Addiction 1

Extent of illicit drug use and dependence, and their contribution to the global burden of disease

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This paper summarises data for the prevalence, correlates, and probable adverse health consequences of problem use of amphetamines, cannabis, cocaine, and opioids. We discuss findings from systematic reviews of the prevalence of illicit drug use and dependence, remission from dependence, and mortality in illicit drug users, and evidence for acute and chronic effects of illicit drug use. We outline the regional and global distribution of use and estimated health burden from illicit drugs. These distributions are likely to be underestimates because they have not included all adverse outcomes of drug use and exclude those of cannabis—the mostly widely used illicit drug. In high-income countries, illicit drug use contributes less to the burden of disease than does tobacco but a substantial proportion of that due to alcohol. The major adverse health effects of cannabis use are dependence and probably psychotic disorders and other mental disorders. The health-related harms of cannabis use differ from those of amphetamine, cocaine, and opioid use, in that cannabis contributes little to mortality. Intelligent policy responses to drug problems need better data for the prevalence of different types of illicit drug use and the harms that their use causes globally. This need is especially urgent in high-income countries with substantial rates of illicit drug use and in low-income and middle-income countries close to illicit drug production areas.

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This is the first in a **Series** of three papers about addiction

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Introduction

Illicit drugs are drugs for which non-medical use has been prohibited by international drug control treaties for half a century because they are believed to present unacceptable risks of addiction to users.[1,2] International control has since been extended from plant-based drugs—heroin, cocaine, and cannabis—to synthetic drugs, such as amphetamines and methylenedioxymetamfetamine (MDMA), and pharmaceutical drugs such as buprenorphine, methadone, and benzodiazepines (panel 1).

In this paper, we summarise data for the prevalence, correlates, and probable consequences of use of the amphetamines, cannabis, cocaine, and opioids—the most commonly used and studied illicit drugs. We discuss findings from systematic reviews of data for the prevalence of illicit drug use and dependence,[3–8] remission from dependence,[9] and mortality in illicit drug users (panel 2).[10–13] We attribute adverse health effects to these drugs using findings from reviews of published studies of the evidence on a range of acute and chronic harms of illicit drug use.[8,14,19,35–41] We provide a brief summary of adverse health effects for different drug types referencing other reviews (webappendix pp 3–5 for more details). We also summarise earlier global burden of disease studies that estimated the regional and global distribution of health burden from illicit drug use and compared this with the burden attributable to alcohol and tobacco use.[29–33]

We do not discuss the prevalence of or disease burden related to MDMA (ecstasy), hallucinogenic drugs, inhalants, or the non-medical use of benzodiazepines and anabolic steroids because information about the prevalence of their use and quantification of their harms is more scarce than it is for the drugs included in this paper (webappendix p 1).[42–46] Their exclusion is because of the scarcity of evidence rather than any judgment about the contribution of these drugs to disease burden. We were also unable to separately discuss the magnitude of adverse outcomes attributable to prescribed pharmaceutical opioids. Although increased prescription of these

Key messages

- The illegality of opioids, amphetamines, cocaine, and cannabis precludes the accurate estimation of how many people use these drugs, how many people are problem users, and what harms their use causes.
- An estimated 149–271 million people used an illicit drug worldwide in 2009: 125–203 million cannabis users; 15–39 million problem users of opioids, amphetamines, or cocaine; and 11–21 million who injected drugs.
- Levels of illicit drug use seem to be highest in high-income countries and in countries near major drug production areas, but data for their use in low-income countries are poor.
- Cannabis use is associated with dependence and mental disorders, including psychoses, but does not seem to substantially increase mortality.
- Illicit opioid use is a major cause of mortality from fatal overdose and dependence; HIV, hepatitis C, and hepatitis B infections from unsafe injection practices are important consequences in people who inject opioids, cocaine, or amphetamines.
- Adverse health outcomes such as mental disorders, road-traffic accidents, suicides, and violence seem to be increased in opioid, cocaine, and amphetamine users. To what extent these associations are causal is unclear, because confounding variables are not always controlled and quantification of risk is poor.
- Global burden of disease estimates suggest that in high-income countries, the contribution of illicit drug use is a substantial proportion of that attributable to alcohol.
- These estimates probably underestimate the true burden because only a few effects of problem use of opioids, cocaine, and amphetamines are included. The global burden of disease 2010 study will address these limitations.

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See Online for webappendix

Panel 1: Major types of illicit drugs

- **Amphetamine-type stimulants** are a class of synthetic, sympathetomimetic amines with powerful stimulant effects on the CNS.
- **Cannabis** is a generic term for preparations (eg, marijuana, hashish, and hash oil) derived from the *Cannabis sativa* plant that produce euphoria and relaxation, heighten the senses, and increase sociability.
- **Cocaine** is an alkaloid that is a powerful CNS stimulant derived from the coca plant (*Erythroxylum coca*).
- **Opioids** include derivatives from the opium poppy (*Papaver somniferum*), such as heroin and morphine, and their synthetic analogues (eg, methadone, fentanyl). Opioids relieve pain, produce euphoria, and can cause coma and respiratory depression in high doses.

Panel 2: Search strategy and selection criteria

We discuss the findings from reviews of published studies of prevalence, natural history, and mortality related to illicit drug use.[3–14] We did searches of peer-reviewed studies (from 1990 to 2008) with methods recommended by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group,[15] systematic searches of online databases,[16,17] internet searches for other evidence of drug use, and consultation with experts in HIV and illicit drug use around the world. Data extraction followed written protocols in line with STROBE guidelines[18] (with cross-checking and tests of internal consistency) and data graded according to predefined variables.

We also draw on systematic reviews of illicit drug use as a cause of adverse health outcomes,[19–23] cross-national studies of illicit drug use and dependence,[24,25] reviews of illicit drug markets,[26–28] and estimates of the contribution of illicit drugs to the global burden of disease.[29–34]

drugs has been accompanied by increases in morbidity and mortality in some countries,[47] data for the magnitude of risks of iatrogenic dependence and mortality in users are not available.[47,48] In countries where use of these drugs has been studied, a substantial proportion of problem users had pre-existing problems with opioids. In these countries, estimates of opioid-dependent people include both heroin and pharmaceutical opioid users.[47]

The prevalence of drug use and dependence

Major challenges exist in the accurate estimation of the prevalence of an illegal, and often stigmatised, behaviour like illicit drug use. This is especially so in cultural settings where illicit drug use can lead to imprisonment, and where research participants cannot be assured of confidentiality or freedom from reprisals for disclosing their drug use behaviours. By necessity, a range of imperfect methods have to be used to estimate the prevalence of use in such areas (panel 3).

The availability and quality of data for estimation varies globally. Evidence[3–7] shows that the four drug classes (opioids, amphetamines, cocaine, and cannabis) are used in most countries, but quantitative estimates of such use are more scarce. This is especially so for estimates of drug dependence.[3–7] The best data come from developed countries in Europe, North America, and Australasia. Consequently, much uncertainty exists in the determination of the global number of people who use illicit drugs.

The 2011 world drug report by the UN Office on Drugs and Crime (UNODC)[28] shows this uncertainty by providing a range of prevalence estimates for countries and regions. UNODC estimated that 149–271 million people aged 15–64 years (3·3–6·1%) had used an illicit drug at least once in 2009. The drugs used varied substantially across regions (table 1), and these numbers are not mutually exclusive, because some people used more than one drug type. The greater uncertainty surrounding estimates for cannabis and amphetamines than for cocaine and opioid use is attributable to the scarcity of credible estimates of their prevalence of use in many countries, and the varying prevalence seen within countries that have made estimates.[3]

The global number of cannabis users was estimated at 125–203 million people (2·8–4·5% of the global population aged 15–64 years in 2009).[28] The highest levels of recorded use were in the established market economies of North America, western Europe, and Oceania. Between 14 million and 56 million people aged 15–64 years were estimated to have used an amphetamine-type stimulant (0·3–1·3%). The highest levels of use were near amphetamine-manufacturing countries in southeast Asia. For cocaine, the number of users worldwide ranged from 14 million to 21 million (0·3–0·5% of the population aged 15–64 years). The largest market was North America, then western and central Europe and South America. The global number of opioid users was estimated at 12–21 million people.[28] More than half these users lived in Asia, and the highest levels of use were along the main drug trafficking routes out of Afghanistan.

