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

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Abstract

Drug use disorders (DUDs) are emerging global public health challenges. Herein, we investigated the global and regional estimates of the prevalence and burden of DUDs, including amphetamine (AUD), cannabis (CAUD), cocaine (CUD), and opioid use disorders (OUD), from 1990 to 2023 for 204 countries and territories by using the Global Burden of Disease Study (GBD) 2023. Overall, trends in global age-standardized DALYs of DUDs increased from 169.3 (95% uncertainty interval [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 particularly higher in high-income countries, particularly in the USA. The most prevalent DUDs in 2023 were CAUD (age-standardized prevalence, 270.8 [95% UI, 201.7-350.0] per 100,000 people) and OUD (205.9 [95% UI, 178.7-235.0]). Particularly, OUD showed a nearly twofold increase in prevalence and burden between 1990 and 2023. In 2023, compared to 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.

Introduction

Drug use disorders (DUDs) present substantial public health challenges, accounting for 1.3 % of all-cause disability-adjusted life-years (DALYs) globally[1]. Among the most globally prevalent DUDs are amphetamine use disorders (AUD), cocaine use disorders (CUD), cannabis use disorders (CAUD), and opioid use disorders (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 significantly vary across regions of the world[1].

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 (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)[3]. Drug use also accompanies risks of various adverse health outcomes. For instance, injecting drugs with non-sterile equipment poses risks of HIV, viral hepatitis, other infectious diseases, and injection-related injuries[4].

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 [5,6]. Pandemic period showed a reduction in hospital admissions, coinciding with a surge in mortality due to drug overdose[5]. The increase in telehealth prescriptions and decreased accessibility of healthcare during the pandemic may have inadvertently contributed to increases in burden of DUDs[5]. These recent shifts are likely to influence international trends in DUDs, highlighting need to understand global and longitudinal trends in prevalence and burden. However, prior 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[5,6].

Herein, 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 (95% uncertainty interval [UI], 134.4-282.0) per 100,000 people in 1990 to 212.0 (95% UI, 179.2-245.6) in 2023 (**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 (**Table 1** and **Supplementary Tables 1-4**). In 2023, the most prevalent DUDs globally were CAUD (21.8 million estimated cases; prevalence, 270.8 [95% UI, 201.7-350.0] cases per 100,000 people) and OUD (17.0 million cases; prevalence, 205.9 [178.7-235.0]), particularly in high-income countries. AUD (9.2 million cases; prevalence, 115.2 [84.7-152.7]) and CUD (4.8 million cases; prevalence, 59.1 [47.4-74.3]) were less common, with CUD being the least prevalent (**Table 1** and **Figure 1)**.

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

The DALYs attributable to DUDs varied significantly between regions (**Figure 1** and **Supplementary Tables 1-4**). The highest drug-attributable burdens were in high-income countries, with DALYs attributable to AUD (DALYs, 61.1), CAUD (DALYs, 20.0), CUD (DALYs, 85.7), and OUD (DALYs, 708.9). **Extended Data Fig. 2** and **Supplementary Tables 5** show the top 30 countries with the highest DALYs of DUDs. In 2023, the USA had the highest burden attributable to DUDs (DALYs, 2229.8), 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 [95% UI, 211.9-373.4] cases per 100,000 people in 1990; 270.8 [201.7-350.0] in 2023; **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 (**Figure 2** and **Table 1)**.

Extended Data Fig. 3 shows age-standardized DALYs per 100,000 individuals by GBD regions from 1990 to 2023. Annual percentage change in DALYs for DUDs by high-income countries from 1990 to 2023 showed significant increases in all DUDs, including AUD, CUD, and OUD, compared to 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 6**).

Distributions of DALYs for DUDs by age and sex

Across all DUDs, age-standardized DALYs were higher for males than females (**Figure 3** and **Supplementary Table 7**). The overall burden attributable to DUDs was higher in males compared to 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 7**.

Associations between DUDs

Some individuals with DUDs reported a combination of each DUD (**Figure 4**). Chord diagram in **Figure 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; **Figure 4**).

Burden attributable to DUDs by cannabis legalization status

Figure 5 illustrates the age-standardized prevalence and DALYs per 100,000 population 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 (**Figure 5** and **Supplementary Table 8**). Compared to 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 [interquartile range, IQR; 104.21] versus 141.85 [172.82] per 100,000 population, 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 to 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; **Figure 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).

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 was modest, which were attributed to increases in population growth offsetting decreases in population aging and epidemiological changes(**Supplementary Table 9**). Similar observations were also observed for DALYs of CAUD. Furthermore, the overall increase 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 1990[3]. In 2023, the age-standardized prevalence and DALYs for all DUDs were significantly 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 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 illegale allowing medical or recreational use, compared to countries where cannabis use remained illegal. These findings provide insights to develop proactive interventions to address the significantly increasing burden of DUDs across the globe.

Disease burden attributable to the DUD 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[7,8]. Societal acceptance likely contributes to higher baseline demand for drugs, which, in turn, leads to a higher disease burden attributable to DUD[9]. Particularly in the USA, irresponsible pharmaceutical marketing, overprescription by healthcare providers, and systemic issues within the healthcare insurance system have further exacerbated the burden of DUDs[7,8,10,11].

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[12,13]. 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 continents[14].

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 United Kingdom, and Finland may be attributed to better access to drugs, higher societal acceptance against drug use, and more resources to obtain substances[1]. 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 "first wave" in 1990s[10,11]. The increasing trends in OUD burden were dominated by increased heroin use during the "second wave" (2010-2013)[10,11]. 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 burden[15]. 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[10,11].

Increased potency of synthetic opioids exacerbates the current opioid crisis, with aggressive marketing strategies from the emergence of Dark Web cryptomarkets[7,8]. 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 (carfentanil)[7]. Rapid emergence of new synthetic opioids, driven by more efficient synthesis methods, alleviated regulatory environments in source countries (e.g., China), and advanced internet commerce, is likely to further intensify the OUD burden[16].

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[17,18]. We also showed significant associations between AUD and OUD, and CUD and OUD, in 2023[19,20]. Likewise, polydrug use, particularly co-use of opioids with stimulants, is increasingly reported[17,18]. A prior survey-based cohort study reported that methamphetamine use tripled among those who reported heroin use from 9.0% in 2015 to 30.2% in 2017[21], 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[7,17]. 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 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 United States Virgin Islands, Puerto Rico, Canada, and Greenland, all characterized by their proximity to major cocaine production regions and higher demands and societal acceptance against drug use. For CAUD, regions with medical or full legalization, such as New Zealand, the United Kingdom, Australia, Belgium, and Canada, reported high disease burdens[22]. In the USA,

243 although cannabis is not federally legalized, several states permit both medical and recreational
244 use, contributing to the significant disease burden. For OUD, except for Kiribati, the top 30
245 countries with the highest DALYs attributable to OUD were predominantly high-income
246 countries or higher SDI countries. As previously mentioned, this trend may be linked to higher
247 demand and greater societal acceptance of opioid use in the West and high SDI regions[1].

