Global burden of disease attributable to illicit drug use and dependence: findings from the Global Burden of Disease Study 2010

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Summary

Background No systematic attempts have been made to estimate the global and regional prevalence of amphetamine, cannabis, cocaine, and opioid dependence, and quantify their burden. We aimed to assess the prevalence and burden of drug dependence, as measured in years of life lived with disability (YLDs), years of life lost (YLLs), and disability-adjusted life years (DALYs).

Methods We conducted systematic reviews of the epidemiology of drug dependence, and analysed results with Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) Bayesian meta-regression technique (DisMod-MR) to estimate population-level prevalence of dependence and use. GBD 2010 calculated new disability weights by use of representative community surveys and an internet-based survey. We combined estimates of dependence with disability weights to calculate prevalent YLDs, YLLs, and DALYs, and estimated YLDs, YLLs, and DALYs attributable to drug use as a risk factor for other health outcomes.

Findings Illicit drug dependence directly accounted for 20·0 million DALYs (95% UI 15·3–25·4 million) in 2010, accounting for 0·8% (0·6–1·0) of global all-cause DALYs. Worldwide, more people were dependent on opioids and amphetamines than other drugs. Opioid dependence was the largest contributor to the direct burden of DALYs (9·2 million, 95% UI 7·1–11·4). The proportion of all-cause DALYs attributed to drug dependence was 20 times higher in some regions than others, with an increased proportion of burden in countries with the highest incomes. Injecting drug use as a risk factor for HIV accounted for 2·1 million DALYs (95% UI 1·1–3·6 million) and as a risk factor for hepatitis C accounted for 502 000 DALYs (286 000–891 000). Suicide as a risk of amphetamine dependence accounted for 854 000 DALYs (291 000–1 791 000), as a risk of opioid dependence for 671 000 DALYs (329 000–1 730 000), and as a risk of cocaine dependence for 324 000 DALYs (109 000–682 000). Countries with the highest rate of burden (>650 DALYs per 100 000 population) included the USA, UK, Russia, and Australia.

Interpretation Illicit drug use is an important contributor to the global burden of disease. Efficient strategies to reduce disease burden of opioid dependence and injecting drug use, such as delivery of opioid substitution treatment and needle and syringe programmes, are needed to reduce this burden at a population scale.

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Introduction

Illicit drugs are drugs whose non-medical use has been prohibited under international drug control treaties.[1,2] They include the plant-based drugs heroin, cocaine, and cannabis, synthetic drugs such as amphetamines, and pharmaceutical drugs such as opioids and benzodiazepines.

The health risks of illicit drug use increase with the frequency and quantity of drugs used. Drug dependence is defined by the International Classification of Diseases 10th Revision (ICD-10)[3] as the presence of three or more indicators of dependence for at least a month within the previous year. These indicators consist of a strong desire to take the substance, impaired control over use, a withdrawal syndrome on ceasing or reducing 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 persistence of drug taking despite the problems that occur. Rates of illicit drug dependence are thought to be increased in developed countries,[4] but no global estimates have been made to date.

Since 1993, estimates of the causes of global disease burden have used the disability-adjusted life year (DALY)[5] to combine disease burden attributable to premature mortality (years of life lost [YLLs]) with that attributable to disability (years of life lived with disability [YLDs]). The operationalised definition of illicit drug use has changed since the original Global Burden of Disease (GBD) study; drug use in GBD 1990 was defined as dysfunctional and harmful drug use overall, without specifying drug type.[6]

In 2002, the GBD comparative risk assessment (CRA) exercise[7] estimated the proportion of disease burden attributable to alcohol, tobacco, and illicit drug use.[7]

WHO estimated that amphetamine, cocaine, and opioid use accounted for 0·9% of global DALYs in 2004.[8] However, this proportion was an underestimate[9] because it did not include burden attributable to cannabis, to infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) from injecting drug use, or drug-related violence (homicide).[10]

The Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010)[11] calculated the burden of illicit drug dependence separately for amphetamines, cocaine, opioids, and cannabis, and assessed more outcomes than did the CRA exercise. This report summarises data for the prevalence and disease burden attributable to these illicit drugs in GBD 2010 and the findings of the CRA[12] for illicit drug use as a risk factor for other health outcomes. We aim to present the global estimates and regional variation in the prevalence of amphetamine, cannabis, cocaine, and opioid dependence; report YLDs, YLLs, and DALYs attributable to each of these forms of drug dependence; and summarise additional burden due to illicit drug use as a risk factor for other health outcomes.

Methods

Overview

The case definitions used for amphetamine, cannabis, cocaine and opioid dependence were based on the International classification of diseases (ICD)[13] and the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, version 4 (DSM-IV).[14] To estimate burden of disease attributable to illicit drug use and dependence, we aggregated disorder-specific epidemiological data and disability weights[15] to calculate prevalent YLDs;[16] multiplied disorder-specific estimates of mortality by standard life expectancy at the age of death to calculate YLLs;[17] summed YLDs and YLLs to generate disorder-specific DALYs;[11] and estimated YLDs, YLLs, and DALYs attributable to drug use as a risk factor for other health outcomes (through use of a CRA).[12]

Systematic reviews of epidemiological data

We obtained data from systematic reviews of studies of the prevalence of illicit drug use and dependence,[18–23] remission from dependence,[24] and excess mortality among illicit drug users.[25–29] These reviews followed PRISMA guidelines, and involved the following components: peer-reviewed literature searches (for articles published in any language between Jan 1, 1990, and Dec 31, 2008); systematic searches of online databases;[30,31] internet searches for other evidence of drug use (media, expert reports, drug-related deaths, drug-related arrests, or persons treated for drug dependence); and consultation with experts in the HIV and illicit drug specialties, including contacting study authors for further data or clarification. Data extraction followed protocols in line with STROBE guidelines,[32] with cross-checking and tests of internal consistency. Data for prevalence, incidence, remission, duration, and excess all-cause mortality were extracted and graded according to predefined variables. Full details have been reported elsewhere.[18–29]

