

Global burden of amphetamine, cannabis, cocaine and opioid use in 204 countries, 1990–2023: a Global Burden of Disease Study

Received: 2 January 2025

Accepted: 20 November 2025

Published online: 16 January 2026

 Check for updates

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Drug use disorders (DUDs) are emerging global public health challenges. Here we investigated the global and regional estimates of the prevalence and burden of DUDs, including amphetamine, cannabis, cocaine and opioid use disorders, from 1990 to 2023 for 204 countries and territories by using the Global Burden of Disease Study 2023. Overall, trends in global age-standardized disability-adjusted life-years of DUDs increased from 169.3 (95% uncertainty interval (95% UI), 134.4–203.9) per 100,000 people in 1990 to 212.0 (95% UI, 179.2–245.6) in 2023. In 2023, both prevalence and burden of DUDs were higher in high-income countries, particularly in the USA. The most prevalent DUDs in 2023 were cannabis use disorder (age-standardized prevalence, 270.8 (95% UI, 201.7–350.0) per 100,000 people) and opioid use disorder (205.9 (95% UI, 178.7–235.0)). Particularly, opioid use disorder showed a nearly twofold increase in prevalence and burden between 1990 and 2023. In 2023, compared with countries where cannabis use was illegal, countries permitting both recreational and medical cannabis use had higher prevalence rates for all types of DUDs. Proactive and effective policies are essential to mitigate the increasing global burden of DUDs.

Drug use disorders (DUDs) present substantial public health challenges, accounting for 1.3% of all-cause disability-adjusted life-years (DALYs) globally¹. Among the most globally prevalent DUDs are amphetamine use disorder (AUD), cocaine use disorder (CUD), cannabis use disorder (CAUD) and opioid use disorder (OUD)². Illicit drugs in most countries include some opioids, such as heroin, morphine, opium and other pharmaceutical opioids; cannabis; amphetamines; and cocaine. Therefore, we refer to all use of drugs, including amphetamine, cocaine, cannabis

and opioids, as drug use. Previous studies suggested that OUD is the largest contributor to burden, and the prevalence and burden of DUDs vary substantially across regions of the world¹.

Drug dependence, a core aspect of DUDs, is defined by a compelling desire for drugs, loss of control over their use, withdrawal symptoms and tolerance. These criteria are specified by definitions from the International Classification of Diseases 10th Revision (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)¹.

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Drug use also accompanies risks of various adverse health outcomes. For instance, injecting drugs with nonsterile equipment poses risks of HIV, viral hepatitis, other infectious diseases and injection-related injuries³.

The COVID-19 pandemic has seen a surge in prevalence of DUDs between 2019 and 2021, particularly in North America, where an opioid crisis has profoundly affected the region^{4,5}. The pandemic period showed a reduction in hospital admissions, coinciding with a surge in mortality due to drug overdose⁴. The increase in telehealth prescriptions and decreased accessibility of healthcare during the pandemic may have inadvertently contributed to increases in burden of DUDs⁴. These recent shifts are likely to influence international trends in DUDs, highlighting need to understand global and longitudinal trends in prevalence and burden. However, previous studies were limited by their focus on the early phase of the pandemic, typically up to 2021, not enough to capture the impact of COVID-19 fully, and by their predominant emphasis on Western countries, particularly North America^{4,5}.

This study utilized the Global Burden of Disease Study (GBD) 2023 to provide insights into global trends in the prevalence and burden of DUDs from 1990 to 2023 and assessed the impact of potential contributors such as the COVID-19 pandemic and cannabis legalization status, which is crucial for understanding their impact on health systems and informing effective intervention strategies.

Results

Global age-standardized prevalence and DALYs (per 100,000) of DUDs in 2023

Overall, age-standardized DALYs of DUDs increased from 169.3 per 100,000 people (95% uncertainty interval (95% UI), 134.4–203.9) in 1990 to 212.0 (95% UI, 179.2–245.6) in 2023 (Supplementary Table 1 and Extended Data Fig. 1). Across all DUDs, high-income countries of GBD regions, particularly in the USA, Canada and Australia, showed higher prevalence and DALY rates (Supplementary Tables 1–5). In 2023, the most prevalent DUDs globally were CAUD (21.8 million estimated cases; prevalence, 270.8 cases per 100,000 people (95% UI, 201.7–350.0)) and OUD (17.0 million cases; 205.9 (178.7–235.0)), particularly in high-income countries. AUD (9.2 million cases; prevalence, 115.2 cases per 100,000 people (95% UI, 84.7–152.7)) and CUD (4.8 million cases; 59.1 (47.4–74.3)) were less common, with CUD being the least prevalent (Fig. 1 and Supplementary Table 1).

In 2023, global DALYs of OUD were the highest (DALYs, 153.7 per 100,000 people (95% UI, 127.4–180.0)). High-income countries, especially the USA and Canada, showed the highest OUD-attributable DALYs of 708.9 per 100,000 people (95% UI, 587.1–833.8; Supplementary Table 2). Globally, AUD and CUD contributed less to the burden, with CAUD having the lowest burden among DUDs (DALYs, 7.8 per 100,000 people (95% UI, 4.8–12.3); Supplementary Table 1).

The DALYs attributable to DUDs showed substantial regional variation (Fig. 1 and Supplementary Tables 2–5). The highest drug-attributable burdens were in high-income countries, with DALYs attributable to AUD (DALYs, 61.1 per 100,000 people), CAUD (DALYs, 20.0), CUD (DALYs, 85.7) and OUD (DALYs, 708.9). Extended Data Fig. 2 and Supplementary Table 6 show the top 30 countries with the highest DALYs of DUDs. In 2023, the USA had the highest burden attributable to DUDs (DALYs, 2,229.8 per 100,000 people), with specific AUD- and OUD-attributable DALY rates also among the highest. Most of the top 30 countries had the highest DALY of OUD.

Global trends in prevalence and DALYs, 1990–2023

Figure 2 illustrates trends in age-standardized prevalence and DALYs from 1990 to 2023. In the longitudinal trend analysis, the global prevalence of CAUD was highest among DUDs, with stable trends from 1990 to 2023 (prevalence, 285.7 cases per 100,000 people (95% UI, 211.9–373.4) in 1990; 270.8 (201.7–350.0) in 2023; Supplementary Table 1).

However, the global DALYs of CAUD were lowest among DUDs during this period. Conversely, overall global DALYs of OUD were highest and showed an increasing trend from 1990 to 2023 (Fig. 2 and Supplementary Table 1).

Extended Data Fig. 3 shows age-standardized DALYs per 100,000 people by GBD regions from 1990 to 2023. Percentage change in DALYs for DUDs by high-income countries from 1990 to 2023 showed pronounced increases in all DUDs, including AUD, CUD and OUD, compared with other regions, except for CAUD (Extended Data Fig. 4). The high DALYs observed in high-income countries aligned with the findings that countries with a high Socio-demographic Index (SDI) exhibit the highest total burden of DALY rates across all DUDs (Extended Data Fig. 5 and Supplementary Table 7).

Distributions of DALYs for DUDs by age and sex

Across all DUDs, age-standardized DALYs were higher for males than females (Fig. 3 and Supplementary Table 8). The overall burden attributable to DUDs was higher in males compared with females, mainly because of CUD and OUD, whereas for AUD and CAUD, the difference between the sexes was minimal. For both sexes, the highest DALYs were for OUD across all age groups, with maximum values at groups aged 30–34 years in Supplementary Table 8.

Associations between DUDs

Some individuals with DUDs reported a combination of each DUD (Fig. 4). The chord diagram in Fig. 4 shows associations between the four types of DUDs. In 2023, OUD had significant associations with all three other DUDs, including AUD (β , 6.46; $P < 0.0001$), CAUD (β , 5.50; $P < 0.0001$) and CUD (β , 1.31; $P < 0.0001$), across 204 countries. Particularly, the strongest association among DUDs was shown in the relationship between OUD and AUD. Furthermore, CAUD co-occurred with other DUDs, including AUD (β , 1.04; $P < 0.0001$), CUD (β , 2.57; $P < 0.0001$) and OUD (β , 5.50; $P < 0.0001$; Fig. 4).

Burden attributable to DUDs by cannabis legalization status

Figure 5 illustrates the age-standardized prevalence and DALYs per 100,000 people for DUDs across countries with different statuses of cannabis legalization in 2023. Significant differences were observed in the burden of DUDs depending on the country's cannabis legalization status (Fig. 5 and Supplementary Table 9). Compared with countries where cannabis use was illegal ($n = 125$), countries permitting both recreational and medical cannabis use ($n = 33$) had higher prevalence for all types of DUDs, including AUD (49.34 per 100,000 people (interquartile range, 104.21) versus 141.85 (172.82), $P < 0.001$), CAUD (197.25 (158.74) versus 436.19 (336.45), $P < 0.001$), CUD (10.04 (23.63) versus 88.58 (106.45), $P < 0.001$) and OUD (90.21 (88.59) versus 120.46 (106.55), $P < 0.001$). Similarly, DALYs attributable to DUDs were higher in countries with more permissive cannabis policies, including those allowing medical or recreational use, compared with countries where cannabis use remained illegal.

Change in the burden of DUDs between pre-pandemic and during COVID-19

Globally, the prevalence of AUDs showed a decreasing trend in the pre-pandemic period and this trend was maintained during the COVID-19 period (change in prevalence: -1.5% in 2015–2019 and -1.3% in 2019–2023; Fig. 6). However, countries with high SDI reported increasing trends in AUD prevalence both before the pandemic and during the COVID-19 period. Increasing trends in CUD and OUD prevalence were observed during the pre-pandemic period, particularly in countries with high SDI. During the pandemic, CUD and OUD prevalence were both increasing; however, the magnitude of increases was halted during the pandemic period (CUD, 6.5% in 2015–2019 versus 3.2% in 2019–2023; OUD, 13.3% in 2015–2019 versus 4.5% in 2019–2023).

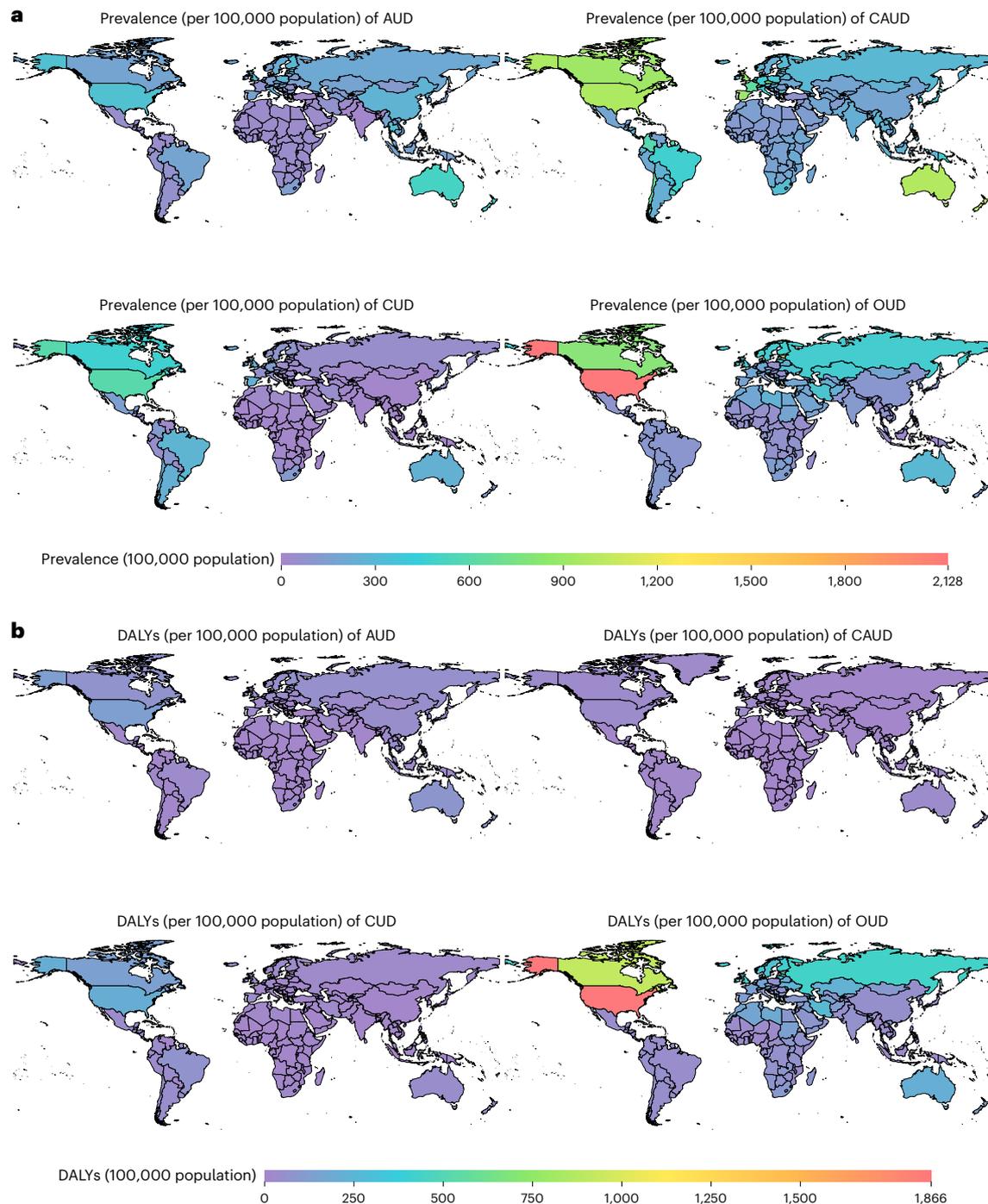


Fig. 1 | World map of age-standardized prevalence and DALYs per 100,000 population attributable to DUDs for both sexes across 204 countries in 2023. a, Prevalence attributed to DUDs. b, DALYs attributed to DUDs. The color

gradient, ranging from purple (low value) to red (high value), indicates the magnitude of each estimate. Data from the Institute for Health Metrics and Evaluation.

