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3 DEPRESSANTS

WORLD DRUG REPORT 2019

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PREFACE

The findings of this year's *World Drug Report* fill in and further complicate the global picture of drug challenges, underscoring the need for broader international cooperation to advance balanced and integrated health and criminal justice responses to drug supply and demand.

With improved research and more precise data from India and Nigeria – both among the 10 most-populous countries in the world – we see that there are many more opioid users and people with drug use disorders than previously estimated. Globally, some 35 million people, up from an earlier estimate of 30.5 million, suffer from drug use disorders and require treatment services. The death toll is also higher: 585,000 people died as a result of drug use in 2017.

Prevention and treatment continue to fall far short of needs in many parts of the world. This is particularly true in prisons, where those incarcerated are especially vulnerable to drug use and face higher risks of HIV and hepatitis C transmission. This gap represents a major impediment to achieving the Sustainable Development Goals and fulfilling the international community's pledge to leave no one behind.

Synthetic opioids continue to pose a serious threat to health, with overdose deaths rising in North America and trafficking in fentanyl and its analogues expanding in Europe and elsewhere. The opioid crisis that has featured in far fewer headlines but that requires equally urgent international attention is the non-medical use of the painkiller tramadol, particularly in Africa. The amount of tramadol seized globally reached a record 125 tons in 2017; the limited data available indicate that the tramadol being used for non-medical purposes in Africa is being illicitly manufactured in South Asia and trafficked to the region, as well as to parts of the Middle East.

The response to the misuse of tramadol illustrates the difficulties faced by countries in balancing necessary access for medical purposes while curbing abuse – with limited resources and health-care systems that are already struggling to cope – and at the same time clamping down on organized crime and trafficking.

Opium production and cocaine manufacture remain at record levels. The amounts intercepted are also higher than ever, with the amount of cocaine seized up 74 per cent over the past decade, compared with a 50 per cent rise in manufacture during the same period. This suggests that law enforcement efforts have become more effective and that strengthened international cooperation may be helping to increase interception rates.

The *World Drug Report 2019* also registers a decline in opiate trafficking from Afghanistan along the "northern" route through Central Asia to the Russian Federation. In 2008, some 10 per cent of the morphine and heroin intercepted globally was seized in countries along the northern route; by 2017 it had fallen to 1 per cent. This may be due in part to a shift in demand to synthetics in destination markets. The increased effectiveness of regional responses may also play a role.

Countries in central Asia, with the support of the United Nations Office on Drugs and Crime (UNODC), have committed considerable resources to strengthening regional cooperation through integrated UNODC country, regional and global programmes, as well as through platforms such as the Central Asian Regional Information and Coordination Centre, the Afghanistan–Kyrgyzstan–Tajikistan Initiative and the Triangular Initiative and its Joint Planning Cell. More research is needed, including to identify lessons learned and best practices that could inform further action.

International cooperation has also succeeded in checking the growth in new psychoactive substances. The Vienna-based Commission on Narcotic Drugs has acted swiftly in recent years to schedule the most harmful new psychoactive substances, and the UNODC early warning advisory has helped to keep the international community abreast of developments.

Political will and adequate funding remain prerequisites for success. Efforts by Colombia to reduce cocaine production following the 2016 peace deal

with the Revolutionary Armed Forces of Colombia (FARC) are a case in point. Alternative development initiatives have enabled farmers in central areas of the country previously under FARC control to abandon coca bush cultivation and join the licit economy. The result has been a drastic reduction in cocaine production. However, in other areas previously controlled by FARC, criminal groups have moved in to fill the vacuum and expand cultivation. Alternative development can succeed, but not without sustained attention and integration into broader development goals.

The successes identified amid the many, formidable problems that countries continue to face in grappling with drug supply and demand highlight that international cooperation works. The challenge before us is to make this cooperation work for more people.

International cooperation is based on agreed frameworks. Nearly every country in the world has reaffirmed its commitment to balanced, rights-based action based on the international drug control conventions. The most recent reaffirmation of that commitment is the Ministerial Declaration on Strengthening Our Actions at the National, Regional and International Levels to Accelerate the Implementation of Our Joint Commitments to Address and Counter the World Drug Problem, adopted at the ministerial segment of the sixty-second session of the Commission on Narcotic Drugs.

UNODC supports countries in putting their commitments into action through the application of international standards on the prevention and treatment of drug use disorders and HIV, as well as standards and norms on the administration of justice and the treatment of prisoners. We provide tailored technical assistance through our field offices and global programmes, and through toolkits and research.

I hope the *World Drug Report 2019* will shed further light on the world drug problem and inform international community responses. By working together and focusing attention and resources, we can help people get the services they need without discrimination, promote security and bring criminals to justice, safeguard health and achieve the Sustainable Development Goals.

Yury Fedotov
Executive Director
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EXPLANATORY NOTES

The boundaries and names shown and the designations used on maps do not imply official endorsement or acceptance by the United Nations. A dotted line represents approximately the line of control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. Disputed boundaries (China/India) are represented by crosshatch owing to the difficulty of showing sufficient detail.

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Countries and areas are referred to by the names that were in official use at the time the relevant data were collected.

All references to Kosovo in the *World Drug Report*, if any, should be understood to be in compliance with Security Council resolution 1244 (1999).

Since there is some scientific and legal ambiguity about the distinctions between "drug use", "drug misuse" and "drug abuse", the neutral term "drug use" is used in the *World Drug Report*. The term "misuse" is used only to denote the non-medical use of prescription drugs.

All uses of the word "drug" and the term "drug use" in the *World Drug Report* refer to substances controlled under the international drug control conventions, and their non-medical use.

All analysis contained in the *World Drug Report* is based on the official data submitted by Member States to the UNODC through the annual report questionnaire unless indicated otherwise.

The data on population used in the *World Drug Report* are taken from: *World Population Prospects: The 2017 Revision* (United Nations, Department of Economic and Social Affairs, Population Division).

References to dollars ($) are to United States dollars, unless otherwise stated.

References to tons are to metric tons, unless otherwise stated.

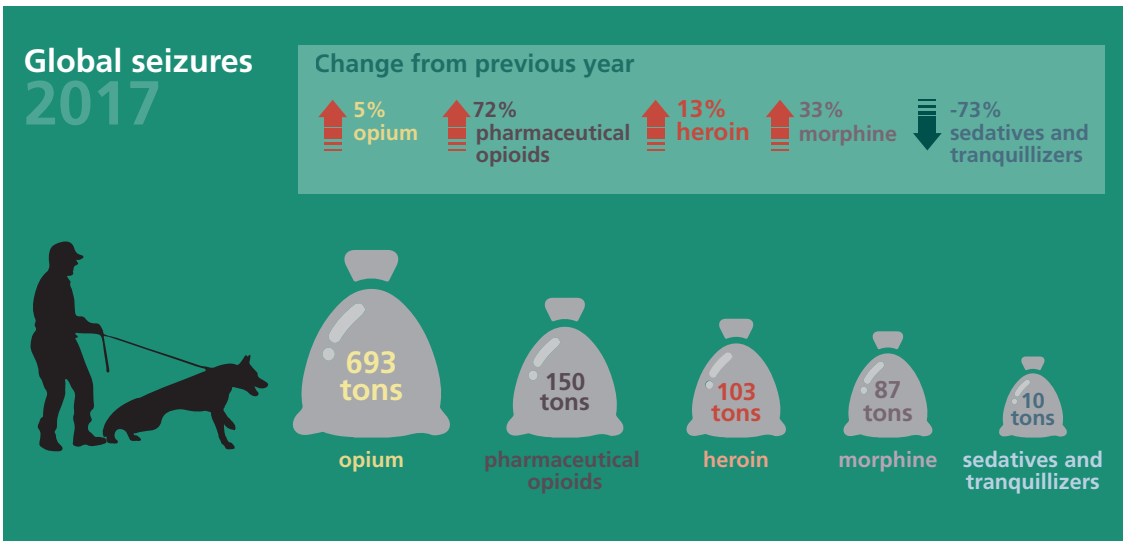
The following abbreviations have been used in the present booklet:

4-ANPP	4-anilino-*N*-phenethyl-4-piperidone
ANPP	4-anilino-*N*-phenethyl-4-piperidone
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
DEA	Drug Enforcement Administration of the United States
GABA	*gamma*-aminobutyric acid
GBL	*gamma*-butyrolactone
GHB	*gamma-hydroxybutyric acid*
INCB	International Narcotics Control Board
NPP	*N*-phenethyl-4-piperidone
NPS	new psychoactive substances
S-DDD	standard defined daily doses
UNODC	United Nation Office on Drugs and Crime
WHO	World Health Organization

SCOPE OF THE BOOKLET

This booklet, the third chapter of the *World Drug Report 2019*, provides an analysis of the market for substances that are broadly known as depressants of the central nervous system, which are primarily used to suppress, inhibit or decrease brain activity. The main classes of depressants discussed in this section include opioids, sedatives, tranquillizers and hypnotics. The sections on drug supply discuss both the depressants that have been diverted from licit sources and those that have been manufactured illicitly, while the sections on drug demand discuss the medical and non-medical use of depressants. To aid understanding of how depressants function in the human body, preliminary information is provided in the relevant sections.

While depressants of the central nervous system are used on their own for the psychoactive effect, they also figure prominently in the polydrug use patterns of people who use different drugs. One pattern of such use is the concurrent use of two or more depressants, such as the use of alcohol and benzodiazepines with opioids, to self-medicate or potentiate the effects of the opioid.[1, 2] In other instances, people who use depressants such as opioids as their primary drug, in response to market dynamics such as changes in the availability, purity and price of a drug, may readily switch to another opioid (for example, from oxycodone to heroin or vice versa) in order to maintain the same level of psychoactive experience.[3] Depressants are also used concurrently or sequentially with stimulants, either to overcome the side-effects of the other substance or to alleviate the adverse effects and severity of withdrawal symptoms.[4, 5]



1 Marc Vogel and others, "Treatment or 'high': benzodiazepine use in patients on injectable heroin or oral opioids", *Addictive Behaviors*, vol. 38, No. 10 (October 2013), pp. 2477–2484.

2 Takahiro Yamamoto and others, "Concurrent use of benzodiazepine by heroin users: what are the prevalence and the risks associated with this pattern of use?", *Journal of Medical Toxicology*, vol. 15, No.1 (January 2019), pp. 4–11.

3 See also *World Drug Report 2016* (United Nations publication, Sales No. E.16.XI.7).

4 Francesco Leri and others, "Understanding polydrug use: review of heroin and cocaine co-use" *Addiction* (2003), 98, pp. 7–22.

5 Keith A Trujillo and others, "Powerful behavioural interactions between methamphetamine and morphine", *Pharmacology, biochemistry and behaviour*, September 2011, vol. 99, No. 3, pp. 451–458.

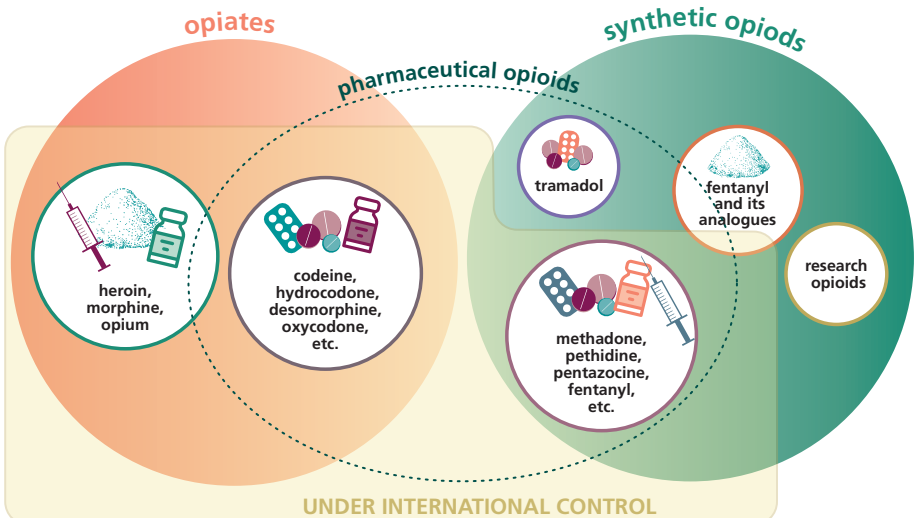
OPIOIDS

Introduction

"Opioids" is a generic term that refers both to opiates and their synthetic analogues.[6] Opiates are naturally occurring alkaloids found in the opium poppy, such as morphine, codeine and thebaine, as well as their semi-synthetic derivatives, such as heroin, hydrocodone, oxycodone and buprenorphine.[7, 8] The term "opioids" also includes synthetic opioids, which are structurally diverse substances. Some are used in medicine mainly for the management of pain resulting from conditions such as trauma, surgery and cancer, and are thus also referred to as pharmaceutical opioids, indicating their medical use.[9] Most pharmaceutical opioids are controlled under the Single Convention on Narcotic Drugs of 1961 with the exception of some, such as buprenorphine, which are controlled under the Convention on Psychotropic Substances of 1971. Tramadol is an example of a pharmaceutical opioid that is currently not controlled under the drug conventions.

Nowadays, most opium is illegally produced for either its non-medical consumption or for the illegal manufacture of morphine and its semi-synthetic derivative, heroin, which are substances controlled at the international level under the 1961 Convention. Opium and opium poppy straw are also produced legally for medical use, mostly for the manufacture of morphine, codeine and thebaine, as well as the subsequent manufacture of a number of semi-synthetic opioids, which also belong to the category of "opiates".

A number of synthetic opioid receptor agonists have been developed by the pharmaceutical industry over the past half century, both for medicinal use, including in veterinary medicine, with the aim of developing more effective medicines for pain management. A few of those substances proved to be effective and were later released into the pharmaceutical market,



Examples of synthetic opioids		
Alphaprodine	Anileridine	Bezitramide
Dextromoramide	Dextropropoxyphene	Diphenoxylate
Dipipanone	Fentanyl and some of its analogues such as alfentanil, remifentanil	Ketobemidone
Levorphanol	Methadone	Pethidine
Phenazocine	Phenoperidine	Pentazocine

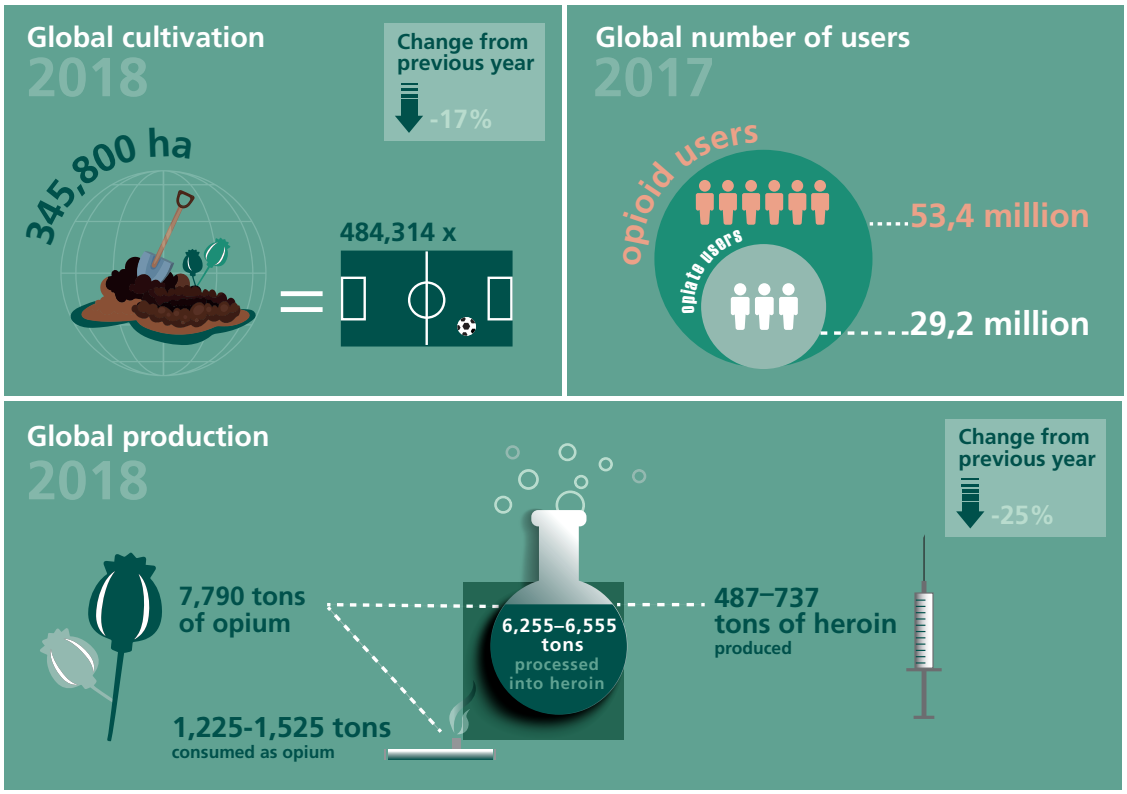
Note: These synthetic opioids are controlled under 1961 Convention, with the exception of pentazocine, which is controlled under the 1971 Convention.