248 Across four types of DUDs, high prevalence of CAUD and OUD presents distinct
249 patterns of estimated disease burden. While the burden of CAUD was the lowest, CAUD is
250 often considered a gateway drug[23], and association analyses indicate positive correlation with
251 other DUDs, including OUD, CUD, and AUD. The "gateway hypothesis" posits that a drug,
252 such as cannabis, could lower the threshold for use and access to other substances, such as
253 opioids[24]. Furthermore, underlying behavioral developmental mechanisms in patients with
254 CAUD coincide with risk factors such as genetic predisposition, trauma, unstable psychiatric
255 symptoms, thrill-seeking, impulsivity, and environmental exposures; these factors can increase
256 the likelihood of subsequent legal and illegal substance use, opioid or other drugs[25]. Delay
257 discounting, which refers to the tendency to devalue larger future rewards in favor of small
258 immediate gratification, is a factor in the decision-making process among individuals with
259 substance misuse. This cognitive bias, along with other factors, can increase the likelihood of
260 subsequent legal and illicit substance use, including opioids or other drugs[25].

261 Conversely, high burden associated with OUD is exacerbated by co-occurrence with
262 other serious conditions, contributing to worse overall disease burden. The International
263 Agency for Research on Cancer (IARC) identified opium consumption as a human carcinogen
264 (Group 1) in September 2020[26]. OUD substantially impacts disease burden due to several
265 factors, including its high dependency potential, the risk of overdose, indiscriminate needle and
266 syringe use for injection, as well as complications such as infectious diseases and mental health
267 disorders[1,24]. The trend of increasing OUD-related disease burden since 1990 in high-income

268 countries can be attributed to several factors due to overprescribing by the medical profession,
269 inadequate regulation, and increased use of illegal heroin and synthetic opioids[10]. The over-
270 prescription of opioid painkillers, particularly in the late 1990s and early 2000s, led to
271 widespread misuse. In addition, the availability of synthetic opioids, such as fentanyl, has
272 further exacerbated the issue due to their high potency and risk of overdose[10,11].

273 Socioeconomic factors, including mental health issues, unemployment, disparity
274 between urban and rural regions, and social instability, contribute to the observed rising trend
275 in DUDs[27,28]. Previous studies show strong associations between poverty, unemployment, and
276 higher drug overdose deaths[29]. Regions with higher poverty and unemployment rates generally
277 have higher rates of retail opioid sales and opioid prescriptions from Medicare[30]. In addition,
278 rural areas often experience poorer healthcare infrastructure compared to urban areas, which
279 can limit access to addiction treatment and prevention services[30]. These factors are often more
280 pronounced in less economically developed regions[30]. These factors combined have led to a
281 sustained increase in OUD burden in high-income countries over the past few decades. The
282 socioeconomic disparities were exacerbated during the COVID-19 pandemic, potentially
283 contributing to a sharp rise in the OUD burden[31].

284 Higher prevalence and burden of DUDs in males compared to females can be attributed
285 to several factors, including sex-specific social and cultural norms, higher rates of risk-taking
286 behaviors, and greater exposure to environments where drugs are more accessible[10]. Previous
287 studies emphasized the need to consider sex and/or gender differences in response to substance
288 use medication[32]. This approach is imperative for developing more effective clinical care
289 guidelines. In addition to sex differences, younger age groups, particularly adolescents and
290 young adults, are often at higher risk due to peer influence, risk-taking behaviors, lower barriers
291 to risky behaviors, and social pressures[33]. In countries with high SDI, the elevated prevalence
292 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 like mental health and unemployment[28].

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 DUDs[34]. 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 disorders [35]. Opioid substitution therapy involving methadone or buprenorphine reduces opioid use, opioid-related morbidity, risk of injection, and mortality, and improves well-being[36,37]. Distributing naloxone, an opioid antagonist, through community-based programs and pharmacies can effectively reverse overdoses and mitigate OUD[38].

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 burden[39]. 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 socioeconomic 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 have previously shown health benefits in tackling DUDs[1]. For example, in the mid-1990s, Australia experienced a similar surge in opioid overdose deaths, but through proactive interventions, mortality rates were reduced [40,41]. 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[40,41].

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 non-fatal burden (YLDs), which may contribute to an underestimation of its overall burden[2]. 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 estimates[31]. 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 are 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 DUD. 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 needs 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 (e.g., 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. Lastly, 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 accurately[1].

In conclusion, our study highlights increasing global burden of DUDs from 1990 to 2023, with high-income countries experiencing the highest prevalence and DALYs. Greatest burden were reported in OUD, exacerbated by its co-occurence with other conditions. Comprehensive strategies, including taxation and regulation of recreational drugs, opioid

367 substitution therapy, distribution of naloxone, needle exchange programs, and regulation of
368 telehealth prescriptions, are essential to mitigate the increasing burden of DUDs.
369

Competing Interests Statement

Our study is official IHME collaborator-lead paper, and, in principle, we will submit a COI list of authors when carrying out a revision status (689 authors).

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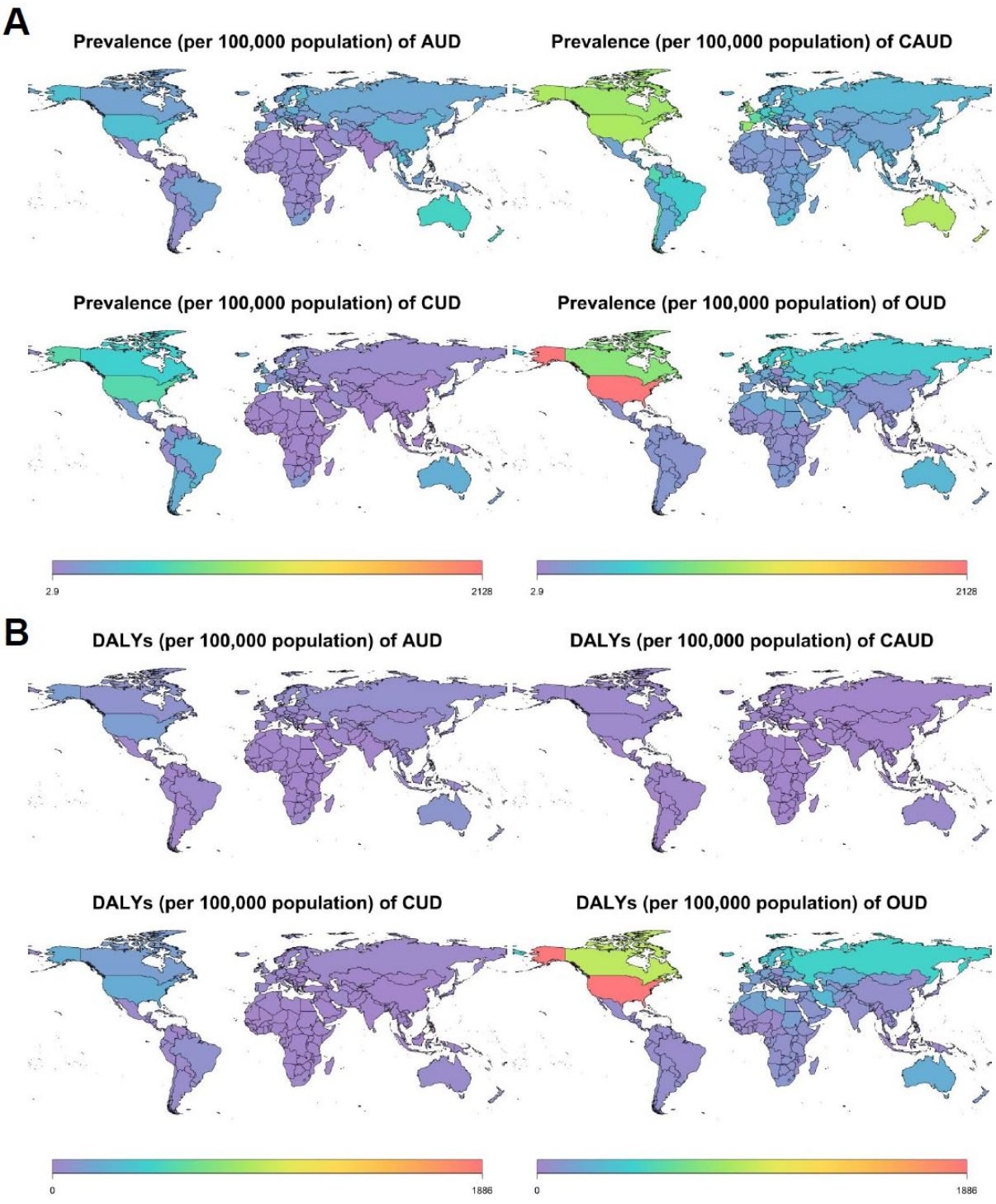