Decomposition analysis

Using Das Gupta decomposition analysis, changes in the number of DALYs cases between 1990 and 2023 were decomposed into three components, including population aging, epidemiological change and population growth (Extended Data Fig. 6). From 1990 to 2023, increases in global DALYs of AUD were modest, which was attributed to increases in population growth offsetting decreases in population aging and epidemiological changes (Supplementary Table 10). Similar observations were also observed for DALYs of CAUD. Furthermore, the overall increases in DALYs of CUD and OUD were both attributed to epidemiological change and population growth.

Discussion

The updated global estimated burden of DUDs from 1990 to 2023 in our study aligned with previous findings, indicating an increase in the prevalence of DUDs since 1990¹. In 2023, the age-standardized prevalence and DALYs for all DUDs were highest in high-income countries, particularly in the USA, Canada and Australia. While CAUD and OUD were the most prevalent DUDs, CAUD contributed the least to burden, whereas OUD accounted for the greatest disease burden with the highest DALYs. Particularly, the prevalence and burden attributable to OUD nearly doubled between 1990 and 2023. Association analyses further exhibited that OUD was associated with all three other DUDs, including

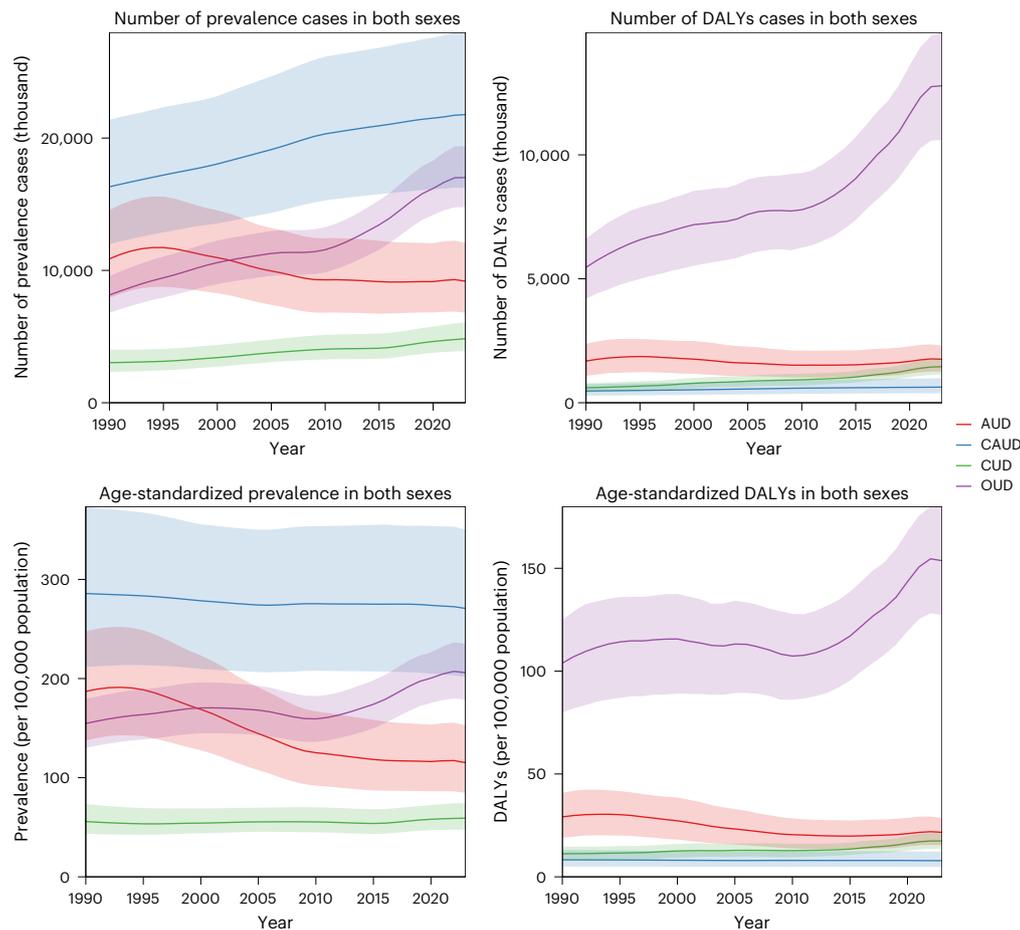


Fig. 2 | Global trends in prevalence and DALYs (numbers and age-standardized rate per 100,000 population) between 1990 and 2023, with 95% UI for the comparison of DUDs by substance type. Solid lines represent median estimates, and shaded areas indicate UIs defined by the 2.5th and 97.5th percentiles of repeated draws across plausible parameter ranges.

AUD, CAUD and CUD. Countries permitting both recreational and medical cannabis use reported higher prevalence of all DUDs and higher DALYs compared with countries where cannabis use remained illegal. These findings provide insights to develop proactive interventions to address the increasing burden of DUDs across the globe.

Disease burden attributable to DUDs varied across geographical locations and was highest in high-income countries, particularly the USA, Canada and Australia. The high attributable burden in high-income countries, despite a substantially higher proportion of health expenditure to address these issues, deserves attention. In the USA and Canada, social norms around drug use may be more permissive, with drug use frequently normalized or even glamorized through social media and celebrity endorsement^{6,7}. Societal acceptance likely contributes to higher baseline demand for drugs, which, in turn, leads to a higher disease burden attributable to DUDs⁸. Particularly in the USA, irresponsible pharmaceutical marketing, over-prescription by healthcare providers and systemic issues within the healthcare insurance system have further exacerbated the burden of DUDs^{6,7,9,10}.

However, relatively lower prevalence in other regions should not be taken as a sign of lesser concern. Countries with lower SDI may report relatively lower prevalence and burden related to diseases, potentially due to underreporting issues influenced by societal and cultural attitudes towards drug use, as well as distinct legal definitions across countries^{11,12}. For instance, region-specific substances such as khat, kratom, raw opium and other locally used drugs, commonly associated with DUDs, are not fully captured in current estimates. In addition, limited surveillance capacity, weak law enforcement, social stigma, lack

of awareness about substances and tolerance of drug-related activities in regions where drug production is a major economic activity can lead to underreporting or misclassification of DUDs, particularly across the African, South American and South Asian continents¹³.

This study indicated that the disease burden of DUDs varies across regions and by the type of drug. Higher prevalence and DALYs in the USA, Canada, the UK and Finland may be attributed to better access to drugs, higher societal acceptance of drug use and more resources to obtain substances¹. In addition, these countries possess more robust health surveillance systems, allowing for better detection and reporting of DUDs. In the USA and Canada, the opioid crisis was driven by prescription opioid practices, referred to as the ‘first wave’ in the 1990s^{9,10}. The increasing trends in OUD burden were dominated by increased heroin use during the ‘second wave’ (2010–2013)^{9,10}. Since 2013, the ‘third wave’ is characterized by a shift toward synthetic opioids (primarily illegally manufactured fentanyl and its analogs), leading to an accelerated OUD burden¹⁴. The USA, partly due to availability of synthetic opioids such as fentanyl, faces a substantial disease burden attributable to OUD, nearly double that of Canada, which has the second highest disease burden^{9,10}.

Increased potency of synthetic opioids exacerbates the current opioid crisis, with aggressive marketing strategies from the emergence of Dark Web cryptomarkets^{6,7}. For example, fentanyl is 30 to 40 times more potent than heroin and can have widely varying strengths from three times that of morphine (acetyl-alpha-methyl fentanyl) to 10,000 times (carfentanyl)⁶. Rapid emergence of synthetic opioids, driven by more efficient synthesis methods, alleviated regulatory environments

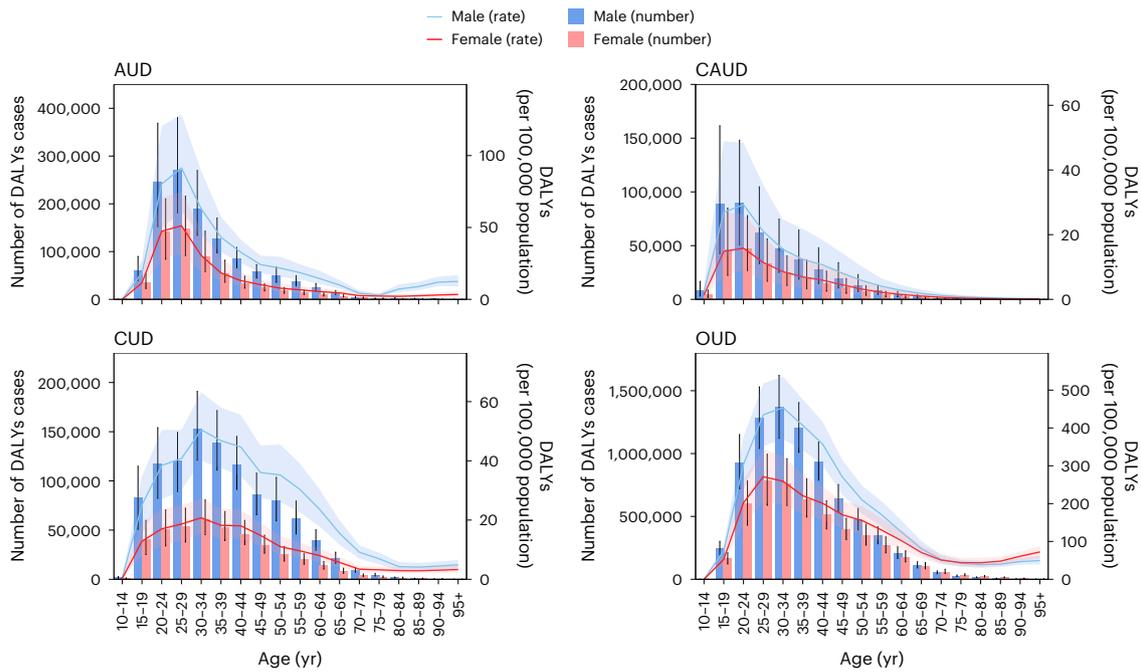


Fig. 3 | Distribution of DALYs numbers and rates per 100,000 population for 2023, with 95% UI for DUDs by age group and sex. Bars represent the number of DALYs cases, and lines indicate DALY rates per 100,000 population for AUD,

CAUD, CUD and OUD. Error bars and shaded areas represent 95% UIs defined by the 2.5th and 97.5th percentiles of repeated draws. The number of cases for AUD and OUD in the 10–14 age group was not available, as this was not estimated.