The health risks of illicit drug use increase with the frequency and quantity of use. People who use these drugs only once or twice have, at most, a very small increase in mortality, which is difficult to detect in epidemiological studies. Problematic drug use, however, most clearly harms the health of users. It is defined by the International Classification of Diseases (10th revision) as "harmful use" and "dependence".[54] A classification of harmful drug use needs evidence that substance use is causing physical (eg, organ damage) or psychological harm (eg, drug-induced psychosis). A classification of drug dependence needs the presence of three or more indicators of dependence for at least a month within the previous year.[54] A similar classification is used by the American Psychiatric Association.[55] Such indicators of dependence include the following: a strong desire to take the substance; an impaired control over use; a withdrawal

syndrome on cessation or reduction of use; tolerance to the effects of the drug; the need for larger doses to achieve the desired psychological effect; a disproportionate amount of time spent by the user obtaining, using, and recovering from drug use; and continuing to take the drug despite the problems that occur. Dependence can occur with all four drug types discussed in this paper.

Findings from a systematic review of data for the prevalence of injecting drug use suggested that, worldwide, 11–21 million people injected drugs in 2007 (figure; table 2).[8] Injecting drug use has been documented in 151 countries;[56] its prevalence has been estimated in 61.[8] Prevalence varies substantially across regions, and between and within countries. National estimates varied from 0·02% of people aged 15–64 years in India and Cambodia, to typically 1–2% in Azerbaijan, Georgia, Mauritius, Russia, Estonia, Malaysia, Canada, Ukraine, Puerto Rico, and Australia. Russia, China, and the USA accounted for more than 40% of the estimated population of injecting drug users (IDUs) worldwide (table 2).[8]

Global and regional estimates have been made of the number of problematic drug users. In 2009, UNODC estimated that there were 15–39 million problem drug users globally (ie, IDUs, or problem users of opioids, cocaine, or amphetamines).[28]

No global estimates of the prevalence of specific forms of drug dependence exist. Drug dependence (combined for all illicit drugs and illicit pharmaceutical use) was assessed in WHO's World Mental Health household surveys in 27 countries in five WHO regions.[57] These surveys recorded substantial geographical variation in rates of illicit drug use[24] and dependence.[57] Generally, rates of drug dependence were higher in more developed countries.[57] The variation is probably attributable to a combination of differences in prevalence and to cultural differences in preparedness to report illicit drug use and related problems. In the past 20 years, nine countries have estimated the prevalence of amphetamine dependence; seven of cannabis; five of cocaine; and 25 of heroin and other opioids (table 3).[3] The scarcity of estimates of specific forms of drug dependence severely limits the ability to make evidence-based statements about the global scale of illicit drug problems.

The estimation of global trends in illicit drug use over time is even more difficult. Drug use is routinely assessed in few high-income countries; assessment of trends in other countries often relies on indirect indicators of drug supply, drug use, and problems related to drug use.[27]

Some indicators suggest that global illicit drug consumption (and its related burden) has increased since 1990. Injecting drug use, for example, is now reported in more countries,[8,58] and HIV in IDUs is more prevalent in eastern Europe, and Asia.[8] The global manufacture of amphetamines has increased, as has the number of problem metamfetamine users in southeast Asia and the Middle East.[59] Opium production and heroin trafficking routes have changed. African countries are now used for transhipment of illicit drugs to European markets and illicit drug use has reportedly increased in these countries. In the established market economies of western Europe, USA, and Australia, cannabis use has stabilised or decreased, whereas the use of MDMA and metamfetamine has increased.[26,59]

Analysts differ in their interpretation of global trends. A UNODC report concluded that illicit drug use had

Panel 3: How do we estimate the number of people who use illicit drugs?

No gold-standard method exists for the estimation of the true size of the population of illicit drug users.[50] No method is ideal for all drugs or all countries. This absence of consistency in measurement and potential biases poses major challenges for cross-national comparisons.[26,51] The best strategy is to look for convergence of results from different indirect methods of estimation.[50] Information adapted from reference 27.

Direct methods

General population or household surveys

In these surveys, participants are asked if they have used various drugs in the past month, the past year, or in their lifetime (monthly, past year, and lifetime prevalence).

The main strength of this approach is that it accurately estimates prevalence if representative population samples are obtained, if people honestly disclose their drug use, and if drug users are equally distributed around the country. The major limitations are that drug users are probably less likely to be available or to agree to an interview if contacted; they might be reluctant to admit drug use (especially if they fear adverse consequences from doing so); illicit drug use is often concentrated in large cities (information that national surveys might not be able to capture); and marginalised groups with high rates of drug use are often missed (eg, homeless people and prisoners). The expense of these surveys limits their use in developing countries. Surveys underestimate the prevalence of the most harmful and stigmatised forms of illicit drug use, such as opioid and injecting drug use,[26] in ways that probably vary between countries and cultures.

School surveys

In these surveys, school-attending children or young people (typically in secondary schools) are asked whether they have used various licit and illicit drugs ever or in the past year, and, if so, how often.

The strength and limitations of this approach are shared with general population surveys. An additional limitation is that they exclude young people who have left school, who are most likely to have used illicit drugs. This population might be a large proportion of young people in some countries.

Indirect methods

These methods use different sources of data to indirectly estimate the total number of drug users.[52] A simple approach is the multiplier method, in which, for example, the number of people who receive drug treatment in a year (an indicator) is multiplied by an estimate of the proportion of drug users who receive treatment in a year (the multiplier) to estimate the total size of the drug-using population. Other indirect methods include capture-recapture and back-projection estimates.[52]

These methods are less expensive than surveys because they use existing data. Their major limitations are uncertainty about the quality of indicator data and the validity of the multipliers. These problems are usually addressed by making multiple indirect estimates with different indicators of illicit drug use (eg, deaths, number in drug treatment, arrests, treatment for complications of drug use), different multipliers, and different methods of estimation. Often, a combined estimate is produced from these different sources.[53]