Figure 1. Age-standardised rates per 100,000 population attributable to drug use disorders for both sexes across 204 countries, 2023.

(A) Prevalence attributed to drug use disorders; **(B)** DALYs attributed to drug use disorders.

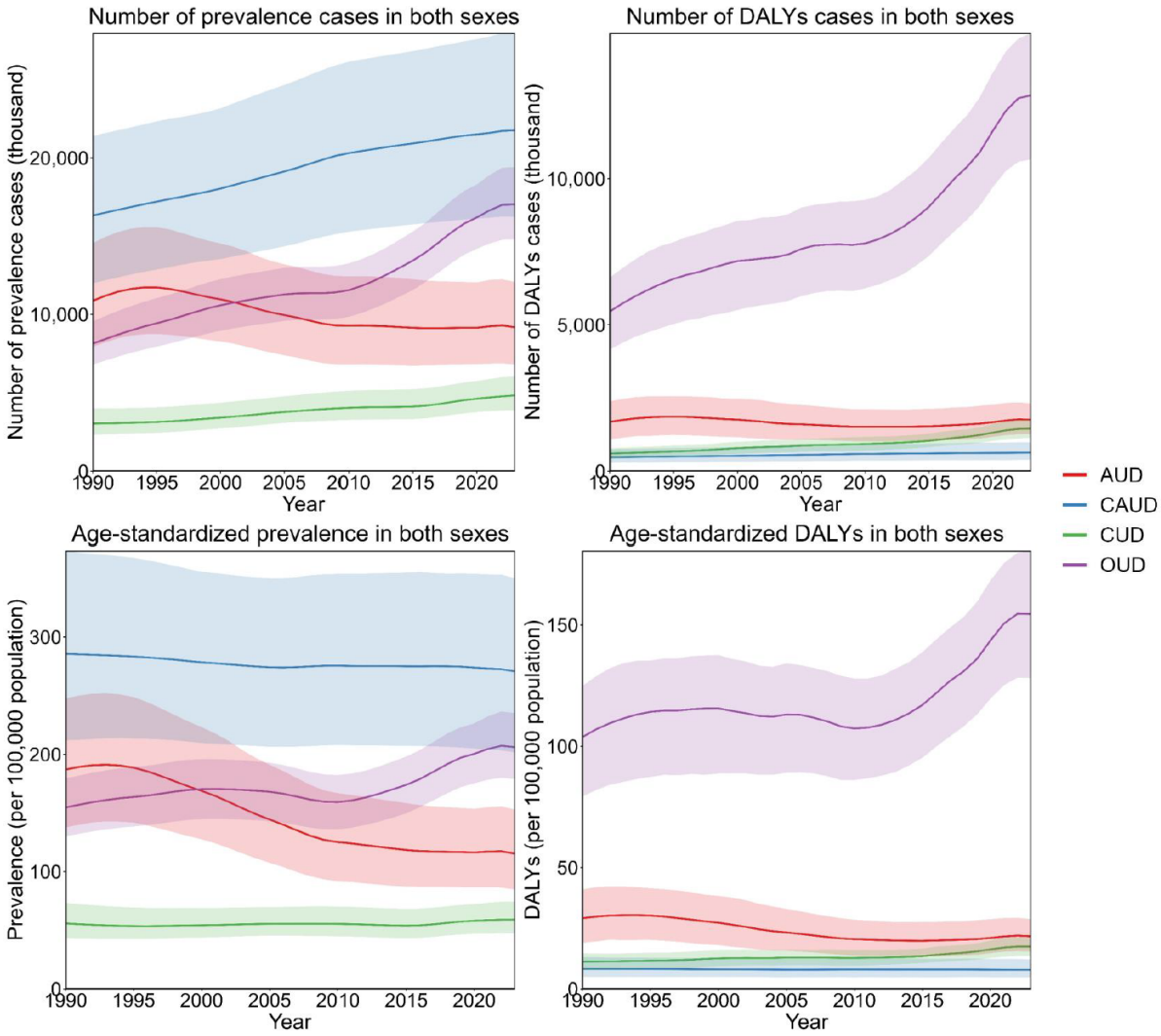


Figure 2. Global trends in prevalence and DALYs for the comparison of drug use disorders by substance type, 1990-2023.