Disease modelling

Although our inclusion criteria ensured minimum study quality, substantial variability existed between the studies identified in our search[18–21,23] because of the different methodological approaches and analyses used. Notable variation also existed in the available data across disorders and regions (appendix). To account for this variability, we modelled outcomes with Dismod-MR, a Bayesian meta-regression technique that was developed from an incidence–prevalence–mortality (IPM) mathematical model.[16,33] For each disorder, DisMod MR estimates prevalence, incidence, duration, and excess mortality separately for 187 countries and 21 world regions, both sexes, 5 year age groups, in 1990, 2005, and 2010. DisMod MR used a generalised negative binomial model that incorporated the following functions: the IPM model to enforce consistency between estimates of each epidemiological parameter; country-level and study-level covariates to account for measurement bias or true variances in the data; and age-specific fixed effects to estimate age patterns. The technique used random effects for country, regions, and super-regions to estimate prevalence in countries with no data. The uncertainty (standard errors or 95% UI) around the epidemiological data was propagated to final prevalence outputs that were used in the calculation of prevalence-based YLDs. This uncertainty was in addition to the uncertainty from fixed effects and random effects for country and regions.[16]

See **Online** for appendix

For **region definitions** see http://www.healthmetricsandevaluation.org/sites/default/files/publication_summary/GBD2010_Regions_countries.pdf

Disability weights

We defined disability as any short-term or long-term health loss resulting from a disorder. We calculated this loss (in the form of disability weights) for each form of drug dependence and multiplied the estimate by the prevalence data to derive YLDs.[15] In response to criticism[34] of the reliability of previous estimates of disability weights,[6] GBD 2010 calculated new disability weights collected from as wide a range of estimates as possible[15] by using representative community surveys in Bangladesh, Indonesia, Peru, Tanzania, and USA and an internet-based survey. Survey participants were shown a number of randomly generated pair-wise comparisons of different health states and asked to choose the healthier option of the pair. To estimate disability weights, responses were transformed into discrete values and anchored between 0 (perfect health) and 1 (death) by use of additional population health equivalence questions.[15]

Severity

For each form of drug dependence, we estimated the proportion of asymptomatic cases from the US National

Epidemiological Survey on Alcohol and Related Conditions 2000–01 and 2004–05,[35] and the Australian National Survey of Mental Health and Wellbeing of Adults 1997.[36] We used these proportions to calculate an average disability weight for each disorder, with asymptomatic cases given a disability weight of 0.[15,16] For all the main physical disorders and most mental and substance use disorders in GBD 2010, some diagnosed individuals reported no additional disability at the time of the survey after disability attributable to comorbid disorders was portioned out. This feature is captured in the proportion of asymptomatic cases. Further details are provided elsewhere.[16]

Comorbidity

We applied a general comorbidity correction to all estimates of YLD using microsimulation methods to create hypothetical populations for each age group, by sex, year, and country. We based the probabilities of having no, one, or several non-fatal health states simultaneously on the prevalence estimates for each health state. For each hypothetical person in the microsimulation, we calculated a combined disability weight for any comorbid health states with a multiplicative function. We then reapportioned disability weights to each health state proportionally to the unadjusted disability weights. We calculated average corrected disability weight for each health state in each age, sex, year, and country stratum, and the decrement compared with the original disability weight was taken as the comorbidity correction for YLD (details in the appendix and elsewhere[15,16]).

Estimation of YLLs

We computed premature mortality attributable to illicit drug dependence as YLLs based on cause of death estimates from 1980 to 2010 for 20 age groups, both sexes, and 187 countries.[17] Mortality was explicitly modelled for illicit drug use disorders. We developed cause of death estimates from analysis of a comprehensive database of vital registration, verbal autopsy, surveillance, and other sources. Ultimately, we used 20 509 country-years of data from 126 countries for mortality estimation. We assessed the quality of every observation, and mapped various revisions of ICD classifications. We reassigned deaths with standardised algorithms when the recorded cause of death was not likely to be the underlying cause of death. Deaths in people who are drug dependent are often characterised