	Cannabis users (N [%])	Opioid users (N [%])	Amphetamines-group users (N [%])	Cocaine users (N [%])
Africa	21 630 000–59 140 000 (3·8–10·4%)	890 000–3 210 000 (0·2–0·6%)	1 180 000–8 150 000 (0·2–1·4%)	940 000–4 420 000 (0·2–0·8%)
North Africa	4 780 000–10 620 000 (3·6–8·0%)	130 000–550 000 (0·1–0·4%)	ND	30 000–50 000 (<0·1–<0·1%)
West and central Africa	11 380 000–31 840 000 (5·2–14·6%)	410 000–1 070 000 (0·2–0·5%)	ND	550 000–2 300 000 (0·3–1·1%)
East Africa	2 340 000–8 870 000 (1·7–6·5%)	140 000–1 310 000 (0·1–1·0%)	ND	ND
Southern Africa	3 130 000–7 810 000 (3·9–9·8%)	210 000–280 000 (0·3–0·3%)	280 000–780 000 (0·4–1·0%)	270 000–730 000 (0·3–0·9%)
The Americas	40 950 000–42 860 000 (6·7–7·0%)	1 180 000–1 910 000 (0·2–0·3%)	5 170 000–6 210 000 (0·8–1·0%)	8 280 000–8 650 000 (1·4–1·4%)
North America	32 520 000–32 520 000 (10·7–10·7%)	1 000 000–1 630 000 (0·3–0·5%)	3 460 000–3 460 000 (1·1–1·1%)	5 690 000–5 690 000 (1·9–1·9%)
Central America	550 000–610 000 (2·2–2·5%)	20 000–20 000 (0·1–0·1%)	320 000–320 000 (1·3–1·3%)	120 000–140 000 (0·5–0·6%)
The Caribbean	440 000–2 060 000 (1·6–7·6%)	50 000–80 000 (0·2–0·3%)	30 000–530 000 (0·1–1·9%)	110 000–330 000 (0·4–1·2%)
South America	7 410 000–7 630 000 (2·9–3·0%)	110 000–170 000 (0·0–0·1%)	1 340 000–1 890 000 (0·5–0·7%)	2 360 000–2 480 000 (0·9–1·0%)
Asia	31 340 000–67 970 000 (1·2–2·5%)	6 440 000–12 020 000 (0·2–0·4%)	4 330 000–38 230 000 (0·2–1·4%)	400 000–2 300 000 (<0·1–0·2%)
East and southeast Asia	5 440 000–24 160 000 (0·4–1·6%)	2 800 000–4 990 000 (0·2–0·3%)	3 480 000–20 870 000 (0·2–1·4%)	400 000–1 070 000 (<0·1–0·2%)
South Asia	16 830 000–28 110 000 (1·9–3·1%)	1 380 000–3 170 000 (0·3–0·4%)	ND	ND
Central Asia	1 950 000–2 260 000 (3·8–4·4%)	320 000–320 000 (0·6–0·6%)	ND	ND
Near and Middle East	6 060 000–12 360 000 (2·4–4·8%)	1 940 000–3 170 000 (0·8–1·4%)	460 000–4 330 000 (0·2–1·7%)	40 000–650 000 (<0·1–0·3%)
Europe	28 730 000–29 250 000 (5·2–5·3%)	3 110 000–3 470 000 (0·6–0·6%)	2 540 000–3 180 000 (0·5–0·6%)	4 300 000–4 750 000 (0·8–0·9%)
West and central Europe	22 750 000–22 860 000 (7·1–7·1%)	1 010 000–1 170 000 (0·3–0·4%)	2 030 000–2 120 000 (0·7–0·7%)	3 990 000–4 090 000 (1·2–1·3%)
East and southeast Europe	5 980 000–6 380 000 (2·6–2·6%)	2 100 000–2 300 000 (0·9–1·0%)	510 000–1 050 000 (0·2–0·5%)	310 000–660 000 (0·1–0·3%)
Oceania	2 160 000–3 460 000 (9·3–14·8%)	40 000–50 000 (0·2–0·3%)	470 000–640 000 (2·0–2·8%)	330 000–400 000 (1·4–1·7%)
Global estimates	124 810 000–202 680 000 (2·8–4·5%)	11 66 000–20 660 000 (0·3–0·5%)	13 690 000–56 410 000 (0·3–1·3%)	14 250 000–20 520 000 (0·3–0·5%)

Data are N and % of population aged 15–64 years in each region. ND=insufficient data for subregional-specific estimate. Data comprised published country-level estimates from the 2010 World Drug Report.[28] Estimates were made only when direct estimates were published for at least two countries with at least 20% of the region's population aged 15–64 years. Regions with fewer data and less certainty have greater ranges. The scarcity of robust data for levels of drug use, particularly in countries such as India and China, preclude an accurate estimate of the global population of illicit drug users. Regions with estimates from more countries have more precise estimates. Adapted from reference 28 by use of regions defined by the UN Office on Drugs and Crime.

Table 1: **Estimated number of people aged 15–64 years who used illicit drugs at least once in the past year, 2009**

stabilised and perhaps decreased between 1998 and 2007.[60] A RAND report undertaken for the EU, by contrast, concluded that globally illicit drug use had, at best, remained stable, and possibly increased during the same period.[26]

The natural history and risk factors for use and dependence

Studies in high-income countries, with high levels of cannabis use, have reported a common temporal ordering of drug initiation—alcohol and tobacco, followed by cannabis use, and then other illicit drugs. This pattern persists after control for possible confounders.[19,61,62] This pattern is not consistent across countries.[25] Use of other illicit drugs is more prevalent than is use of cannabis in some countries (eg, Japan), and the association between initiation of alcohol, tobacco, and cannabis, and other illicit drug use is stronger in some countries (eg, the USA) than in others (eg, the Netherlands).[25] Variations in patterns of drug initiation between countries and cultures suggest that entry into illicit drug use is dependent on social factors and drug availability, as well as characteristics of users and social settings that facilitate or deter use.

Drug use is consistently more common in boys and men than in girls and women.[24,63] Rates of cannabis use peak in young adulthood and decrease as young people enter relationships, marry, have children, engage in further education, and enter the workforce. People who do not make these transitions are more likely to persist in their drug use.[63]

The natural history of dependence on illicit drugs has been poorly studied in prospective cohort studies. Most of these studies have recruited cohorts of users seeking treatment or entering the criminal justice system, groups whose trajectory of use can differ from users who do not enter these systems. The restricted evidence suggests that a minority of individuals will no longer meet criteria for dependence a year after diagnosis.[9] This proportion is higher for cannabis and amphetamines than it is for heroin and cocaine.[9]

Most of what we know about risk factors for problem use of opioids comes from retrospective studies of treatment populations rather than prospective studies of representative cohorts of young people.[64] We know most from cohort studies about risk factors and pathways for regular cannabis use in developed countries.[65] Similar risk factors seem to predict early cannabis use in developing countries.[65] These risk factors can be divided into social and contextual factors, family factors, individual factors, and peer affiliations during adolescence.

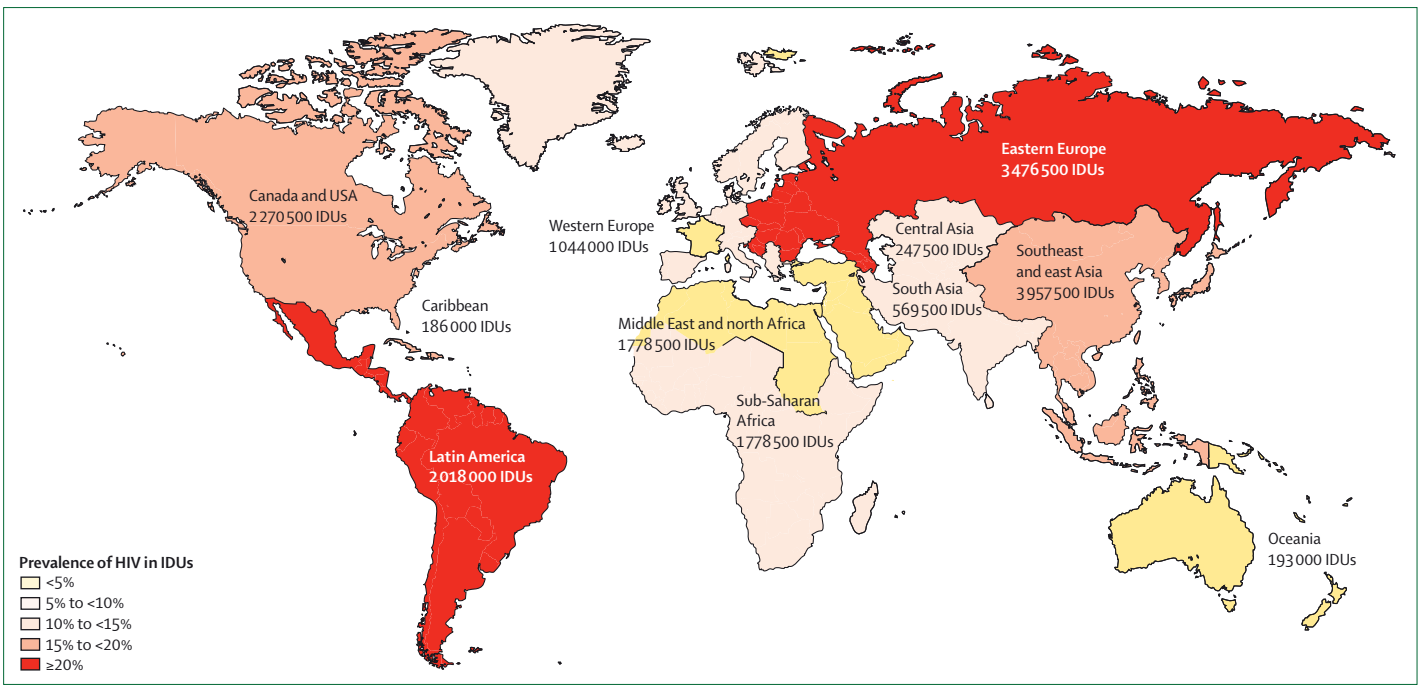

Figure: **Estimated number of injecting-drug users (IDUs) and regional prevalence of HIV in people who inject drugs**
Adapted from reference 8.