6 WHO, *Lexicon of Alcohol and Drug Terms* (Geneva, 2014).

7 Ibid.

8 All opiates are controlled under the Single Convention on Narcotic Drugs of 1961, except for buprenorphine, which is controlled under Schedule III of the Convention on Psychotropic Substances of 1971.

9 See, for example, *World Drug Report 2017* (United Nations publication, Sales No. E.16.XI.6).



but many were not developed further and were never marketed as pharmaceutical opioids. Some discarded substances, including many fentanyl analogues and research opioids, such as U-47700 and AH-7921, are derived from information provided in the research publications of pharmaceutical companies and have now been introduced into the illicit drug markets. A few of those substances, such as furanylfentanyl and U-47700, have recently been placed under international control; substances not under international control are classified as NPS with opioid effects.

Opioid receptors

In the human body there are three types of opioid receptors – mu (μ), delta (Δ) and kappa (K) receptors – that mediate the activity of both exogenous opioids (drugs) and endogenous peptides such as the endorphins. Extensively present in the brain, brainstem and the spinal cord, opioid receptors are responsible for triggering brain reward systems and producing analgesia (pain relief) by decreasing pain transmission. The location of opioid receptors in specific parts of the body, such as the "respiratory centre" in the brain, intestines and the peripheral neurons, produces other effects such as suppression of breathing, constipation and sensations of warmth in association with the use of opioids.[10] In addition to these effects, opioid peptides impact a wide variety of other functions such as the regulation of stress responses, feelings, mood, learning, memory and immune functions.[11]

Pharmaceutical opioids for medical purposes

Pharmaceutical opioids have been used for the management and control of acute and chronic pain that can result from physical trauma and post-surgical care, and for palliative therapy for cancer and other chronic conditions. In addition, pharmaceutical opioids such as buprenorphine and methadone are on the WHO Model List of Essential Medicines for

10 UNODC, "Understanding the global opioid crisis", Global SMART Update, vol. 21 (March 2018).

11 WHO, *Neuroscience of Psychoactive Substance Use and Dependence* (Geneva, 2004).

the treatment of opioid use disorders. In some countries, heroin is used in a medical context as part of heroin-assisted treatment directed at people for whom other opioid treatment options have previously failed. Such treatments can help those people to remain in treatment, limit their use of street drugs, reduce their illegal activities, and possibly reduce their likelihood of overdose and mortality. In such heroin-assisted programmes, heroin is administered, preferably in a clinical setting as unadulterated, subsidized or even cost-free.[12] In addition, some of the opioids that are available over the counter are also used to relieve cough and severe diarrhoea.

TABLE 1 Pharmaceutical opioids and their use

Indication or condition	Main opioids used for treatment
Severe pain	Fentanyl, hydromorphone, morphine and pethidine
Moderate to severe pain	Buprenorphine, oxycodone and tramadol
Mild to moderate pain	Codeine, dihydrocodeine and dextropropoxyphene
Induce or supplement anaesthesia	Fentanyl and its analogues such as alfentanil and remifentanil
Cough suppressant	Codeine, dihydrocodeine, pholcodine and ethylmorphine
Gastrointestinal disorders such as diarrhoea	Codeine and diphenoxylate
Opioid use disorders	Buprenorphine and methadone

Source: INCB, *Narcotic Drugs: Estimated World Requirements for 2018 – Statistics for 2016* (E/INCB/2017/1), para. 36.

According to INCB, the consumption for medical purposes of pharmaceutical opioids that are under international control more than doubled from 1998 to 2010 (as expressed in defined daily doses), followed a stable trend from 2010 to 2014, then decreased by 10 per cent until 2017.[13]

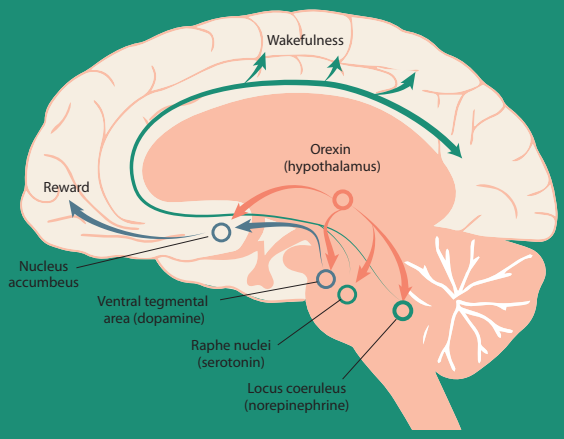
12 Marica Ferri, Marina Davoli and Carlos A. Perucci, "Heroin maintenance for chronic heroin-dependent individuals", *Cochrane Database of Systematic Reviews*, No. 12 (2011).

13 INCB, *Narcotics Drugs: Estimated World Requirements for 2019 – Statistics for 2017* (E/INCB/2018/2) and previous years.

Mesolimbic dopamine system

The mesolimbic dopamine system, involving the ventral tegmental area and the nucleus accumbens in the brain, is involved in the stimuli-reward-motivation processes.[a] Dopamine is the main neurotransmitter involved in this system and is responsible for mediating feelings of reward, pleasure motivation, drive and aggression, among others, and related stress conditions.

While cocaine and other amphetamine-like psychostimulants are known to block dopamine transporters, increasing dopamine concentration in the synaptic space, opioids have been reported to increase dopamine release in the nucleus accumbens, which is one of the principal mechanisms of the rewarding effects.[b]



The associative learning properties related to the release of dopamine strengthen the reinforcing effects of the drug as well as of the environment and emotional reactions associated with its use (stimuli and reward) and establish the compulsive conditioned behaviour known as "addiction".

a WHO, Neuroscience of Psychoactive Substance Use and Dependence (Geneva, 2004).

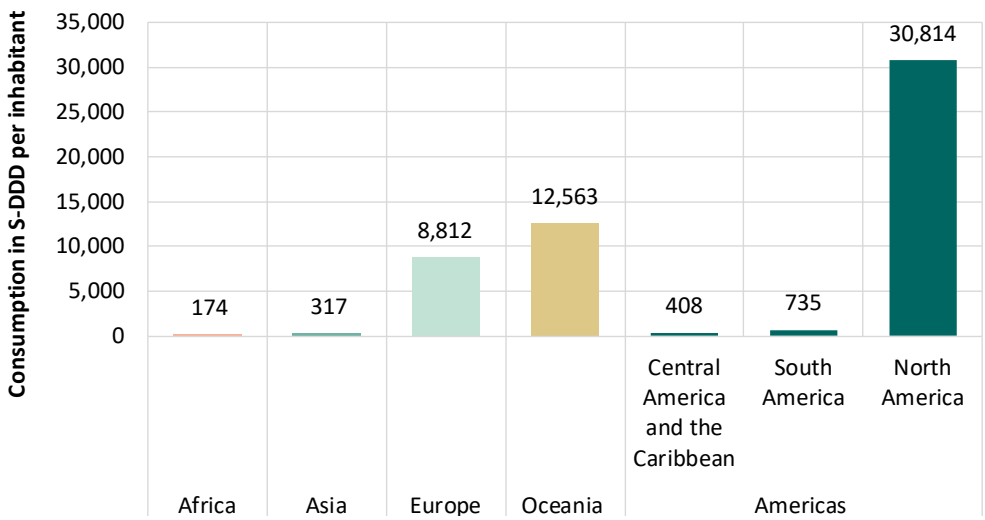
b Ide Soichrion and others, "Distinct roles of opioid and dopamine systems in lateral hypothalamic intracranial self-stimulation", *International Journal of Neuropsychopharmacology*, vol. 20, No. 5 (May 2017), pp. 403–409.

Increase in the medical use of fentanyl

Until the 1980s, fentanyl was mainly used for the induction of anaesthesia and, in combination with other substances, for anaesthesia in short-term surgical interventions. Since the early 1990s, the applications of the drug have proliferated. Controlled-release preparations (patches) of fentanyl have been introduced, as have new delivery methods, including a sublingual spray that helps cancer patients cope with severe pain. Increasingly used in all parts of the world for the treatment of severe pain, fentanyl in all its applications has created a rapidly growing licit demand for the expansion of the manufacture of the substance, which only came to a halt in recent years after reports of increasing numbers of overdose deaths attributed to the non-medical use of fentanyl and its analogues (notably in North America). This is despite the fact that, in many cases, the fentanyl and fentanyl analogues that actually caused the overdose deaths appear to have been illicitly manufactured and trafficked.[a]

[a] INCB, *Narcotic Drugs: Estimated World Requirements for 2018 – Statistics for 2016* (E/INCB/2017/2).

FIG. 1 Availability of pharmaceutical opioids for medical use (in defined daily doses per million inhabitants), average over 2015–2017



Source: INCB, *Narcotic Drugs: Estimated World Requirements for 2019 – Statistics for 2017* (E/INCB/2018/2).

Note: Consumption is measured in terms of reported wholesale sales to medical doctors, pharmacies and hospitals. For the purposes of the 1961 Convention, a drug is regarded as "consumed" when it has been supplied to any person or enterprise for retail distribution, medical use or scientific research.

The marked increase in the manufacture and sale of pharmaceutical opioids in the first decade of the new millennium increased the global per-capita consumption of those substances. The increase has been uneven, however, with extremely high levels of per-capita consumption in North America, particularly in the United States of America, while per-capita consumption of pharmaceutical opioids in the rest of the Americas, Africa and Asia remained relatively low over the period 2015–2017 (expressed in standard daily doses), suggesting a severe ongoing lack of accessibility to, and availability of, pain medication for the majority of the inhabitants of middle- and low-income countries.[14]

14 INCB, *Narcotics Drugs: Estimated World Requirements for 2019 – Statistics for 2017* (E/INCB/2018/2) and previous years.

In parallel to the strong increase in the production and sale of opioids for medical use, in North America there has been an increase in the non-medical use of pharmaceutical opioids and its adverse consequences, with an alarming increase in the number of fatal and non-fatal opioid overdose cases reported. Other subregions, such as North Africa, West and Central Africa and the Near and Middle East, have also reported the spread of the non-medical use of tramadol, an opioid not under international control. At the global level, concerns about the non-medical use of pharmaceutical opioids has created a challenge due to the concomitance of two opposing needs. On the one hand, the supply of and accessibility to pain medication are insufficient to treat pain in many regions (particularly in middle- and low-income countries) where people suffer disproportionately from a lack of medication for pain management; on the other hand, rigorous marketing and the over-prescription of opioids, particularly in North America, have had the consequences of iatrogenic addiction and fatal and non-fatal overdose cases in people requiring pain management. Some of these concerns have prompted measures, in North America, for example, aimed at gradually strengthening the overall control system for prescribing and dispensing pharmaceutical opioids and developing guidelines for the management of chronic pain.[15, 16]

Non-medical use of opioids

Overview of the use of opioids in different regions

In 2017, an estimated 53 million people (range 47–60 million) globally, or 1.1 per cent of the population aged 15–64, used opioids at least once in the past year, of whom half were past-year users of opiates (heroin and opium). The highest prevalence of non-medical use of opioids is estimated in North America, at nearly 4 per cent of the population aged 15–64, representing one quarter of global opioids users. The major opioids of concern in North America remain pharmaceutical opioids, hydrocodone, oxycodone, codeine and tramadol, which are used for non-medical purposes. The annual prevalence of opiates (mainly heroin) use in 2017 is also estimated to be higher (0.7 per cent) in North America than the global average of 0.6 per cent. The use of opioids in Australia and New Zealand also remains much higher than the global average (3.3 per cent of the adult population), with the non-medical use of pharmaceutical opioids also being the main opioids of concern.

As the prevalence of opioid use in Asia is also high, with nearly 1 per cent of the population estimated to be past-year users, the size of the population of the region means that more than half of global opioid users reside in Asia (29 million past-year opioid users). Within Asia, the Near and Middle East and South-West Asia have a high prevalence of opioid use (2.3 per cent of the adult population) with a total of almost 8.5 million past-year opioid users in those two subregions combined. The high prevalence of opioid use in those subregions is driven by use in Afghanistan, Iran (Islamic Republic of) and Pakistan; however, there are differences in the nature of the opioid problem in those countries. In Afghanistan, opium remains the predominant opioid, with nearly 70 per cent of opioid users reporting using opium, but there is also substantial use of heroin and non-medical use of pharmaceutical opioids.[17] In the Islamic Republic of Iran, nearly 90 per cent of opioid users report using opium or the condensed extract of smoked opium ashes (shireh).[18, 19] In Pakistan, opioid use is more mixed: in 2012, notwithstanding polydrug use among opioid users, of the estimated 2.7 million opioid users, 1.6 million also reported the non-medical use of pharmaceutical opioids, whereas over 1 million people were estimated to be regular opiate users, of whom the majority were heroin users (860,000) while one third were opium

15 See, for instance, Deborah Dowell, Tamara M. Haegerich and Roger Chou, "CDC guidelines for prescribing opioids for chronic pain", *Morbidity and Mortality Weekly Report*, vol. 65, No. 1 (March 2016), pp. 1–49.