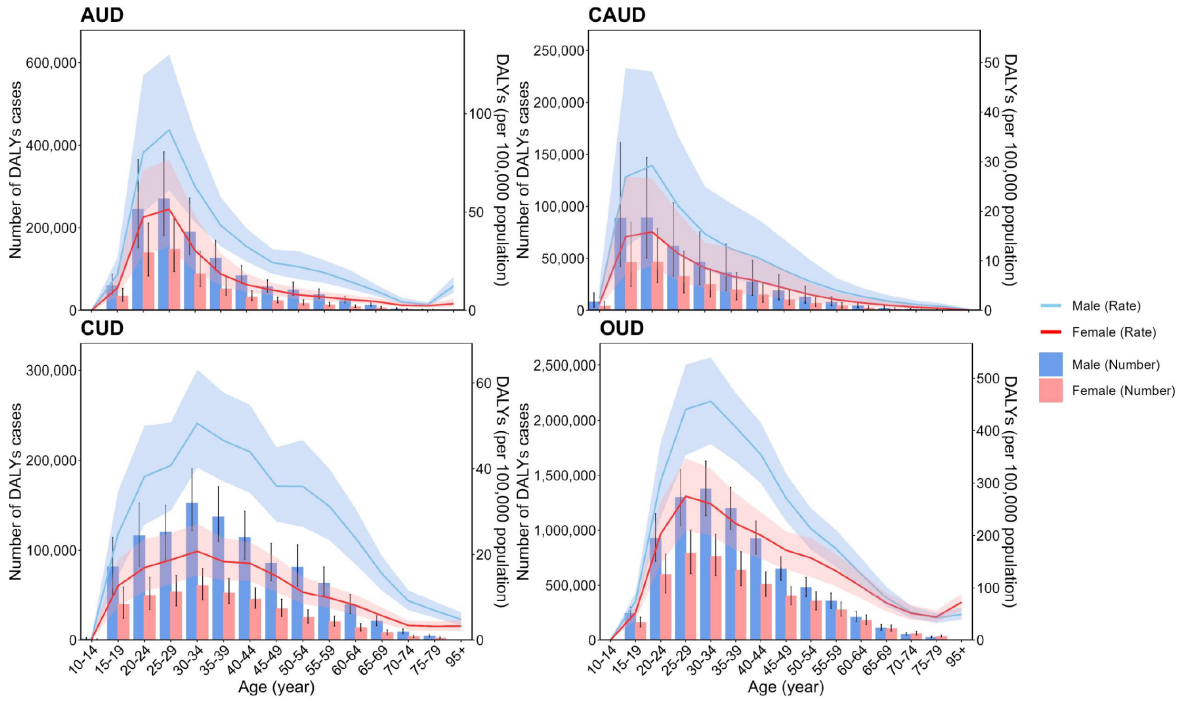
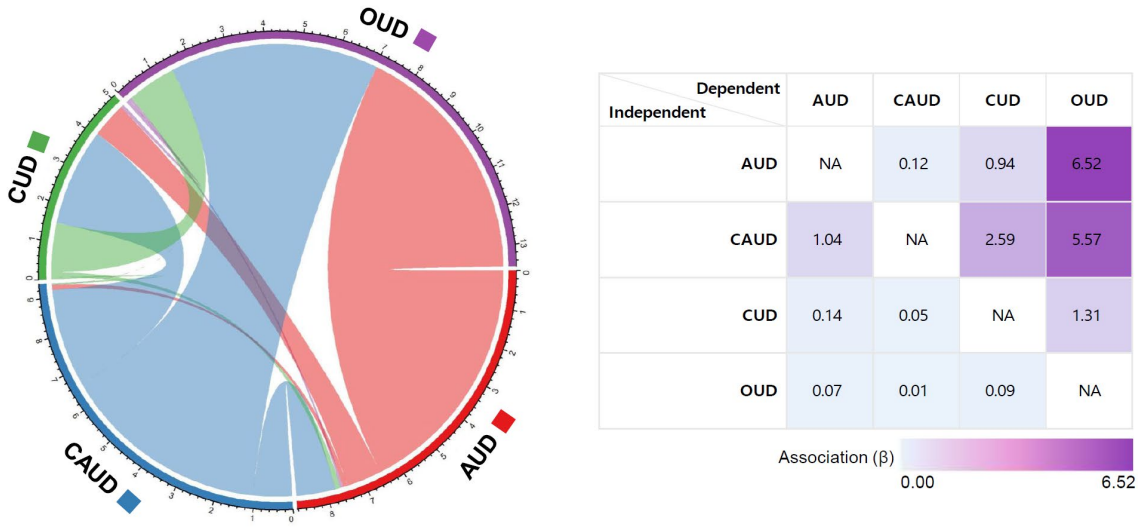


Figure 3. Distribution of DALYs numbers and rates per 100,000 population for drug use disorders by age group and sex, 2023.



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515 **Figure 4.** Age-standardized DALYs rate per 100,000 population for drug use disorders
516 attributed to each drug disorder, adjusted for the legalization level of cannabis use across 204
517 countries, 2023.

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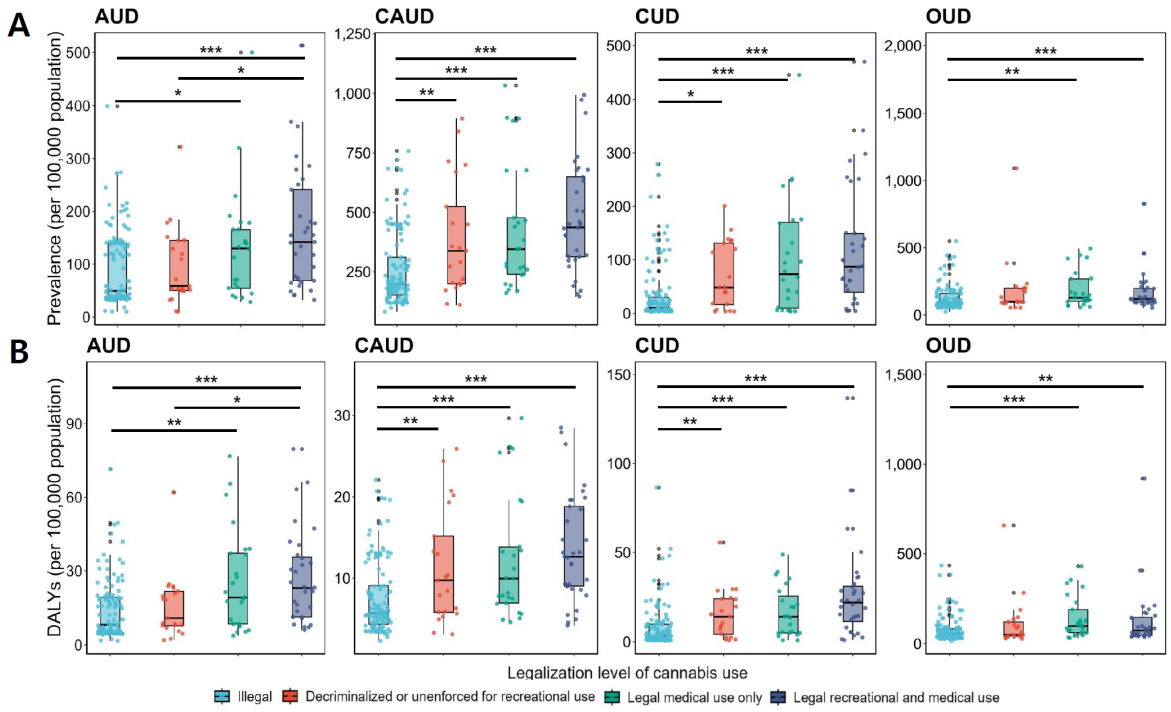

523

524 **Figure 5.** Age-standardized prevalence and DALYs per 100,000 population by drug use
525 disorders and cannabis legalization level across 204 countries, 2023. **(A)** Age-standardized
526 prevalence among cannabis legalization level; **(B)** Age-standardized DALYs among cannabis
527 legalization level.