	Estimated number of people who inject drugs			Estimated regional mid-point IDU prevalence (%)	Estimated number of people with HIV who inject drugs			Estimated regional mid-point HIV prevalence in IDUs (%)
	Low	Middle	High		Low	Middle	High	
Eastern Europe	2 540 000	3 476 500	4 543 500	1·50%	18 500	940 000	2 422 000	27·0%
Western Europe	816 000	1 044 000	1 299 000	0·37%	39 000	114 000	210 500	10·9%
East and southeast Asia	3 043 500	3 957 500	4 913 000	0·27%	313 000	661 000	1 251 500	16·7%
South Asia	434 000	569 500	726 500	0·06%	34 500	74 500	135 500	13·1%
Central Asia	182 500	247 500	321 000	0·64%	16 500	29 000	47 000	11·8%
Caribbean	137 500	186 000	241 500	0·73%	6000	24 000	52 500	12·9%
Latin America	1 508 000	2 018 000	2 597 500	0·59%	181 500	580 500	1 175 500	28·8%
Canada and USA	1 604 500	2 270 500	3 140 000	0·99%	127 000	347 000	709 000	15·3%
Pacific Islands	14 500	19 500	25 000	0·36%	<250	500	500	1·4%
Australia and New Zealand	105 000	173 500	236 500	1·03%	500	2500	6000	1·5%
Middle East and north Africa	89 000	121 000	156 500	0·05%	1500	3500	6500	2·9%
Sub-Saharan Africa*	534 500	1 778 500	3 022 500	0·43%	26 000	221 000	572 000	12·4%
Extrapolated global estimates	11 008 500	15 861 500	21 222 000	0·37%	764 000	2 997 500	6 589 000	18·9%

Adapted from reference 8 by use of regional groupings defined by the the Joint UN Programme on HIV/AIDS. IDU=injecting drug user. *The estimates for sub-Saharan Africa should be viewed with caution because the prevalence estimates were derived from three of 47 countries in the region (South Africa, Mauritius, and Kenya). Furthermore, the estimated range of IDU for this region was derived by applying the regional observed error; this large error band shows the substantial uncertainty around these estimates.

Table 2: **Injecting drug use and HIV in people aged 15–64 years who inject drugs, 2008**

The major social and contextual factors that increase the likelihood of use are drug availability, use of tobacco and alcohol at an early age (ie, early adolescence),[66] and social norms for the toleration of alcohol and other drug use.[67] Socioeconomic background is also an important correlate of use, with people from more disadvantaged backgrounds more likely to use illicit drugs.[68] Less well studied structural risk factors include poverty and social and cultural factors. Family factors that increase risk during adolescence include poor quality of parent–child relationships,[69] parental conflict,[25,70,71] and parental and sibling drug use.[69,72,73]

	Studies identified	Regions	Range of adult past-year prevalence estimates
Amphetamines	Nine countries: four indirect prevalence estimates and five representative household survey-based estimates	Western Europe, eastern Europe, North America, Australia, southeast Asia	0·10–0·73%
Cannabis	Seven countries: all representative household survey-based estimates	Western Europe, North America, Australia, southeast Asia	0·10–1·50%
Cocaine	Five countries: one indirect prevalence estimate and four representative household survey-based estimates	Western Europe, southeast Asia, North America	0·07–0·52%
Heroin and other opioids	25 countries: 17 indirect prevalence estimates and eight representative household survey-based estimates	Western Europe, eastern Europe, North America, southeast Asia, Australia, south Asia	0·11–0·82%

Age ranges varied across studies so not all estimates were directly comparable. Only national estimates are included in these ranges; additional studies had sub-national estimates.[3-7]

Table 3: **Systematic reviews of prevalence studies of dependence on illicit drugs**

Individual risk factors include being male,[71] the personality traits of novelty[74] and sensation seeking,[75] early oppositional behaviour and conduct disorders in childhood,[73,76] and poor school performance, low commitment to education, and early school leaving.[77,78] Affiliating with antisocial and drug-using peers is one of the strongest predictors of adolescent alcohol and other drug use[79,80] that operates independently of individual and family risk factors.[78,81]

These risk factors often co-occur. Young people who initiate substance use at an early age are often exposed to many social and family disadvantages, come from families with problems and a history of parental substance use, are impulsive, have performed poorly at school, and are affiliated with delinquent peers. Young people with many of these risk factors start alcohol, tobacco, and illicit drug use at an early age, and often develop problem drug use.[79]

Risk factors for drug dependence can differ between countries, although few studies have directly examined this.[24] A study[24] of initiation and progression to dependence in 17 countries showed that the following variables predicted the development of illicit drug dependence in users: earlier onset of drug use, use of multiple types of illicit drugs, and development of externalising (eg, conduct disorder) and internalising (eg, depression) disorders before the age of 15 years. These findings are lent support by those from cohort studies in high-income countries, which have recorded that early onset drug use, and mental health problems, are risk factors for dependent drug use,[82] and that mental health problems increase the risk of problem drug use.

Health consequences of illicit drug use

Four broad types of adverse health effects of illicit drug use exist:[1] the acute toxic effects, including overdose; the acute effects of intoxication, such as accidental injury and violence; development of dependence; and adverse health effects of sustained chronic, regular use, such as chronic disease (eg, cardiovascular disease and cirrhosis), blood-borne bacterial and viral infections, and mental disorders (tables 4, 5). Many people who use illicit drugs will use more than one of the four drug types discussed in this paper. Therefore, the acute and long-term health effects of their drug use might be even greater than it is for people using only one drug type. Little work has quantified these potential interactions, but they are likely to be important.

Many studies have recorded associations between illicit drug use and various health-related harms, but determination of whether such associations are causal is more difficult. To make a causal inference it is necessary to document an association between drug use and the adverse outcome, confirm that drug use preceded the outcome, and exclude alternative explanations of the association, such as reverse causation and confounding.[90] Cohort studies of problem amphetamine, cocaine, and heroin users suggest that these drugs increase the risk of premature death, morbidity, and disability. These studies have rarely controlled for social disadvantage, but the mortality excess is too large to be wholly accounted for by this confounding;[91] the major causes of increased mortality are plausibly and directly related to illicit drug use.[36]

Tables 4 and 5 compare the availability of evidence, the quality of evidence, and the strength of associations seen for each drug type for a range of putative acute and chronic outcomes. Several things are apparent. First, the risks of cannabis use are much smaller than those of other illicit drugs, largely because cannabis does not produce fatal overdoses and it cannot easily be injected. Second, the quality of evidence varies widely across drug and health outcomes—data for cannabis are largely from prospective population-based cohorts, whereas data for the other drug types are from selected cohorts of treated opioid, cocaine, and amphetamine users.