	Cannabis		Amphetamines		Cocaine		Opioids	
	N	Prevalence, % (95% UI)	N	Prevalence, % (95% UI)	N	Prevalence, % (95% UI)	N	Prevalence, % (95% UI)
High-income Asia Pacific	390 000	0·28 (0·18–0·41)	372 000	0·24 (0·17–0·34)	257 000	0·06 (0·05–0·07)	456 000	0·28 (0·17–0·44)
Central Asia	197 000	0·22 (0·17–0·29)	203 000	0·23 (0·18–0·29)	52 000	0·02 (0·01–0·02)	209 000	0·24 (0·18–0·33)
East Asia	2 402 000	0·17 (0·09–0·28)	2 634 000	0·18 (0·12–0·26)	234 000	0·16 (0·11–0·24)	2 180 000	0·14 (0·08–0·24)
South Asia	2 649 000	0·15 (0·13–0·18)	3 993 000	0·24 (0·16–0·37)	1 086 000	0·07 (0·04–0·10)	4 331 000	0·26 (0·22–0·31)
Southeast Asia	977 000	0·15 (0·11–0·19)	2 724 000	0·42 (0·34–0·54)	114 000	0·02 (0·01–0·02)	956 000	0·15 (0·11–0·20)
Australasia	154 000	0·68 (0·60–0·78)	98 000	0·41 (0·29–0·56)	32 000	0·14 (0·09–0·20)	110 000	0·46 (0·41–0·53)
Caribbean	69 000	0·16 (0·12–0·21)	88 000	0·20 (0·16–0·25)	143 000	0·33 (0·26–0·42)	109 000	0·26 (0·18–0·36)
Central Europe	249 000	0·23 (0·18–0·29)	365 000	0·31 (0·27–0·37)	63 000	0·05 (0·04–0·06)	230 000	0·19 (0·15–0·26)
Eastern Europe	432 000	0·22 (0·15–0·33)	298 000	0·14 (0·11–0·19)	117 000	0·05 (0·04–0·07)	607 000	0·27 (0·17–0·44)
Western Europe	1 141 000	0·34 (0·28–0·41)	938 000	0·26 (0·24–0·28)	641 000	0·18 (0·16–0·19)	1 318 000	0·35 (0·32–0·39)
Andean Latin America	62 000	0·11 (0·08–0·15)	76 000	0·14 (0·12–0·17)	145 000	0·26 (0·20–0·34)	153 000	0·28 (0·18–0·42)
Central Latin America	220 000	0·09 (0·07–0·13)	710 000	0·30 (0·23–0·39)	274 000	0·12 (0·09–0·14)	572 000	0·24 (0·17–0·35)
Southern Latin America	169 000	0·28 (0·19–0·43)	153 000	0·26 (0·20–0·33)	184 000	0·30 (0·21–0·42)	208 000	0·35 (0·22–0·54)
Tropical Latin America	286 000	0·14 (0·08–0·23)	708 000	0·33 (0·26–0·43)	920 000	0·43 (0·30–0·59)	491 000	0·23 (0·12–0·39)
North Africa and Middle East	735 000	0·14 (0·12–0·18)	1 145 000	0·24 (0·20–0·28)	691 000	0·14 (0·11–0·17)	1 374 000	0·29 (0·22–0·37)
High-income North America	1 755 000	0·60 (0·53–0·68)	717 000	0·23 (0·18–0·28)	1 604 000	0·53 (0·39–0·72)	959 000	0·30 (0·25–0·36)
Oceania	21 000	0·20 (0·13–0·31)	25 000	0·26 (0·18–0·37)	3000	0·03 (0·02–0·05)	19 000	0·20 (0·12–0·31)
Central sub-Saharan Africa	151 000	0·16 (0·11–0·23)	207 000	0·24 (0·17–0·34)	40 000	0·05 (0·03–0·07)	118 000	0·15 (0·09–0·23)
Eastern sub-Saharan Africa	589 000	0·16 (0·13–0·20)	798 000	0·24 (0·20–0·29)	105 000	0·03 (0·03–0·04)	488 000	0·15 (0·12–0·19)
Southern sub-Saharan Africa	149 000	0·18 (0·12–0·28)	188 000	0·24 (0·17–0·34)	37 000	0·05 (0·03–0·07)	157 000	0·21 (0·13–0·35)
Western sub-Saharan Africa	276 000	0·08 (0·06–0·11)	742 000	0·24 (0·19–0·32)	149 000	0·05 (0·04–0·07)	435 000	0·15 (0·11–0·20)
Women	4 696 000	0·14 (0·12–0·16)	6 256 000	0·18 (0·16–0·22)	2 090 000	0·06 (0·05–0·07)	4 698 000	0·14 (0·12–0·16)
Men	8 377 000	0·23 (0·20–0·27)	10 928 000	0·31 (0·27–0·37)	4 801 000	0·14 (0·12–0·16)	10 781 000	0·31 (0·27–0·35)
Overall	13 073 000	0·19 (0·17–0·21)	17 184 000	0·25 (0·22–0·28)	6 891 000	0·10 (0·09–0·11)	15 479 000	0·22 (0·20–0·25)

Prevalence estimates were standardised by age, by use of direct standardisation to the global standard population produced by WHO in 2001.[37]

Table 1: **Estimated number of cases and age-standardised and sex-standardised prevalence of cannabis, amphetamine, cocaine, and opioid dependence in 2010, by region**

as accidental poisonings. Deaths coded as accidental poisonings from drugs that were included in the drug use disorder category were narcotics, hallucinogens, sedative-hypnotic, or psychotropic drugs. These events were recorded as deaths from drug use disorders, unless they involved children. Further detail on the mortality modelling can be found in the appendix and elsewhere.[17]

Calculation of YLDs, YLLs, and DALYs

GBD 2010 estimated prevalent YLDs by multiplying prevalence estimates (ie, DisMod-MR prevalence output) by the disability weight. DisMod-MR prevalence estimates and burden estimates were stratified by sex, age, year (1990, 2005, and 2010), 187 countries, and 21 regions (appendix).

Using methods outlined elsewhere,[11,16] we also decomposed the change in DALYs between 1990 and 2010 (both estimated in this study) into effects of the following factors: population growth, population ageing, and changes in the global prevalence of drug dependence. We calculated DALYs in 2010 for each disorder on the basis of two scenarios: first, if population growth increased to the 2010 level but the population age and sex structure and DALY rates remained the same as in 1990; and second, if the population age and sex structure was set to the 2010 level while DALY rates were the same as they were in 1990.

When we report comparisons of prevalence and DALYs by country or region, we use age-standardised values with direct standardisation to the global standard population proposed by WHO in 2001.[37]

Comparative risk assessment

Overview

GBD 2010 also quantified burden attributable to drug use as risk factors for other health outcomes in a CRA.[12] We used literature reviews to estimate relative risks (RRs) for drug use as a risk factor for other health outcomes (eg, suicide or mental disorders). We used estimates of RR together with DisMod-MR exposure output to calculate population-attributable fractions. These fractions were multiplied by relevant cause-specific DALYs to calculate attributable burden.[12]

Cannabis use and schizophrenia

In the previous global CRA, cannabis use was not included as a risk factor for any disease because of concerns about the quality of the evidence.[9] In the intervening years, a steady increase in the number and quality of epidemiological studies on cannabis use and psychosis (or schizophrenia) suggested that cannabis use probably precipitates schizophrenia in susceptible individuals. We defined the exposure as use of cannabis weekly or more often in the previous year and modelled two possible effects of cannabis use on schizophrenia: first, increased disorder severity in individuals who used cannabis regularly who had schizophrenia (ie, more time spent in the acute state for schizophrenia as modelled in GBD 2010), and second, early onset of schizophrenia in regular cannabis users. We did two systematic literature reviews on the global epidemiology of weekly or more cannabis use[19,23] and schizophrenia.[38,39] We used estimates of cannabis use by age (for each year of age), sex, country, and year (1990, 2005, and 2010) and assumed that the prevalence of regular cannabis use was the same in individuals with and without schizophrenia. Estimates of the number of incident cases and the corresponding duration of schizophrenia by age, sex,