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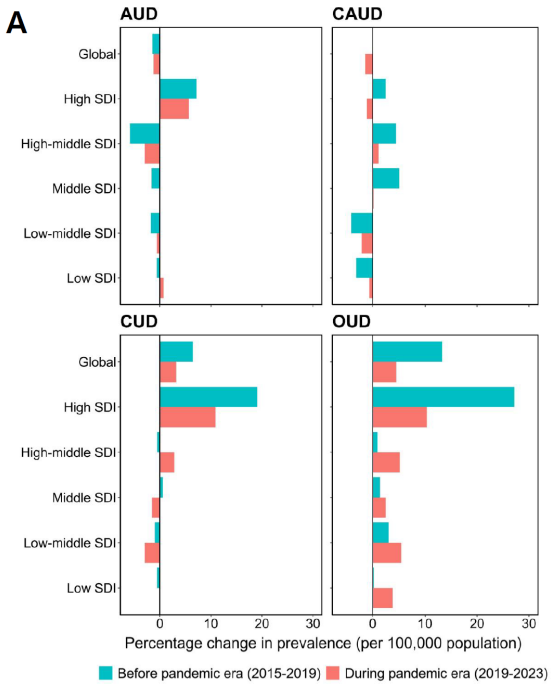

B

	Prevalence (per 100,000 population)		
	Percentage change in before pandemic (2015-2019), %	Percentage chanes in after pandemic (2019-2023), %	Difference in percentage (2015-2019 vs. 2019-2023), %
AUD			
Global	-1.4	-1.3	0.2
High SDI	7.2	5.6	-1.5
High-middle SDI	-5.8	-2.9	2.9
Middle SDI	-1.6	0.1	1.7
Low-middle SDI	-1.8	-0.6	1.2
Low SDI	-0.6	0.7	1.3
CAUD			
Global	-0.1	-1.5	-1.4
High SDI	2.5	-1.1	-3.6
High-middle SDI	4.5	1.1	-3.4
Middle SDI	5.1	0.2	-4.9
Low-middle SDI	-4.1	-2.1	2.0
Low SDI	-3.2	-0.7	2.5
CUD			
Global	6.5	3.2	-3.3
High SDI	19.1	10.9	-8.2
High-middle SDI	-0.5	2.9	3.4
Middle SDI	0.6	-1.5	-2.1
Low-middle SDI	-1.0	-2.9	-1.9
Low SDI	-0.5	0.1	0.6
OUD			
Global	13.3	4.6	-8.7
High SDI	27.2	10.3	-16.9
High-middle SDI	0.9	5.3	4.3
Middle SDI	1.4	2.5	1.2
Low-middle SDI	3.1	5.5	2.4
Low SDI	0.2	3.9	3.6

Figure 6. Age-standardized annual percentage change in prevalence of drug use disorders by socio demographic index, before and during pandemic periods (2017-2019 and 2019-2023). **(A)** Annual changes in prevalence rates per 100,000 population; **(B)** Difference in annual percent change and comparison between pre- and pandemic periods.

Table 1. Number of cases and age-standardized rate per 100,000 population for global prevalence and DALYs of drug use disorders, 1990 and 2023.

	1990		2023		Percentage change in prevalent cases, 1990-2023	Percentage change in age-standardized prevalence rate, 1990-2023
	Prevalent cases, in thousands (95% UI)	Age-standardized prevalence rate per 100,000 population (95% UI)	Prevalent cases, in thousands (95% UI)	Age-standardized prevalence per 100,000 population (95% UI)		
Drug use disorders						
Global	39072.9 (33443.6-45567.5)	698.0 (601.2-805.4)	53843.1 (46576.3-60704.5)	662.9 (571.3-749.6)	37.8	-5.0
Southeast Asia, East Asia, and Oceania	14026.1 (11868.1-16884.0)	720.5 (617.0-857.2)	11720.5 (9803.2-13853.3)	563.0 (467.5-679.4)	-16.4	-21.9
Central Europe, Eastern Europe, and Central Asia	3405.7 (2921.7-3968.0)	798.5 (681.5-940.4)	3038.5 (2689.7-3430.0)	783.6 (678.4-896.9)	-10.8	-1.9
High-income	12352.0 (10435.4-14290.8)	1324.9 (1112.6-1553.3)	20494.3 (18384.4-22649.9)	2062.4 (1842.3-2310.4)	65.9	55.7
Latin America and Caribbean	2775.7 (2268.9-3423.3)	672.0 (554.6-806.3)	4561.6 (3865.7-5298.1)	741.2 (626.8-863.8)	64.3	10.3
North Africa and Middle East	1290.7 (1093.6-1534.1)	396.6 (342.7-460.4)	2953.9 (2591.8-3405.1)	442.5 (388.4-510.8)	128.9	11.6
South Asia	3784.6 (3068.7-4681.7)	364.4 (295.7-441.4)	7497.4 (6056.9-8906.3)	368.1 (298.4-435.8)	98.1	1.0
Sub-Saharan Africa	1438.1 (1136.3-1832.7)	322.1 (264.5-389.0)	3576.9 (2816.9-4559.1)	305.1 (249.0-371.6)	148.7	-5.3
Amphetamine use disorders						
Global	10876.0 (7933.9-14560.0)	187.0 (137.7-247.7)	9181.7 (6800.6-12075.8)	115.2 (84.7-152.7)	-15.6	-38.4
Southeast Asia, East Asia, and Oceania	7604.7 (5655.3-10148.7)	369.3 (276.4-491.7)	4751.4 (3473.3-6325.8)	242.2 (174.8-326.7)	-37.5	-34.4
Central Europe, Eastern Europe, and Central Asia	705.5 (505.3-947.5)	166.2 (118.3-222.1)	637.6 (474.5-835.0)	175.7 (128.3-234.5)	-9.6	5.7
High-income	1683.8 (1169.4-2350.9)	177.4 (123.2-248.1)	2200.5 (1653.0-2861.6)	233.2 (173.9-307.5)	30.7	31.5
Latin America and Caribbean	439.7 (300.2-606.6)	105.0 (72.6-142.7)	602.3 (420.0-814.0)	97.6 (67.6-132.7)	37.0	-7.0
North Africa and Middle East	115.4 (78.6-160.3)	33.8 (23.7-45.8)	244.3 (171.7-330.4)	36.6 (25.7-49.6)	111.7	8.4