Third, the magnitude of the effect is often poorly quantified. Especially in view of the known potential for serious adverse health and social consequences from opioids and psychostimulants, a clear need exists for more prospective, quantitative, longitudinal studies of specific patterns of drug use (or common combinations) and specific outcomes of such use, to produce better

	Cannabis				Opioids				Amphetamines				Cocaine			
	Effect	Level of evidence	Size of effect	Reference	Effect	Level of evidence	Size of effect	Reference	Effect	Level of evidence	Size of effect	Reference	Effect	Level of evidence	Size of effect	Reference
Acute toxic effects (fatal overdose)	×	..	0	19, 38	√	C	CMR 0·7	11	√	C	?	13, 39, 109	√	C	?	12, 39
Acute intoxication effects																
Accidental injury	?	..	..	19, 38	√	C	CMR 0·16	11	?	..	..	13, 39	?	..	..	12, 39
Motor vehicle accidents	√	D	?	19, 38, 41	?	..	..	41	?	..	..	13, 41	?	..	..	12, 41
Drug-induced psychotic symptoms	√	A	OR 2–3	19, 38, 21	×	..	0	39	√	A	?	37, 39	√	E	?	39, 84
Myocardial infarction	?	E	..	19, 38	×	..	0	39	√	E	?	37, 39	√	E	?	39
Dependence (lifetime risk %)	√	A	9%	61	√	A	23%	101	√	A	11%	101	√	A	16%	101
Adverse health effects of chronic use																
Cardiovascular pathology	?	..	..	19, 38	√	E	?	39	√	C	?	39	√	E	?	39
Liver disease	×	..	0	19, 38	√	C	?	39	?	C	?	37, 39	?	..	..	39
Pulmonary disease	?	..	..	19, 38	√	E	?	39	?	C	?	39	?	..	..	39
Cancers	?	..	..	10, 19, 38	?	C	?	11, 85	?	..	..	39	?	..	..	39
Neurotoxic effects	?	C	..	19, 38	×	..	..	39	√	..	?	37	√	..	?	39
Psychotic disorders	√	B	OR 2–3	19, 20 ,23	×	..	0	39	√	D	?	86	√	D	?	84
Common mental disorders	?	B	..	19, 23	√	D	?	87	√	D	?	86	√	D	?	87
Suicide	×	B	0	10	√	C	CMR 0·12	11	?	..	?	37, 86, 87	?	..	?	37
Increased mortality (standardised mortality ratios)	×	B	1	10	√	C	14·7 (95% CI 12·8–16·5)*	11	√	C	6·2†	13	√	C	4·7–7·6‡	12

A=experimental or controlled evidence supports this finding. B=findings across cohorts, representative population-based. C=findings across cohorts of drug users. CMR=crude mortality rate per 100 person-years. D=findings across cross-sectional studies, representative population-based, or case-control studies. E=cross-sectional associations in non-representative samples of drug users, case series suggesting outcome. n/a=not applicable. OR=odds ratio. SMR=standardised mortality ratio. ×=this drug does not seem to have an effect on the outcome. √=the outcome might be increased by the use of this drug. ?=Insufficient data exists for this drug and this outcome to allow conclusions about the association between the two. *Pooled SMR estimated from random effects meta-analysis (very high heterogeneity existed across studies; stratified analyses investigated this heterogeneity in further analyses and demographic and regional differences were clearly evident). †Only one study from the Czech Republic reported SMRs (this should be interpreted with caution). ‡Range from several studies only—interpret with caution.

Table 4: **Major potential acute and chronic consequences of illicit drug use**

estimates of expressed risk. Nonetheless, the major causes of increased mortality are plausibly and directly related to illicit drug use.[36] Tables 4 and 5 indicate that although evidence links opioid, cocaine, and amphetamine use with more adverse outcomes than cannabis, gaps remain in knowledge about the causal nature and magnitude of the risks.

Drugs differ in their most direct effects. To overdose fatally on cannabis is difficult, if not impossible, whereas fatal overdose is a well-known risk for the other major illicit drugs. The risk of overdose is increased when opioids are used in combination with other CNS depressants, such as alcohol and benzodiazepines,[92,93] and when an individual resumes opioid use after periods of abstinence during drug treatment or imprisonment.[36] Stimulant-related

	Cannabis		Opioids, amphetamines, and cocaine
	Effect	Size of effect	
HIV	×	0	Risk of HIV infection via injection with an HIV-infected needle: about 1 in 125 injections[88] (figure, table 2).
Hepatitis C	×	0	The prevalence of hepatitis C antibodies varies widely in IDUs, from 1% to greater than 90% prevalence.[14,22]
Hepatitis B	×	0	Prevalence substantially increased.[14]
Infective endocarditis	×	0	Most infections due to *Staphyloccus aureus*.[39] Risk rarely quantified; two US cohorts of cocaine IDUs noted 3–10% of deaths due to sepsis or endocarditis.[12]
Tuberculosis	×	0	Has been noted in some countries as especially prevalent as an HIV co-infection.[89]

×=this drug does not seem to have an effect on the outcome.

Table 5: **Consequences of unsafe drug injection**

overdoses can trigger fatal cardiac arrhythmias and strokes,[39,94,95] which are otherwise very rare causes of death in healthy young adults.[39,96] Few cohort studies have been done to examine the magnitude of risk in stimulant users, making the estimation of the magnitude of overdose risk difficult, although the evidence that does exist suggests that crude mortality rates for drug overdose do not differ much from those seen across cohorts of opioid users.[12,13] More thorough study of the rates and causes of death in psychostimulant users is needed.

Cannabis use impairs cognitive and behavioural functions,[97] especially for sustained-attention tasks, so the risk of road-traffic accidents can increase if users drive while intoxicated. Controlled studies have recorded statistically significant deficits in driving performance, but studies under more realistic road conditions report more impairment to a lesser extent.[19,38,41] Case-control studies have recorded weak associations between cannabis use and culpability for road-traffic accidents, with higher risks in individuals who use more cannabis.[19,38] These risks are less than those for alcohol, and fewer drivers use cannabis—the estimated proportion of road-traffic accidents attributable to cannabis in France between 2001 and 2003 was 3% (*vs* 30% for alcohol).[98] The relative contribution of cannabis use to road-traffic accidents will vary between countries according to the prevalence of cannabis use and access to motor vehicles.

Other illicit drugs can adversely affect an individual's ability to drive,[41] although data for the effect of opioids and stimulants on driving is equivocal.[41] Nonetheless, road-traffic accidents, falls, drowning, and related injuries are a more common cause of death in opioid and stimulant users than in their non-using peers. The contribution of these causes to drug-related disease burden might have been underestimated, because few cohort studies report deaths from trauma, and such deaths in drug users might not have been recorded as drug-related.[36] A pooled estimate from cohort studies of opioid users suggested that the trauma-related crude mortality rate was 0·16 per 100 person-years (95% CI 0·12–0·21).[11]

In the USA, an estimated 20% of people who use an illicit drug will meet the criteria for dependence;[99] the proportion reported in Australia is much the same.[101] Illicit drugs differ in their dependence risk,[100,101] ranging from 9% of lifetime cannabis users to 23% of lifetime heroin users in one study (webappendix p 2).[101] Such variance is attributable to differences in pharmacological effects (drugs with a rapid onset and shorter duration of effect have a higher dependence risk) and route of administration (drugs that are smoked or injected have a higher dependence risk than do those that are swallowed or used intranasally). More heroin injectors meet dependence criteria than do cannabis smokers.[101] Amphetamine and cocaine users who smoke or inject have a higher risk of dependence than do those who use intranasally.[102,103]

A consistent association exists in longitudinal studies between early onset of cannabis use, regular cannabis use, and a later diagnosis of schizophrenia, which increasing evidence suggests is not caused by confounding.[19,20,104–106] Meta-analyses of prospective population-based studies have noted a doubling of the risk of psychotic outcomes in regular cannabis users, after controlling for confounders,[20,23] and that the age of onset of schizophrenia is about 2·7 years earlier for cannabis users who develop the disorder.[107] Cannabis use is a biologically plausible contributory cause of schizophrenia in vulnerable individuals.[21]

A less consistent association exists between cannabis use and depression, and the evidence for a causal role between cannabis use and depression is less convincing than it is for psychotic symptoms and disorders.[19,23] Anxiety, depression, and other illicit drug use are very strongly associated,[99] but to ascertain whether these disorders precede and contribute to the development of problem drug use, or are exacerbated by such use, is difficult. For example, conduct disorders, depression, and anxiety disorders, which develop in adolescence and early adulthood, predispose young adults to use illicit drugs at an early age, thereby increasing the risk of their developing dependence. Longitudinal studies provide strong evidence that heavy alcohol use is a causal factor in depressive disorders.[108] Similar longitudinal analyses are needed to understand the relation between different types of illicit drug use and depression and other mental disorders.