	Overall	Male individuals	Female individuals
Cannabis dependence			
YLDs	2057000 (1348000–2929000)	1323000 (849000–1936000)	734000 (481000–1063000)
YLLs	..	..	..
DALYs	2057000 (1348000–2929000)	1323000 (849000–1936000)	734000 (481000–1063000)
Amphetamine dependence			
YLDs	2596000 (1460000–3957000)	1657000 (928000–2562000)	939000 (522000–1502000)
YLLs	21000* (6000–15000)	15000* (4000–13000)	5000* (1000–4000)
DALYs	2617000 (1470000–4109000)	1673000 (933000–2653000)	944000 (524000–1520000)
Cocaine dependence			
YLDs	1085000 (633000–1639000)	760000 (443000–1168000)	325000 (187000–503000)
YLLs	25000* (7000–22000)	18000* (5000–17000)	6000* (2000–5000)
DALYs	1110000 (645000–1727000)	778000 (452000–1200000)	331800 (189500–518700)
Opioid dependence			
YLDs	7170000 (5143000–9258000)	5017000 (3550000–6536000)	2153000 (1484000–2877000)
YLLs	1981000 (1233000–3133000)	1460000 (771000–2419000)	522000 (287000–792000)
DALYs	9152000 (7066000–11443000)	6477000 (4860000–8298000)	2675000 (1963000–3453000)
Other drug use disorders			
YLDs	3503000 (2108000–5170000)	2306000 (1380000–3439000)	1198000 (723000–1821000)
YLLs	1555000 (1008000–2552000)	1114000 (590000–1941000)	441000 (249000–739000)
DALYs	5059000 (3555000–7042000)	3420000 (2390000–4798000)	1639000 (1128000–2348000)
All drugs			
YLDs	16411000 (11837000–21584000)	11063000 (7934000–14572000)	5349000 (3763000–7095000)
YLLs	3582000 (2225000–5683000)	2607000 (1340000–4409000)	975000 (538000–1510000)
DALYs	19995000 (15255000–25367000)	13670000 (10214000–17454000)	6324000 (4715000–8199000)

Data are mean (95% UI). YLDs=years of life lived with disability. YLLs=years of life lost. DALYs=disability-adjusted life years. *Mean value was outside of the 95% UI because the full distribution of 1000 draws is asymmetric with a long tail and therefore a few high values in the uncertainty distribution can raise the mean above the 97·5 percentile of the distribution.

Table 2: **Estimated YLDs, YLLs, and DALYs for drug use disorders, by sex, in 2010**

country, and year were based on the model for schizophrenia (appendix).

Opioid, amphetamine, and cocaine dependence as risk factors for suicide

We regarded opioid, amphetamine, and cocaine dependence as risk factors for suicide on the basis of a systematic search of studies reporting the suicide mortality rates in persons with such dependence.[12] We identified 21 cohort studies for opioid dependence, three studies for cocaine dependence, and one study for amphetamine dependence. We pooled relative-risk (RR) estimates for amphetamine and cocaine dependence to estimate an RR for psychostimulant dependence.[12] This RR was used with disorder-specific exposure data to calculate population attributable fractions for each disorder (appendix).

Injecting drug use as a risk factor for HIV, HBV, and HCV infection

We estimated the burden of disease from HIV, HBV, and HCV infection that was attributable to injecting drug use from systematic reviews of the epidemiological literature and exposure estimates.[22,40] The exposure was current or past year injecting drug use. We assessed specific consequences in terms of the following outcomes: HIV; the sum of acute hepatitis B, liver cancer secondary to hepatitis B, and cirrhosis of the liver secondary to hepatitis B; and the sum of acute hepatitis C, liver cancer secondary to hepatitis C, and cirrhosis of the liver secondary to hepatitis C. We used cohort data examining HIV and HCV seroconversion rates in injecting drug users with different levels of drug use (including abstinence) to examine differences in incidence (appendix).[3]

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Opioid and amphetamine dependence were the two most common forms of illicit drug dependence worldwide, although millions of people were also dependent on cannabis or cocaine (table 1). Most individuals dependent on drugs were male (64% each for cannabis and amphetamines and 70% each for opioids and cocaine).

Geographical distribution of individuals with drug dependence resulted from variations in prevalence and country populations (table 1). We estimated that 9·3 million individuals with amphetamine dependence were living in Asian regions (57·8% of all cases), with the highest prevalence estimates for southeast Asia and Australasia (table 1). 1·8 million people were estimated to be dependent on cannabis in high-income North America (13·4% of all cases), which also had a high population prevalence compared with other GBD regions (table 1). The highest prevalence of cocaine dependence was in high-income North America and Latin