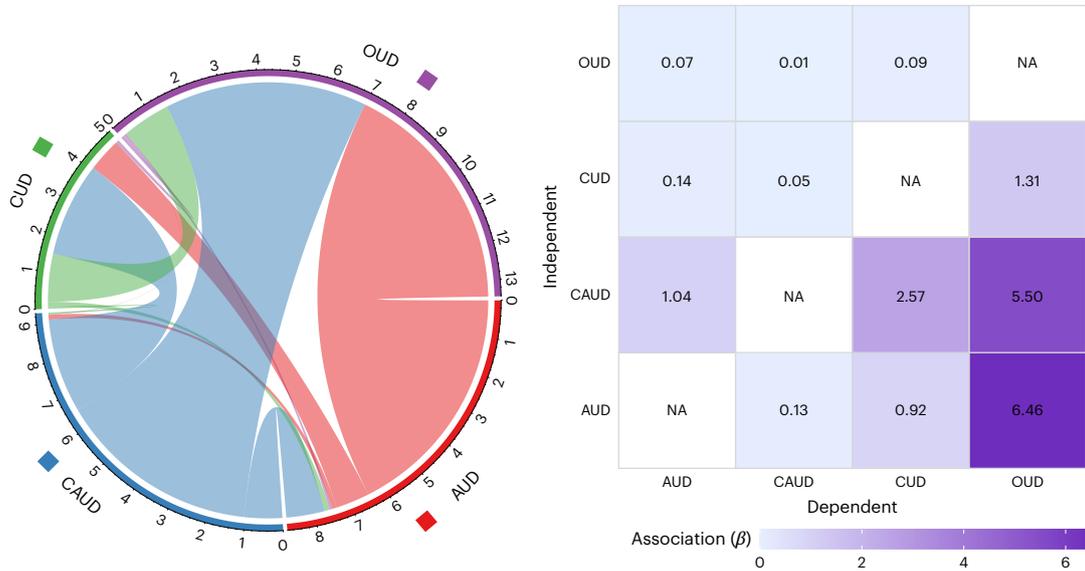


Fig. 4 | Age-standardized DALYs per 100,000 population for DUDs attributed to each drug disorder in 2023, adjusted for the legalization level of cannabis use across 204 countries. Regression coefficients (β) from linear regression models quantify associations between age-standardized DALYs per 100,000

population for each disorder (AUD, CAUD, CUD and OUD). Models were adjusted for country-level cannabis use legalization status based on 2021 classifications across the 204 countries. NA, not available.

in source countries (for example, China) and advanced internet commerce, is likely to further intensify the OUD burden¹⁵.

Previous studies have raised concerns about the growing trend of combined use of opioids with stimulants such as methamphetamine and cocaine, which can lead to more severe health outcomes^{16,17}. We also showed significant associations between AUD and OUD, and CUD and OUD, in 2023^{18,19}. Likewise, polydrug use, particularly co-use of opioids with stimulants, is increasingly reported^{16,17}. A previous survey-based cohort study reported that methamphetamine use tripled among those who reported heroin use from 9.0% in 2015 to 30.2% in 2017²⁰,

partly implying the rise in stimulant-related deaths, which is especially a concern when the drug was co-used with fentanyl. In the USA, deaths driven by synthetic opioids co-occur with deaths attributable to cocaine, methamphetamine and other stimulants^{6,16}. However, further research is needed to fully elucidate potential consequences of shifting drug use behaviors toward the co-use of opioids with stimulants.

CUD burdens were highest in high-income countries and Latin America. This pattern reflected that Latin America acted as major production and trafficking regions of cocaine, such as Colombia and Bolivia (top global producers of cocaine) and Mexico, Guatemala and

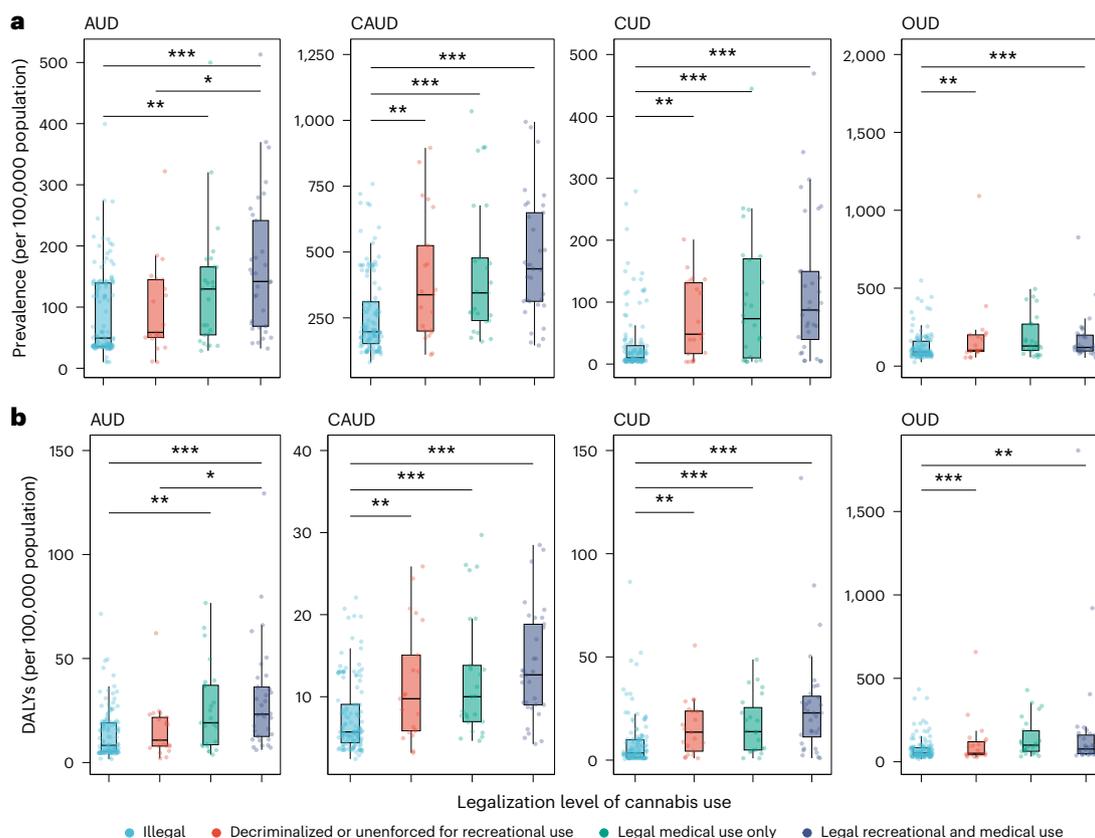


Fig. 5 | Age-standardized prevalence and DALYs per 100,000 population by DUDs and cannabis legalization level across 204 countries in 2023. a, Age-standardized prevalence among cannabis legalization level. **b,** Age-standardized DALYs among cannabis legalization level. Countries were classified according to their cannabis use legalization status in 2021 as follows: illegal in 125 countries, decriminalized or unenforced for recreational use in 21 countries, legal for

medical use only in 25 countries and legal for both recreational and medical use in 33 countries. Post hoc analysis using Dunn's test (two-sided) was conducted to assess differences among legalization groups, with significance levels defined as $***P < 0.001$, $**P < 0.01$ and $*P < 0.05$. Boxplots show the median at the center, the 25th–75th percentile range, and whiskers extending to values within 1.5× the interquartile range.

Honduras (key transit points)², and high-income countries served as primary consumer markets. Consequently, the top five regions for CUD disease burden are the USA, the US Virgin Islands, Puerto Rico, Canada and Greenland, all characterized by their proximity to major cocaine production regions and higher demands and societal acceptance of drug use. For CAUD, regions with medical or full legalization, such as New Zealand, the UK, Australia, Belgium and Canada, reported high disease burdens²¹. In the USA, although cannabis is not federally legalized, several states permit both medical and recreational use, contributing to the significant disease burden. For OUD, except for Kiribati, the top 30 countries with the highest DALYs attributable to OUD were predominantly high-income countries or higher SDI countries. As previously mentioned, this trend may be linked to higher demand and greater societal acceptance of opioid use in the West and high SDI regions¹.

Across four types of DUDs, high prevalence rates of CAUD and OUD present distinct patterns of estimated disease burden. While the burden of CAUD was the lowest, CAUD is often considered a gateway drug²², and association analyses indicate positive correlation with other DUDs, including OUD, CUD and AUD. The 'gateway hypothesis' posits that a drug, such as cannabis, could lower the threshold for use and access to other substances, such as opioids²³. Furthermore, underlying behavioral developmental mechanisms in patients with CAUD coincide with risk factors such as genetic predisposition, trauma, unstable psychiatric symptoms, thrill-seeking, impulsivity and environmental exposures; these factors can increase the likelihood of subsequent legal and illegal substance use, opioid or other drugs²⁴. Delay discounting, which refers to the tendency to devalue larger future rewards in favor

of small immediate gratification, is a factor in the decision-making process among individuals with substance misuse. This cognitive bias, along with other factors, can increase the likelihood of subsequent legal and illicit substance use, including opioids or other drugs²⁴.

Conversely, a high burden associated with OUD is exacerbated by co-occurrence with other serious conditions, contributing to worse overall disease burden. The International Agency for Research on Cancer identified opium consumption as a human carcinogen (Group 1) in September 2020²⁵. OUD substantially impacts disease burden due to several factors, including its high dependency potential, the risk of overdose, indiscriminate needle and syringe use for injection, as well as complications such as infectious diseases and mental health disorders^{1,23}. The trend of increasing OUD-related disease burden since 1990 in high-income countries can be attributed to several factors due to overprescribing by the medical profession, inadequate regulation and increased use of illegal heroin and synthetic opioids⁹. The over-prescription of opioid painkillers, particularly in the late 1990s and early 2000s, led to widespread misuse. In addition, the availability of synthetic opioids, such as fentanyl, has further exacerbated the issue due to their high potency and risk of overdose^{9,10}.

Socio-economic factors, including mental health issues, unemployment, disparity between urban and rural regions and social instability, contribute to the observed rising trend in DUDs^{26,27}. Previous studies show strong associations between poverty, unemployment and higher drug overdose deaths²⁸. Regions with higher poverty and unemployment rates generally have higher rates of retail opioid sales and opioid prescriptions from Medicare²⁹. In addition, rural areas

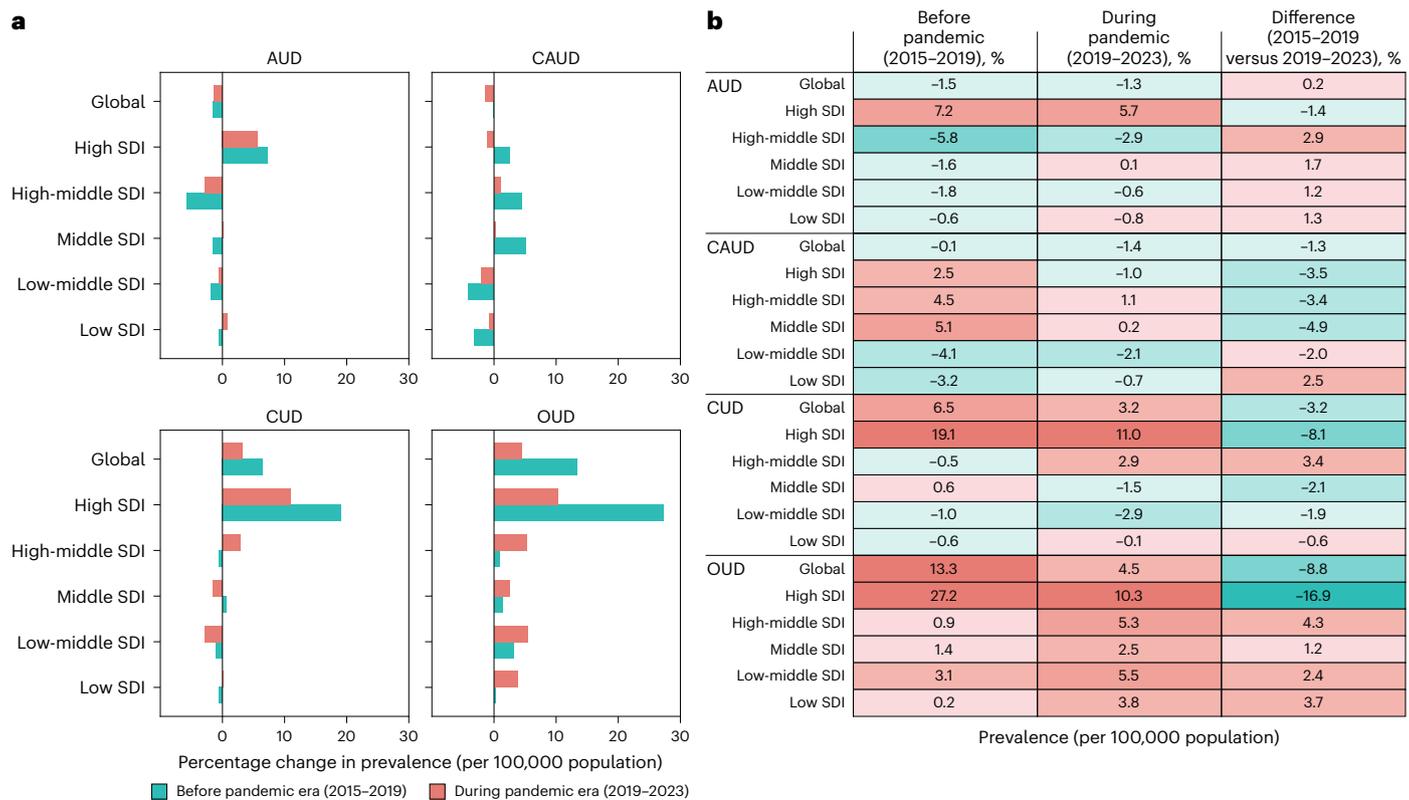


Fig. 6 | Age-standardized percentage change in prevalence of DUDs by SDI, before and during pandemic periods (2015–2019 and 2019–2023). **a**, Percentage change in prevalence per 100,000 population. **b**, Difference in percentage change and comparison between pre- and during pandemic periods.