Reviews have concluded that insufficient evidence is available to decide whether a causal relation exists between cannabis use and suicide.[10,19] By contrast, rates of self-reported suicide attempts in problem opioid, cocaine, and amphetamine users[109] are much higher than they are in non-drug-using peers of the same age, sex, and socioeconomic status.[110] The association is probably mediated by depression, rates of which are high in problem drug users.[36] The intoxicating effects of these drugs, and the stresses of an illicit-drug-dependent lifestyle, probably increase suicide risk in depressed drug users. Meta-analyses have produced a pooled crude mortality rate for suicide in opioid-dependent individuals of 0·12 per 100 person-years (95% CI 0·08–0·16).[11]

Because cannabis cannot be readily injected, the risks of unsafe injecting arise from only opioid, cocaine, and amphetamine use. HIV infection risk after injection with an HIV-contaminated syringe has been estimated at 0·67%.[88] The sharing of other contaminated drug-use paraphernalia presents an unquantified but probably lower risk. The risk of sexual transmission of HIV between HIV-positive IDUs and their sexual partners is much lower at 0·02–0·05% per heterosexual sex act;[111–113] risk during receptive anal intercourse between men can be 0·82% (95% CI 0·24–2·76%).[114]

Pronounced geographical variations exist in the prevalence of injecting drug use and HIV infection in IDUs (figure; table 2). Injecting drug use has been reported in 151 countries,[36] with 0·8–6·6 million (of an

estimated 11–21 million injectors in 2007) estimated to be living with HIV.[8] Existing estimates of drug-related HIV have been insufficient in their account of its geographical variation; new estimates being made for the 2010 global burden of disease analysis will be more accurate, in view of the increase in the amount of data for the extent of both injecting drug use and HIV in people who inject drugs.

The viruses that cause hepatitis B and hepatitis C infections are also spread by sharing contaminated injection equipment.[115,116] Large proportions of IDUs are infected with hepatitis C, with an estimated 10·0 million (range 6·0–15·2 million) injectors thought to be positive for hepatitis C antibodies in 2010:[14] 75–85% of these develop chronic hepatitis C infections[117–119] that can potentially lead to cirrhosis, liver failure, and hepatocellular carcinoma.[120] The proportion of people with hepatitis C who develop cirrhosis is estimated at 7% after 20 years of infection, and 20% after 40 years.[121] Additional stresses on the liver from heavy alcohol intake, liver fibrosis, and HIV or hepatitis B co-infection, can increase rates and speed of the development of complications.[121] Many individuals living with hepatitis C report fatigue, poor sleep, and abdominal pain, which impair quality of life as much as diabetes does.[122] In countries with low rates of HIV infection in IDUs, the burden of hepatitis C in IDUs might be comparatively higher.

Findings from reviews show no evidence that cannabis use increases overall mortality,[10,19] which contrasts with mortality from other types of illicit drug use (webappendix p 6). A meta-analysis of mortality in opioid users calculated a pooled standardised mortality ratio of 14·7 (95% CI 12·8–16·5).[11] These risks varied geographically, with, for example, lower increases in mortality in Australia, and higher increases in Italy.[11] Fewer cohort studies of cocaine and amphetamine users[12,13] report increased premature mortality; mortality increases in these cohorts seem less pronounced than they are for opioid users.

Burden of disease attributable to illicit drug use

Since 1993, estimates of the causes of global disease burden have used disability-adjusted life years (DALY)[124]3to combine disease burden from premature mortality with that from disability. This metric allows a comparison of the contribution across diseases, injuries, and risk factors. In 2002, the comparative risk assessment exercise[124] estimated the proportion of disease burden attributable to alcohol, tobacco, and injecting drug use. These estimates explicitly accounted for variations in prevalence of different diseases or injuries, considered age and sex differences, and included mortality as well as morbidity.

Global mortality attributable to illicit opioid use was estimated at 100 000 deaths in 1990, 62% of which were in high-income countries.[125] An estimate for 2000 (which defined illicit drug use as injecting or problem use of amphetamines, cocaine, or opioids) estimated all-cause mortality, and mortality attributable to AIDS, overdose, suicide, and trauma from cohort studies of problem illicit drug users (table 6).[29] Major regional differences were recorded in the quality of data for the prevalence of use, and estimates relied heavily on studies of mortality in problem drug users in high-income countries.[126] Use of findings from such studies is a major limitation of these estimations—reviews have since shown that mortality in drug users varies geographically and according to country income.[11]

The 2000 study estimated that the median number of deaths attributed to illicit drugs was about 200 000 (241 000 from summing all four causes, and 197 000 with an estimate of all-cause mortality).[29] Uncertainty intervals around each estimate were wide (102 000–322 000 and 82 000–408 000, respectively); nonetheless, the 2000 estimate[29] was double the 1990 estimate.[125] WHO estimates of global DALYs attributable to amphetamine, cocaine, or opioid use in 2004 suggested that use of these drugs accounted for 0·9% of global DALYs, varying widely across regions

	AIDS mortality			Opioid overdose mortality			Suicide mortality			Trauma mortality			Illicit drug all-cause mortality			Alcohol all-cause (middle)	Tobacco all-cause (middle)
	Low	Middle	High	Low	Middle	High	Low	Middle	High	Low	Middle	High	Low	Middle	High		
Africa	2000	5000	9000	1000	2000	3000	<1000	1000	2000	1000	4000	7000	13 000	28 000	42 000	213 000	158 000
Americas	12 000	17 000	30 000	7000	8000	11 000	806	1000	5261	2000	7000	12 000	37 000	61 000	83 000	279 000	802 000
Europe	1000	2000	10 000	7507	14 000	20 000	2000	7000	15 000	2000	5000	7000	17 000	33 000	47 000	538 000	1 605 000
Eastern Mediterranean	2000	5000	10 000	7000	17 000	26 000	1000	3000	4000	1000	4000	6000	9000	15 000	22 000	16 000	186 000
Southeast Asia	6000	59 000	111 000	3000	23 000	45 000	2000	15 000	28 000	2000	4000	6000	8000	17 000	26 000	229 000	1 035 000
Western Pacific	5000	11 000	18 000	3000	4000	4000	<1000	1000	3000	8000	10 000	12 000	17 000	44 000	104 000	526 000	978 000
Total	26 000	105 000	191 000	29 000	69 000	111 000	8000	32 000	57 000	18 000	34 000	50 000	102 000	197 000	322 000	1 804 000	4 800 000

Adapted from references 29,30,32,131. WHO regional definitions used.[31–33]

Table 6: **Estimated mortality attributable to injecting or problematic drug use according to several major causes, compared with alcohol and tobacco—2000 Global Burden of Disease comparative risk assessment**

