr>
<td>Uncontrolled before-and-after</td>
<td>4 (3.5)</td>
<td>2 (10.5)</td>
<td>2 (2.1)</td>
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<td>Sampling approach</td>
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<td></td>
<td></td>
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<tr>
<td>Convenience</td>
<td>22 (19.3)</td>
<td>5 (26.3)</td>
<td>18 (18.8)</td>
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<td>Population-based</td>
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<td>13 (68.4)</td>
<td>74 (77.1)</td>
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<td>Administrative records</td>
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<td>6 (31.6)</td>
<td>39 (40.6)</td>
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<td>Household survey</td>
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<td>5 (26.3)</td>
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<tr>
<td>Unspecified</td>
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<td>1 (5.3)</td>
<td>4 (4.2)</td>
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</table>

*Combined total exceeds number of studies because some evaluated both decriminalisation and legal regulation.
†One global study and one multi-country European study including Belgium and Portugal.
Notably, one study assessed self-reported impaired driving, while others assessed the proportion of fatally injured drivers screening cannabis-positive or the overall prevalence of driving with detectable tetrahydrocannabinol (THC) concentrations in blood. Remaining metrics were measured in less than 5% of studies (Figure 1). Some pre-specified metrics were not represented in any of the articles, including infectious disease incidence (e.g., HIV, hepatitis C), environmental impacts (e.g., drug production waste, discarded needles) and labour market participation.

Studies outside the US

Of the 10 studies conducted outside the USA, 6 focussed on cannabis decriminalisation. All three studies from Australia examined the prevalence of cannabis use post-decriminalisation, while one also measured perceived cannabis availability. Following cannabis decriminalisation, one European multi-country study including Belgium and Portugal examined the prevalence of cannabis use and uptake of cannabis-related addictions treatment and one Czech study considered the age of first cannabis use. An international study using United Nations Office on Drugs and Crime data from 102 countries compared availability, as reflected by cannabis seizures and plant eradication, in countries that had decriminalised cannabis use and uptake of cannabis-related addictions treatment and one Czech study considered the age of first cannabis use. An international study using United Nations Office on Drugs and Crime data from 102 countries compared availability, as reflected by cannabis seizures and plant eradication, in countries that had decriminalised cannabis use and uptake of cannabis-related addictions treatment and one Czech study considered the age of first cannabis use.

Impacts of decriminalisation and legal regulation

Results of individual studies are provided in online supplemental table 1. Online supplemental table 2 tallies findings and average quality scores for each of the metrics; here we summarise findings for metrics examined in more than 5% of studies, in descending order based on the number of datapoints. Across all three substance use metrics (prevalence of use, frequency of use and use of other alcohol or drugs), drug law reform was most often not associated with use (with null findings for 48.0% to 52.4% of outcome measures falling under these metrics). With respect to change in perceived harmfulness of the decriminalised or regulated drug, mixed results were found in half of cases, with heterogeneity detected on the basis of age, gender and state. For example, legal regulation of cannabis for medical use was associated with greater perceived harmfulness of cannabis among eighth graders but not older students in an analysis of US Monitoring the Future data while a study employing US National Survey on Drug Use and Health data found greater perceived harmfulness of cannabis among young adults aged 18 to 25 but not adolescents aged 12 to 17. Among nine studies that employed health service utilisation metrics, harmful effects were reported for 6 of 12 outcome measures, with increases in emergency department visits and/or hospitalisations attributed to decriminalisation or legal regulation. However, all but one of those studies assessed change over time in one jurisdiction, without a control group. Further, two studies that also examined changes in acute care use for non-cannabis drugs found reductions in those visits or admissions following cannabis decriminalisation or legal regulation. In contrast, six of nine prescription drug use associations were beneficial, with reductions observed in rates of opioid and other drug prescribing attributed to legal regulation of cannabis for medical use.

Figure 3

Number of included studies from countries that implemented decriminalisation or legal regulation by 2017. Note: Policy changes were classified, following the review inclusion criteria, based on the implementation of a change to national or subnational law to decriminalise drug use and/or possession or to legalise at least one class of drugs. We did not evaluate the extent to which legal changes were reflected in policing and criminal justice practice. Implementation of cannabis legalisation for medical purposes only is not reflected in this map.
use; outcomes in this category came from studies of higher average quality (X=16.3). Perceived availability of the decriminalised or regulated drug appeared largely unaffected by decriminalisation (null associations for five of nine outcome measures) but two studies indicated increased perceived availability of cannabis among Colorado, US, adolescents following legal regulation for adult use, and among adults in US states with legal regulation for medical use. Across the subset of seven outcome measures for overdose or poisoning by the decriminalised or regulated drug (cannabis), in all cases an increase in calls to poison control centres or unintentional paediatric exposures was reported. However, studies assessing the impacts of cannabis regulation on overdose or poisoning by drugs other than cannabis concluded that the effects were either beneficial (four outcome measures) or mixed/null (three outcome measures). Driving with detectable concentrations of THC was most often found to increase following decriminalisation or legal regulation (five of eight outcome measures), but these studies were of lower average quality (X=12.0).