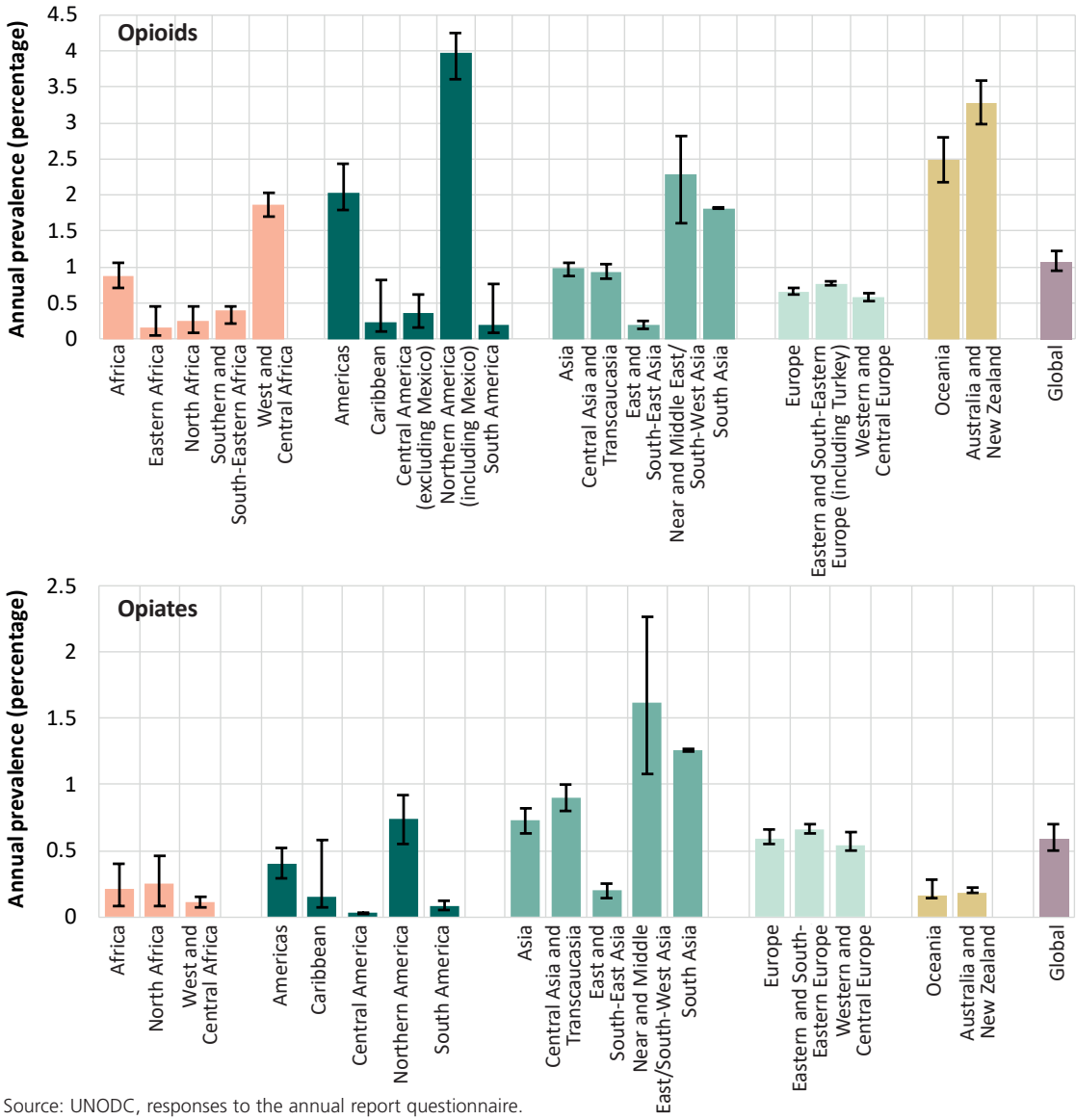
16 Nora D. Volkow and A. Thomas McLellan, "Opioid abuse in chronic pain: misconceptions and mitigation strategies", *New England Journal of Medicine*, vol. 374 (March 2016), pp. 1253–1263.

17 United Nations Office on Drugs and Crime (UNODC), "Drug use in Afghanistan: 2009 survey" (2009).

18 Official statistics reported by the Drug Control Headquarters, Islamic Republic of Iran.

19 Masoumed Amin-Esmaeili and others, "Epidemiology of illicit drug use disorders in Iran: prevalence, correlates, comorbidity and service utilization results from the Iranian Mental Health Survey", *Addiction*, vol 111, No. 10, (October 2016).

FIG. 2 Use of opioids and opiates, by region, 2017



Source: UNODC, responses to the annual report questionnaire.

users (320,000 users).[20] Although the use of opiates (heroin and opium) was much higher among men than among women in Pakistan, a similar proportion of men and women reported non-medical use of pharmaceutical opioids in the country.[21]

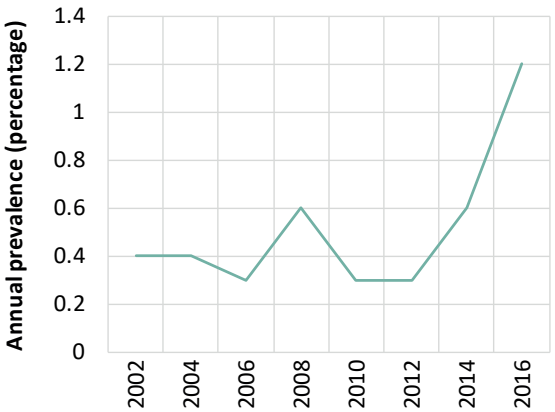
In South Asia, 1.8 per cent of the adult population or 19 million people, comprising 35 per cent of the global estimate, are past-year opioids users. These estimates are driven by India, where 2.1 per cent of the population aged 10–75, a total of 23 million people, are estimated to be past-year opioid users (2018).[22] Among opioids, heroin is the most prevalent substance, with a past-year prevalence of use of 1.1 per cent among the population aged 10–75,

20 UNODC and Pakistan, Ministry of Interior and Narcotics Control, *Drug Use in Pakistan 2013* (Islamabad, 2014).

21 Ibid.

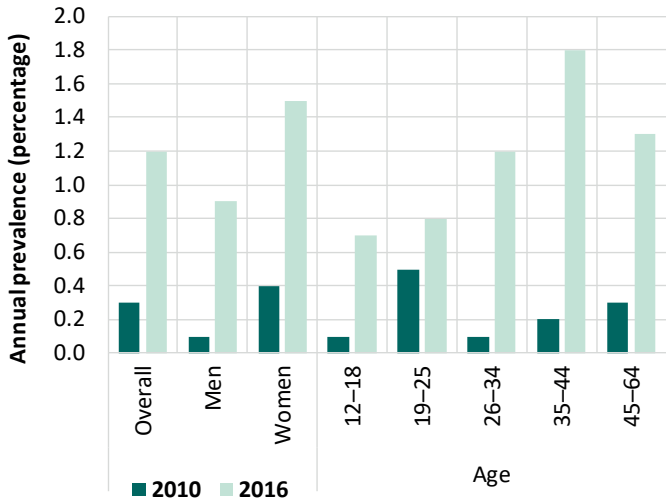
22 Atul Ambekar and others, *Magnitude of Substance Use in India 2019* (New Delhi, Ministry of Social Justice and Empowerment, 2019).

FIG. 3 Non-medical use of pharmaceutical opioids, Chile, 2002–2016



Source: Chile, Ministry of the Interior and Public Security, Twelfth national study of drug use among the public of Chile, 2016 (*Décimo Segundo Estudio Nacional de Drogas en Población General de Chile*).

FIG. 4 Non-medical use of opioids by sex and age group, Chile, 2010 and 2016



Source: Chile, Ministry of the Interior and Public Security, Twelfth national study of drug use among the public of Chile, 2016 (*Décimo Segundo Estudio Nacional de Drogas en Población General de Chile*).

followed by non-medical use of pharmaceutical opioids, the prevalence of which is almost 1 per cent of the general population, and opium, the prevalence of which is almost 0.5 per cent. The past-year use of opioids is much higher among men in general (4 per cent of the male population) than women (0.2 per cent of the female population). Moreover, 1.8 per cent of adolescents aged 10–17 are estimated to be past-year opioid users. Of the total 23 million past-year opioid users, roughly one third, or 7.7 million people, are considered to be suffering from opioid use disorders in India. The states with the highest prevalence of opioid use in the country are those in the north-east (Mizoram, Nagaland, Arunachal Pradesh, Sikkim, Manipur), along with Punjab, Haryana and Delhi, in the north of the country.

West and Central Africa is also a subregion with a high prevalence of non-medical use of opioids (1.9 per cent or an estimated 5 million opioid users), which is dominated by the non-medical use of pharmaceutical opioids, in particular of tramadol. However, the lack of data on the prevalence of drug use in Africa makes it difficult to quantify its trends and level. In Nigeria, for example, the prevalence of pharmaceutical opioids in 2017 was estimated at 4.7 per cent of the population aged 15–64 (corresponding to an estimated 4.6 million past-year users), most of which can be attributed to the non-medical use of tramadol and, to a lesser extent, the non-medical use of codeine and morphine.[23]

The estimated prevalence of opioid use in Europe in 2017 was estimated at 0.7 per cent of the adult population, or nearly 3.8 million opioid users. In Western and Central Europe, where there are an estimated 2 million opioid users (0.6 per cent of the adult population), the use of opioids is dominated by heroin use. However, in recent years there have been indications of an increase in the non-medical use of pharmaceutical opioids in the subregion, with methadone, buprenorphine and fentanyl reported as the main pharmaceutical opioids misused.[24]

The non-medical use of opioids in South America in 2017 was estimated at 0.2 per cent and 0.4 per cent, respectively. Most of the countries in those subregions report the non-medical use of pharmaceutical opioids more than of heroin. Among countries in South America, in Chile, one country where recent information on non-medical use of pharmaceutical opioids has been reported, the past-year prevalence of non-medical use of pharmaceutical

23 UNODC, *Drug Use in Nigeria 2018* (Vienna, 2018).

24 EMCDDA, *European Drug Report 2018: Trends and Developments* (Luxembourg, Publications Office of the European Union, 2018).

opioids increased from 0.3 per cent in 2012 to 1.2 per cent in 2016. In 2016, the non-medical use of opioids was particularly high among women, although it has increased markedly among men as well as among the age groups 26–34 and 35–44.[25]

Drivers of the opioid epidemic in the United States

In the United States of America, the increase in the non-medical use of pharmaceutical opioids since 1997 has been attributed in part to a number of reasons, including the organization of the health system's structures for regulation and control of access to those drugs, prescription practices, the medical dispensing culture and patient expectations.[26] The number of opioid prescriptions dispensed from retail pharmacies in the United States increased from 174 million in 2000 to 256.9 million in 2009.[27] This increase in combination with high dosages and the longer duration of opioid prescriptions, primarily for the management of acute to chronic non-cancer pain, resulted in further diversion and misuse of pharmaceutical opioids and the development of opioid use disorders among users.[28, 29]

Attributed mainly to the availability of pure and cheaper heroin in the market, a gradual increase in heroin use has also been observed in parts of the United States since 2006. It has been hypothesised that the transition from the non-medical use of prescription opioids to the use of heroin, especially among young people, could be part of the progression of addiction in a subgroup of non-medical users of prescription opioids who considered it costly to maintain their patterns of consumption and switched to heroin use as they considered it more reliably available through drug dealers, more potent and more cost effective than pharmaceutical opioids.[30, 31]

Another major change in the market for pharmaceutical opioids in the United States occurred in 2010, when changes were made in the formulation of OxyContin® (oxycodone) one of the main opioids misused in the country. The new abuse-deterrent formulation of OxyContin® made it controlled release[32] and tamper proof so that it could no longer be crushed and snorted or injected.[33] However, the increase in heroin use in the United States had already begun and therefore preceded the changes introduced in policies and practices related to prescription opioids. Nevertheless, given the large number of non-medical users of pharmaceutical opioids, even a small proportion switching to heroin use has translated into a much larger number of people using heroin.[34]

Between 2002 and 2011, pooled data from the National Survey on Drug Use and Health showed that, among new initiates to heroin use, the likelihood of initiation of heroin use among people who had reported non-medical use of pharmaceutical opioids was 19 times higher than among those who had not reported non-medical use of pharmaceutical opioids. The rate of heroin initiation increased, as the frequency of past-year non-medical use of pharmaceutical opioids and among people with opioid use disorders increased. Conversely, only a small percentage (3.6 per cent) of those who had initiated the non-medical use of pharmaceutical opioids had initiated heroin use within the five-year period following their first non-medical use of pharmaceutical opioids.[35, 36]

25 Chile, Ministry of the Interior and Public Security, *Décimo Segundo Estudio Nacional de Drogas en Población General de Chile*.

26 Benikt Fischer and others, "Non-medical use of prescription opioids and prescription opioid-related harms: why so markedly higher in North America compared to the rest of the world?", *Addiction*, vol. 109, No. 2 (February 2014), pp.177–181,

27 Nicholas B. King and others, "Determinants of increased opioid-related mortality in the United States and Canada, 1990–2013: a systematic review", *American Journal of Public Health,* vol. 105, No. 8 (August 2014), pp. e32–e42.

28 Wilson M. Compton and others, "Relationship between nonmedical prescription-opioid use and heroin use", *New England Journal of Medicine*, vol. 374, No. 2 (January 2016), pp. 154–163.

29 Theodore J. Cicero and others, "Effect of abuse-deterrent formulation of OxyContin", *New England Journal of Medicine,* vol. 367, No. 2 (July 2012), pp. 187–189.

30 Compton and others, "Relationship between nonmedical prescription-opioid use and heroin use".

31 Daniel Ciccarone, "The triple wave epidemic: Supply and demand drivers of the US opioid overdose crisis", *International Journal of Drug Policy* (February 2019).

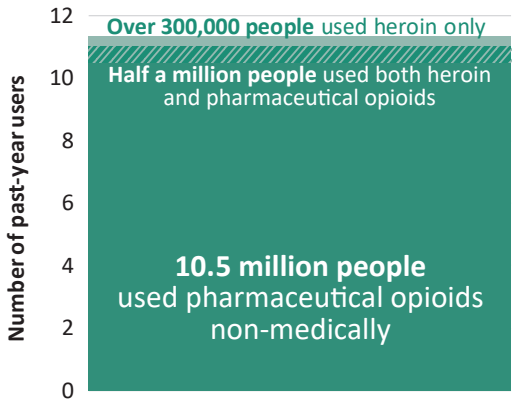
32 Controlled release formulation is designed to achieve optimal therapeutic levels over a defined period.

33 Cicero and others, "Effect of abuse-deterrent formulation of OxyContin".

34 Compton and others, "Relationship between non-medical prescription opioid use and heroin use".

35 Pradip K. Muhuri, Joseph C. Gfroerer and Christine Davies,

FIG. 5 The overlap between non-medical use of pharmaceutical opioids and heroin in the United States, 2017



Source: United States, Substance Abuse and Mental Health Services Administration, *Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health* (Rockville, Maryland, 2018).

In 2017, people who used heroin were also more likely to have previously used pharmaceutical opioids and switched to heroin use or continued to use both substances. Out of an estimated 11.1 million people in the United States in 2017 who had used opioids non-medically in the past year, 10.5 million of them (95 per cent) had primarily used pharmaceutical opioids and 5 per cent, about half a million, had also used heroin. This accounts for more than half of the estimated 886,000 people who had primarily used heroin in the past year.[37]

Up until 2013 sporadic outbreaks of fentanyl and fentanyl analogues containing heroin were causing deaths among heroin users in the United States.[38]

The appearance of fentanyls and their subsequent proliferation in the United States heroin market from 2013/14 added to the dynamics of the opioid market in that country. In subsequent years, the availability of heroin, synthetic opioids and other drugs containing fentanyls, their profitability, and increasing restrictions on prescription opioids, with a large population misusing pharmaceutical opioids, could have contributed further to the opioid epidemic in the United States. Fentanyls have been used as an adulterant of heroin and cocaine and also sold as falsified prescription opioids, such as oxycodone or hydrocodone and even as falsified benzodiazepines, to a large population of opioid users who were unaware of the actual contents.[39, 40] This has resulted in incidents with fatal consequences for opioid users, as seen in the dramatic increase in the number of fatal and non-fatal overdose cases in the United States.[41] It appears also that many people who have used fentanyl have often experienced or encountered a non-fatal overdose and therefore they consider that use of fentanyl should be avoided.[42, 43] However, demand for fentanyl itself has emerged within small groups of users and may be reported in certain areas where high-frequency users with tolerance to heroin and other opioids may seek out fentanyl.

The rapid expansion of fentanyl is also visible in seizures. Since 2014, the number of seized samples that the National Forensic Laboratory Information System of DEA in the United States has analysed and identified as fentanyl has been increasing considerably. In 2017, fentanyl represented a third of the pharmaceutical opioids that were identified in

"Associations of nonmedical pain reliever use and initiation of heroin use in the United States", CBHSQ Data Review (Rockville, Maryland, Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, August 2013).

36 See also, Theodore J. Cicero and others, "Increased use of heroin as an initiating opioid of abuse: Further considerations and policy implications", vol. 87 (December 2018), pp 267–271.

37 Substance Abuse and Mental Health Services Administration, *Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health*, HHS Publication No. SMA 18-5068, NSDUH Series H-53 (Rockville, Maryland, Center for Behavioral Health Statistics and Quality, 2018).