	HIV/AIDS DALYs		Drug use disorders* DALYs		Poisoning DALYs		Suicide/ self-inflicted injuries DALYs		Trauma† DALYs		Total illicit drugs DALYs		Total alcohol DALYs		Total tobacco DALYs	
	Number (000s)	%	Number (000s)	%	Number (000s)	%	Number (000s)	%	Number (000s)	%	Number (000s)	%	Number (000s)	%	Number (000s)	%
Africa	0	0	939 000	100	9000	0·8	46 000	3·7	136 000	0·7	1131 000	0·3	7759 000	2·1	1930 000	0·5
Americas	231 000	10·7	2446 000	100	55 000	9·3	81 000	5·0	297 000	2·8	3110 000	2·2	13 102 000	9·1	8837 000	6·1
Europe	620 000	52·5	1369 000	100	23 000	1·1	170 000	5·5	213 000	1·7	2395 000	1·6	17 342 000	11·4	17 725 000	11·7
Eastern Mediterranean	199 000	21·6	1675 000	100	7000	1·7	68 000	6·2	168 000	1·1	2117 000	1·5	763 000	0·5	2793 000	2·0
Southeast Asia	588 000	9·6	1252 000	100	17 000	0·9	445 000	6·2	283 000	0·6	2585 000	0·6	12 066 000	2·7	12 764 000	2·8
Western Pacific	788 000	54·1	674 000	100	22 000	1·7	39 000	0·7	363 000	1·4	1886 000	0·7	18 393 000	6·9	12 848 000	4·8
Global DALYs	2426 000	4·1	8355 000	100	133 000	1·8	849 000	4·3	1460 000	1·1	13 223 000	0·9	69 424 000	4·5	56 897 000	3·7

Extracted from reference 31. WHO regional definitions used.[31-33] *Cannabis was not included in these estimates. †Included road-traffic accidents, falls, fires, drownings, and other unintentional injuries—these estimates specifically excluded violence as a potential consequence of illicit drug use.

Table 7: **Estimated disability-adjusted life years (DALYs) attributable to illicit drug use according to several major causes, compared with alcohol and tobacco, 2004**

(table 7). Drug dependence (excluding cannabis) was the largest of the four causes of global illicit drug burden assessed (68%), followed by HIV/AIDS (18%).

These estimates indicate that illicit drug use is a substantial global cause of premature mortality and morbidity. They were acknowledged to be underestimates because they did not include cannabis and MDMA, or the burden attributable to hepatitis B, hepatitis C, or drug-related violence.[29] The Australian burden of disease study included a greater number of drug-related outcomes, and its findings suggest that existing global figures substantially underestimate illicit-drug-related burden (panel 4; table 8).

Comparison of illicit drugs with tobacco and alcohol

Although far from perfect, the existing global burden of disease estimates provide a common metric to compare the harms caused by illicit drugs with those of alcohol and tobacco—regionally and globally—while taking account of differences in prevalence and harms. Comparison of existing estimates of use and burden of disease for illicit drugs, alcohol, and tobacco (table 9) draws attention to four main points. Globally, many fewer people use illicit drugs than use alcohol (roughly one-tenth). Nonetheless, estimated levels of problem use of opioids, cocaine, or amphetamines are an appreciable proportion of those for alcohol use disorders (0·3–0·9% *vs* 1·2%). Tobacco use is far more widespread, and so its contribution to disease burden was greater than that for alcohol or illicit drugs. Finally, the estimated number of attributable deaths and DALYs were much higher for alcohol use disorders than for problem illicit-drug use (3·8% and 4·5% for alcohol and 0·4% and 0·9% for illicit drugs, respectively). The higher number of years of life lost from illicit drug use (2·1 million *vs* 1·5 million for alcohol) shows the concentration of illicit drug deaths in younger people, whereas alcohol and tobacco deaths occur in middle-aged and older adults.

Harms of illicit drug use not captured in burden of disease estimates

Burden of disease estimates do not include the adverse social effects on drug users, such as stigma and discrimination, or the adverse effects that drug users' behaviours have on public amenity (eg, public drug use, drug dealing, and discarded injection equipment) and public safety (eg, violence between drug dealers, and property crime to finance illicit drug use).

Interactions also exist between illicit drug policy and drug-related harm. Both internationally and nationally, policies focus on the reduction of supply and use by criminalisation of drug use and supply. Criminalisation increases the price of illicit drugs,[132] and probably discourages some people from using these drugs. The prevalence of illicit drug use is therefore probably lower than it might be if their sale and use was as legal as alcohol and tobacco. This is not true for solely removing criminal penalties for use.[133]

Conversely, the higher price of illicit drugs probably makes it more likely that some who use illicit drugs will engage in criminal activities to finance their use (eg, by drug dealing, property offences, and fraud).[134] Furthermore, violence is often associated with illicit drug markets, presenting a risk to the wellbeing of drug users.[135] Cohort studies of opioid users suggest a pooled homicide crude mortality rate of 0·10 per 100 person-years (95% CI 0·07–0·13),[11] and findings from a meta-analysis of toxicological studies of homicide victims show that about 6% of victims tested positive for cannabis, 11% for cocaine, and 5% for opioids.[136] A review[35] concluded that "the distal factors surrounding illicit drug markets appear to play a larger role in illicit drug-related homicide than the proximal effects of [these] substances". Drug-related law enforcement often comprises a large proportion of the social costs of illicit drug use.[137,138] Countries that are sites of illicit drug production or trafficking might have substantial social, political, and health disruption from the activities of the

Panel 4: The burden of disease attributable to illicit drugs, tobacco, and alcohol in Australia

The disease burden attributable to opioids, amphetamines, cocaine, and cannabis in Australia (table 8) is of international relevance, because Australia has good data for mortality, and rates of most types of illicit drug use (cocaine excepted) are much the same as those in other high-income countries. A 2003 study examined more consequences of drug use than had previous global studies,[127] allowing some assessment of the extent to which global estimates underestimate disease burden.

In 2003, illicit drug use in Australia caused similar levels of disease burden as did alcohol (2·0% *vs* 2·3%).[127] More deaths were attributed to illicit drugs than to alcohol, on the assumption that moderate alcohol use reduced cardiovascular heart disease mortality in middle-aged adults. Injecting drug use and opioid and polydrug use accounted for more than half the contribution of illicit drugs to disease burden. Cannabis dependence, psychosis, suicide, and road-traffic crashes accounted for 0·2% of the total disease burden and 10% of the burden for all illicit drugs.[127] The inclusion of cannabis use, hepatitis C, and hepatitis B produced an estimate that was 1·6 times greater than one based on the fewer outcomes included in the 2000 global burden of disease estimates.

The estimates for the 2010 global burden of disease project[128,129] will include estimates of disease burden attributable to cannabis use, and a greater number of illicit drug use disorders and adverse consequences of illicit drug use.[128] The Australian data suggest that the new global estimates will be substantially higher than previous ones.

	Deaths		Disability-adjusted life years (DALYs)	
	Number	% total	Number	% total
Heroin and polydrug use	263	0·2	16758	0·6
Hepatitis C	759	0·6	11709	0·4
Cannabis use	0	0·0	5206	0·2
Suicide and self-inflicted injuries	204	0·2	4458	0·2
Hepatitis B	329	0·2	3637	0·1
Other	150	0·1	9696	0·4
Total				
Illicit drugs	1705	1·3	51463	2·0
Alcohol	1084	0·8	61091	2·3
Tobacco	15511	11·7	204788	7·8

Adapted from reference 127.