Countries were categorized into five SDI groups according to the GBD SDI classification, low (32 countries), low-middle (41 countries), middle (40 countries), high-middle (47 countries) and high (44 countries).

often experience poorer healthcare infrastructure compared with urban areas, which can limit access to addiction treatment and prevention services²⁹. These factors are often more pronounced in less economically developed regions²⁹. These factors combined have led to a sustained increase in OUD burden in high-income countries over the past few decades. The socio-economic disparities were exacerbated during the COVID-19 pandemic, potentially contributing to a sharp rise in the OUD burden³⁰.

Higher prevalence and burden of DUDs in males compared with females can be attributed to several factors, including sex-specific social and cultural norms, higher rates of risk-taking behaviors and greater exposure to environments where drugs are more accessible⁹. Previous studies emphasized the need to consider sex and/or gender differences in response to substance use medication³¹. This approach is imperative for developing more effective clinical care guidelines. In addition to sex differences, younger age groups, particularly adolescents and young adults, are often at higher risk due to peer influence, risk-taking behaviors, lower barriers to risky behaviors and social pressures³². In countries with high SDI, the elevated prevalence and burden of DUDs are driven by factors such as greater availability and access to drugs, higher rates of prescription drug misuse and socio-economic stressors such as mental health and unemployment²⁷.

The increasing global burden of DUDs, particularly in high-income countries, necessitates comprehensive policy interventions. Taxation and regulation of availability and prescription effectively reduce harms associated with cannabis and prescribed drugs. Given the potential role of cannabis as a ‘gateway drug’, its legalization for medical and/or recreational use, coupled with taxation and regulation, can control its use and potentially reduce the risk and burden of other DUDs³³. Policies must address the high prevalence and burden of OUD due to

over-prescription and availability of synthetic opioids. Psychosocial interventions have been shown to benefit patients with cannabis and psychostimulant use disorders³⁴. Opioid substitution therapy involving methadone or buprenorphine reduces opioid use, opioid-related morbidity, risks of injection and mortality, and improves well-being^{35,36}. Distributing naloxone, an opioid antagonist, through community-based programs and pharmacies can effectively reverse overdoses and mitigate OUD³⁷.

Injection drug use, such as with opioids, increases the risk of infectious diseases transmitted via needles. Needle and syringe programs, opioid agonist therapy and HIV antiretroviral therapy can reduce this burden³⁸. Policies should focus on improving the accessibility of treatment, reducing stigma and implementing preventive measures such as needle exchange programs, supervised injection sites and opioid substitution therapies. Addressing socio-economic factors, enhancing mental health support and ensuring accurate reporting and diagnosis are critical for mitigating the burden of DUDs. Additionally, in regions considered major suppliers of drugs or countries with lower SDI, such as Latin America, Africa and South Asia, there are concerns about the reliability and uncertainty of data reporting DUDs. Therefore, regular surveys and a robust reporting system are needed to improve data accuracy and reliability.

Implementation of proactive policies has previously shown health benefits in tackling DUDs¹. For example, in the mid-1990s, Australia experienced a similar surge in opioid overdose deaths, but through proactive interventions, mortality rates were reduced^{39,40}. Australia implemented key initiatives, such as expanding methadone treatment, implementing syringe and needle exchange programs, reforming law enforcement practices and establishing the first medically supervised injection center in 2001^{39,40}.

GBD 2023 has several limitations. First, data sources varied in quality and reliability, particularly in countries with lower SDI. In addition, missing data from regions, especially the African continent, may have impacted the global estimates due to underreporting and thus interpretations of findings. Second, the GBD did not include CAUD-specific mortality estimates, resulting in DALYs based solely on nonfatal burden (years lived with disability), which may contribute to an underestimation of its overall burden². Likewise, the reliance on DSM-IV and ICD-10 diagnostic criteria, while ensuring comparability, may result in underestimation of disease burden, especially attributable to CAUD. Third, we focused on DUDs within substance use disorders, excluding alcohol use disorders and nicotine use disorders. In addition, our research primarily covered amphetamine, cannabis, cocaine and opioid use, while excluding drugs such as lysergic acid diethylamide, methamphetamine and 3,4-methylenedioxymethamphetamine due to limitations of data sources. Furthermore, regional and cultural differences in drug use patterns and reporting may have introduced biases in prevalence and burden estimates³⁰. Fourth, DUD often co-occurs with other mental health disorders or chronic conditions with higher rates of comorbidity. Our analysis had inherent limitations in accurately measuring and attributing the burden to individual conditions when comorbidities were present. Consequently, there is a possibility that we may not have fully accounted for the synergistic effects of co-occurring disorders, potentially resulting in an underestimation of the actual disease burden. Fifth, the observation period of the study included significant changes in drug policy, particularly the legalization of cannabis in several countries. These policy changes likely contributed to altered reported estimates of DUDs. Therefore, further analyses are needed to suggest the impact of changing legal frameworks, such as cannabis legalization, on estimates. Sixth, the association analysis and the comparisons across cannabis legalization levels need to be interpreted with caution. The observed associations among different types of DUDs do not establish causality, and the higher burden of DUDs in countries with cannabis legalization may be influenced by increased surveillance and reporting rather than a direct effect of legalization. Therefore, further controlled prospective studies with longer observation periods are needed to gain a more in-depth understanding of the impacts of cannabis legalization. Seventh, despite efforts to standardize data integration and modeling approaches, variations in data quality and availability across regions may introduce uncertainties in the estimated burden of DUDs. Specifically, the use of stringent diagnostic criteria based on DSM-IV and ICD-10 likely excludes subclinical or less severe cases that may be captured by surveys using broader definitions (for example, the National Survey on Drug Use and Health in the USA). Additionally, the global statistical modeling framework employed by GBD, while designed to ensure cross-national comparability, may smooth out regional variability and result in systematically conservative prevalence estimates, particularly in regions with high-quality surveillance data. Last, while we provide global trends in the prevalence and burden of DUDs, further well-designed prospective studies controlling for confounding factors are needed to estimate the risks of DUDs more accurately¹.

In conclusion, our study highlights an increasing global burden of DUDs from 1990 to 2023, with high-income countries experiencing the highest prevalence and DALYs. The greatest burdens were reported for OUD, exacerbated by its co-occurrence with other conditions. Comprehensive strategies, including taxation and regulation of recreational drugs, opioid substitution therapy, distribution of naloxone, needle exchange programs and regulation of telehealth prescriptions, are essential to mitigate the increasing burden of DUDs.

Online content

Any methods, additional references, Nature Portfolio reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions

and competing interests; and statements of data and code availability are available at <https://doi.org/10.1038/s41591-025-04137-0>.

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Methods

Study design

The GBD 2023 quantified the burden of disease attributable to 375 diseases from 1990 to 2023¹². This comprehensive analysis estimated prevalence, incidence, DALYs, years of life lost, years lived with disability and death for all diseases, covering 204 countries, and was stratified by year, age, sex and region. In this study, we examined the burden of disease attributable to AUD, CAUD, CUD and OUD. The analysis included data from 204 countries over 34 years (1990–2023), stratified by 15 age groups (from 10–14 years to 95 years and older, in 5-year intervals), sex (male, female and both sexes), seven super-regions (Southeast Asia, East Asia and Oceania; Central Europe, Eastern Europe and Central Asia; high-income countries; Latin America and the Caribbean; North Africa and Middle East; South Asia; and Sub-Saharan Africa; Supplementary Table 11)¹ and SDI (low SDI, low-middle SDI, middle SDI, high-middle SDI and high SDI; Supplementary Table 12)¹². The classification for super-regions in this study follows the GBD 2023 definitions, which consider not only geographic location but also factors such as country-level gross domestic product, reflecting variations in health and development. Age-standardized rates were calculated for overall estimation to account for changes in population distribution within each country over time. All analyses adhered to the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER)⁴¹. The data used in this analysis can be accessed at the Global Health Data Exchange (GHDx; <https://ghdx.healthdata.org/gbd-2023/sources>), and the detailed methodology has been comprehensively outlined in previous publications^{42,43}.

Case definition and input data

The case definition for nonfatal estimation of each disorder was established using datasets derived from the DSM-IV, text revision (TR) and ICD-10 codes. To meet the DSM-IV-TR criteria, a diagnosis was applied when the following symptoms were reported at least three times within a 12-month period^{12,44}:

- Tolerance, indicated by either:

A requirement for increased substance amounts to reach intoxication; or

A significantly reduced effect when using the same quantity of the substance over time.

- Withdrawal, identified by either:

The presence of withdrawal symptoms commonly associated with dependence; or

The use of the same or a similar substance to prevent withdrawal symptoms.

- Consuming the substance in progressively larger quantities or over an extended duration.
- Persistent attempts to cut down or control substance use, which prove unsuccessful.
- Spending an excessive amount of time obtaining, using or recovering from the substance.
- Neglecting important responsibilities or activities due to substance use.
- Continuing substance use despite being aware of its negative physical or psychological effects.

The ICD and DSM-IV-TR codes for the diagnosis of nonfatal and fatal DUDs are summarized in Supplementary Table 13. The input data used for these estimations include vital registration records, verbal autopsy reports, surveillance databases and systematic reviews. Data from countries with sparse and heterogeneous records were excluded, as they tend to exaggerate fluctuations in mortality counts and produce unreliable regional patterns. These excluded datasets were primarily from low-income countries.

Data redistribution

To accurately determine the cause of death, nonspecific, unreliable or intermediate garbage codes that were not primary ICD cause of death codes were redistributed to appropriate categories for assigning the underlying cause of death. ICD codes commonly associated with DUDs as garbage codes included those for accidental poisonings (X40–X44 and X49), exposure to unspecified factors (X59) and external causes of undetermined intent (Y34)⁴³. To systematically reallocate these garbage-coded deaths to valid underlying causes of death, a structured redistribution process was applied⁴³. First, garbage codes were grouped based on their diagnostic relatedness to ensure that nonspecific or unreliable ICD codes were classified according to their probable association with valid causes of death. Second, a multiple cause analysis was performed to determine the most probable cause to which each garbage-coded death should be reassigned. Multiple cause of death data, which include all causes listed on a death certificate, were utilized to enhance the accuracy of this reassignment⁴⁵. To refine this reassignment, various statistical methods, including multinomial regression, Bayesian regression and coarsened exact matching, were applied to estimate redistribution probabilities based on demographic and historical mortality patterns. GBD 2019 and 2020 updates introduced least absolute shrinkage and selection operator regression to refine potential underlying causes by eliminating weaker associations and generalized linear model-based modeling to estimate the proportion of deaths attributable to each intermediate cause⁴³. Data sources were excluded where more than 50% of all deaths in a specific location-year were attributed to major garbage codes to reduce the potential bias.