38 Armenian and others, "Fentanyl, fentanyl analogues and novel synthetic opioids".

39 Ibid.

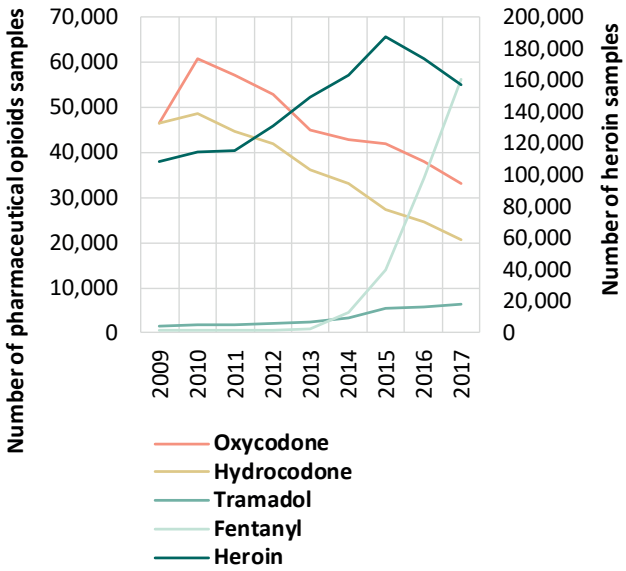
40 United States, Department of Justice, DEA, *2018 National Drug Threat Assessment* (October 2018).

41 Alana M. Vivolo-Kantor and others, "Vital signs: trends in emergency department visits for suspected opioid overdoses – United States, July 2016–September 2017", *Morbidity and Mortality Weekly Report,* vol. 67, No. 9 (March 2018).

42 Jennifer J. Carroll and others, "Exposure to fentanyl-contaminated heroin and overdose risk among illicit opioid users in Rhode Island: a mixed methods study", *International Journal of Drug Policy*, vol. 46 (August 2017), pp. 136–145.

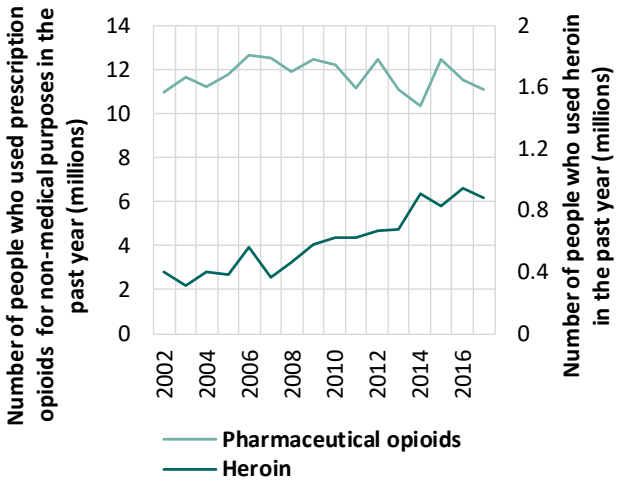
43 Tess M. Kilwein, Preston Hunt and Alison Looby, "A descriptive examination of nonmedical fentanyl use in the United States: characteristics of use, motives, and consequences", *Journal of Drug Issues*, vol. 48, No. 3 (April 2018), pp. 409–420.

FIG. 6 Number of substances submitted to and analysed by forensic laboratories, by type of drug identified, United States, 2009–2017



Source: United States, Department of Justice, DEA, National Forensic Laboratory Information System, reports for different years.

FIG. 7 Use of heroin and non-medical use of pharmaceutical opioids in the United States, number of people, 2002–2017



Source: United States, Substance Abuse and Mental Health Services Administration, *Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health* (2018).

different samples, but the spread of fentanyl use has been uneven in the United States. In 2017, fentanyl made up the highest percentage of seized pharmaceutical opioid samples in the North-east and the Midwest (55 per cent and 34 per cent, respectively),[44] which are regions with a comparatively higher prevalence of heroin use in the United States.

Trends in opioid use in the United States

According to survey data, in the United States, since the increase over the period 2013–2014, the prevalence of heroin use has remained relatively stable, at 0.3 per cent of the population aged 12 and older, or around 900,000 past-year users, while the annual prevalence of non-medical use of pharmaceutical opioids decreased from a peak in 2015 of 4.7 per cent of the population aged 12 and older (12.5 million past-year users) to around 4.2 per cent of the population aged 12 and older (11 million past-year users) in 2017.[45] Considering that the national household survey excludes institutionalized and homeless populations, which may have disproportionately higher rates of non-medical use of opioids, these estimates are probably an underestimation of the extent of such use in the United States. For example, the number of chronic heroin users[46] estimated in 2010 at 1.5 million[47] was more than twice the number of past-year users (620,000) or six times the number of past-month heroin users (240,000) estimated in the national household survey in the same year.

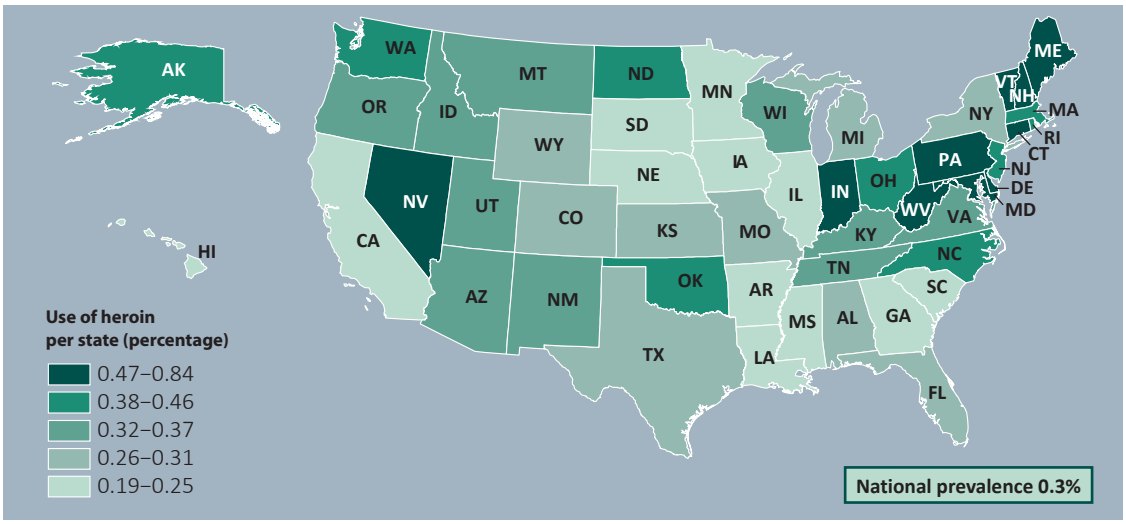
44 United States, Department of Justice, DEA, Diversion Control Division, "National Forensic Laboratory Information System: NFLIS-Drug 2017 annual report" (Springfield, Virginia, 2018).

45 Substance Abuse and Mental Health Services Administration, *Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health*.

46 Defined as those who had used heroin for four days or more in the past month.

47 Jonathan P Caulkins and others, "Cocaine's fall and marijuana's rise: questions and insights based on new estimates of consumption and expenditures in US drug markets", *Addiction*, vol. 110, No. 5 (May 2015), pp 728–36.

MAP 1 Heroin use in the past year among the population aged 12 and older in the United States, by state, 2017

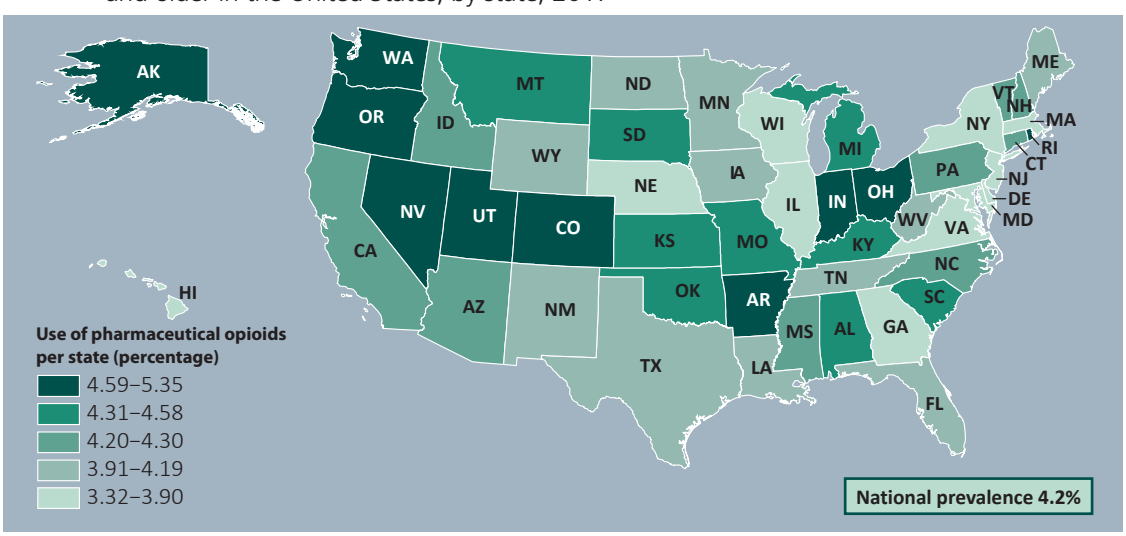


Source: SAMISHA, Center for Behavioral Health Statistics and Quality, NSDUH, 2016 and 2017.

The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.

The extent of past-year non-medical use of pharmaceutical opioids and of heroin varies considerably from region to region in the United States, but heroin use seems more geographically concentrated than non-medical use of prescription opioids. Estimated past-year non-medical use of pharmaceutical opioids in the western part of the country (4.5 per cent of the population aged 12 and older) was higher in 2017 than the estimated national prevalence (4.2 per cent), while the estimated past-year prevalence of heroin use was higher in the north-eastern part of the country (0.45 per cent). Non-medical use of

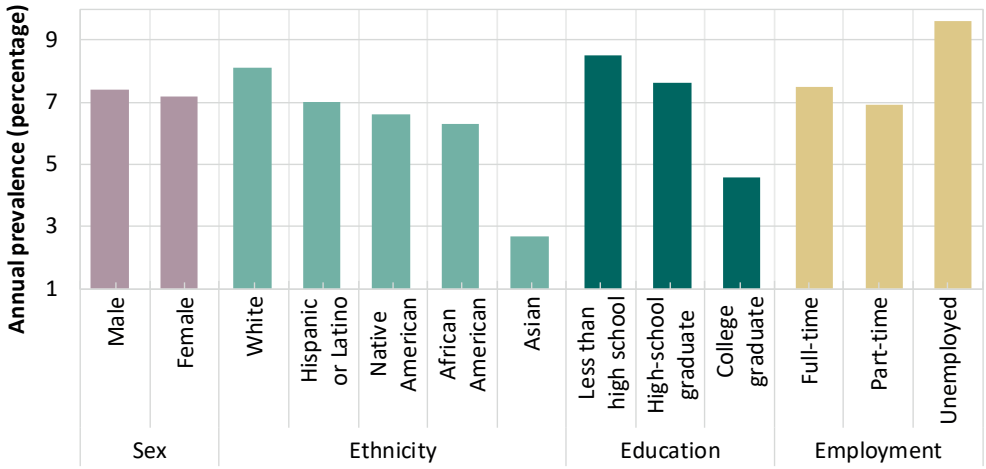
MAP 2 Non-medical use of pharmaceutical opioids in the past year among the population aged 12 and older in the United States, by state, 2017



Source: SAMISHA, Center for Behavioral Health Statistics and Quality, NSDUH, 2016 and 2017.

The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.

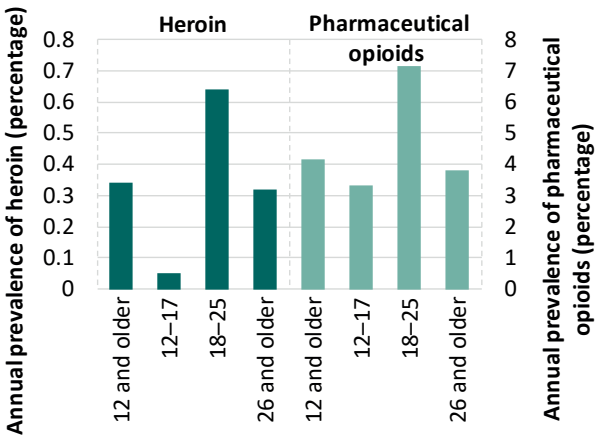
FIG. 8 Opioid use among people aged 18–25, by sociodemographic characteristics, United States, 2017



Source: United States, Substance Abuse and Mental Health Services Administration, *Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health* (2018).

pharmaceutical opioids was more prevalent in completely rural counties (4.3 per cent) and small metropolitan counties (4.3 per cent) than in large metropolitan (3.9 per cent) and urbanized counties (3.9 per cent).[48]

FIG. 9 Use of opioids in the United States, by age group, 2017



Source: United States, Substance Abuse and Mental Health Services Administration, *Key Substance Use and Mental Health Indicators in the United States: Results from the 2017 National Survey on Drug Use and Health* (2018).

48 United States, Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, *Results from the 2017 National Survey on Drug Use and Health: Detailed Tables* (Rockville, Maryland, 2018).

Opioid use in Canada

Information on the non-medical use of opioids in Canada is very limited. In 2017, around 85,000 people or nearly 0.4 per cent of the population aged 15–64 reported the past-year use of pharmaceutical opioids in order to "get high", with the highest rates being among young adults aged 20–24 (1.1 per cent) and young people aged 15–19 (0.8 per cent,).[49, 50] There is insufficient information on the extent of non-medical use of opioids among women and most age groups for the country.[51]

Trends and patterns of opioid use in Europe

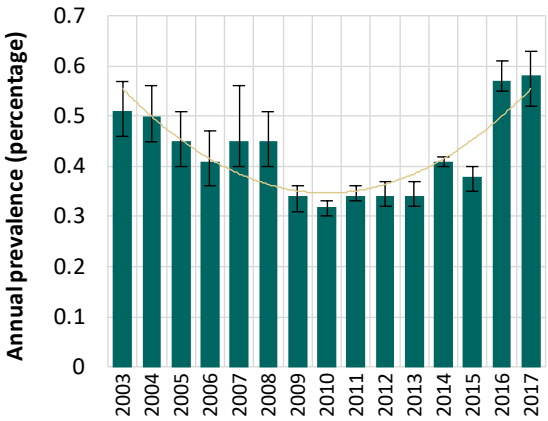
The annual prevalence of opioid use in Europe in 2017 is estimated at 0.7 per cent of the population aged 15–64, with heroin remaining the most commonly used opioid in the region. In Eastern and South-Eastern Europe, the prevalence of opiate use (heroin and opium) remains higher (0.7 per cent) than in other subregions, although there was a decrease in the preceding years in the overall use of

49 Canadian Tobacco, Alcohol and Drugs Survey, February–December 2017.

50 Owing to "high sampling variability", these results are to be interpreted with caution.

51 Owing to "high sampling variability", the prevalence among women and other age groups cannot be estimated.

FIG. 10 Opiate use in Western and Central Europe, 2003–2017



Source: UNODC, responses to the annual report questionnaire.

opioids in the subregion, driven primarily by the decrease in the number of registered opioid users in the Russian Federation. In the Russian Federation, which used to have a high prevalence of opioid use, the opioid market has started to change in recent years, and synthetic drugs other than opioids have started to dominate. The number of first-time entrants into treatment for opioid use (mostly heroin use) decreased by more than three quarters over the period 2006–2017.