**Impacts of decriminalisation**

Of the 19 studies evaluating impacts of decriminalisation, six measured the prevalence of use of the decriminalised drug with eight unique outcome measures. No association was detected for all but three outcomes; following cannabis decriminalisation lifetime use increased among adults in South Australia, while past-month use increased among 12th graders but not younger students in California, relative to the rest of the country in both cases. After peyote use for ceremonial purposes was decriminalised in the USA in 1994, self-reported use increased among American Indians. Three studies evaluated relationships between decriminalisation and drug-related criminal justice involvement in Mexico and the USA. One high-quality study found that decriminalisation positively influenced criminal justice involvement: in five US states, arrests for cannabis possession decreased among youth and adults. When possession of small amounts of cannabis was decriminalised in the 1970s in Nebraska, however, the mean monthly number of arrests did not change, while cannabis-related prosecutions increased among youth. In Tijuana, Mexico, decriminalisation of all drugs had no apparent impact on the number of drug possession arrests. Two historical and one recent study measured healthcare utilisation. US states that decriminalised cannabis in the 1970s saw greater emergency department visits related to cannabis, but decreased visits related to other drugs. In Colorado, US, decriminalisation was associated with increased emergency department visits for cyclic vomiting. Addiction treatment utilisation, healthcare and non-healthcare costs, driving after use, price of drugs, availability of drugs, frequency of use, attitudes towards use and perceived harmfulness were each evaluated in only one or two studies of decriminalisation.

**DISCUSSION**

This systematic review identified 114 peer-reviewed publications and conference abstracts evaluating the impacts of drug decriminalisation or legal regulation from 1970 to 2018. Within this search period, 88.6% were published in 2014 or later. This rapid growth in scholarship was driven by the implementation and subsequent evaluation of cannabis legalisation in a number of US states beginning in 2012, and knowledge production will surely continue to accelerate as longer-term data become available and as other jurisdictions (eg, Canada and Uruguay) analyse the effects of recently implemented cannabis legalisation. Indeed, a first study on the impacts of cannabis legalisation on adolescent use in Uruguay was published in May 2020 (finding no impact on risk of use). The present study provides an overview of the emerging literature based on our systematic review and suggests three key patterns.

First, peer-reviewed longitudinal evaluations of drug decriminalisation and legal regulation are overwhelmingly geographically concentrated in the US and focussed on cannabis legalisation. Importantly, the lack of non-US studies evaluating legal regulation of cannabis for medical use may reflect the more tightly controlled nature of medical cannabis regulation in other countries, and thus the more limited potential for population-level effects. It is notable that decriminalisation in the absence of legal regulation was evaluated in only 18 studies (15.8%), despite being far more common globally than legal regulation. These gaps may hamper evidence-based drug law reform in countries that are less well-developed, that play a substantial role in drug production and transit or that have different baseline levels of substance (mis)use as compared with the US.

Second, prevalence of use was the predominant metric used to assess the impact of drug law reform, despite its limited clinical significance (eg, much cannabis use is non-problematic) and limited responsiveness to drug policy. This is because ecological analyses have indicated little relationship between drug policies and prevalence of use, as have studies assessing within-state change in use related to legal regulation. These findings are supported by the preponderance of evidence synthesised in this review, although some variation is evident in relation to the specific provisions of legal reforms (eg, liberal vs tightly regulated medical markets). Impacts of legal cannabis regulation on prevalence and frequency of use continue to be evaluated, with recent data suggesting small increases among adults, but not youth. Drug policies may be more able to influence the types of drugs that people use, drug-related risk behaviours and modes of drug consumption. Metrics to assess these outcomes, however, were lacking in the reviewed literature. For example, only one study (0.8%) investigated whether legal regulation of cannabis was associated with changes in the mode of cannabis consumption. Although the prevalence of use was often measured alongside more clinically or socially significant metrics (eg, prevalence...
of substance use disorders, educational outcomes among young adults), 42.2% of studies assessing substance use prevalence included that metric alone or in combination with a single drug-related attitude metric.

Third, there was a lack of alignment between the stated policy objectives of drug law reform and the metrics used to assess its impact in the scientific literature. For instance, removal of criminal sanctions to prevent their negative sequelae is a key rationale for decriminalisation and legal regulation, but only four studies (3.5%) evaluated changes in drug-related criminal justice involvement following drug law reform. Similarly, improving the physical and mental health of people who (already) use drugs is a motivation for drug policy reform but no included studies examined mental or physical health outcomes (aside from substance use disorders) in this population. As a result, there is a risk that decisions on drug policy may be informed by inappropriate metrics. Promisingly, in recent months, additional studies assessing legal regulation that employ a range of criminal justice metrics have been published. Finally, despite ample evidence of the impact of criminalisation on infectious disease transmission and acquisition risks, we found no studies evaluating the impact of decriminalisation on these outcomes.