In addition, previous studies have shown that over 90% of drug poisonings result from exposure to narcotics, psychodysleptics and other drugs, predominantly occurring among individuals aged 15 to 65⁴³. This indicated that the cases are not accidental ingestions but rather unexpected addictions following intentional intake⁴⁶. Therefore, to correct the misassignment of drug overdose deaths as other unintentional poisonings, the GBD 2023 utilized a drug-specific redistribution algorithm to determine the most probable substance responsible for the fatality⁴¹. Since many cases involve multiple substances, Supplementary Table 14 outlines the selection process used to assign a single underlying cause. This algorithm prioritized substances with higher fatality risks, such as opioids, when multiple drugs were recorded and were also followed in the drug-specific redistribution process for garbage codes (X40–X44).

Data processing and adjustment for burden estimates

To ensure consistent comparisons across cause, age, sex, location and time, corrections were implemented at several stages of data processing. Burden estimates with insufficient age information or missing both age and sex data were allocated to appropriate GBD age groups and sexes by splitting these records⁴². When studies reported estimates for broad age groups by sex along with estimates for specific age groups combining both sexes, age–sex-specific estimates were derived using the reported sex ratio and uncertainty bounds. If within-study sex ratios were unavailable, a meta-analytic sex ratio estimated through Bayesian, regularized, trimmed meta-regression (MR-BRT) was applied¹². In addition, estimates covering wide age ranges were further disaggregated into 5-year age groups based on age-specific patterns estimated using the Bayesian meta-regression tool (DisMod-MR 2.1). These adjustments ensured consistency across age, sex and location while accounting for potential bias in reported estimates.

If there were differences between study definitions and the optimal case definition required for analysis, additional data adjustments were conducted to ensure comparability across causes and locations, even when reported estimates were available⁴¹. For CAUD, most studies reported prevalence based on either ‘any use’ or ‘regular use’, requiring a two-step adjustment process⁴⁷. First, ‘any use’ estimates were converted to ‘regular use’ using a meta-analysis, which applied

meta-analytic techniques to adjust the estimates downward. Second, ‘regular use’ estimates were converted to cannabis dependence, using a logit-difference coefficient estimated through MR-BRT. Given that the data patterns for individuals under 25 years of age and those aged 25 years and older differed, separate age-specific models were applied for CAUD. For AUD, CUD and OUD both direct and indirect estimation methods were employed. Direct methods relied on self-reported data on drug use and dependence. Indirect methods combined multiple data sources to estimate the total number of cases indirectly, utilizing multiplier methods, back-projection and capture–recapture approaches. Since direct estimation methods tend to underestimate prevalence due to reporting bias and stigma, indirect methods were considered more reliable¹². To account for discrepancies between these two approaches, the MR-BRT Crosswalk model was applied. Given the similarity in data patterns for AUD and CUD, data from both disorders were combined to derive a single adjustment factor. For OUD, when direct prevalence data were insufficient, the indirect multiplier method was used to integrate incomplete datasets¹². In this process, government records on the number of individuals receiving substitution therapy for opioid dependence and literature sources reporting the percentage of individuals with opioid dependence in treatment were utilized. A spatiotemporal Gaussian process regression (ST-GPR) model was applied to estimate coverage across year, location and sex⁴². The total population of individuals with opioid dependence was then calculated using the following formula: opioid population = number in treatment/ST-GPR estimated coverage; year, sex and location. The estimated opioid-dependent population was subsequently divided by the total population to derive the prevalence of OUD.

The GBD 2023 employed the concepts of severity and disability weight to assess the burden of disease associated with DUDs, including CAUD, CUD, AUD and OUD. The severity of the DUD was classified into three categories (asymptomatic, mild and moderate to severe) based on its impact on daily functioning as well as mental and physical health. Disability weights were applied to quantify the impact of each severity level on quality of life. To determine the disability weight, data from sources such as the US National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), the Comorbidity and Trauma Study and other surveys were utilized^{42,48}. The severity distribution was determined based on NESARC data. In cases where drug-specific data were lacking, adjustments were applied using MR-BRT, and the burden was estimated with DisMod-MR 2.1 to account for variations by age, sex and country.

Modeling strategy

DisMod-MR 2.1 was the primary modeling strategy employed to estimate nonfatal outcomes such as prevalence, incidence and excess mortality. To account for country-specific characteristics, country-level covariates were incorporated into the model. For cocaine and amphetamine, log per capita income was considered. For opioids, log-transformed estimates of defined daily doses for statistical purposes (consumption per day per million population) were included, modeled using ST-GPR with data provided by the International Narcotics Control Board. In addition, age-standardized prevalence of intravenous drug use and the Healthcare Access and Quality Index were included as covariates.

To assess fatal estimates such as cause-specific mortality of four types of DUDs, the Cause of Death Ensemble model (CODEm) was employed, stratified by year, age, sex and region for each disorder¹². CODEm is a modeling tool specifically developed for the GBD, which evaluates the predictive accuracy of different statistical models and covariate combinations, then aggregates these findings to calculate cause-specific mortality burden estimates. Building on this approach, the CoDCorrect process was applied to maintain internal consistency by aligning the unadjusted estimates of specific disorders (AUD, CAUD, CUD and OUD) with the overall distribution of deaths attributed to the

broader ‘parent’ category of DUDs⁴³. This adjustment ensured that the sum of specific cause estimates did not exceed the total deaths estimated for the parent category.

Uncertainty estimation

Uncertainty estimation was calculated by randomly sampling 500 draws from the parameter distributions, with this uncertainty then propagated throughout each stage of the analysis. The final estimates used the 2.5th and 97.5th percentiles of the posterior distribution to determine the 95% UI.

Estimating association between burden and SDI

The SDI is an indicator used to assess development status, which is closely related to health outcomes. It calculates the geometric mean of three components: the total fertility rate for individuals under the age of 25, the average education level for those aged 15 and older and log per capita income⁴⁹. On this scale, ranging from 0 to 1, an SDI of 0 indicates the lowest level of development related to health, while an SDI of 1 represents the highest level. For 2021, locations were categorized into quintiles: low SDI (0.00–0.47), low-middle SDI (0.47–0.62), middle SDI (0.62–0.71), high-middle SDI (0.71–0.81) and high SDI (0.81–1.00)⁴³. Each year, an SDI score was assigned to each GBD location. This study utilized the SDI to investigate the association with DALYs attributable to AUD, CAUD, CUD and OUD.

Statistical analysis

To comprehensively explore the associations of the disease burdens attributed to AUD, CAUD, CUD and OUD, additional analyses were conducted using GBD 2023. First, to examine the burdens of prevalence and DALY of the four disorders across different levels of cannabis use legalization, 204 countries were classified based on their legalization status as of 2021 into four groups: illegal, decriminalized or unenforced for recreational use, legal medical use only and legal recreational and medical use (Supplementary Table 15). Post hoc analysis using Dunn’s test was conducted to assess the statistical significance of differences among groups, with a significance level defined at $P < 0.05$ (ref. 50). Second, an association analysis was performed to intuitively understand the relationships and potential interdependencies among the disorders (AUD, CAUD, CUD and OUD). The analysis incorporated cannabis use legalization status in each country as an adjustment factor, based on its status in 2021. A linear regression model was used to estimate the β values, quantifying the influence of independent variables on dependent variables. We included 2023 estimates of DALYs from each of the 204 countries, calculated through GBD modeling. Third, to examine changes before and after the COVID-19 pandemic, the analysis considered two 3-year periods: 2015–2019 (pre-pandemic) and 2019–2023 (during pandemic), using 2019 as the reference point. Percentage change was calculated for each period, and the analysis was stratified by SDI levels to reflect variations across different socio-demographic contexts. Fourth, a decomposition analysis was conducted to assess the effects of population growth, aging and epidemiological changes on AUD, CAUD, CUD and OUD from 1990 to 2023⁵¹. The analysis, formulated by Das Gupta, utilizes population data, age structure and the rate of DUDs to calculate how each factor contributes to the overall changes^{52,53}. Epidemiological changes refer to the adjusted change in DUDs, accounting for age-specific structure and population size. The impacts of evaluated factors were shown as either increases or decreases in total cases, indicated by positive and negative values, respectively. All additional analyses and visualizations were performed using R Statistical Software (v.4.1.2; R Foundation, Vienna, Austria; <https://www.R-project.org/>).

Ethics and inclusion statement

This study utilized secondary data from the GBD 2023, a large-scale collaborative scientific initiative designed to enable cross-comparison

of health outcomes by age, sex and geographical location. The authors did not have access to individual-level participant data. Importantly, the study's findings provide region-specific estimates that are directly relevant for policymakers and researchers. By highlighting geographic variations in disease burden and associated risk factors, the results can inform the development of targeted interventions, guide resource allocation and support evidence-based health policy planning tailored to local and regional contexts.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The findings from this study were produced using data available in public online repositories or in the published literature, data that are publicly available on request from the data provider and data that are not publicly available due to restrictions by the data provider and which were used under license for the current study. Details on data sources can be found on the GHDx website, including information about the data provider and links to where the data can be accessed or requested (where available). To download the data used in these analyses, please visit the Global Health Data Exchange GBD 2023 website (accessed on 18 September 2025) at <https://ghdx.healthdata.org/gbd-2023/sources>.

Code availability

Our study follows the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER; Supplementary Table 16). All code used for the GBD 2023 analyses is publicly available online at <https://ghdx.healthdata.org/gbd-2023/code>.

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Acknowledgements

This study was funded by the Gates Foundation, the Australian National Health and Medical Research Council and the Queensland Department of Health, Australia. This paper was developed as part of the GBD Collaborator Network and GBD Protocol with support from the GBD Secretariat, IHME and the GBD Collaborator Network under the IHME ID: 4251 (GBD 2023 Substance Use Collaborators). This work was supported by the Yonsei Fellowship, funded by Lee Youn Jae (to J.I.S.). This research was supported by the Ministry of Science and ICT (grant nos. RS-2024-00509257 and IITP-2024-RS-2024-00438239 to D.K.Y.) and the Ministry of Health & Welfare (grant no. RS-2025-02220492 to D.K.Y.), South Korea. The funder 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 the study data and had final responsibility for the decision to submit for publication.

Author contributions

J.K., H.J.K., M.S.K., J.I.S. and D.K.Y. conceptualized and designed the study. J.K., H.J.K., M.S.K., J.I.S. and D.K.Y. were responsible for the methodology. J.K., H.J.K., M.S.K., J.I.S. and D.K.Y. were responsible for data acquisition. J.K., H.J.K., M.S.K., J.I.S. and D.K.Y. performed statistical analysis and data curation. J.K., H.J.K., M.S.K., J.I.S. and D.K.Y. performed the validation. J.K., H.J.K., M.S.K., J.I.S. and D.K.Y. were responsible for data interpretation. J.K., H.J.K., M.S.K., J.I.S. and D.K.Y. performed the visualization. J.K., H.J.K., M.S.K., J.I.S. and D.K.Y. were responsible for managing the estimation or publications process. J.K., H.J.K. and M.S.K. wrote the original draft of the paper. All authors provided critical revision to the paper. J.I.S. and D.K.Y. supervised the study. J.I.S. and D.K.Y. were responsible for project administration. J.I.S. and D.K.Y. were responsible for funding acquisition. Contributions by the GBD 2023 Global Substance Use Collaborators are described in Supplementary Information.