South Asia	113.2 (77.2-158.9)	11.0 (7.6-15.1)	233.7 (162.5-320.1)	11.4 (8.0-15.5)	106.4	3.7
Sub-Saharan Africa	213.7 (144.7-297.8)	47.1 (33.0-64.8)	511.9 (347.4-709.6)	42.8 (30.1-58.5)	139.5	-9.1
Cannabis use disorders						
Global	16318.4 (11983.5-21401.7)	285.7 (211.9-373.4)	21772.5 (16243.7-27949.6)	270.8 (201.7-350.0)	33.4	-5.2
Southeast Asia, East Asia, and Oceania	3370.1 (2418.2-4497.1)	174.0 (126.1-228.2)	4457.3 (3246.6-5815.0)	216.7 (155.1-290.1)	32.3	24.6
Central Europe, Eastern Europe, and Central Asia	1252.2 (864.4-1724.8)	302.7 (207.6-419.4)	979.4 (705.7-1325.5)	272.7 (192.6-375.5)	-21.8	-9.9
High-income	6341.2 (4844.2-7895.1)	700.3 (532.2-881.9)	6333.4 (4933.1-7835.9)	693.1 (533.1-865.7)	-0.1	-1.0
Latin America and Caribbean	1472.2 (1004.0-2070.2)	344.9 (241.3-477.9)	2232.3 (1652.8-2910.7)	366.0 (269.3-479.6)	51.6	6.1
North Africa and Middle East	418.1 (272.9-623.4)	118.5 (82.0-169.6)	902.8 (617.4-1298.3)	135.1 (92.8-194.2)	115.9	14.0
South Asia	2647.4 (1927.2-3496.4)	247.6 (184.4-320.4)	4772.1 (3415.9-6157.9)	231.9 (166.8-297.7)	80.3	-6.4
Sub-Saharan Africa	817.2 (539.5-1208.8)	170.0 (120.0-241.8)	2095.2 (1393.8-3136.7)	167.2 (115.6-237.4)	156.4	-1.7
Cocaine use disorders						
Global	3029.9 (2323.1-4012.7)	55.8 (43.4-73.4)	4837.6 (3904.5-6063.2)	59.1 (47.4-74.3)	59.7	6.0
Southeast Asia, East Asia, and Oceania	97.9 (61.3-143.5)	5.2 (3.2-7.5)	91.7 (58.4-136.6)	4.3 (2.6-6.5)	-6.3	-16.7
Central Europe, Eastern Europe, and Central Asia	181.0 (134.3-241.6)	42.4 (31.4-56.7)	136.6 (102.6-183.1)	35.0 (26.2-47.2)	-24.5	-17.3
High-income	2085.9 (1610.3-2725.2)	219.4 (167.4-288.4)	3127.7 (2550.3-3862.8)	307.7 (247.7-387.1)	49.9	40.3
Latin America and Caribbean	470.9 (343.8-631.1)	116.5 (88.0-155.7)	1076.5 (857.1-1353.4)	175.0 (139.0-220.0)	128.6	50.2
North Africa and Middle East	76.4 (52.5-107.1)	24.0 (17.2-33.1)	152.8 (110.3-208.1)	23.3 (16.9-31.5)	100.0	-2.6
South Asia	47.3 (30.3-68.9)	4.9 (3.4-6.9)	94.4 (64.8-132.7)	4.8 (3.4-6.7)	99.9	-2.1
Sub-Saharan Africa	70.4 (48.6-95.7)	17.9 (12.9-24.4)	157.9 (109.8-215.1)	15.5 (11.3-20.5)	124.2	-13.0
Opioid use disorders						
Global	8141.7 (6805.0-9569.8)	154.7 (130.2-179.4)	17016.2 (14791.4-19390.7)	205.9 (178.7-235.0)	109.0	33.1
Southeast Asia, East Asia, and Oceania	2681.4 (2228.5-3135.0)	155.1 (131.8-178.3)	2054.1 (1706.3-2402.2)	85.6 (70.0-100.8)	-23.4	-44.8

Central Europe, Eastern Europe, and Central Asia	1190.1 (1024.1-1400.2)	270.3 (231.8-316.6)	1197.5 (1035.6-1357.2)	282.7 (244.2-324.8)	0.6	4.6
High-income	2062.2 (1779.8-2351.2)	210.8 (181.7-240.7)	8700.3 (7638.9-9789.7)	824.7 (724.7-939.9)	321.9	291.3
Latin America and Caribbean	369.8 (277.2-466.4)	97.9 (75.4-120.6)	600.4 (468.1-735.0)	95.0 (73.5-116.5)	62.4	-3.0
North Africa and Middle East	620.7 (498.9-768.8)	198.3 (161.4-241.8)	1495.3 (1269.9-1762.5)	224.4 (190.8-264.9)	140.9	13.2
South Asia	910.3 (700.6-1112.1)	93.5 (74.3-112.4)	2235.2 (1786.6-2718.3)	111.6 (90.5-134.1)	145.6	19.4
Sub-Saharan Africa	307.4 (236.8-375.7)	78.7 (63.3-93.9)	733.4 (567.5-899.9)	71.3 (57.8-84.2)	138.6	-9.4
Other drug use disorders						
Global	945.4 (724.2-1224.1)	18.8 (14.7-24.3)	1515.2 (1200.0-1894.6)	18.0 (14.2-22.4)	60.3	-4.7
Southeast Asia, East Asia, and Oceania	338.9 (259.1-430.4)	20.2 (15.7-25.7)	405.4 (313.0-524.1)	16.3 (12.5-21.4)	19.6	-19.3
Central Europe, Eastern Europe, and Central Asia	97.6 (74.6-124.3)	21.9 (16.7-28.1)	104.4 (82.2-133.1)	22.3 (17.2-28.1)	7.0	1.6
High-income	304.6 (235.8-390.3)	30.6 (23.6-39.4)	504.1 (417.2-608.1)	43.9 (35.8-53.1)	65.5	43.4
Latin America and Caribbean	36.5 (26.5-48.8)	10.7 (7.9-14.3)	74.3 (55.9-97.9)	11.5 (8.6-15.1)	103.8	7.1
North Africa and Middle East	63.4 (47.6-79.3)	23.0 (17.8-29.8)	167.3 (129.5-210.3)	24.3 (18.9-30.3)	164.0	5.7
South Asia	71.9 (52.2-95.6)	7.9 (5.9-10.5)	174.4 (128.6-231.0)	8.9 (6.6-11.7)	142.5	13.1
Sub-Saharan Africa	32.5 (23.6-42.6)	9.2 (6.8-12.1)	85.2 (62.0-112.1)	8.9 (6.6-11.7)	162.4	-3.1

	DALYs cases, in thousands (95% UI)	**Age-standardized DALYs rate per 100,000 population (95% UI)**	**DALYs cases, in thousands (95% UI)**	**Age-standardized DALYs per 100,000 population (95% UI)**	**Percentage change in DALYs cases, 1990-2023**	**Percentage change in age-standardized DALYs rate, 1990-2023**
Drug use disorders						
Global	9118.5 (7217.7-10976.1)	169.3 (134.4-203.9)	17576.0 (14901.6-20347.0)	212.0 (179.2-245.6)	92.8	25.2
Southeast Asia, East Asia, and Oceania	4142.5 (3179.9-5163.8)	225.8 (175.1-282.0)	2169.6 (1645.8-2673.2)	97.3 (73.4-120.4)	-47.6	-56.9