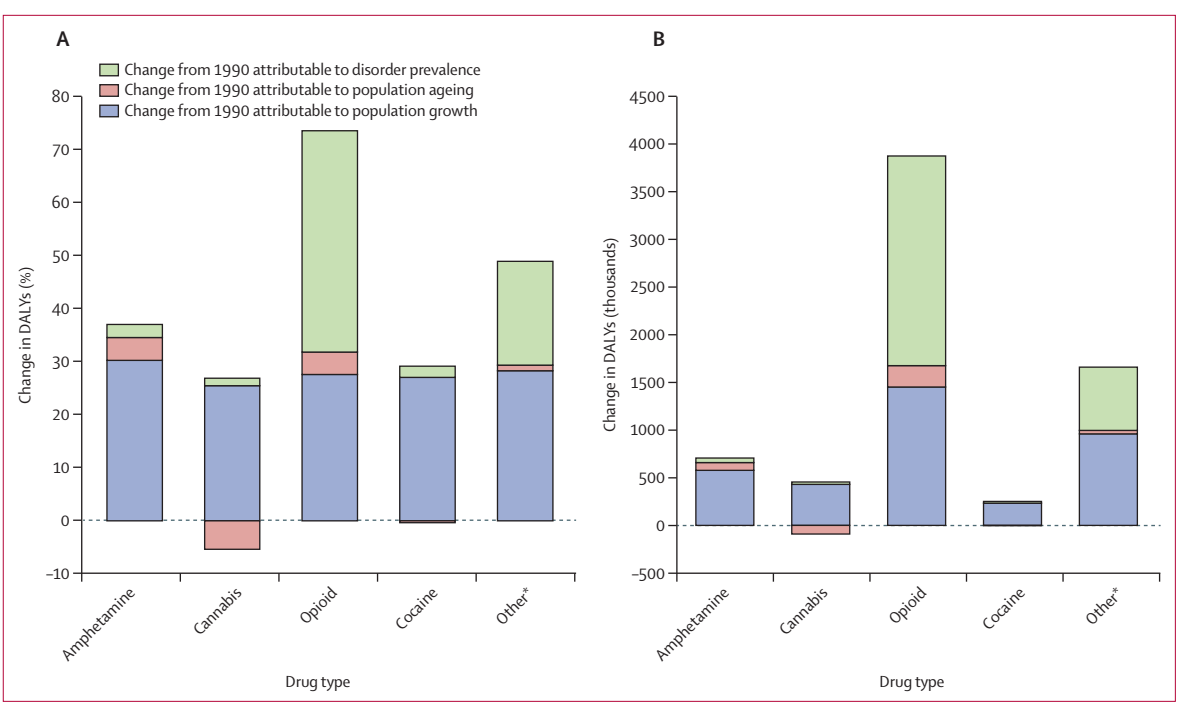


Figure 1: **Estimated change in crude DALYs attributable to illicit drug dependence between 1990 and 2010**
(A) Proportional change. (B) Absolute change. DALYs=disability-adjusted life years. *Non-specific category that could include any other illicit drug, but not alcohol or tobacco.

America. Australasia had among the highest prevalence of opioid dependence, although the largest overall populations were in east Asia and south Asia. The estimated prevalence of illicit drug dependence was generally lowest in African and Asian regions.

Drug use disorders directly accounted for almost 20 million DALYs in 2010 (table 2), 0·8% (95% UI 0·6–1·0) of all-cause DALYs. This figure is an increase of 52% from GBD 2010 estimates for 1990 (which used the same methods), when the direct burden accounted for 13·1 million DALYs (9·7 million–17·2 million) or 0·5% (0·4–0·7) of all-cause DALYs. Population growth accounted for 28%, population ageing 2%, and increased prevalence for the remaining 22% of the increase in DALYs between 1990 and 2010 (figure 1).

Substantial variation existed between drug types in the nature and magnitude of changes between 1990 and 2010 (figure 1). Much of the change over time could be attributed to population growth with the exception of opioid dependence, for which 42% of the increase was attributed to an increase in prevalence of that disorder between 1990 and 2010. Overall, the burden of opioid dependence increased by 74% across the period, amounting to almost 4 million additional DALYs in 2010.

For simplicity, the rest of the Results section focuses on 2010 findings. Table 2 shows that 69·4% (95% CI 59·4–76·8) of all drug disorder DALYs were explained by YLDs and 30·6% (23·2–40·6) by YLLs. Opioid dependence accounted for the highest proportion (45·9% [40·1–52·2]) of illicit drug burden and cocaine dependence accounted for the smallest burden (5·5% [3·8–7·5]; table 2). Cannabis dependence was not estimated to cause any YLLs but contributed about 2 million DALYs in the form of YLDs (10·3% of illicit drug dependence burden; table 2). Of about 78 000 deaths due to illicit drug use disorders in 2010, more than half (55%, 43 000 deaths) were attributable to opioid dependence.

About 70% of DALYs from opioid and cocaine use were accounted for by men, as were 64% of DALYs for amphetamine and cannabis dependence. This sex difference was apparent in all age groups (figure 2). Each of the drug use disorders followed a fairly consistent age pattern: DALYs rose sharply between the ages of 15 years and 24 years, peaked between 20 years and 30 years, and steadily declined thereafter, with the steepest decline in cannabis disorders (figure 2).

The proportion of all-cause DALYs attributed to drug dependence was more than 20 times higher in some regions than in others, with a higher proportion of burden noted in countries with higher incomes. Overall, the largest proportion of DALYs occurred in Australasia and high-income North America (appendix). The lowest proportion of overall DALYs attributable to illicit drugs occurred in central sub-Saharan Africa and western sub-Saharan Africa.

We also noted substantial variation in age-standardised DALY rates at a country level for the four major drug types (appendix). The rates for cocaine dependence burden were highest in the Americas and opioid dependence burden was high in western European countries, Australia, the USA, and Russia.

Regular cannabis use as a risk factor for schizophrenia was estimated to account for around 7000 DALYs worldwide (table 3), all of which were YLDs, through bringing forward the onset of schizophrenia and increasing time spent in the acute disease state. Injecting drug use as a risk factor for HIV accounted for about 2·1 million DALYs. Its contribution to HCV