Competing interests

S. Afzal reports support for the present manuscript from the Institute of Public Health Lahore; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from the Dean Institute of Public Health Lahore; support for attending meetings and travel from the Dean Institute of Public Health Lahore; participation on a data safety monitoring board or advisory board with Pakistan National Bioethics Committee, Institution Review Board of Fatima Jinnah Medical University, Ethical Review Board and Data Monitoring Board with the Institute of Public Health Lahore Pakistan, and is in charge of the Clinical Research Organization King Edward Medical University; leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, with Pakistan Higher Education Commission Research Committee, Pakistan Medical and Dental Research Commission Research and Journals Committee, Pakistan Society of Internal medicine, Pakistan Association of Medical Editors, Medical Microbiology and Infectious Diseases Society, Fellow of Leads International, Fellow of Faculty of Public Health UK and Fellow of College of Physicians and Surgeons Pakistan; receipt of equipment, materials, drugs, medical writing, gifts or other services from the Bergen University of Norway for research writing; and other financial

or nonfinancial interests from Dean Public Health and Preventive Medicine King Edward Medical University; outside the submitted work. M.S. Aslam reports two grants from Xiamen University Malaysia Research Fund (XMUMRF). Grant no.: XMUMRF/2025-C15/ITCM/0006. Project title: Therapeutic and Toxicity Evaluation of Selected Medicinal Herbs for NAFLD: Exploring the Inter-Organelle Contact Sites Modulation. Theory Role: Co-Investigator Dates: January 2025–December 2027 (ongoing). Internal XMUMRF research grant administered by Xiamen University Malaysia, funds disbursed to institutional research accounts only; no salary, honoraria or personal payments to author. Grant no.: XMUMRF/2023-C11/ISEM/0041. Project title: Children's Rights Education in the Early Years of Divorce: An Exploration of Adolescents' Perspectives. Role: Co-Investigator Dates: January 2023–December 2025 (ongoing). Internal XMUMRF research grant administered by Xiamen University Malaysia; funds disbursed to institutional research account only; no salary, honoraria or personal payments to author; all outside the submitted work. A.S.B. reports support for attending meetings and/or travel to the American Public Health Conference 2022, 2023 and 2024; American College of Epidemiology 2023, 2024 and 2025; Military Health System Conference 2024; and from the University of Virginia Biomedical Data Science Innovation Lab and Seminar series; leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, as a member of the Board of Directors of the American College of Epidemiology 2024–present; former co-chair of the Publications Committee of the American College of Epidemiology in 2023 and 2024; liaison for the Publications Committee of the American College of Epidemiology in 2024 and 2025; Communications Chair for the American Public Health Association, Health Informatics and Information Technology Section; Associate Editor, *Annals of Epidemiology Journal*; all outside of the submitted work. S.B. reports grants or contracts from the Japan Society for the Promotion of Science (JSPS), Japanese Ministry of Education, Culture, Sports, Science and Technology (MEXT), Grant-in-Aid for Scientific Research (KAKENHI; Grant ID 23KFO126), JSPS and the Australian Academy of Science, JSPS International Fellowship (Grant ID P23712); leadership or fiduciary roles in other board, society, committee or advocacy groups, paid or unpaid, as District Chair, Diversity, Equity, Inclusion & Belonging of Rotary District 9675 (Sydney, Australia), as Chair, Founding Member and Manager of the Global Health & Migration Hub Community, Global Health Hub Germany (Berlin, Germany), as Editorial Board Member of *PLOS One*, *BMC Neurology*, *Frontiers in Neurology*, *Frontiers in Stroke*, *Frontiers in Public Health*, *Journal of Aging Research*, *Neurology International*, *Diagnostics* and *BMC Medical Research Methodology*; as a member of the College of Reviewers, Canadian Institutes of Health Research (CIHR), Government of Canada; as the Director of Research of World Headache Society (Bengaluru, India); as Expert Adviser/Reviewer of Cariplo Foundation (Milan, Italy); as Visiting Director of National Cerebral and Cardiovascular Center, Department of Neurology, Division of Cerebrovascular Medicine and Neurology, Suita (Osaka, Japan); as Member, Scientific Review Committee of Cardiff University Biobank (Cardiff, UK); as Chair of Rotary Reconciliation Action Plan; and Healthcare and Medical Adviser at Japan Connect (Osaka, Japan); outside the submitted work. A. Caye reports consulting fees from EMS, Knight Therapeutics; outside the submitted work. S.R.C. reports grants or contracts from Janssen Cilag Australia Investigator Initiated Research Grants; Australian NHMRC, MMRF Research Grants; NIMH Research Grants; and XWPharma contract research; all funds paid to the University of Adelaide; consulting fees from Insight Timer and Preventative Health SA; all funds paid to the University of Adelaide; and payment or honoraria for lectures, presentations, speakers bureaus, manuscripts writing or educational events from Servier, Lundbeck-Otsuka, all funds paid to the University of Adelaide; leadership or fiduciary role in other board, society, committee or

advocacy group, unpaid, with the Board of Mental Health Foundation of Australia; outside the submitted work. X.D. reports all support for the present manuscript from the Institute for Health Metrics and Evaluation and University of Washington. E.E. reports grants or contracts from Grand Challenges Canada, Canadian Institutes of Health Research, funds paid to their institution; and leadership or fiduciary role in other board, society, committee or advocacy group, unpaid, with Global Implementation Society; outside the submitted work. I.F.E.B. reports leadership or fiduciary role in other board, society, committee or advocacy group as Editor in Chief of *Recent Advances in Infectious Diseases* and as an Editor for *Texila American Journals*; outside the submitted work. O.F.F. reports leadership or fiduciary role in other board, society, committee or advocacy group, unpaid, with the African Tobacco Control Alliance; outside the submitted work. A. Faro reports support for the present manuscript from the National Council for Scientific and Technological Development (CNPq, Brazil). J.F. reports grants or contracts from the National Institute of Mental Health and the National Institute on Drug Abuse; outside the submitted work. J.J.J. reports payment for honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Novartis, Adamed, Amgen, Boehringer Ingelheim and Sevier; outside the submitted work. S.V.K. reports grants or contracts from the National Institute for Health & Care Research, funds paid to their institution; outside the submitted work. M. Kosci reports grants or contracts from NPO 'Systemic Risk Institute' number LX22NPO5101, funded by the European Union – Next Generation EU (Ministry of Education, Youth, and Sports); outside the submitted work. P. Meylaks reports grants or contracts from the Center for Comparative Research of Social Wellbeing, HSE University; outside the submitted work. T.R.M. reports grants or contracts from the National Institute of Mental Health, payments made to their employer; payment for expert testimony for opioid litigations, payments made to their employer; and from Opioid litigation, Evre, LLC, payments made to them; outside the submitted work. L. Monasta reports support for the present manuscript from the Italian Ministry of Health, payments made to their institution. R.F.P.-A. reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Angelini, Casen Recordati, Lundbeck, Neuraxpharm, Rubió, Servier and Takeda; support for attending meetings and/or travel from Angelini, Italfarmaco, Advanz Pharma, Takeda, Lundbeck and Camurus; all outside the submitted work. S.K.P. reports support for the present manuscript from Siksha 'O' Anusandhan (Deemed to be University); grants and contracts from File no. 17-59/2023-24/CCRH/Tech./Coll./ICMR-Diabetes/960; outside the submitted work. G.D.P. reports support for attending meetings and/or travel from Roche Hellas and Bayer Greece; outside the submitted work. R. Passera reports participation on a Data Safety Monitoring Board or Advisory Board with the Data Safety Monitoring Board dello studio 'Consolidation with ADCT-402 (loncastuximab tesirine) after immunochemotherapy: a phase II study in BTKitreated/ineligible Relapse/Refractory Mantle Cell Lymphoma (MCL) patients' – FIL, Fondazione Italiana Linfomi, Alessandria (Italy); leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, with EBMT Statistical Committee, European Society for Blood and Marrow Transplantation, Paris, France; and is a former member from 2020 to 2023 of the IRB/IEC Comitato Etico AO SS. Antonio e Biagio Alessandria-ASL AL-VC (Italy); outside the submitted work. A.E.P. reports support for the present manuscript from the Australian National Health and Medical Research Council (Grant no. APP2009306). V. Sharma acknowledges support from DFSS (MHA)'s research project (DFSS28(1)2019/EMR/6) at Institute of Forensic Science & Criminology, Panjab University, Chandigarh, India, and RUSA grant to Panjab University by Ministry of Education, Govt. of India; outside the submitted work. J.I.S. reports support from the Yonsei Foundation, funded by Lee Youn Jae. J.P.S. reports support for

the present manuscript from the Portuguese Foundation for Science and Technology. L.M.L.R.S. reports grants or contracts with SPRINT – Sport Physical Activity and Health Research e Innovation Center, Polytechnic of Guarda, 6300-559 6 Guarda, Portugal; and collaboration with RISE–UBI, Health Sciences Research Centre, University of Beira Interior, 6201-506 Covilhã, Portugal; outside the submitted work. J.A.S. reports consulting fees from ROMTech, Atheneum, Clearview Healthcare Partners, American College of Rheumatology, Yale, Hulio, Horizon Pharmaceuticals, DINORA, ANI/ Exeltis, USA Inc., Frictionless Solutions, Schipher, Crealta/Horizon, Medisys, Fidia, PK Med, Two labs Inc., Adept Field Solutions, Clinical Care Options, Putnam Associates, FocusForward, Navigant Consulting, Spherix, MediQ, Jupiter Life Science, UBM LLC, Trio Health, Medscape, WebMD, Practice Point Communications and the National Institutes of Health; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Simply Speaking; support for attending meetings and/or travel from OMERACT, an international organization that develops measures for clinical trials and receives arm’s length funding from 12 pharmaceutical companies, as past steering committee member to attend their meeting every 2 years; participation on a Data Safety Monitoring Board or Advisory Board with FDA Arthritis Advisory Committee (unpaid); leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, as a past steering committee member of the OMERACT; stock or stock options in Atai Life Sciences, Kintara Therapeutics, Intelligent Biosolutions, Acumen Pharmaceutical, TPT Global Tech, Vaxart Pharmaceuticals, Atyu Biopharma, Adaptimmune Therapeutics, GeoVax Labs, Pieris Pharmaceuticals, Enzolytics Inc., Seres Therapeutics, Tonix Pharmaceuticals Holding Corp., Aebona Pharmaceuticals and Charlotte’s Web Holdings, Inc., and previously owned stock options in Amarin, Viking and Moderna Pharmaceuticals; all outside the submitted work. D.J.S. reports consultancy honoraria from Discovery Vitality, Kanna, L’Oreal, Lundbeck, Orion, Servier, Seaport Therapeutics, Takeda and Wellcome. R.T.-S. reports grants or contracts from Valencian Regional Government’s Ministry of Education (PROMETEO/CIPROM/2022/58) and the Spanish Ministry of Science, Innovation and Universities (PID2021-129099OB-I00). The funders were not involved in the design of the manuscript or decision to submit the manuscript for publication, nor will they be involved in any aspect of the study’s conduct; all outside the submitted work. S.J.T. reports grants or contracts from part of the 2023/4 Adult Psychiatric Morbidity Survey team, collecting epidemiological data on community-based adults living in England. This is a contracted study from NHS Digital, via the Department of Health and Social Care. S.J.T. has also contributed to multiple chapters of the 2023/4 Adult Psychiatric Morbidity Survey report, payments made to the University of Leicester. S.J.T. led a study funded by the National Institute for Health and Care Research Clinical Research Network, on optimizing survey design for people with learning disability and autistic people, payments made to the University of Leicester. S.J.T. led a study from the National Institute for Health and Care Research related to reviewing a national training program for health and social care

professionals relating to learning disability and autism, payments made to the University of Leicester. S.J.T. was co-applicant on a study funded by the National Institute for Health and Care Research related to identification, recording and reasonable adjustments for people with a learning disability and autistic people in NHS electronic clinical record systems, payments made to the University of Leicester. S.J.T. was co-applicant on a study funded by the National Institute for Health and Care Research related to medication support interventions and strategies for people with learning disabilities, payments made to the University of Leicester. S.J.T. was lead applicant on a study funded by the Baily Thomas Charitable Fund investigating barriers, enablers and interventions to facilitate deprescribing for people with intellectual disability, payments made to the University of Leicester. S.J.T. reports support for attending meetings and/or travel from the Royal College of Psychiatrists for accommodation and travel to conference events due to their role as academic secretary in the faculty of the Psychiatry of Intellectual Disability, as well as additional conference fees waived for Royal College of Psychiatrists; leadership or fiduciary roles as Academic Secretary for the Neurodevelopmental Psychiatry Special Interest Group and Psychiatry of Intellectual Disability Faculty at the Royal College of Psychiatrists; Associate Editor for *Journal of Mental Health Research in Intellectual Disabilities*; Editorial Board Member for *Progress in Neurology and Psychiatry*, *Advances in Mental Health and Intellectual Disability*, *Advances in Autism*, *BMC Psychiatry* and *BJPsych Open* (no payments received for these roles); royalties received as Editor of *Psychiatry of Intellectual Disability Across Cultures* (Oxford University Press); outside the submitted work. A.C.T. reports support for the present manuscript from the US National Institutes of Health (K34DA061696); leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid, from Elsevier, Inc. as Co-editor in Chief of *SSM – Mental Health*, and from BMJ Publishing Group, Ltd, as Clinical Editorial Advisor for *The BMJ*; outside the submitted work. M.Z. is an Alexion, AstraZeneca Rare Disease employee.