Central Europe, Eastern Europe, and Central Asia	1002.0 (787.8-1202.8)	228.8 (179.4-274.1)	1316.2 (1066.7-1561.8)	309.9 (248.8-367.0)	31.4	35.4
High-income	2216.8 (1750.8-2628.4)	230.1 (181.1-272.7)	9915.9 (8405.8-11588.2)	917.4 (776.2-1069.1)	347.3	298.8
Latin America and Caribbean	360.6 (265.6-449.5)	91.2 (67.3-113.9)	739.4 (580.3-894.8)	118.3 (92.5-143.2)	105.1	29.7
North Africa and Middle East	446.5 (323.6-571.9)	144.9 (106.0-184.9)	1135.7 (875.9-1384.4)	170.6 (131.5-207.8)	154.3	17.7
South Asia	674.7 (504.9-861.8)	69.8 (52.2-88.8)	1564.9 (1186.4-1917.1)	79.3 (60.5-97.5)	131.9	13.6
Sub-Saharan Africa	275.4 (199.7-358.6)	69.0 (50.2-90.2)	734.3 (548.4-944.7)	70.1 (52.6-91.1)	166.6	1.7
Amphetamine use disorders						
Global	1682.3 (1085.2-2378.4)	29.1 (19.0-40.9)	1755.2 (1250.0-2307.4)	21.6 (15.3-28.6)	4.3	-25.7
Southeast Asia, East Asia, and Oceania	1217.1 (800.7-1711.2)	60.0 (39.7-84.7)	728.6 (465.5-1058.2)	36.5 (23.0-53.5)	-40.1	-39.2
Central Europe, Eastern Europe, and Central Asia	103.7 (65.8-151.9)	24.4 (15.4-35.6)	124.6 (88.4-166.7)	33.1 (23.2-45.0)	20.1	35.5
High-income	236.5 (143.7-348.9)	24.9 (15.1-36.8)	641.4 (479.8-811.8)	61.1 (45.3-76.8)	171.1	145.4
Latin America and Caribbean	58.6 (34.8-88.4)	14.0 (8.4-21.0)	91.5 (56.8-132.6)	14.8 (9.1-21.5)	56.1	5.4
North Africa and Middle East	17.6 (10.7-25.6)	5.3 (3.2-7.6)	49.0 (30.8-69.0)	7.4 (4.6-10.4)	178.7	39.7
South Asia	19.8 (11.4-31.4)	1.9 (1.1-3.1)	47.3 (29.4-67.8)	2.3 (1.5-3.4)	138.8	21.1
Sub-Saharan Africa	29.0 (16.8-43.3)	6.4 (3.8-9.6)	72.9 (44.3-108.9)	6.2 (3.8-9.1)	151.6	-3.4
Cannabis use disorders						
Global	472.3 (283.6-748.0)	8.3 (5.0-13.0)	629.0 (383.6-991.6)	7.8 (4.8-12.3)	33.2	-5.3
Southeast Asia, East Asia, and Oceania	97.9 (55.9-157.4)	5.1 (2.9-8.1)	129.7 (76.3-206.2)	6.3 (3.6-10.0)	32.4	24.9
Central Europe, Eastern Europe, and Central Asia	36.4 (19.9-58.7)	8.8 (4.8-14.3)	28.5 (16.4-45.0)	7.9 (4.5-12.7)	-21.8	-9.8
High-income	183.5 (109.8-281.5)	20.3 (12.1-31.0)	182.1 (110.8-281.7)	20.0 (12.0-30.9)	-0.7	-1.5
Latin America and Caribbean	42.5 (23.4-69.7)	9.9 (5.6-15.8)	64.3 (38.4-101.4)	10.6 (6.3-16.6)	51.2	6.1
North Africa and Middle East	12.1 (6.5-20.8)	3.4 (1.9-5.7)	26.3 (14.5-43.4)	3.9 (2.2-6.5)	116.5	14.1
South Asia	76.3 (44.3-118.4)	7.1 (4.2-11.0)	137.5 (82.6-219.0)	6.7 (4.0-10.5)	80.2	-6.2
Sub-Saharan Africa	23.6 (12.7-39.6)	4.9 (2.7-8.1)	60.6 (33.0-103.3)	4.8 (2.7-8.1)	156.9	-1.5

Cocaine use disorders						
Global	602.3 (415.8-789.1)	11.2 (7.9-14.7)	1453.9 (1142.3-1769.6)	17.4 (13.6-21.3)	141.4	55.3
Southeast Asia, East Asia, and Oceania	44.7 (25.9-72.5)	2.5 (1.5-4.0)	29.0 (18.3-41.5)	1.3 (0.8-1.8)	-35.3	-48.8
Central Europe, Eastern Europe, and Central Asia	57.5 (43.3-76.0)	13.1 (9.8-17.3)	46.1 (34.6-60.0)	11.0 (8.0-14.3)	-19.8	-16.4
High-income	335.5 (217.3-455.7)	35.2 (22.8-48.1)	946.4 (739.4-1184.2)	85.7 (65.1-106.5)	182.0	143.8
Latin America and Caribbean	88.4 (60.0-121.5)	22.0 (15.2-29.7)	268.0 (206.2-329.5)	43.1 (32.9-53.0)	203.3	96.0
North Africa and Middle East	23.0 (14.1-33.7)	7.8 (4.8-11.4)	52.4 (32.6-76.6)	8.0 (5.0-11.6)	127.8	2.3
South Asia	33.3 (17.3-59.3)	3.6 (1.9-6.4)	65.1 (38.0-107.2)	3.4 (2.0-5.7)	95.3	-5.1
Sub-Saharan Africa	19.8 (12.5-31.4)	5.1 (3.3-7.9)	47.0 (28.0-78.6)	4.6 (2.8-7.5)	137.3	-8.5
Opioid use disorders						
Global	5459.6 (4189.1-6615.1)	103.9 (79.9-124.8)	12785.5 (10598.8-14934.0)	153.7 (127.4-180.0)	134.2	48.0
Southeast Asia, East Asia, and Oceania	2141.0 (1572.0-2657.7)	123.4 (91.2-152.2)	1129.7 (863.5-1438.5)	47.0 (35.8-59.4)	-47.2	-61.9
Central Europe, Eastern Europe, and Central Asia	746.1 (574.0-903.6)	169.3 (130.3-205.4)	1016.2 (829.3-1235.0)	234.7 (189.5-284.6)	36.2	38.7
High-income	1350.2 (1060.0-1606.7)	138.4 (108.6-164.7)	7680.7 (6376.5-8962.6)	708.9 (587.1-833.8)	468.9	412.2
Latin America and Caribbean	159.6 (112.5-212.3)	42.3 (29.7-55.3)	272.0 (192.9-354.8)	43.0 (30.4-56.1)	70.4	1.7
North Africa and Middle East	365.9 (259.2-474.8)	118.9 (84.9-152.2)	927.2 (701.1-1139.7)	139.3 (105.3-171.3)	153.4	17.1
South Asia	502.1 (354.5-653.2)	52.4 (37.3-67.8)	1228.7 (909.3-1551.9)	62.2 (46.6-78.3)	144.7	18.7
Sub-Saharan Africa	194.8 (136.1-257.7)	50.4 (35.6-67.1)	531.2 (378.1-702.0)	52.2 (38.1-68.4)	172.7	3.6
Other drug use disorders						
Global	901.9 (649.2-1233.0)	16.8 (12.2-22.8)	952.4 (824.4-1104.5)	11.4 (9.8-13.2)	5.6	-32.4
Southeast Asia, East Asia, and Oceania	641.8 (418.7-968.8)	34.9 (22.9-52.8)	152.7 (111.3-214.2)	6.3 (4.6-8.8)	-76.2	-82.0
Central Europe, Eastern Europe, and Central Asia	58.2 (45.9-74.4)	13.3 (10.4-17.0)	100.9 (75.0-134.7)	23.2 (17.2-31.3)	73.3	74.6
High-income	111.1 (92.0-130.9)	11.3 (9.4-13.3)	465.3 (384.2-564.5)	41.8 (34.4-50.7)	319.0	268.4