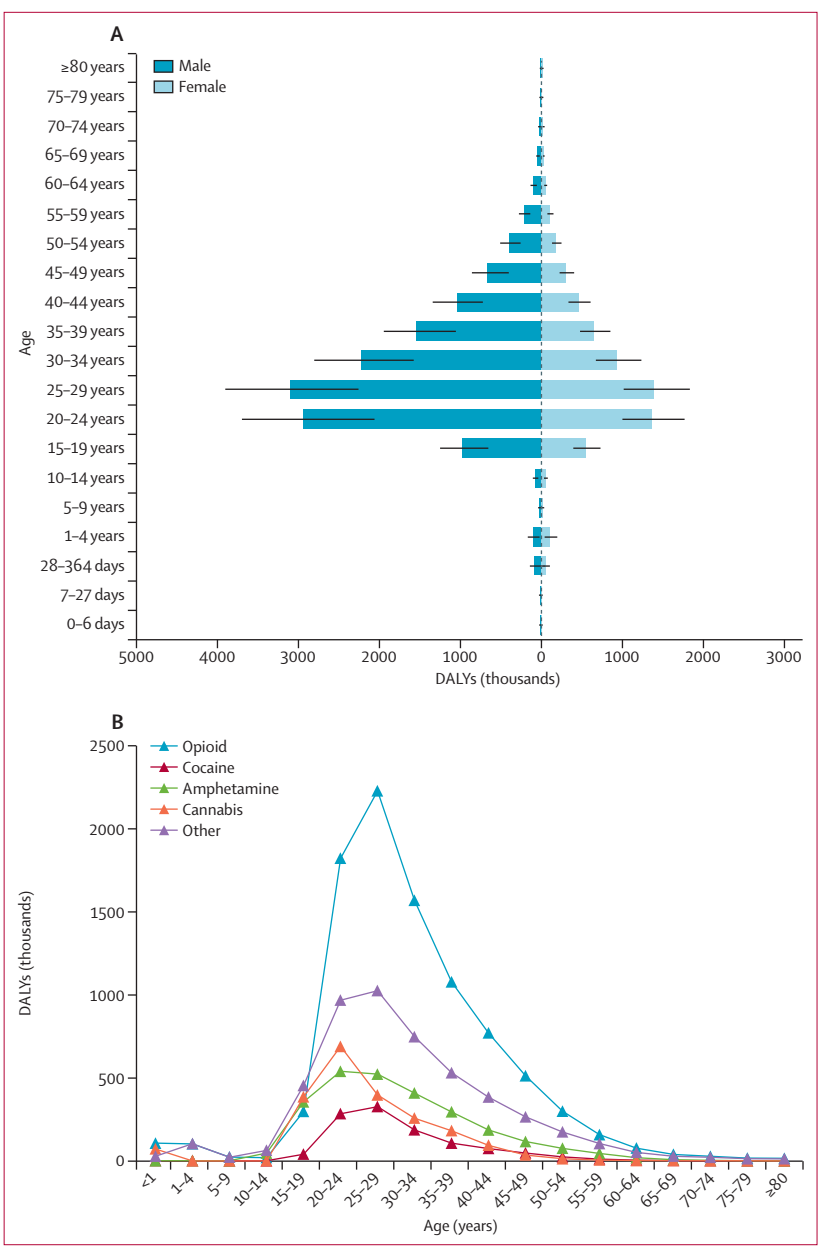


Figure 2: **Total burden (DALYs) of drug dependence by age and sex in 2010**
(A) DALYs attributable to drug dependence, by age and sex. (B) DALYs attributable to each type of drug dependence by age. DALYs=disability-adjusted life years.

accounted for a further 502 000 DALYs. Injecting drug use as a risk factor for hepatitis B made a smaller contributor to burden (63 000 DALYs). Suicide attributable to amphetamine, opioid, and cocaine dependence accounted for a substantial number of DALYs (table 3). For these latter outcomes most of the burden was attributable to years of life lost.

Figure 3 shows 2010 country-level DALY rates (age-standardised, per 100 000) for drug dependence as well as the risks of drug use considered previously. Countries with the highest overall illicit drug burden (>650 DALYs per 100 000) included, among others, the USA, UK, Russia, and Australia (for country-level DALY rates see appendix pp 15–18).

	Overall	Male individuals	Female individuals
Cannabis use as a risk factor for schizophrenia*			
DALYs	7000 (3000–13 000)	5000 (2000–10 000)	2000 (1000–4000)
YLDs	7000 (3000–13 000)	5000 (2000–10 000)	2000 (1000–4000)
YLLs	..	..	..
Injecting drug use as a risk factor for hepatitis C†			
DALYs	502 000 (286 000–891 000)	323 000 (183 000–578 000)	179 000 (93 000–336 000)
YLDs	8000 (4000–16 000)	5000 (2000–9000)	4000 (2000–8000)
YLLs	494 000 (281 000–878 000)	318 000 (180 000–570 000)	175 000 (90 000–330 000)
Injecting drug use as a risk factor for hepatitis B‡			
DALYs	63 000 (29 000–122 000)	46 000 (21 000–89 000)	17 000 (7000–34 000)
YLDs	1100 (400–2500)	700 (200–1600)	400 (100–1000)
YLLs	61 000 (28 000–120 000)	45 000 (21 000–88 000)	17 000 (7000–33 000)
Injecting drug use as a risk factor for HIV			
DALYs	2 117 000 (1 176 000–3 590 000)	1 461 000 (811 000–2 493 000)	657 000 (364 000–1 109 000)
YLDs	137 000 (69 000–246 000)	95 000 (46 000–176 000)	42 000 (21 000–77 000)
YLLs	1 980 000 (1 093 000–3 382 000)	1 366 000 (755 000–2 348 000)	615 000 (340 000–1 044 000)
Opioid dependence as a risk factor for suicide			
DALYs	671 000 (329 000–1 173 000)	441 000 (208 000–793 000)	230 000 (95 000–435 000)
YLDs	7000 (3000–13 000)	4000 (2000–8000)	3000 (1000–5000)
YLLs	664 000 (324 000–1 163 000)	437 000 (205 000–787 000)	228 000 (93 000–431 000)
Cocaine dependence as a risk factor for suicide			
DALYs	324 000 (109 000–682 000)	225 000 (74 000–481 000)	99 000 (29 000–219 000)
YLDs	3000 (1000–7000)	2000 (1000–4000)	1000 (0–3000)
YLLs	320 000 (107 000–675 000)	223 000 (73 000–477 000)	97 000 (29 000–217 000)
Amphetamine dependence as a risk factor for suicide			
DALYs	854 000 (291 000–1 791 000)	554 000 (186 000–1 172 000)	300 000 (88 000–656 000)
YLDs	10 000 (3000–20 000)	6000 (2000–13 000)	4000 (1000–8000)
YLLs	844 000 (287 000–1 772 000)	548 000 (183 000–1 162 000)	296 000 (87 000–650 000)

Data are mean (95% UI). *Modelled with two effects; an earlier onset of schizophrenia in people who use cannabis regularly; and increased time spent in the acute state of schizophrenia. †Included attributable acute hepatitis C, liver cancer secondary to hepatitis C, and cirrhosis secondary to hepatitis C. ‡Included attributable acute hepatitis B, liver cancer secondary to hepatitis B, and cirrhosis secondary to hepatitis B.