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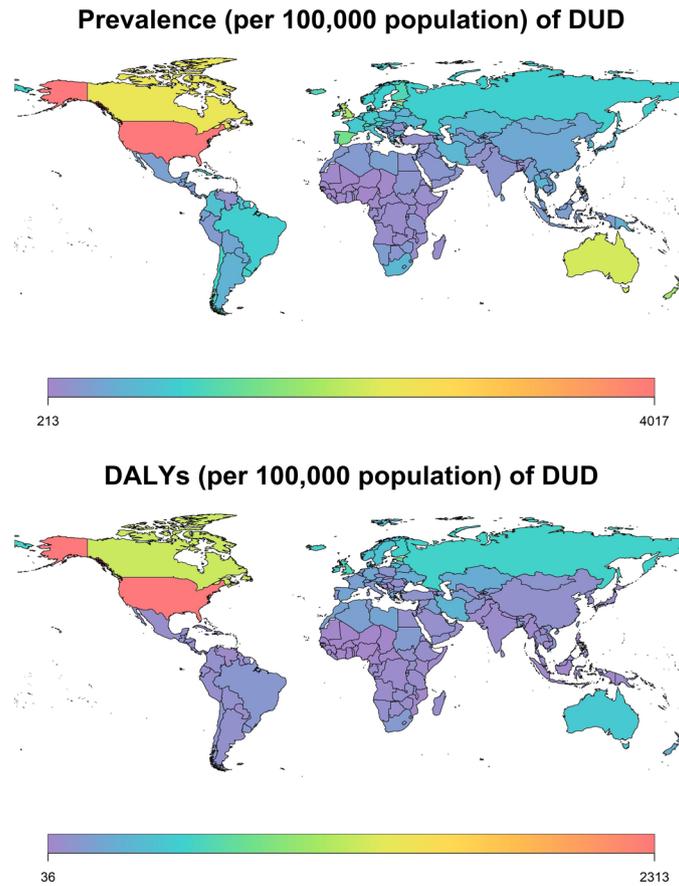
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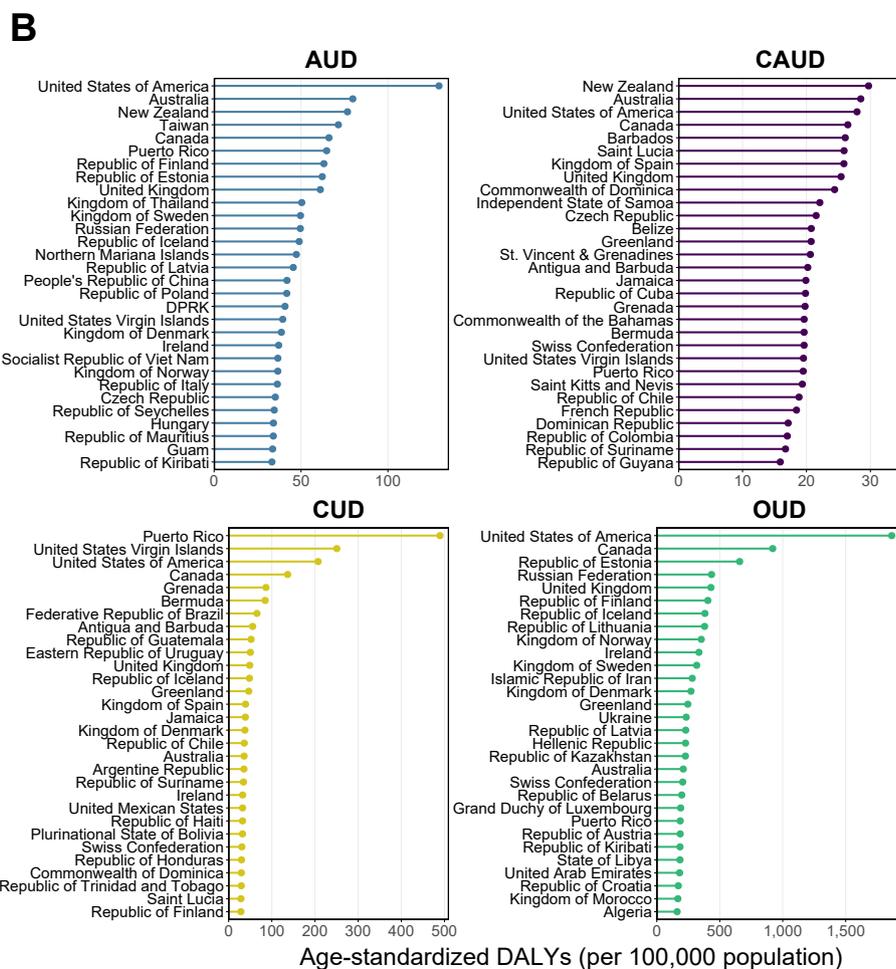
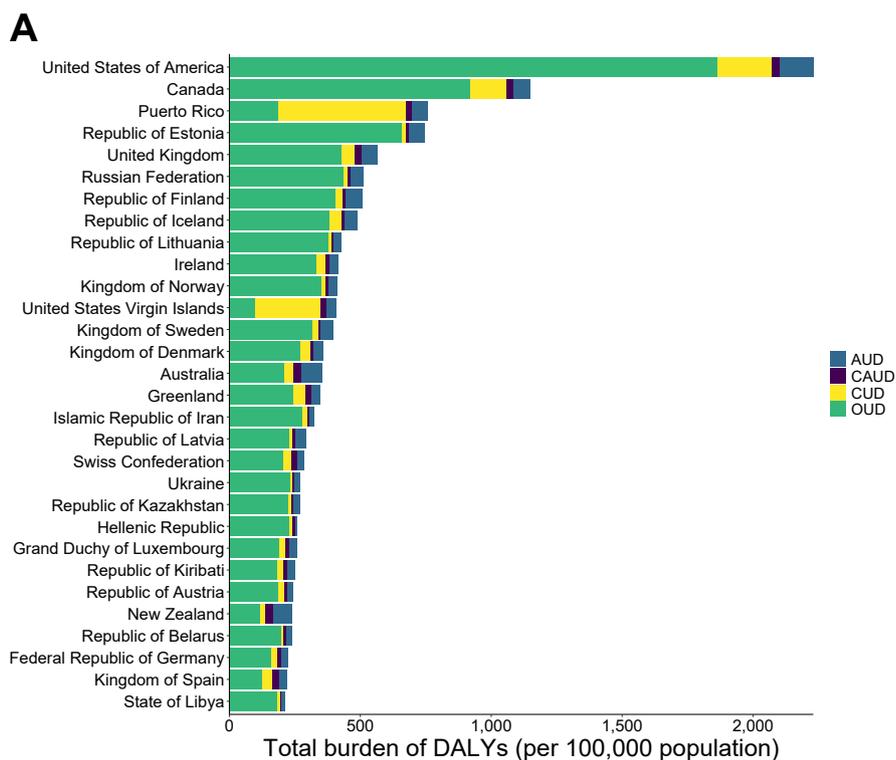
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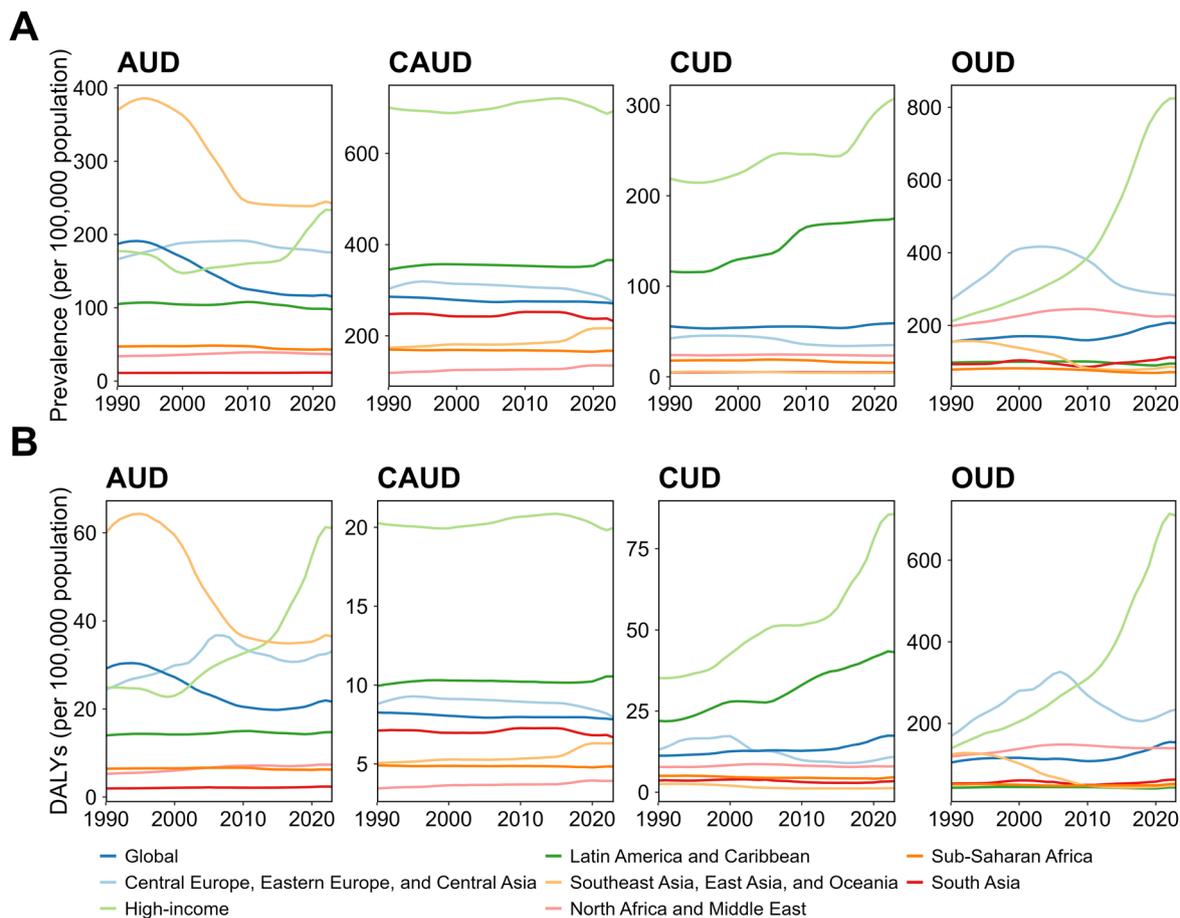
Extended Data Fig. 1 | World map of age-standardized prevalence and DALYs rates per 100,000 population attributable to overall drug use disorders for both sexes across 204 countries, 2023. Abbreviations: DALYs,

disability-adjusted life year; DUD, drug use disorders. The color gradient, ranging from purple (low value) to red (high value), indicates the magnitude of each estimate. Data from the Institute for Health Metrics and Evaluation.



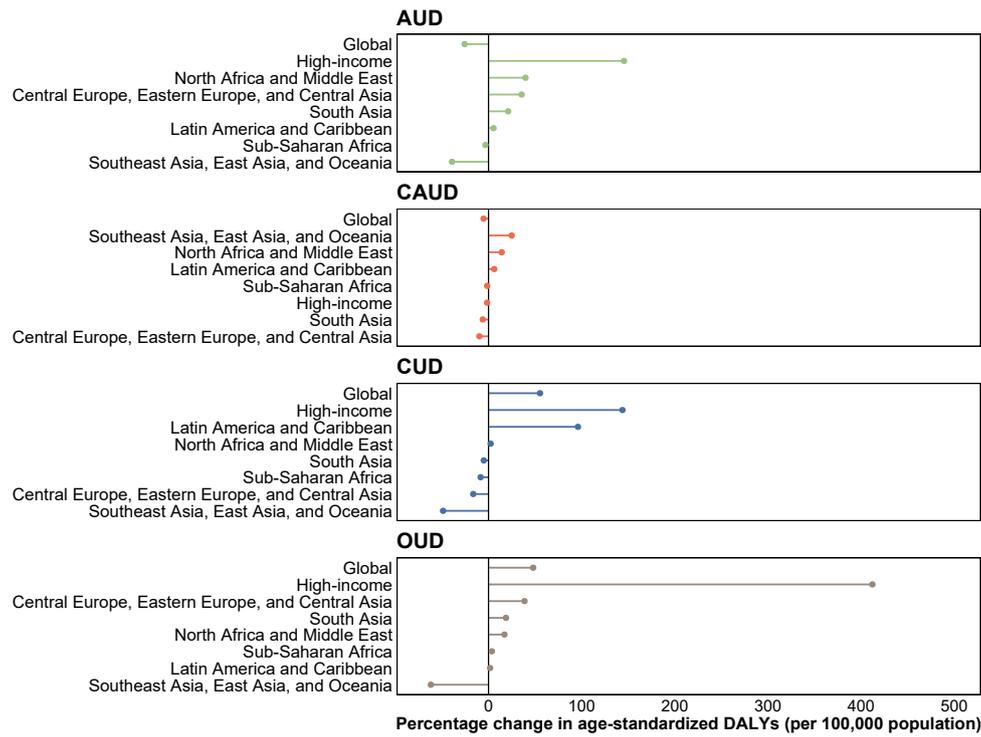
Extended Data Fig. 2 | Age-standardized DALYs per 100,000 population attributable to drug use disorders for both sexes across the top 30 countries, 2023. (A) Total burden of DALYs for drug use disorders; (B) DALYs rate for each

drug use disorder. Abbreviations: AUD, amphetamine use disorders; CAUD, cannabis use disorders; CUD, cocaine use disorders; DALYs, disability-adjusted life year; OUD, opioid use disorders.