Both the included studies and our systematic review have important strengths and limitations. To our knowledge, we conducted the first review of all global literature on decriminalisation and legal regulation and applied no language restrictions. All eligible articles identified were published in English; this may reflect a paucity of evaluation research published in other languages and/or limitations of our search strategy (eg, some non-English journals may not be indexed in the 10 databases searched). In addition, we excluded grey literature, non-original research and study designs that are not suited to evaluating policy effects (eg, cross-sectional studies), but these restrictions narrowed the geographical scope of included studies. For example, two articles on Portugal were excluded as non-original research, but nevertheless provide important insight on impacts of decriminalisation. Despite restricting eligibility to more rigorous study designs, most included studies used relatively weaker eligible designs that are known to be vulnerable to pre-existing trends and confounding; only 22.8% and 5.3%, respectively, used controlled before-and-after or interrupted time series designs to address these threats to validity. The use of these study designs may be related to limited resources for prospective drug policy evaluations, with many studies relying on publicly available, routinely collected data. That the US is unique in the extent to which data on drug use and related harms are routinely collected helps to explain its over-representation in our review. Scoping reviews inclusive of grey literature and cross-sectional designs would be valuable for describing the full range of evaluations that have been conducted globally.

While beyond the scope of our high-level synthesis, the implementation and specific provisions of drug policies vary widely. Decriminalisation policies vary in their definitions of quantities for personal use, application of administrative penalties and the extent to which the law ‘on the books’ is reflected in policing and criminal justice practice. Indeed, in some jurisdictions with nominal decriminalisation, arrests for possession of small quantities of the decriminalised drugs remain routine. Legal regulation models for cannabis are also heterogeneous. For example, policies legally regulating cannabis for medical use may or may not allow for legal dispensaries, and this provision has been shown to substantially modify the impact of legal regulation on cannabis use. To the extent that individual studies employed crude exposure measures (eg, presence vs absence of a law), they may have obscured context-dependent effects of drug law liberalisation. Further, the impact of drug laws on drug use and related outcomes may be limited by a lack of public awareness of the details of local laws.

Our use of vote-counting in this synthesis (ie, categorising individual outcome measures as indicating beneficial, harmful, mixed/subgroup-specific or no statistically significant associations) is subject to the same limitation. Vote-counting should also be interpreted with caution in light of the heterogeneity of outcome definitions, the inherent arbitrariness of statistical significance thresholds and the key distinction between statistical and clinical significance. In addition, many included studies are evaluating the same policies (eg, cannabis legalisation in western US states), sometimes using overlapping data but drawing different conclusions based on analytical choices and timeframes. The existence of multiple datapoints for a particular outcome does not imply that the outcome has been well-studied across diverse contexts such that scientific consensus on its effects has been reached. Moreover, as illustrated by a recently published extension of the included article by Bachhuber et al, multiple high-quality studies may generate results that are later revealed to be spurious as additional follow-up data become availability. Specifically, Shover et al demonstrated that the positive association reported between medical cannabis legalisation and opioid overdose mortality in 1999 to 2010 was reversed direction in later years, suggesting that earlier findings of a protective effect should not be given causal interpretations. This was foreshadowed in the included article by Powell et al, which found that the purportedly positive effect of medical cannabis legalisation was attenuated in 2010 to 2013. This scientific back-and-forth can be expected given that most included articles are evaluating legal changes introduced rather recently, and thus are examining early impacts with limited years of follow-up. Longer-term impacts of non-medical cannabis legalisation, and how they might be influenced by increased commercialisation, are yet to be seen.

Conclusions

The findings of this review indicate a need for a broadening of the metrics used to assess the impacts of drug decriminalisation and legal regulation. Given the
growing number of jurisdictions considering decriminalisation or legal regulation of psychoactive drugs,\textsuperscript{14-16} the disproportionate emphasis on metrics assessing drug use prevalence, as well as the limited geo-cultural diversity in evaluations, are concerning. Experts have called for a more fulsome approach to evaluating drug policies in line with public health and the United Nations Sustainable Development Goals, with attention to the full breadth of health and social domains potentially impacted, including human rights and social inclusion (eg, stigma), peace and security (eg, drug market violence), development (eg, labour market participation), drug market regulation (eg, safety of the drug supply) and clinically-significant health metrics (eg, drug-related morbidity).\textsuperscript{105}

Drawing on methods such as multi-criterion decision analysis,\textsuperscript{19} the engagement of both scientists and policymakers in priority-setting may help to produce evidence that provides a more comprehensive understanding of the breadth of impacts that should be anticipated with drug law reform efforts. Funding will also be required to support rigorous prospective evaluations of legal reforms.

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DW and AIS conceptualised and supervised the review. CZ designed and conducted the literature searches. AIS drafted the manuscript. SC, ZM and AIS conducted screening and data extraction. NM contributed to drafting the manuscript and developing figures. All authors contributed to interpretation of findings and revising the manuscript for important intellectual content.

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\textbf{Map disclaimer}

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