Table 3: **Estimated DALYs attributable to illicit drug use as a risk factor for other health outcomes, 2010**

Discussion

To our knowledge, this study is the first attempt to estimate the global, regional, and country level prevalence of dependence and burden of disease attributable to drug dependence for four major illicit drug types (amphetamines, cannabis, cocaine, and opioids). Several key findings emerged. First, age and sex patterns of dependence and burden were striking. All forms of drug dependence and disease burden were highest in men aged 20–29 years. These disorders adversely affect young adults at a crucial time in their lives. At a global level, illicit drug dependence was the eighth largest contributor to disability in male individuals, up from tenth in 1990.[16]

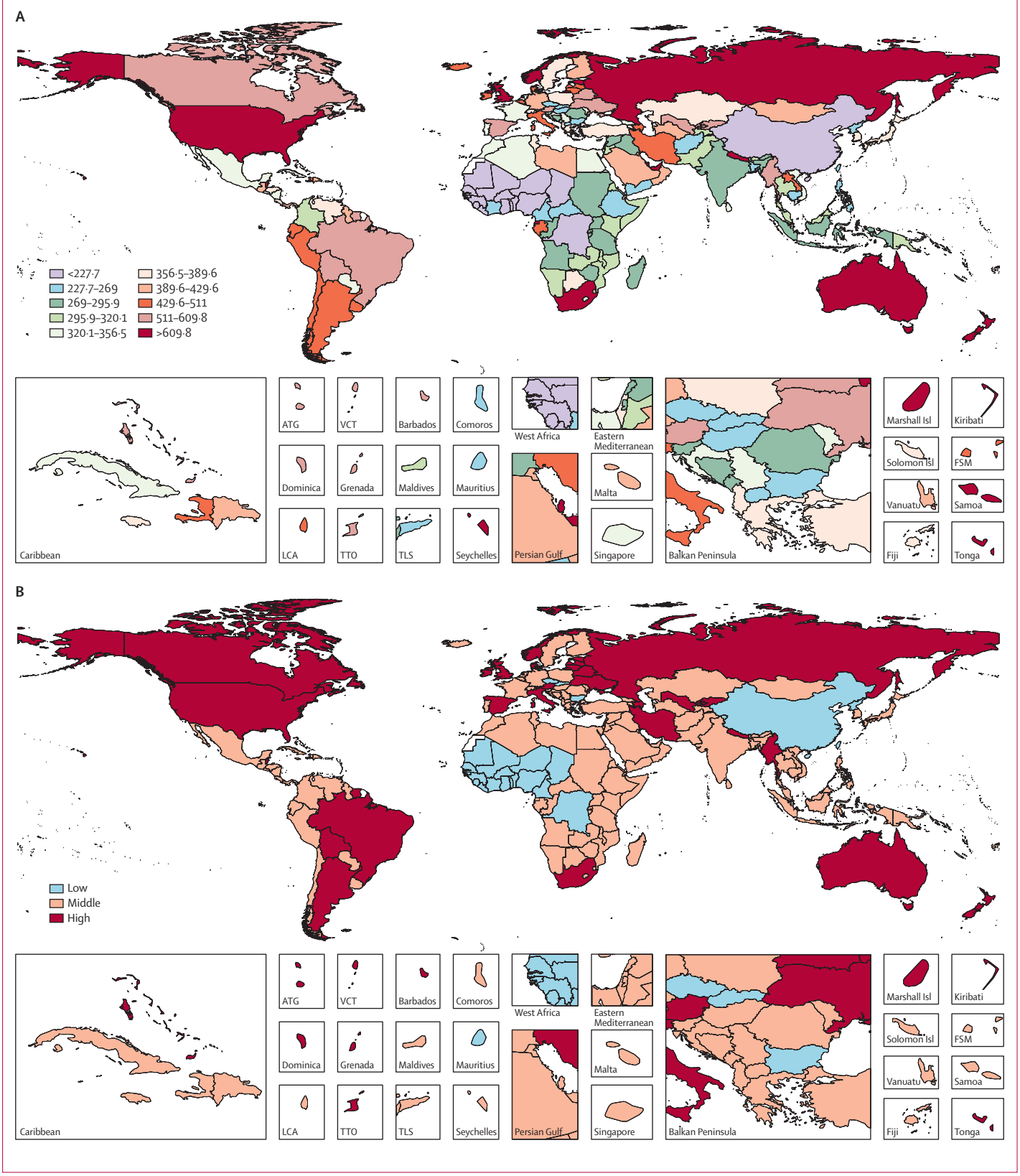
Second, although cannabis is by far the most commonly used illicit drug worldwide,[10,41] the prevalence of cannabis dependence was lower than that for amphetamines and opioids. Cocaine dependence had the lowest estimated prevalence, and seemed most geographically concentrated in North America and South America.

The highest estimated global burden was attributable to opioid dependence (9·2 million DALYs, or almost half of direct illicit drug burden). This finding was attributable to opioid's substantial contribution to premature mortality, high disability weight, and the comparatively large population of dependent opioid users. The opioid DALY estimates were around eight times those for cocaine dependence, and 4·5 times those for cannabis dependence.

The key findings from estimates of other outcomes of illicit drug use (from the CRA component) were as follows. First, regular cannabis use made a very small contribution to disease burden through its contribution as a risk factor for schizophrenia (~7000 DALYs globally). Second, by contrast, injecting drug use had a

Figure 3 (next page): **Age-standardised disability-adjusted life years (DALYs) attributed to illicit drug use in 2010**

(A) Age-standardised DALYs per 100 000 population. (B) Age-standardised DALYs compared with the global mean. Analyses include DALYs attributable to cannabis, cocaine, amphetamine, opioid, and other drug dependence, as well as the following risks of illicit drug use: cannabis use as a risk factor for schizophrenia; injecting drug use as a risk factor for HBV, HCV, and HIV; and opioid, cocaine, and amphetamine dependence as risk factors for suicide. Low=significantly lower than the global mean. Middle=not significantly different from the global mean. High=significantly higher than the global mean. ATG=Antigua and Barbuda. VCT=Saint Vincent and the Grenadines. Isl=Islands. FSM=Federated States of Micronesia. LCA=Saint Lucia. TTO=Trinidad and Tobago. TLS=Timor-Leste.


A
<227·7
227·7–269
269–295·9
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320·1–356·5
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389·6–429·6
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511–609·8
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Caribbean
ATG
VCT
Barbados
Comoros
West Africa
Eastern Mediterranean
Dominica
Grenada
Maldives
Mauritius
Malta
LCA
TTO
TLS
Seychelles
Persian Gulf
Singapore
Balkan Peninsula
Marshall Isl
Kiribati
Solomon Isl
FSM
Vanuatu
Samoa
Fiji
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Solomon Isl
FSM
Vanuatu
Samoa
Fiji
Tonga

notable additional contribution to burden of disease by increasing the risks of infection by the three modelled blood-borne viruses. HIV was the largest contributor (2·1 million DALYs), with attributable HCV, estimated for the first time, contributing an additional 0·5 million DALYs. Third, suicide was another significant contributor to illicit drug burden because it is a common cause of death in regular users of opioids, cocaine, or amphetamines.