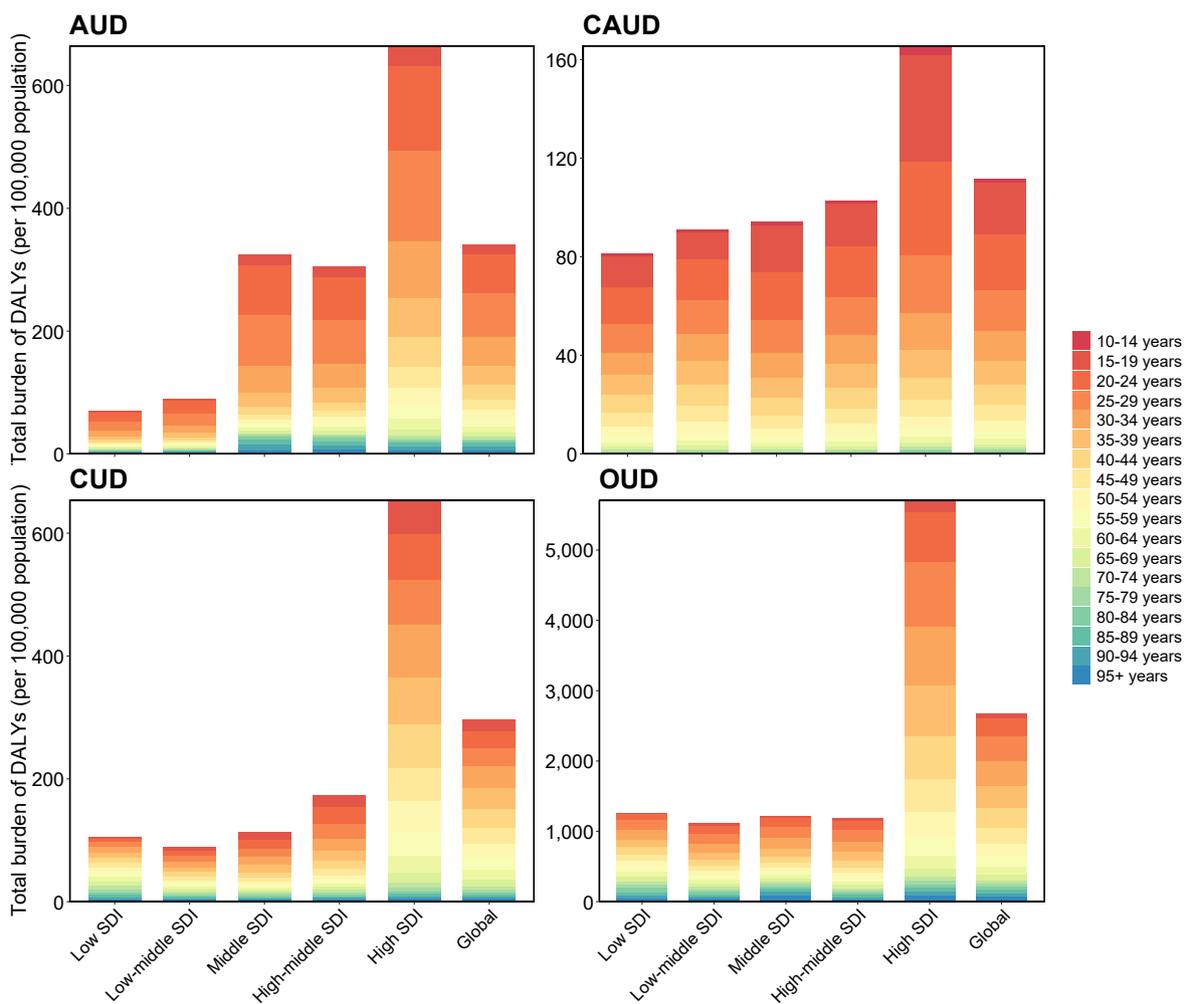


Extended Data Fig. 3 | Regional trends in prevalence and DALYs per 100,000 population for drug use disorders by GBD regions, 1990-2023. (A) Total burden of DALYs rate for drug use disorders; **(B)** DALYs rate for each drug use disorder.

Abbreviations: AUD, amphetamine use disorders; CAUD, cannabis use disorders; CUD, cocaine use disorders; DALYs, disability-adjusted life year; OUD, opioid use disorders.

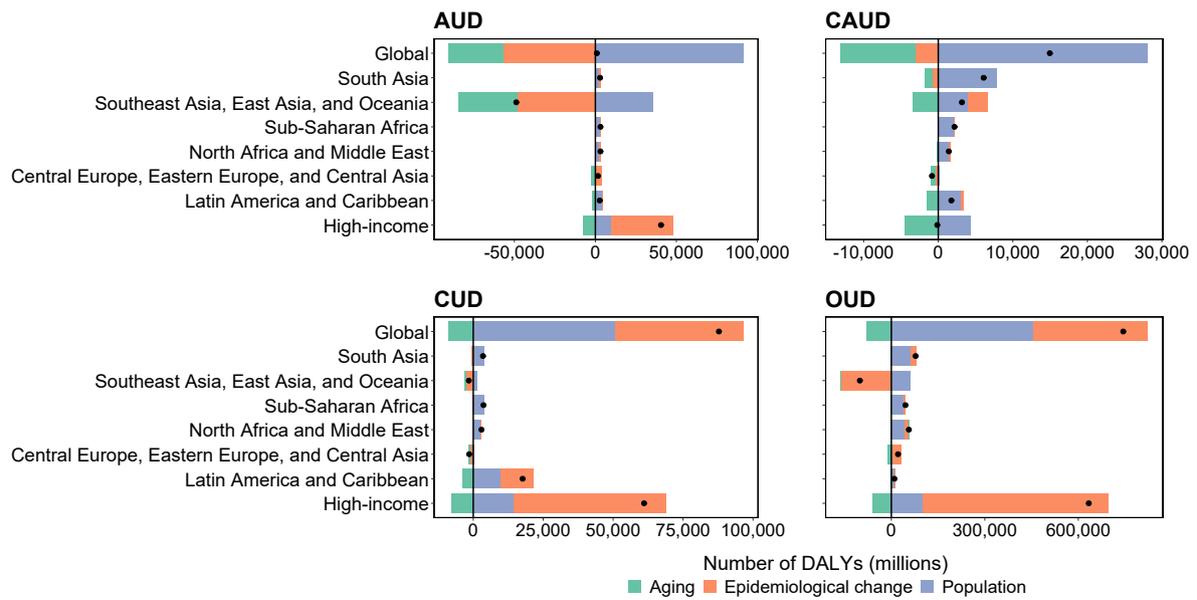


Extended Data Fig. 4 | Percentage change in age-standardized DALYs per 100,000 population for drug use disorders by GBD regions, 2023. Abbreviations: AUD, amphetamine use disorders; CAUD, cannabis use disorders; CUD, cocaine use disorders; DALYs, disability-adjusted life year; OUD, opioid use disorders.



Extended Data Fig. 5 | DALY per 100,000 population of drug use disorders for both sexes by SDI and age group, 2023. Countries were categorized into five SDI groups according to the GBD SDI classification, low (32 countries), low-middle (41 countries), middle (40 countries), high-middle (47 countries),

and high (44 countries). Abbreviations: AUD, amphetamine use disorders; CAUD, cannabis use disorders; CUD, cocaine use disorders; DALYs, disability-adjusted life year; OUD, opioid use disorders; SDI, socio demographic index.



Extended Data Fig. 6 | Changes in the number of DALYs cases (millions) associated with aging, epidemiological change, and population by each drug use disorders, 1990-2023. Abbreviations: AUD, amphetamine use disorders; CAUD, cannabis use disorders; CUD, cocaine use disorders; DALYs, disability-adjusted life year; OUD, opioid use disorders.

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Data collection

No primary data collection was carried out of these analyses. Relevant data from population surveys, published studies, and government reports were extracted by a reviewer using a data collection.

Data analysis

All data analyses and visualizations were performed using R Statistical Software (v4.1.2; R Core Team 2023, R Foundation for Statistical Computing, Vienna, Austria; <https://www.R-project.org/>). Our study follows the Guidelines for Accurate and Transparent Health Estimate Reporting (GATHER; Supplementary Table 16). All code used for the GBD 2023 analyses is publicly available online at <https://ghdx.healthdata.org/gbd-2023/code>.

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Reporting on sex and gender

This study did not involve primary human participants. All analyses used aggregated, de-identified population-level data from the Global Burden of Disease Study (GBD) 2023. The underlying data sources included nationally representative household surveys, census data, administrative health records, and epidemiological studies, covering individuals across the full age range (0–95+ years), both sexes, and all global regions. GBD estimates are stratified by age, sex, location, and Socio-demographic Index (SDI), which capture key covariate-relevant population characteristics for modeling drug use disorders.

No primary data collection was carried out for this analysis, so the study does not involve human research participants. As stated in the Methods section, we conducted the sex-stratified analysis to investigate the sex differences in drug use disorders.

Reporting on race, ethnicity, or other socially relevant groupings

No primary data collection was carried out for this analysis, so the study does not involve human research participants. The estimates were stratified by Socio-demographic Index (SDI), which may capture aspects of socio-economic status, but the analysis did not explicitly assess race or ethnicity.

Population characteristics

No primary data collection was carried out for this analysis, so the study does not involve human research participants. The analysis utilized data from the Global Burden of Disease Study 2023 and examined the prevalence and burden of drug use disorders across various population subgroups. These subgroups were stratified by age, sex, geographic region, and SDI, providing a comprehensive understanding of the disparities in drug use disorders across different populations.

Recruitment

No primary data collection was carried out for this analysis, so we did not recruit participants.

Ethics oversight

This study was approved by the University of Washington IRB committee.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

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Life sciences study design

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Sample size

Sample size was defined as the population of every location used in our analysis. Country-, region-, super-region, and global level populations are estimated as part of the Global Burden of Disease Study 2023. Detailed methods are described in [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(25\)01917-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(25)01917-8/fulltext). This study did not involve laboratory or experimental replication. All analyses were conducted using standardized Global Burden of Disease (GBD) 2023 computational pipelines, which are applied independently to each location-year-sex group. Uncertainty was quantified through 250-1,000 posterior draws for every estimate, providing the basis for 95% uncertainty intervals.

Data exclusions

We carefully evaluated all data sources for inclusion in our study. Sources were excluded if they lacked necessary survey weight factors or crucial demographic information such as sex or age variables. In addition, we omitted data deemed unreliable, based on assessments by survey administrators or through our own detailed examination. This careful section process ensured the quality and completeness of the information used in our analysis.

Replication	This a meta-analysis of existing studies with many years of cohort and other existing data. When re-applying the method to the same data, we got the same results.
Randomization	Randomizations was not relevant to this study. This analysis is a meta-analysis of existing studies and thus, there were no experimental groups.
Blinding	Blinding was not relevant to this study, as it was an observational study using survey and surveillance data.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input checked="" type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Plants

Seed stocks	<i>Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.</i>
Novel plant genotypes	<i>Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.</i>
Authentication	<i>Describe any authentication procedures for each seed-stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.</i>