In Western and Central Europe (mainly the States members of the European Union), heroin remains the main opioid used. Opioid use in the subregion remained stable over the past decade, but there have been signs of an increase or resurgence in the opioid market since 2013, with a major increase observed at the subregional level in the prevalence of opioid use in 2016. The increase was primarily the result of higher opiate use estimates reported by Poland, reflecting not only an increase in the prevalence of heroin use, from 0.1 per cent of the population aged 15–64 in 2014 to 1.1 per cent in 2016, but also high levels of use of "kompot" (1.7 per cent), a home-made heroin preparation manufactured from poppy straw in that country.

France, Germany, Italy, Spain and the United Kingdom, which account for some 60 per cent of the population of the European Union, are estimated to account for three quarters of the estimated high-risk opioid users in the European Union. Notwithstanding an increase in the prevalence of opioid use in Poland in 2016, opioid use in the rest of Western and Central Europe has remained quite stable over the past five years. In Western and Central Europe there seems to be an ageing cohort of opioid users who have been in contact with drug treatment services, and who present a range of chronic medical conditions associated with ageing as well as problems associated with long-term opioid use.[52, 53]

Apart from heroin, some of the most common opioids reported in countries in the European Union in recent years are opium, morphine, methadone, buprenorphine, tramadol and various fentanyl analogues.[54] Some of those opioids may be diverted from legitimate pharmaceutical supplies, while others are illicitly manufactured and sold. The non-medical use of pharmaceutical opioids in Western and Central Europe is mainly observed in the context of users seeking alternatives to heroin. The prevalence of the non-medical use of pharmaceutical opioids remains quite low in the subregion and is essentially linked to the diversion of methadone or buprenorphine for non-medical use among opioid users, including self-medication outside treatment settings.[55]

In recent years, an increasing number of countries in Western and Central Europe have reported that more than 10 per cent of opioid users who enter treatment do so for problems related to opioids other than heroin.[56] The non-medical use of buprenorphine is reported by around one third of opioid users in treatment in Czechia, while the non-medical use of methadone is reported by almost a quarter of opioid users in treatment in Denmark. In Cyprus

52 Anne Marie Carew and Catherine Comiskey, "Rising incidence of ageing opioid users within the EU-wide treatment demand indicator: the Irish opioid epidemic from 1996 to 2014", *Drug and Alcohol Dependence*, vol. 192 (November 2018), pp. 329–337.

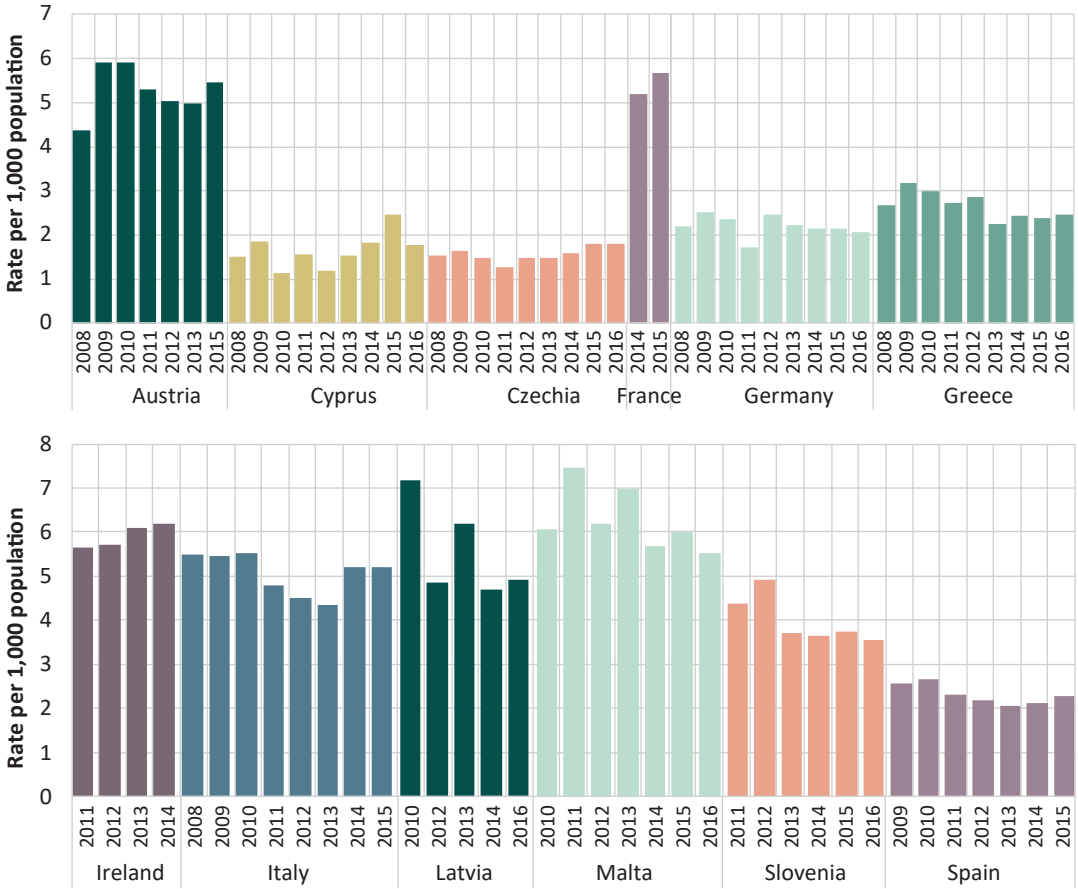
53 Anne Marie Carew and Catherine Comiskey, "Treatment for opioid use and outcomes in older adults: a systematic literature review", *Drug and Alcohol Dependence*, vol. 182 (January 2018), pp. 48–57.

54 EMCCDA, *European Drug Report 2018*.

55 Paul Griffiths, Michael Evans-Brown and Roumen Sedefov, "The misuse of psychoactive medicines: getting the balance right in complex system", *Addiction*, vol. 109, No. 2 (February 2014), pp. 182–188.

56 EMCCDA, *European Drug Report 2018*.

FIG. 11 Trends in high-risk opioid use in countries in Western and Central Europe



Source: EMCDDA, Statistical Bulletin 2018.

Note: High-risk opioid use is defined by EMCDDA as recurrent drug (opioid) use that causes actual harms (negative consequences) to the person (including dependence, but also other health, psychological and social problems) or places the person at a high probability/risk of suffering such harms.

and Poland, between 20 per cent and 30 per cent of opioid users are in treatment for problems related to the use of opioids such as oxycodone (Cyprus), and "kompot" in Poland.[57]

Over the past two decades, Estonia and Finland have experienced a transition from the use of heroin to the use of fentanyl (in the case of Estonia) and buprenorphine (in the case of Finland). Following a decline in heroin availability in Estonia, 3-methylfentanyl first appeared in the drug market in 2002. By 2005, 3-methylfentanyl and 3-methylfentanyl -fentanyl mixtures accounted for the majority of opioids seized and had replaced heroin use in the country.[58] Although national estimates of opioid use are not available for Estonia, the majority of people who inject drugs there reportedly inject 3-methylfentanyl and, since 2015, other fentanyl analogues such as furanylfentanyl, acrylfentanyl, carfentanil, and ocfentanil.[59]

In Finland, the proportion of clients entering treatment for non-medical use of buprenorphine

57 Ibid.

58 Ilkka Ojanperä and others, "An epidemic of fatal 3-methylfentanyl poisoning in Estonia", *International Journal of Legal Medicine,* vol. 122, No. 5 (September 2008), pp. 395–400.

59 EMCDDA, "Estonia: Estonia drug report 2018" (June 2018).

increased from 3 per cent in 1998 to more than one third in 2008[60] and as of 2018 accounted for almost all opioid users in treatment.[61] It is noteworthy that concurrent use of amphetamines and opioids is quite common among problem drug users in Finland. In 2014, a smaller proportion of clients in treatment also reported the use of the opium derivatives, tramadol, oxycodone, codeine preparations and fentanyl.[62]

Tramadol: the other opioid crisis

In recent years, tramadol, a synthetic opioid not under international control, has emerged as an opioid of public health concern in many subregions, in particular West, Central and North Africa. The non-medical use of tramadol is also reported in the Middle East and in other parts of Asia as well as in Europe and North America. In middle-income and developing countries, the non-medical use of pharmaceutical opioids such as tramadol seems to occur in contexts where health-care systems, including for the dispensing of prescription opioids, are not well developed or regulated, and where falsified or illicitly manufactured/trafficked pharmaceutical opioids are available to meet the demand for the non-medical use of the substances.[63]

In Egypt, for example, since 2000 there has been an increase in the non-medical use of tramadol among people entering treatment for drug use disorders. However, there has been a change in their source of supply, as most patients report having obtained tramadol from pharmacies in the early 2000s by bypassing the regulations for dispensing prescription painkillers, whereas over the next 10 to 15 years most reported resorting to the illicit market to obtain tramadol, which had been illicitly manufactured and smuggled into Egypt.[64] In a small-scale study conducted in the Islamic Republic of Iran, of the 162 people who had obtained tramadol from a pharmacy, more than half did not have a prescription. More than 60 per cent of those interviewed matched the criteria of dependence and had a prior history of substance use disorders, more than half were aged 18 or under and two thirds had taken at least two courses of tramadol, each for more than one week's duration, without a prescription during the previous year.[65]

Various studies suggest that the high level of non-medical use of tramadol in the above subregions is the result of the drug's easy availability in pharmacies and on the illicit ("black") market, its low price in comparison with controlled drugs and the perception among users, especially young people, that since tramadol is a medication, its use does not carry the same level of risk and stigma as the use of other controlled drugs.[66, 67, 68, 69]

National-level prevalence estimates of the non-medical use of tramadol for most countries in the Middle East and West and Central and North Africa are not available, but different studies and surveys in a few countries point to a widespread non-medical use of tramadol in those subregions.[70] For example, in 2016 in Egypt, 3 per cent of the adult population reported non-medical use of tramadol in the past year, while nearly 68 per cent of people in treatment for drug use disorders were being treated for

60 Hanna Uosukainen and others, "Twelve-year trend in treatment seeking for buprenorphine abuse in Finland", *Drug and Alcohol Dependence*, vol. 127, Nos. 1–3 (January 2013), pp. 207–214.

61 EMCDDA, "Finland: Finland drug report 2018" (June 2018).

62 Finland, National Institute for Health and Welfare, *Finland Drug Situation 2014*, report 3/2015 (Tampere, Finland, 2015).

63 *Report of the International Narcotics Control Board for 2012* (E/INCB/2012/1).

64 Samir Abou El Magd and others, "Tramadol misuse and dependence in Egypt and the UAE: user characteristics and drug-use patterns", *International Addiction Review,* vol. 2, No. 1 (April 2018), pp. 6–13.

65 Ebrahim Zabihi and others, "Potential for tramadol abuse by patients visiting pharmacies in Northern Iran", *Substance Abuse: Research and Treatment,* vol. 5 (2011), pp. 11–15.

66 Samir Abou El Magd and others, "Tramadol misuse and dependence in Egypt and the UAE: user characteristics and drug-use patterns", *International Addiction Review,* vol. 2, No. 1 (April 2018), pp. 6–13.

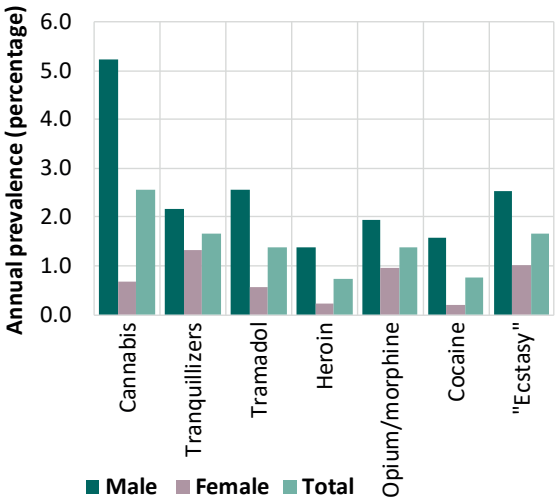
67 Saeed Bashirian, Majid Barati and Yadollah Fathi, "Prevalence and factors associated with tramadol abuse among college students in West of Iran: an application of the theory of planned behaviour", *Avicenna Journal of Neuropsychiatry*, vol. 1, No. 1 (August 2014), pp. 26–30.

68 Nabil R. Mohamed and others, "An epidemiological study of tramadol HCl dependence in an outpatient addiction clinic at Heliopolis Psychiatric Hospital", *Menoufia Medical Journal*, vol. 28, No. 2 (2015), pp. 591–596.

69 Medhat M Bassiony and others, "Adolescent tramadol use and abuse in Egypt", *The American Journal of Drug and Alcohol Abuse*, vol. 41, N0. 3 (2015), pp. 2016–211.

70 See *World Drug Report 2017* and *World Drug Report 2018* (United Nations publications, Sales No. E.18.XI.9).

FIG. 12 Drug use among secondary school students in Egypt, 2016



Source: MedSPAD 2016 in Egypt: Results of the First Mediterranean School Survey Project on Alcohol and other Drugs (MedSPAD) in Egypt.

tramadol use.[71] In the State of Palestine, among the estimated 10,000 high-risk male drug users in 2016 (1.8 per cent of the male population aged 15 and older) in Gaza, although polydrug use was a common phenomenon, almost all were using tramadol non-medically and almost half of those who did used it for 4–7 days per week. Tramadol was also the first substance that the majority had initiated at around 20 years of age.[72]

The non-medical use of tramadol is also reported as being quite common among young people and university students. A study among university students in Egypt (2012–2013) revealed that the past-year prevalence of the non-medical use of tramadol was 12.3 per cent, with the average age of onset being 17. The non-medical use of tramadol among university students was correlated with the use of cannabis and alcohol as most (85 per cent) tramadol users reported concurrent use of more than one substance.[73] Another study, in 2014, among college students (aged 18–30) in the west of the Islamic Republic of Iran showed that 11 per cent of respondents had used tramadol non-medically in the past year and that the majority of those users (75 per cent) had also used it in the past month.[74] A significant proportion of students also reported high levels of social pressure for the non-medical use of tramadol. The first ever survey among secondary school students in Egypt also showed a high prevalence of the non-medical use of tramadol as well as of the use of opium and morphine among 15–19-year-old students in 2016.[75]

Another study of people with tramadol use disorders in treatment in Egypt and the United Arab Emirates in 2018 showed that the non-medical use of tramadol was more common among young people aged 26–35, those with a primary or secondary school education (as opposed to little or no schooling, or with university education), and those who were currently unemployed or were skilled workers.[76]

A number of studies in the Middle East and North Africa have shown that tramadol is used non-medically for a number of reasons, including: for its pleasurable effect, i.e., to improve mood; for the prolongation of the duration of sexual intercourse; to delay the sensation of fatigue; because of the perception that its effects last long; and as self-medication for pain relief or the relief of symptoms of depression, anxiety or other comorbid psychiatric disorders.[77, 78] The non-medical use of

71 Egypt, General Secretariat of Mental Health of the Ministry of Health, "Report of the General Secretariat of Mental Health and Addiction Treatment on tramadol" (2017).

72 Palestinian National Institute of Public Health and UNODC, *Estimating the Extent of Illicit Drug Use in Palestine* (November 2017).

73 Medhat M. Bassiony and others, "Opioid use disorders attributed to tramadol among Egyptian university students", *Journal of Addiction Medicine,* vol. 12, No. 2 (March 2018), pp. 150–155.

74 Bashirian, Barati and Fathi, "Prevalence and factors associated with tramadol abuse among college students in West of Iran".

75 Egypt, General Secretariat of Mental Health and Addiction Treatment, and Pompidou Group, Council of Europe, *MedSPAD: Results of the First Mediterranean School Survey Project on Alcohol and Other Drugs (MedSPAD) in Egypt* (December 2017).

76 Samir Abou ElMagd and others, "Tramadol misuse and dependence in Egypt and the UAE: user characteristics and drug-use patterns", *International Addiction Review,* vol. 2, No. 1 (April 2018), pp 6–13.