Table 8: **Burden of disease attributable to illicit drugs, alcohol, and tobacco in Australia, 2003**

	Illicit drugs		Alcohol		Tobacco	
	N	Global %	N	Global %	N	Global %
Past-year users	149–272 million*	3·3–6·1%	2830 million†	44%	..	..
Problem or dependent users	15–39 million‡	0·3–0·9%	76·3 million§	1·2%§	1670 million¶	26%¶
Attributable deaths†	0·25 million	0·4%	2·25 million	3·8%	5·11 million	8·7%
Years of life lost due to use disorders†	2·1 million	0·23%	1·5 million	0·17%	NR	NR
Attributable DALYs†	13·22 million	0·9%	69·42 million	4·5%	56·90 million	3·7%

*Any illicit drug (including cannabis); estimates refer to individuals aged 15–64 years made by the UN Office on Drugs and Crime for 2009.[27,28] †These data refer to 2004, and were extracted from WHO Global Burden of Disease spreadsheets[31]—cannabis is not included in the estimates for illicit drugs. ‡Estimates made by the UN Office on Drugs and Crime for 2009 in individuals aged 15–64 years, and refer to problem drug users, not necessarily dependent drug users—problem or dependent cannabis users are excluded in this definition.[27,28] §These data are reported in the 2004 WHO Global Status of Alcohol Report,[130] and refer to individuals aged 15 years or older with alcohol use disorders—prevalence estimate approximated from population data reported in references 31 and 132. ¶These data refer to current smokers aged 15 years or older in 2004 and are from references 31 and 32. NR=not specifically reported.

Table 9: **Comparison of existing estimates of use and burden of disease for illicit drugs, alcohol, and tobacco**

large-scale criminal networks involved, as is the case in Afghanistan and Mexico.[139]

The dominant policy focus on supply reduction and criminalisation of drug use can also adversely affect the health and wellbeing of illicit drug users in the following ways: by increasing the health risks of illicit drug use (eg, if users engage in risky injecting to avoid arrest by police);[140,141] by increasing risks of engaging in sex work or other illegal activities to finance drug use, exposing users to violence and sexual risk; by discouraging treatment-seeking (for fear of negative consequences);[141,142] by reducing access to interventions that reduce risk, through creating legal obstacles to, or policy limits on, service provision;[140–143] and by increasing the risks of imprisonment and its attendant health risks.[140,142,144]

Some countries have been successful in ensuring that services are accessible to, and accessed by, people who use drugs. Some have achieved high coverage of HIV prevention services for IDUs,[56] and others provide good access to drug treatment and other services for dependent drug users.[56,145] However, globally, a very low proportion of the population who inject drugs has access to interventions to reduce HIV infection.[56] Treatment coverage globally is also low, with structural factors (including policy and legal bans—eg, on use of agonist opioids) a major impediment to improved coverage.[142,143]

Discussion

A substantial proportion of young adults in developed countries have used an illicit drug at some time in their lives. Worldwide, around one in 20 people aged 15–64 years might have done so in the past year. Cannabis is the drug most often used and the most widely available because of widespread domestic production in many countries. A minority of individuals who use illicit drugs become dependent on or inject them. The prevalence of dependence on these drugs has rarely been directly assessed, but it seems to be more common in high-income countries.

Many important questions cannot be answered. How many people who use a drug will go on to become dependent? How long do people use drugs for? And for how long do they remain dependent on them? Does the risk of dependence vary over time and between individuals? Do users move in and out of harmful and dependent use, and if so, when and why? How large is the risk for adverse outcomes, including early death? Do these risks vary between countries, and demographic subgroups? How much does criminalisation of drugs reduce their prevalence of use? How much of the harm related to illicit drugs derives from their illegal status? Until we have better answers to these questions, statements about the exact magnitude of the health, social, and financial burden of illicit drug use cannot be made with accuracy. This makes the formulation of evidence-informed drug policies and programmes difficult.[1] Without knowing the size of the population at risk, identification of appropriate interventions and the size of target populations is difficult.

On the basis of available evidence, most of the disease burden attributable to illicit drugs is concentrated in problem or dependent drug users, especially people who inject drugs. Existing estimates underestimate the contribution of illicit drugs to the global burden of disease because they do not include all adverse outcomes of illicit drug use. Even so, these estimates suggest that drug dependence, HIV infection, and drug overdose are important causes of drug-related disease burden. Causes of burden might also be changing in high-income countries—as mortality from HIV decreases, the burden attributable to chronic hepatitis C infection in IDUs might increase. As yet, we have no estimates of the global burden attributable to cannabis use.

In high-income countries, the contribution of illicit drugs to burden of disease is less than that of tobacco, but may be similar to alcohol (if moderate alcohol use truly has protective effects on cardiovascular mortality). This outcome is the product of the following: the lower prevalence of problem illicit drug use than of alcohol and tobacco use (reducing the number of individuals exposed), the occurrence of adverse outcomes of illicit drug use at much younger ages than those for alcohol and tobacco (increasing the years of life lost or lived with disability due to illicit drug use), and the consequences of injection of opioids and stimulants (with injecting-related blood-borne viral infections being major contributors to burden that are not experienced by cannabis, alcohol, or tobacco users). Estimates of disease burden are much less certain in low-income and middle-income countries.

In many high-income countries, illicit opioid use seems to be the most hazardous type of illicit drug use in terms of mortality. The risks of amphetamine and cocaine use have not been as well studied as those of opioids, but are probably less hazardous than opioids in terms of fatal overdose. They nonetheless cause dependence, drug-induced psychosis, violence, and HIV and hepatitis C infections when injected with non-sterile equipment.

Much of the burden attributable to injecting drug use can be prevented or reduced by needle and syringe programmes, opioid substitution treatment, and antiretroviral therapy.[143] Burden is also probably worsened by the criminal status and stigmatisation of injecting drug use, high rates of imprisonment, and little political interest in funding interventions to reduce these risks.[140–143]

The major adverse health effect of cannabis use is dependence, which in young adults is correlated with, and probably a contributory cause of, psychosis and other mental disorders. The health-related harms of cannabis use have never been quantified on a global scale, but they are qualitatively different from the other major drug types, in that cannabis contributes more to morbidity than mortality because it cannot be injected and does not cause fatal overdose.

A major unintended consequence of the criminalisation of drug use is the inability to collect high quality data for patterns of use and harms. High-income countries often use general population and school surveys to monitor trends in drug use, but these probably underestimate the use of more highly stigmatised drugs that account for most of the harms (panel 3). Routinely collected mortality and morbidity data can be used to monitor trends in those that are more directly related to drug use (such as overdose deaths and numbers seeking treatment). However, even in high-income countries with good research infrastructure, illicit drug use might not always be recognised (or recorded) as a contributory cause of death or hospitalisation.

Data for patterns of use and harm are very scarce for synthetic drugs that have emerged within the past two decades. Policies towards newly emerging drugs (eg, mephedrone) are often made in response to media stories and in ignorance of the scale of their use and the problems arising from it.[146] Decisions are often made on an implicit precautionary principle: when in doubt, prohibit the use of a new substance. Once use of a drug has been prohibited, the decision is rarely revisited.

Intelligent policy responses to drug problems need much better data for the prevalence of different types of illicit drug use and the harms that their use causes to users and society, especially in high-income countries with substantial rates of illicit drug use. It is equally important in developing countries that are close to source countries, or whose citizens have ready access to precursor chemicals to illicitly manufacture synthetic drugs. A need exists for the global community, including UN agencies, to address the technical and political challenges that many countries face in developing this capacity. The second paper in this Series[133] examines evidence for the effectiveness of a range of interventions that aim to reduce the extent of drug use and harms related to such use.

Contributors
LD and WH both contributed to the overall structure of and idea for the paper. LD retrieved data presented in the paper and led the writing with substantial input from WH. Both authors approved the final draft.

Conflicts of interest
WH and LD have been consultants to WHO for the purposes of providing scientific advice on illicit drug epidemiology (LD, WH), burden of disease (LD, WH), and reviewing evidence for the comparative harms of cannabis, tobacco, and alcohol (WH). LD has consulted to the UNODC, providing advice on presentation, analysis, and interpretation of data for illicit drugs. LD has also consulted to UNAIDS on injecting drug use, HIV, and effective responses, including reviewing data for monitoring and assessment including data from the UN General Assembly 26th Special Session.

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