Overall, we estimated illicit drugs to be the cause of 0·9% of DALYs worldwide in 2010, the 19th leading risk factor overall, compared with 6·3% (5·5–7·0) for tobacco smoking (including second-hand smoke) and 3·9% (3·5–4·3) for alcohol.[12]

Opioid dependence and injecting drug use are significant contributors to global burden and much of this burden could be averted by scaling up needle and syringe programmes, opioid substitution treatment, and HIV antiretroviral therapy.[42,43] Accumulating evidence suggests that not only HIV[42] but also HCV[43] burden can be reduced through needle and syringe programmes; HCV burden can also be decreased by effective treatment of chronic HCV infection.[43] The release of more effective and less toxic HCV drugs is expected to strikingly improve what have been extremely low rates of HCV treatment uptake in people who inject drugs.[44]

Effective responses to reduce burden attributable to stimulant dependence are not as clear as those for opioid and injecting drug use. Various pharmacological interventions have been trialled for treatment of amphetamine and cocaine dependence without production of effective agonist pharmacotherapies.[45] Behavioural interventions are effective for treatment of psychostimulant and cannabis dependence.[46,47] Much more research is needed, however, into how to scale up these behavioural approaches to reduce the population prevalence of such disorders.[47]

Our study had limitations. We did not explicitly estimate the prevalence and disease burden related to MDMA (3,4-methylenedioxy-methamphetamine or ecstasy), hallucinogens, inhalants, or the non-medical use of benzodiazepines, because comparatively little information exists on prevalence of use and quantification of harms. However, the inclusion of the other drug use disorders category was a crude attempt to capture this burden.

We did not separately estimate burden attributable to any form of ICD-10 harmful use or DSM-IV abuse, because of concerns about the validity of these diagnostic categories, limitations in existing epidemiological data, and the probable low disability caused by these disorders. Future updates of the GBD estimates might reconsider this decision. Any update will also need to deal with the effects of changes to the fifth revision of the DSM, which defines use disorder with three levels of severity, and no longer distinguishes between abuse and dependence.

Although this study made use of advanced modelling to impute results when data were not available, and propagate uncertainty, a substantial amount of research is needed to document even the most basic epidemiological parameters for drug dependence in most countries. Until such work is done, much uncertainty will remain around the exact size of global disease burden attributable to illicit drug use.

Our estimates might have been affected by changes in classification systems used to diagnose dependence over time. We believe, however, that the absence of data is responsible for much more of the uncertainty than are diagnostic changes.

As noted previously, the causes of drug-related deaths are often misattributed. However, research on the most common forms of misattribution was too limited to produce a credible redistribution scheme apart from the codes in ICD for accidental poisoning, as described. Future iterations of the GBD will need to take account of surveys validating causes of death to better capture miscoded deaths related to drugs.

The much improved derivation of new disability weights,[15] involving surveys of the general population, were not without their limitations. As discussed elsewhere,[15] whether brief lay descriptions can accurately capture the complexity of disability due to drug dependence is uncertain. Considerations other than health status might also have influenced respondents' views of which state was healthier, because describing drug use disorders without mentioning the specific drug was difficult.

Our estimates of illicit drug burden are probably conservative because various potential health outcomes of illicit drug use were not included in our estimates. First, although systematic reviews suggested increased risks of unintentional injuries and homicide in opioid, cocaine, and amphetamine dependence, they were not included because confounding had not been well addressed in studies of these outcomes. This condition excluded some of the most common causes of death among illicit drug users from our estimates.[28,29] Second, the evidence for a causal association was regarded as too weak to include a range of possible outcomes of cannabis use—namely, suicide, cancer, and accidental injuries.[25] Finally, many putative consequences of illicit drug use exist for which we did not attempt to quantify the magnitude of any possible association, because the level of evidence was too low.[10] These consequences included the incidence of mental disorders, myocardial infarction, and cardiovascular pathology. Well-designed prospective studies are needed for these consequences of illicit drug use that properly control for key forms of confounding.

Finally, in GBD, the notion of disability was intended to capture only the health loss of an individual. It did not include social or other effectors such as the family, social, and economic consequences of mental and substance use disorders. To that extent, our estimates of illicit drug disease burden are part estimates of the adverse effects that illicit drug use has upon society.

Illicit drug use is an important contributor to the global disease burden, larger than many mental disorders and greater than all maternal conditions combined.[11] Our estimates of this burden can be improved with future iterations of GBD, but we now have the first global picture of this cause of health loss. Moreover, much can be done to reduce this burden. Although we have fewer means of responding to some causes of burden, such as cocaine and amphetamine dependence, well-evaluated and effective interventions can substantially reduce two major causes of burden—opioid dependence and injecting drug use. The challenge will be to deliver these efficiently and on a scale needed to have an effect on a population level.

Contributors

LD, HAW, AJB, AJF, and FJC worked with the members of the Global Burden of Diseases, Injuries, and Risk Factors Study core group (TV and CJLM) to undertake the systematic reviews, the epidemiological modelling, and prepare the burden estimates. RB provided the analyses on severity distributions and NJ analysed mortality data for drug use disorders. GF and REE provided input into the comparative risk assessment component. LD prepared the first draft of the paper with assistance from HAW, AJB, AJF, FJC, and WDH; all other authors contributed to subsequent drafts. All authors contributed to and approved the final report.

Conflicts of interest

WDH has been a member of the International Narcotics Control Board since May 2012: this membership did not have a role upon the conduct of this work or the decision to submit the manuscript. LD has received untied educational grant funding from Reckitt Benckiser (RB) to conduct postmarketing surveillance of buprenorphine-naloxone in Australia. The design, conduct, reporting, and interpretation of the results of that work were determined by the study investigators. RB had no knowledge of the present report.

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For **details of the contributors** see http://www.gbd.unsw.edu.au/gbdweb.nsf/page/Contribution of Data

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