77 Ibid.

78 Nabil R. Mohamed and others, "An epidemiological study of tramadol HCl dependence in an outpatient addiction clinic at Heliopolis Psychiatric Hospital", *Menoufia Medical Journal*, vol. 28, No. 2 (2015), pp. 591–596.

Non-medical use of opioids in Nigeria

The first ever comprehensive survey of drug use in Nigeria, in 2018, revealed that the past-year prevalence of the non-medical use of pharmaceutical opioids (mainly tramadol) was 6 per cent among men and 3.3 per cent among women. Corresponding to 4.6 million past-year users of pharmaceutical opioids aged 15–64 in Nigeria, the non-medical use of opioids was second only to the use of cannabis, which had an estimated prevalence of 10.8 per cent among the population aged 15–64.

The mean age of initiation of the non-medical use of pharmaceutical opioids (mainly tramadol) was 21 and, on average, past-year opioid users had regularly used opioids for 12 years. Nearly 80 per cent of all opioid users were daily or near-daily users and spent around $3.60 per day on pharmaceutical opioids, compared with $10 on heroin. The past-year prevalence of the non-medical use of pharmaceutical opioids (tramadol, codeine, morphine) was high among almost all age groups but was particularly high among people aged 35–39 and 60–64. Polydrug use was also a common feature among opioid users, with more than half reporting using concurrently or sequentially 4–5 substances, including cannabis, pharmaceutical opioids (tramadol, codeine, morphine), cough syrup and tranquilizers.

The majority of opioid users suffered from a severity of dependence that would require intervention to address their drug use disorders, with nearly 40 per cent of opioid users reporting that they wanted help or treatment for their drug problems but were unable to get it. High scores of severity of dependence, in general, have been associated with a high risk of injecting and sexual behaviours that were observed among opioid users in the survey.

Nearly half of drug users reported problems at home, school or workplace as the main problems they face as a consequence of their regular drug use. Other drug users reported being in physical danger or having relationship issues with family or friends or trouble with law enforcement officials because of their drug use. Many high-risk drug users also reported committing petty crimes such as theft, shoplifting and burglary to finance their drug use. Moreover, almost one out of eight people in the general population had suffered a negative experience in the past 12 months as a result of a person using drugs in their family, neighbourhood or community.

Source: UNODC and Government of Nigeria, Drug use in Nigeria 2018.

pharmaceutical opioids in the Middle East and North Africa seems to be less a result of "iatrogenic addiction", when non-medical use of those substances occurs after receiving treatment for a legitimate medical condition, and seems to be more led by the desire, especially among young people and people with substance use disorders, to use them for non-medical purposes.[79, 80] Given its dual properties of being an opioid while also acting on the serotonergic and noradrenergic receptor system,[81] tramadol, in contrast to other opioids, is also perceived by people using it for non-medical purposes as an energy and mood booster. This makes tramadol attractive to broad sections of society, including students during examinations and bus and taxi drivers in a number of developing countries, who would not otherwise be using any opioids.[82]

Non-medical use of tramadol is also reported in other parts of the world. In 2018, for example, of 130,000 respondents to the Global Drug Survey, although a non-representative sample (young people, mainly aged between 18 and 35, who have access to the Internet, and mostly in developed countries), 2.3 per cent reported past-year non-medical use of

79 Sahba Jalali and others, "Higher Regulatory Control of Tramadol to Prevent its Abuse and Dependence", *Journal of Drug Policy Analysis* (January 2017).

80 Medhat M Bassiony and others, "Opioid use disorders attributed to tramadol among Egyptian university students", *Journal of Addiction Medicine,* vol. 12, No. 2 (March/April 2018), pp. 150–155(6).

81 WHO Expert Committee on Drug Dependence, "Annex 1: extract from the report of the forty-first meeting of the Expert Committee on Drug Dependence – fentanyl analogues, synthetic cannabinoids, cathinones, and medicines: pregabalin and tramadol" (Geneva, 2019).

82 See, for example, *World Drug Report 2018*.

The non-medical use of tramadol in West Africa: early findings from an ongoing study

The non-medical use of tramadol in West Africa has raised concerns in recent years. There is a severe lack of quantitative information on drug use in West Africa, but several countries in the region have reported tramadol as one of the drugs most consumed (in a non-medical context), after cannabis. The only country with recent scientific data, Nigeria, indicates that pharmaceutical opioids (tramadol, codeine, and morphine) were the second most misused drugs after cannabis in 2017.[a, b] In West Africa, the non-medical use of tramadol is reported by authorities across all ages, genders and socioeconomic classes, both in urban and rural areas. One particularly worrying finding is that there are reports of tramadol being misused by children in schools.

Most tramadol tablets or capsules appear to be bought on the informal market (street markets, itinerant sales people, tea sellers, etc.) with packaging mentioning a dosage higher than that available in pharmacies. While the regulation of supply chains of pharmaceutical opioids in most West African countries may be vulnerable to risks of diversion for the non-medical use of pharmaceutical drugs, it seems that the majority of the tramadol used non-medically is derived from illegally imported shipments, rather than from the diversion of legally imported products.

Interviews with non-medical users of tramadol show that they are looking for a number of different effects. Some consume tramadol for its calming, analgesic and anti-fatigue effects in order to improve intellectual, physical and working performances, and to lessen the need for sleep and decrease appetite. In farming communities, there are reports of tramadol being used by humans and fed to cattle to enable them to work under extreme conditions.[b] Others use tramadol as a recreational drug on account of its stimulant and euphoric effects, or to improve sexual stamina. Drug users also use tramadol as a substitute for heroin, to ease withdrawal symptoms and cravings. Attractive packaging encourages the recreational use of tramadol and the fact that it is a medicine makes its use without a prescription perceived as non-harmful. As stated by WHO, however, the non-medical use of tramadol "has the potential to precipitate drug abuse and/or dependence in humans".[c]

Polydrug use is common among people who use tramadol non-medically in West Africa. Tramadol is reported to be used along with coffee, alcohol, cannabis and with substances such as taurine and caffeine; some users mix tramadol and codeine. The use of diazepam and other benzodiazepines seems to be common among people who use tramadol non-medically, together with, or instead of, tramadol.

Source: Tramadol Trafficking in West Africa (provisional title), UNODC, forthcoming.

[a] See box on non-medical use of opioids in Nigeria.

[b] UNODC and Government of Nigeria, *Drug Use in Nigeria 2018.*

[c] Souvik Kusari and others, "Synthetic origin of tramadol in the environment", *Angewandte Chemie International Edition* (2015).

[d] WHO, *Critical review Report: Tramadol, Expert Committee on Drug Dependence*, 41st Meeting, Geneva, 12-16 November 2018.

tramadol, compared with 0.8 per cent who reported the use of heroin and 0.6 per cent who reported use of opium.[83]

Opioid overdose deaths

One major toll of opioid use observed globally is the high burden of disease attributed to opioid use disorders. This is particularly the case in North America", where it accounts for nearly 4.4 million healthy years of life lost due to disability and premature death.[84] While population surveys indicate an overall decline in the non-medical use of opioids, including heroin, between 2015 and 2017, opioid-related deaths continue to increase in the United States. Opioids, mainly synthetic opioids (a category comprising fentanyl and tramadol), are the main driver of overdose deaths in the United States. In

83 Adam R. Winstock and others, *Global Drug Survey (GDS) 2018: Key Findings Report 2018* (London, 2018).

84 Institute for Health Metrics and Evaluation, *Global Burden of Disease Study 2017*, Global Health Data Exchange. Available at http://ghdx.healthdata.org/gbd-2017.

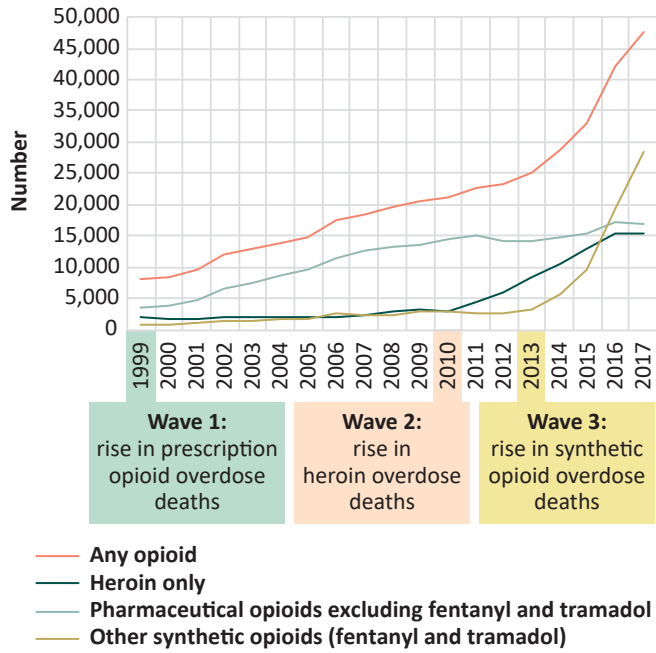
2017, nearly 68 per cent (47,600) of all overdose deaths (70,237) were attributed to the use of opioids, corresponding to a rate of 14.6 deaths per 100,000 population. Of those, the largest number of overdose deaths were attributed to synthetic opioids such as fentanyl and its analogues, which increased from over 19,000 overdose deaths in 2016 to over 28,000 in 2017. Overdose deaths attributed to other pharmaceutical opioids and heroin remained stable, at high levels, from 2016 to 2017.

Drug overdose rates, including opioid overdose deaths, which were higher than the national rate of 14.6 per 100,000, were mainly reported in states in the eastern United States. From 2013 to 2017, the overdose death rate increased significantly in 35 states (out of 50), including the District of Columbia. Fifteen of the 20 states, for which quality overdose data were available, reported a significant increase in the overdose death rate involving synthetic opioids in the previous year; they included eight states west of the Mississippi river (Arizona, California, Colorado, Minnesota, Missouri, Oregon, Texas and Washington). Over the period 2016–2017, opioid overdose deaths increased significantly among both sexes, among opioid users aged 25–44, across most ethnic groups and in metropolitan areas with a population between 250,000 and 1 million inhabitants (referred to as "medium metro counties") and suburban areas with a population of 1 million or more (referred to as "large fringe metro" areas). Overall, the overdose epidemic in the United States continues to worsen, with the increasing involvement of both pharmaceutical and illicitly sourced drugs: in 2016, synthetic opioids (primarily illicitly sourced fentanyls) were involved in 24 per cent of deaths involving pharmaceutical opioids, 37 per cent of those involving heroin, and 40 per cent of those involving cocaine.[85]

In Canada, 3,998 opioid-related deaths were reported in 2017, corresponding to a rate of 10.9 deaths per 100,000 population. Opioid overdose deaths increased by 33 per cent over the period 2016–2017. Moreover, in the first six months of 2018, 2,066 opioid overdose deaths, or 11.2 deaths per 100,000 population, were reported, the majority being attributed to fentanyls. In 2017, the largest numbers of opioid overdose deaths were reported in British Columbia (1,482: 30.8 deaths per 100,000 population) Ontario (1,265: 8.9 deaths per 100,000 population) and Alberta (745 deaths: 17.4 deaths per 100,000 population), and, overall, among males and among people aged 30–39.[86]

In Europe, Estonia has recorded a high rate of opioid overdose deaths (10.6 per 100,000 population) attributed to the use of fentanyls. After a peak in the number of opioid overdose deaths in 2012 (170 deaths), the rate decreased steadily until 2015 then increased in 2016 (114 deaths: 13.4 deaths per 100,000 population). Results of toxicological examinations attributed the majority of those deaths to synthetic opioids, mainly 3-methylfentanyl and other fentanyl analogues such as carfentanil, furanylfentanyl and acrylfentanyl.[87]

FIG. 13 Opioid overdose deaths in the United States, 1999–2017



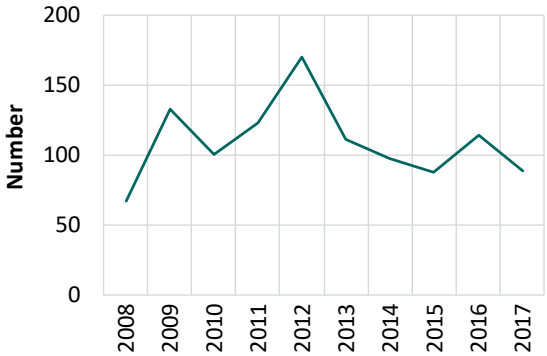
Source: United States, Centers for Disease Control and Prevention, National Center on Health Statistics, Wide-ranging Online Data for Epidemiologic Research (CDC WONDER).

85 Lawrence Scholl and others, "Drug and opioid-involved overdose deaths: United States, 2013–2017", *Morbidity Mortality Weekly Report*, vol. 67, No. 5152 (January 2019), pp. 1419–1427.

86 Canada, "Overview of national data on opioid-related harms and deaths", 12 December 2018.

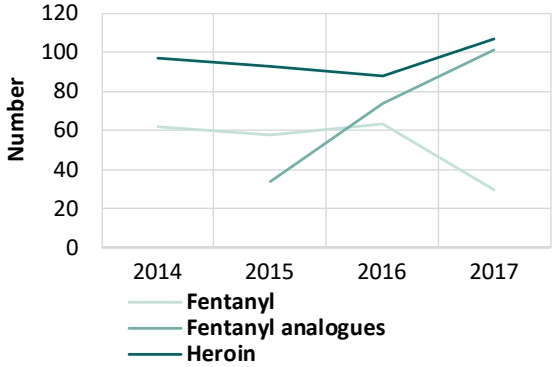
87 EMCDDA, "Estonia drug report 2018".

FIG. 14 Trends in fentanyl overdose deaths in Estonia



Source: Estonian causes of death registry.

FIG. 15 Opioid overdose deaths in Sweden

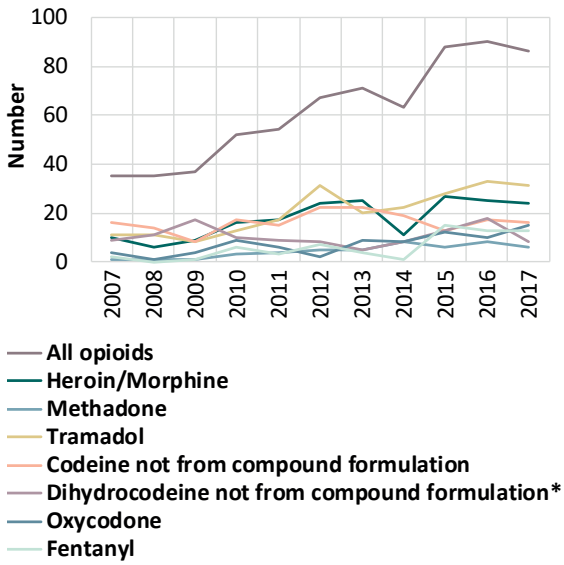


Source: "Swedish National Threat Assessment on fentanyl analogues and other synthetic opioids" (October 2018).

Sweden has also experienced overdose deaths attributed to the use of opioids, including heroin, fentanyl and fentanyl analogues. A total of 590 overdose deaths were reported in Sweden in 2016 (9.5 per 100,000 population), of which opioids accounted for over 90 per cent. Fentanyl analogues were introduced into the drug market in Sweden in 2014, through online sales of illicit fentanyl analogues, mainly in the form of nasal spray but also in the form of tablets, powder and capsules.[88] Since 2015, fentanyl analogues have resulted in an increasing number of overdose deaths. While the number of heroin overdose deaths remained high in Sweden over the period 2015–2017, fentanyl and fentanyl analogues accounted for a larger number of overdose deaths; however, the majority of those deaths involved more than one substance.[89] Overall, most fentanyl analogue deaths in 2015 were attributed to acetylfentanyl (31 cases), while in 2016 most were attributed to acrylfentanyl (43 cases) and in 2017 to cyclopropylfentanyl (72 cases). In 2017, people who died from a fentanyl overdose were older on average (median age: 44.6) than those whose overdose was caused by fentanyl analogues (median age: 32.9).[90]

In Northern Ireland, the number of opioid-related deaths has been increasing since 2013. In 2017, a total of 136 drug-related deaths were reported (almost 7 drug-related deaths per 100,000 population), of which 40 per cent were attributed to opioids. Tramadol and heroin were the main opioids found in those deaths, but smaller numbers of deaths caused by codeine, oxycodone and fentanyl have also been reported and are considered to be

FIG. 16 Opioid-related deaths in Northern Ireland, 2007–2017



Source: Northern Ireland Statistics and Research Agency, "Drug related and drug misuse deaths 2007–2017", 4 March 2019.