Latin America and Caribbean	11.5 (9.2-14.1)	3.0 (2.4-3.7)	43.7 (36.6-52.3)	6.9 (5.8-8.3)	280.1	130.5
North Africa and Middle East	28.0 (17.9-44.6)	9.5 (6.2-15.2)	80.9 (51.6-123.3)	12.1 (7.7-18.5)	189.3	26.9
South Asia	43.2 (25.9-67.0)	4.7 (2.9-7.2)	86.3 (54.6-136.9)	4.6 (2.9-7.2)	99.8	-2.2
Sub-Saharan Africa	8.3 (5.4-11.8)	2.2 (1.4-3.1)	22.7 (14.7-33.8)	2.3 (1.5-3.4)	174.1	4.8

Abbreviation: DALYs, disability-adjusted life year; UI, uncertainty interval.

Figure Legends

Figure 1. Age-standardized per 100,000 population attributable to drug use disorders for both sexes across 204 countries, 2023.

(A) Prevalence attributed to drug use disorders; **(B)** DALYs attributed to drug use disorders.

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

Figure 2. Global trends in prevalence and DALYs (numbers and age-standardized rate per 100,000 population) for the comparison of drug use disorders by substance type, 1990-2023.

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

Figure 3. Distribution of DALYs numbers and rates per 100,000 population for drug use disorders by age group and sex, 2023.

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

Figure 4. Age-standardized DALYs per 100,000 population for drug use disorders attributed to each drug disorder, adjusted for the legalization level of cannabis use across 204 countries, 2023.

Abbreviations: AUD, amphetamine use disorders; CAUD, cannabis use disorders; CUD, cocaine use disorders; DALYs, disability-adjusted life year; NA, not available; OUD, opioid use disorders.

Figure 5. Age-standardized prevalence and DALYs per 100,000 population by drug use disorders and cannabis legalization level across 204 countries, 2023.

(A) Age-standardized prevalence among cannabis legalization level; **(B)** Age-standardized DALYs among cannabis legalization level.

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

Figure 6. Age-standardized percentage change in prevalence of drug use disorders by SDI, before and during pandemic periods (2015-2019 and 2019-2023).

(A) Percentage change in prevalence per 100,000 population; **(B)** Difference in percent change and comparison between pre- and pandemic periods.

Abbreviations: AUD, amphetamine use disorders; CAUD, cannabis use disorders; CUD, cocaine use disorders; OUD, opioid use disorders; SDI, socio-demographic index.

Methods

Study design

The GBD 2023 quantified the burden of disease attributable to 371 causes of death from 1990 to 2023[42]. This comprehensive analysis estimated prevalence, incidence, DALYs, years of life lost (YLLs), years lived with disability (YLDs), 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; Latin America and the Caribbean; North Africa and Middle East; South Asia; and Sub-Saharan Africa; **Supplementary Table 10**)[1], and SDI (low SDI, low-middle SDI, middle SDI, high-middle SDI, and high SDI; **Supplementary Table 11**)[43]. 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 (GDP), 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)[44]. The data used in this analysis can be accessed at Global Health Data Exchange (GHDx; https://ghdx.healthdata.org/gbd-2023/sources), and the detailed methodology has been comprehensively outlined in previous publications[45,46].

Case definition and input data

The case definition for non-fatal estimation of each disorder was established using datasets derived from the DSM-IV-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[47,48]:

- 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 non-fatal and fatal DUDs were summarized in **Supplementary Table 12**. 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)[49]. To systematically reallocate these garbage-coded deaths to valid underlying causes of death (UCoD), a structured redistribution process was applied[50]. First, grouping garbage codes based on their diagnostic relatedness to ensure that non-specific or unreliable ICD codes are 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 includes all causes listed on a death certificate, was utilized to enhance the accuracy of this reassignment[49]. 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 cause[50]. Data sources were excluded where more than 50% of all deaths in a specific location-year were attributed to major garbage codes in order 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 65[49]. This indicated that the cases are not accidental ingestions but rather unexpected addictions following intentional intake[51]. 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 fatality[49]. Since many cases involve multiple substances, **Supplementary Table 13** 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 records[46]. 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 applied. In addition, estimates covering wide age ranges were further disaggregated into five-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.

Differences between study definitions and the optimal case definition required for analysis conducted additional data adjustments to ensure comparability across causes and locations, even when reported estimates were available[46]. For CAUD, most studies reported prevalence based on either "any use" or "regular use," requiring a two-step adjustment process[46]. 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 reliable[46]. 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 datasets[46]. 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 sex[52]. 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 DUD, including cannabis, cocaine, amphetamine, and opioid use disorders. The severity of 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 U.S. National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), the Comorbidity and Trauma Study, and other surveys were utilized[46,53]. 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 non-fatal 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 (LDI) was considered. For opioids, log-transformed estimates of defined daily doses for statistical purposes (SDDD; 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 (HAQ) Index were included as covariates.

To assess fatal estimates such as cause-specific mortality of four types of DUD, the Cause of Death Ensemble model (CODEm) was employed, stratified by year, age, sex, and

region for each disorder[54]. 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 DUDs[42]. 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 (TFU25), the average education level for those aged 15 and older (EDU15+), and LDI per capita[55]. 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)[56]. 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 burden 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 14**). Post-hoc analysis using Dunn's test was conducted to assess the statistical significance of differences among groups, with a significance level defined at $p<0.05$[57]. 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 three-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 2023[58]. 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[59,60]. Epidemiological changes refer to the adjusted change in DUDs, accounting for age-specific and population size. The impact of evaluated factors was 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 (version 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.

Data Availability Statement

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 at https://ghdx.healthdata.org/gbd-2023/sources.

Code Availability Statement

Our study follows the Guidelines for Accurate and Transparent Health Estimate Reporting (GATHER; Supplementary Table 15). All code used for the GBD 2023 analyses is publicly available online at https://ghdx.healthdata.org/gbd-2023/code.

Methods-only References

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