Note: Drug-related deaths are defined as deaths of which the underlying cause recorded on the death certificate is drug poisoning, drug abuse or drug dependence. Drug-misuse deaths occur when the underlying cause is drug poisoning, drug abuse or drug dependence and when any of the nationally controlled substances is involved in the death.

88 Swedish Police Authority, National Operations Department, "Swedish National Threat Assessment on fentanyl analogues and other synthetic opioids" (October 2018).

89 Ibid.

90 Sweden, National Board of Forensic Medicine.

increasing. It is noteworthy that almost half of recorded drug overdose deaths involved three or more drugs, of which diazepam was the most commonly reported substance. The most deaths resulting from drug misuse were reported to be those of young males aged 25–34.[91]

Emergence of new psychoactive substance opioids

With the aim of developing more effective medications for pain management, both for medicinal and veterinary use, a number of synthetic opioid receptor agonists have been developed by the pharmaceutical industry in the past five decades. After initial research, however, many of the substances were not further developed, or were considered "not suitable for human consumption". In recent years, along with fentanyl analogues, many opioid receptor agonists, which are derived from information published in the research publications of pharmaceutical companies or patents, have emerged in the illicit drug markets. In the scientific literature they are often referred to as "research opioids" or "novel synthetic opioids".[92] From the perspective of UNODC, since these substances are not under international control they have been labelled as "NPS with opioid effects" or "NPS opioids". Synthetic opioid receptor agonists are of varying potency and, as with other opioids, their clinical effects are dose dependent. Although they are structurally unrelated to morphine, NPS opioids are full agonists of the μ-opioid receptors, which account for profound depression of the central nervous system and respiratory system; this is responsible for significant morbidity and mortality associated with their use.[93] In cases of toxicity with NPS opioids, larger doses of naloxone are required to reverse the effects than in cases of overdose with many other opioids.[94]

NPS opioids appear to be an expanding group of substances that are being introduced into the drug market for non-medical use. Among the new NPS reported in 2017 to the UNODC early warning advisory, nearly one third were synthetic opioid receptor agonists, the majority of these 22 substances being fentanyl analogues while a few were from other families of research opioids, such as U-48800 and U-51754. In addition, in recent years other opioid receptor agonists, such as AH-7921, MT-45, and U-4700, or similarly named substances, have been reported, seized and analysed.[95, 96]

Many synthetic opioid receptor agonists, including AH-7921, MT-45 and U-4700 have been sold as such to regular opioid users.[97] Other synthetic opioids, including fentanyl analogues, are reportedly sold in drug markets as replacements for controlled drugs, and in many instances as falsified prescription painkillers such as oxycodone, and even as falsified benzodiazepines.[98] In other instances, synthetic opioids have been used as adulterants to heroin and other drugs, such as cocaine, and those buying them, sometimes marginalized opioid users, are not usually aware of their exact contents and often miscalculate their doses, with deleterious consequences.[99]

Many fentanyl analogues are marketed for non-medical use directly to users and almost exclusively on the Internet.[100] The proliferation of e-commerce has also facilitated the sale of synthetic opioids through both the conventional Internet and the darknet.[101, 102] As reported in recent cases in Sweden, unlabelled nasal sprays containing acryloylfentanyl (acrylfentanyl) have been offered for purchase online;[103] there are also reports of "e-liquids" containing fentanyl analogues that can be vaped using

91 Northern Ireland Statistics and Research Agency, "Drug related and drug misuse deaths 2007–2017", 4 March 2019.

92 Armenian and others, "Fentanyl, fentanyl analogues and novel synthetic opioids".

93 Ibid.

94 Ibid.

95 EMCDDA, *EMCDDA-Europol Joint Report on a New Psychoactive Substance – 1-cyclohexyl-4-(1,2-diphenylethyl) piperazine ('MT-45')*, Joint Report Series, MT-45 (Luxembourg, Publication Office of the European Union, 2014).

96 "Swedish National Threat Assessment on fentanyl analogues and other synthetic opioids".

97 Ibid.

98 *2018 National Drug Threat Assessment*.

99 Ibid.

100 EMCDDA, *Fentanils and Synthetic Cannabinoids: Driving Greater Complexity into the Drug Situation – An Update from the EU Early Warning System* (Luxembourg, Publication Office of the European Union, 2018).

101 Armenian and others, "Fentanyl, fentanyl analogues and novel synthetic opioids".

102 EMCDDA, *Fentanils and Synthetic Cannabinoids*.

103 "Swedish National Threat Assessment on fentanyl analogues and other synthetic opioids".

electronic cigarettes.[104] Overall, synthetic opioids are becoming a major concern that requires regular monitoring by law enforcement, toxicological laboratories, chemists, pharmacists and physicians, in order to improve understanding of their emergence and provide guidance for responding to the threat to individual and public health that they pose.

Supply of opiates

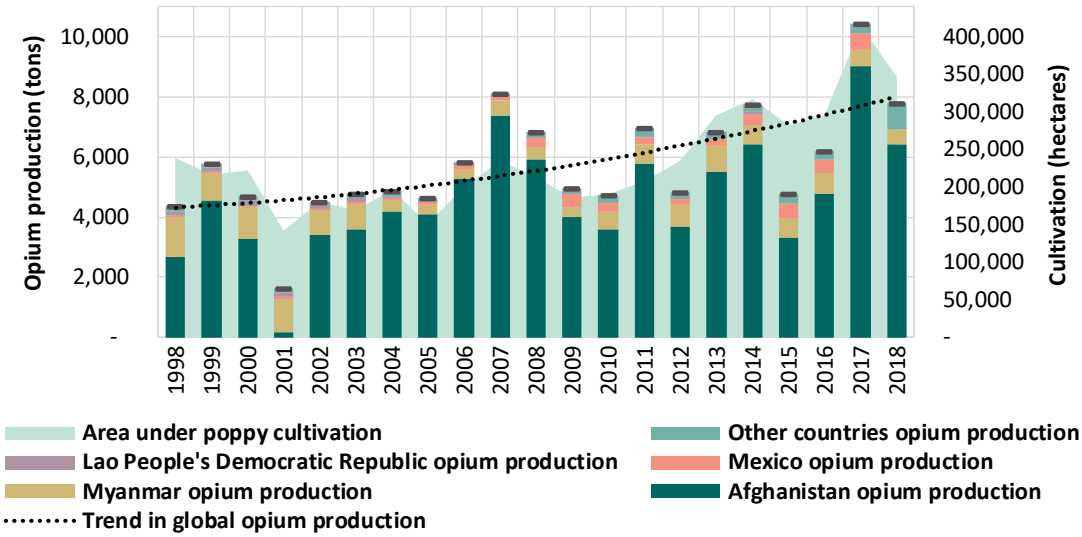
Opium is illicitly produced in some 50 countries worldwide, although production is highly concentrated in Afghanistan, Myanmar and Mexico, which accounted for roughly 96 per cent of global opium production over the period 2014–2018.

Opiates produced in Afghanistan, the single largest opium producer, have a global reach. They supply markets in neighbouring countries, Europe, the Near and Middle East, South Asia, Africa and a small proportion of the markets in North America (mainly Canada) and Oceania. In South-East Asia, Myanmar and, to a lesser extent, the Lao People's Democratic Republic supply the heroin markets in East and South-East Asia and Oceania. In Latin America, Mexico and, to a lesser extent, Colombia and Guatemala provide most of the heroin supply to the United States and supply the comparatively small heroin market in South America.

Global area under opium poppy cultivation and opium production declined in 2018

Despite a decrease in size of 17 per cent from the previous year, the global area under illicit opium poppy cultivation remained at a high level of around 346,000 ha in 2018. Global opium production also decreased in 2018, by 25 per cent, but the estimate is still among the highest in the past two decades. Of the estimated 7,790 tons of opium produced worldwide in 2018, it is estimated that some 1,225–1,525 tons remained unprocessed for consumption as opium, while the rest was manufactured into heroin, resulting in an estimated 486–736 tons of heroin (expressed at export purity) being manufactured in 2018. Both opium and heroin prices continued to decline in 2018 in Afghanistan and Myanmar, implying that there is no sign of a possible shortage of opiates on the market as a result of the decline in global opium production in 2018.

FIG. 17 Opium poppy cultivation and production of opium, 1998–2018*



Source: UNODC calculations, based on UNODC illicit crop monitoring surveys and annual report questionnaire.
Note: Data for 2018 are still preliminary; notably no new data for Mexico for the year 2018 were available at the time of writing this report.

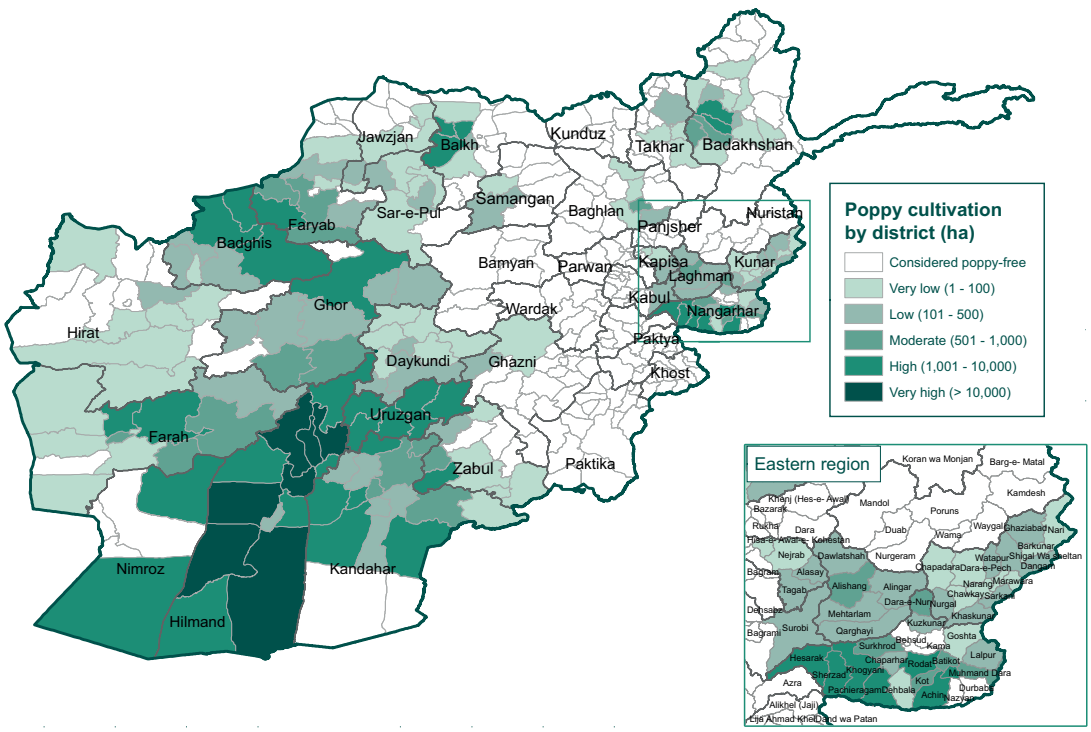
104 EMCDDA, *Fentanils and Synthetic Cannabinoids.*

Decline in opium production mainly due to decreases reported in Afghanistan

The global decline in opium production in 2018 was primarily related to Afghanistan where, following years of an upward trend, the area under opium poppy cultivation shrank by 20 per cent from its record 2017 level, although the estimated area for 2018 is still the second largest ever reported for that country. As the opium yield fell, overall opium production decreased by 29 per cent in Afghanistan in 2018. Nonetheless, Afghanistan remains the world's largest opium-producing country, accounting for 82 per cent of global illicit opium production.

More than two thirds (69 per cent) of opium production in the country continues to take place in southern Afghanistan, most notably in the provinces of Helmand (52 per cent of the total) and Kandahar (9 per cent). However, cultivation and production declined in all regions in 2018, in particular in the northern, western and central parts of the country and, to a lesser extent, in eastern, southern and north-eastern Afghanistan.[105] This was mainly the result of a severe drought that affected not only rain-fed but also irrigated land. As it had not snowed sufficiently in the mountains in the winter of 2017/2018, there was not sufficient groundwater for irrigating many parts of the country, including areas under opium poppy cultivation. The subsequent lack of rain negatively affected rain-fed opium poppy cultivation in western and northern Afghanistan.[106] The drought not only affected opium production but also agriculture in general. This caused a humanitarian crisis in several parts of the country, in particular in western and northern part

MAP 3 Opium poppy cultivation in Afghanistan, 2018



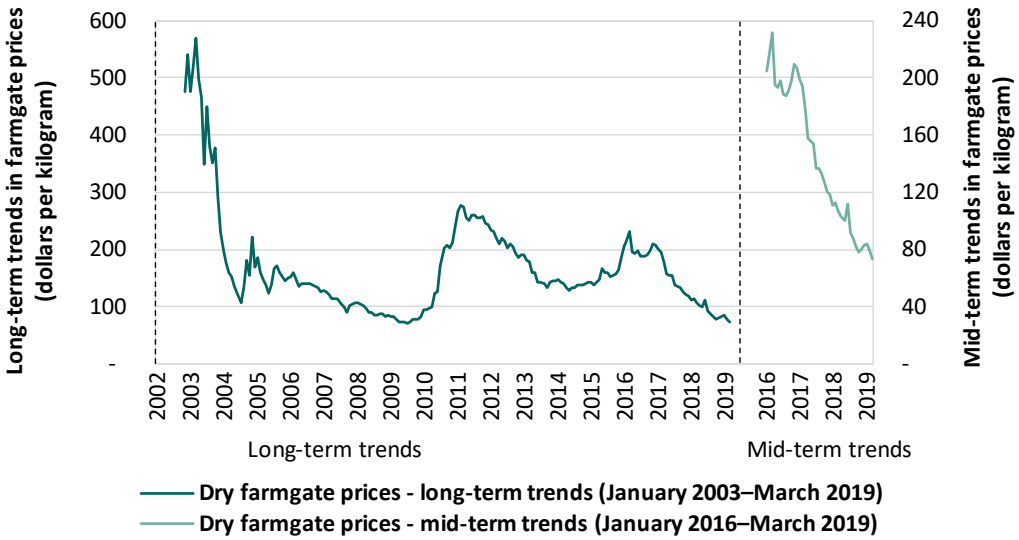
Source: UNODC and Afghanistan, Ministry of Counter Narcotics, *Afghanistan Opium Survey 2018: Cultivation and Production* (November 2018).

The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.

105 UNODC and Afghanistan, Ministry of Counter Narcotics, *Afghanistan Opium Survey 2018: Cultivation and Production* (November 2018).

106 Ibid.

FIG. 18 Average dry opium farm-gate prices in Afghanistan, November 2002–March 2019



Source: Afghanistan, Ministry of Counter Narcotics and UNODC, "Afghanistan drug price monitoring monthly report" (March 2019 and previous years).

of the country, where 1.4 million people were considered at risk of acute food insecurity as a result of the drought in the spring of 2018, and that situation led to a forecast decrease in cereal production of some 28 per cent in 2018 from the average for the period 2013–2017.[107]

Apart from the drought, sharply falling opium prices – probably a consequence of the record opium production in 2017 – might have acted as a disincentive for farmers to grow opium poppy in 2018. Opium prices continued to decline in 2018,[108] while the indebtedness of many Afghan farmers increased as a consequence of the drought. Research has shown that growing indebtedness, often in the form of "salaam" arrangements, in which the following year's opium harvest is sold in advance in exchange for immediate cash payments, may prompt farmers, irrespective of a decrease in opium prices, to revert to opium poppy production in order to repay their debts.[109] Cultivating opium poppy is one of the many coping strategies that a rural household may employ for securing its livelihood. Income for covering basic needs, including food, medical expenses and debt were the three most common uses of opium income reported by farmers in Afghanistan in 2017.[110] In particular, "infrequent poppy farmers" cited the need to repay loans as a key reason for cultivating opium poppy.[111]

Decline in opium production also reported in Myanmar

Opium poppy cultivation in Myanmar, home to the world's second largest area under opium poppy cultivation, continued to decline in 2018, with the country accounting for 11 per cent of the global area under illicit opium poppy cultivation worldwide that year. Some 37,300 hectares of opium poppy are estimated to have been cultivated in the country in 2018, which represents a decline of 12 per cent from the previous year and of one third since 2015.[112] Opium production in Myanmar also

107 Food and Agriculture Organization of the United Nations, Global Information and Early Warning System on Food and Agriculture, "Country brief: Afghanistan", 21 June 2018.

108 Afghanistan, Ministry of Counter Narcotics and UNODC, "Afghanistan drug price monitoring monthly report" (March 2019).

109 Mohammad Ehsan Zia and others, *Rural Finance in Afghanistan and the Challenge of the Opium Economy*, Report No. 33275 (Washington D.C., World Bank, July 2005).

110 UNODC and Islamic Republic of Afghanistan, *Afghanistan Opium Survey 2017 – Challenges to sustainable development, peace and security*, (May 2018).

111 Ibid.

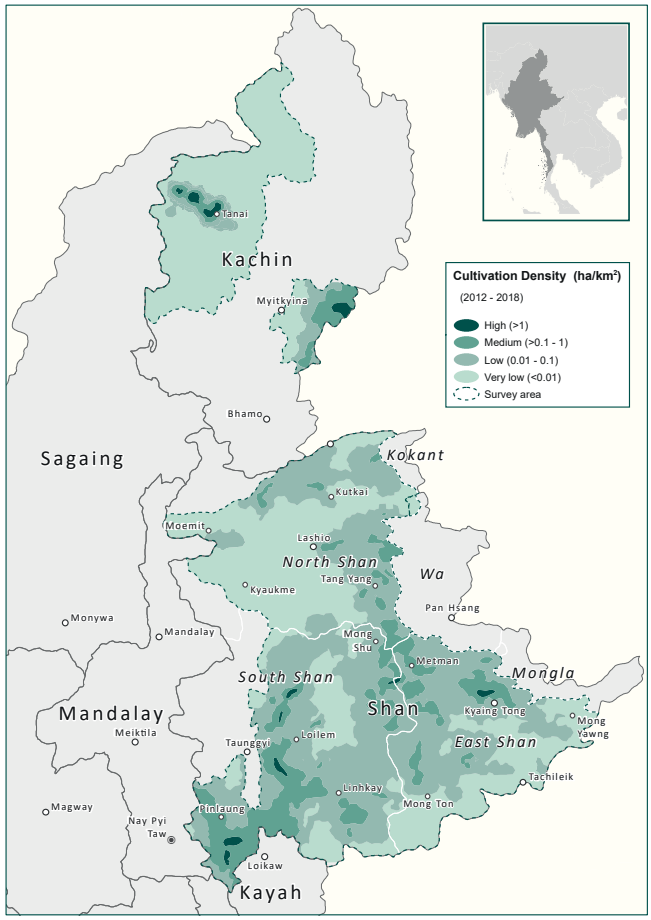
112 Percentage decline estimated based on the regions where estimates were available in both 2017 and 2018 (Shan and

declined in 2018 to an estimated 520 tons (7 per cent of global opium production), its lowest level since 2010.

Almost 90 per cent of the opium poppy in Myanmar continued to be cultivated in Shan State, while most of the remainder was cultivated in neighbouring Kachin State, in the north of the country. Smaller pockets of opium poppy cultivation were also found in Kayah State, in the south, and in Chin State, in the west. [113] The most marked declines in opium poppy cultivation in Myanmar in 2018 were in areas with a comparatively good security situation. There were also declines in parts of North Shan and Kachin states, where there had been a protracted state of conflict in recent years and central government control is limited.

Apart from the security situation, a number of structural vulnerabilities are frequently associated with opium poppy cultivation in Myanmar, such as income inequality, lack of employment opportunities and of infrastructure, such as access to markets and availability of health clinics. Those vulnerabilities continued to play a role in the areas where there is a high concentration of opium poppy cultivation. Moreover, the presence of organized crime groups in those areas is also associated with the manufacture and trafficking of heroin.[114] Lower opium prices might also have played a role, as in the period 2015–2018 farm-gate prices of dry opium decreased by around 45 per cent in Myanmar, possibly a consequence of a shift from the use of opiates to the use of synthetic drugs, particularly methamphetamine, in several parts of East and South-East Asia.

MAP 4 Opium poppy cultivation density map in Myanmar, June 2017–May 2018



Source: UNODC and Myanmar, Central Committee for Drug Abuse Control.
The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.

Opium production on the increase in Mexico

The latest available estimates of the annual opium harvest for the period July 2016–June 2017 indicated a continued increase in the area under opium poppy cultivation in Mexico, by 21 per cent from the previous year, to 30,600 hectares.[115] In general, opium poppy cultivation in Mexico is found in areas that are not easily accessible and are characterized by a low level of economic development.[116] The main areas under opium poppy cultivation in 2017 continued to be in the states that form part of the Sierra Madre Occidental, i.e., the states near the Gulf of California, in particular Sinaloa, Durango, Chihuahua and Nayarit, as well as further south, in the states of the Sierra Madre del Sur, which are located along the Pacific Coast, in particular the

Kachin States).

113 UNODC and Myanmar, Central Committee for Drug Abuse Control, *Myanmar Opium Survey 2018: Cultivation, Production and Implications* (Bangkok, December 2018).

114 UNODC, Socioeconomic report on evidence for enhancing reliance on opium poppy cultivation in Shan State, Myanmar (draft report, quoted in the *Myanmar Opium Survey 2018*).

115 UNODC and Mexico, *México: Monitoreo de Cultivos de Amapola 2015–2016 y 2016–2017* (November 2018).

116 Ibid.

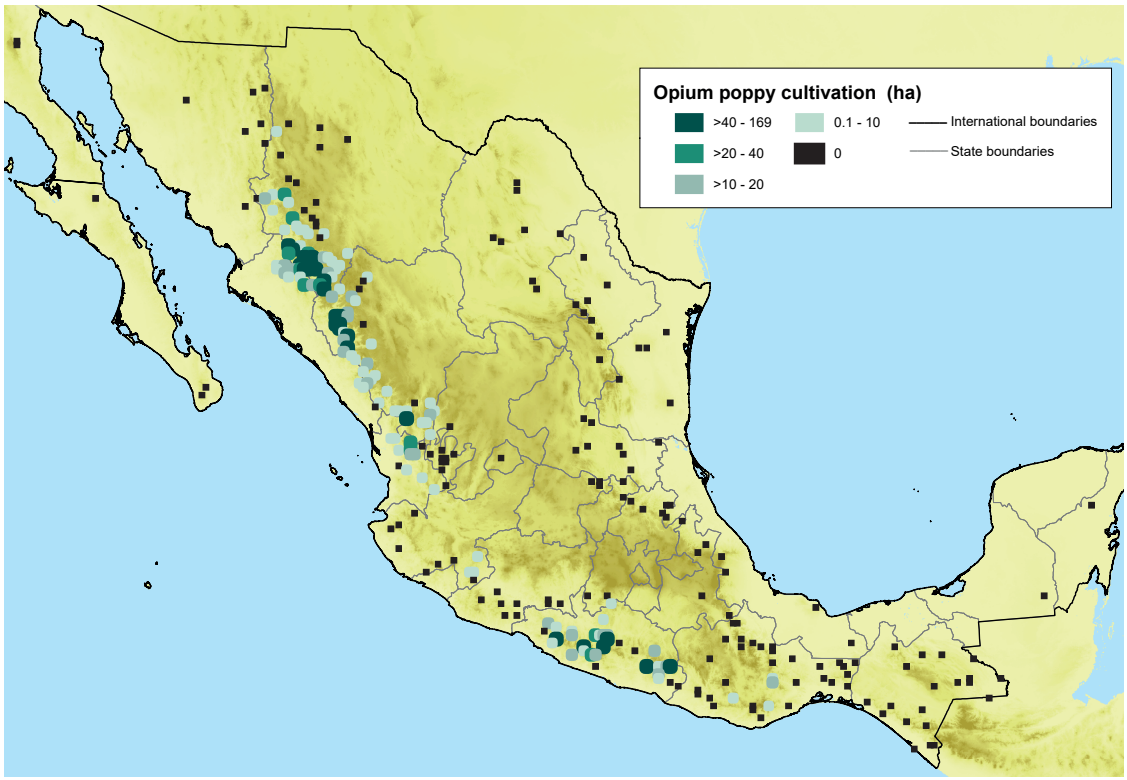
State of Guerrero, which surrounds Acapulco, and the State of Oaxaca.[117]

The states of Sinaloa, Chihuahua and Durango, also known as the "Golden Triangle" of Mexico, are not only known for opium poppy cultivation but also for widespread cultivation of cannabis, which is mainly destined for the United States market. Reports suggest a shift in the activities of organized crime groups in Mexico as cannabis grown in the country appears to have lost its competitive advantage in the United States market, where the production of high-quality cannabis has been on the increase following the legalization of cannabis supply for recreational use in several states.[118]

The reported increase in the area under opium poppy cultivation in Mexico went in parallel with a number of law enforcement activities, including a 32 per cent increase in the eradication of poppy cultivation in Mexico in 2017, a 44 per cent increase in the quantities of heroin and morphine seized in the country, a tripling in the quantity of opium gum seized and a tripling in the number of clandestine heroin laboratories dismantled in Mexico in 2017.[119] Meanwhile, the quantity of heroin seized by United States authorities along the south-west border with Mexico increased by 36 per cent from a year earlier (fiscal year of 2017).

Based on forensic profiling, United States authorities estimated that in 2016, 86 per cent of the heroin analysed (744 samples taken from 1.6 tons of heroin seized in the United States) had originated in Mexico, up from 20 per cent in 2006.[120] Most indicators point to an expansion of the heroin

MAP 5 Opium poppy cultivation density in Mexico, 2016–2017



Source: UNODC and Mexico, *Mexico: Monitoreo de Cultivos de Amapola 2015–2016 y 2016–2017* (November 2018).

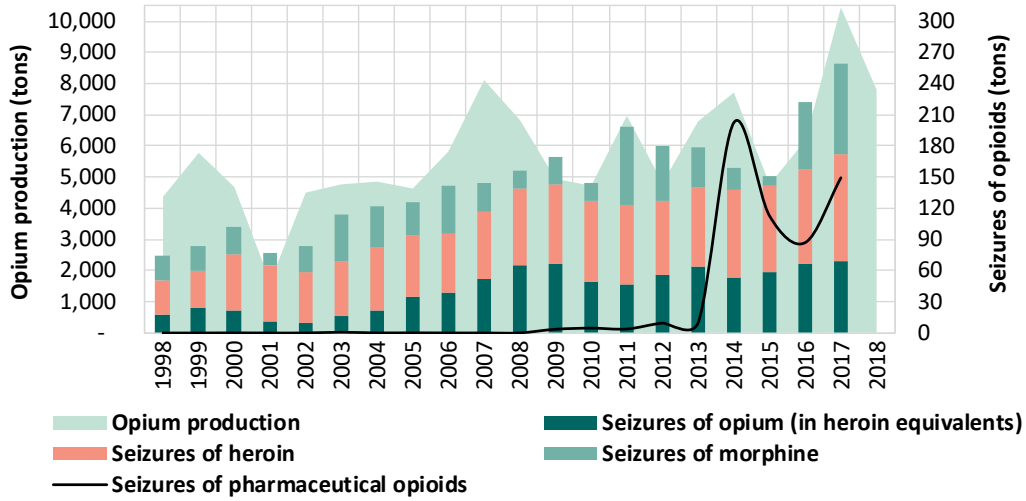
The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.

117 Ibid.

118 *2018 National Drug Threat Assessment.*

119 *México: Monitoreo de Cultivos de Amapola 2015-2016 y 2016-2017.*

FIG. 19 Global opium production and quantities of opioids[a] seized, 1998–2018



Sources: UNODC, responses to the annual report questionnaire and other Government sources.
[a] *A ratio of 10:1 was used to convert opium into heroin equivalents.*

market in the United States in recent years:[121] overall, heroin seizures in the country more than tripled between 2006 and 2016, to 7.1 tons, then increased further, to 8.1 tons in 2017, while the number of heroin-related deaths in the United States rose sevenfold over the period 2007–2017, or, excluding the involvement of other, synthetic opioids, fourfold.[122]

Opium production has been fluctuating greatly but global opiate seizures have increased steadily over the past two decades

At the global level, annual opium production has been fluctuating more than annual heroin seizures and global opiate use, suggesting the existence of opium inventories. By offsetting fluctuations in opium production, such inventories appear to ensure a smooth supply of heroin to the main consumer markets and explain the comparatively smaller year-on-year changes in heroin seizures. The overall upward trend in quantities of opiates seized over the past two decades has been more pronounced than the upward trend in opium production,[123] suggesting that law enforcement authorities may have become increasingly successful in intercepting trafficked opiates worldwide, although changes in purity could also partially explain the difference.

Opiate seizures increased to new record levels in 2017 and remained concentrated in Asia, especially in South-West Asia

In 2017, quantities of opiates seized globally reached an all-time high, with a 5 per cent increase from the previous year in the quantity of opium seized (to 693 tons), a 13 per cent increase in heroin seized (to 103 tons) and a 33 per cent increase in morphine seized (to 87 tons). Expressed in common heroin equivalents, heroin seizures continued to exceed those of morphine and opium in 2017.

Most seizures of opiates continued to be reported in, or close to, the main opium production areas. Thus, with more than 90 per cent of global illicit opium production taking place in Asia, the region accounted for 86 per cent of all quantities of opiates seized (expressed in heroin equivalents) in 2017.

120 *2018 National Drug Threat Assessment.*

121 For further details of the increasing demand for heroin in the United States, see the section on the demand for opioids.

122 National Institute on Drug Abuse, "Overdose death rates", revised January 2019.

123 Notwithstanding possible changes in heroin purity seizures (not accounted for in the calculation).

The vast majority of those opiates continued to be seized in the Near and Middle East/South-West Asia in 2017 (79 per cent of global opiates seized, expressed in common heroin equivalents), particularly opium (97 per cent of global opium seizures) and morphine (99 per cent of global morphine seizures).

Accounting for 39per cent of the global total, the largest quantity of opiates (expressed in heroin equivalents) continued to be seized in the Islamic Republic of Iran in 2017, followed by Afghanistan (26 per cent) and Pakistan (14 per cent). The next largest seizures of opiates were reported by Turkey (7 per cent), the United States and China (4 per cent each).

Quantities of heroin and morphine seized continue to increase in all regions except Oceania

The quantities of heroin and morphine intercepted in Asia more than doubled in 2016 and increased by a further 14 per cent in 2017. This primarily reflected increases in the quantities of morphine and heroin seized in the Near and Middle East/South-West Asia, a consequence of marked increases in Afghan opiate production in 2016 and 2017, as well as ongoing law enforcement operations in those subregions.

In East and South-East Asia, the quantities of heroin and morphine seized decreased in 2016 but increased in 2017. The majority of heroin and morphine seizures in that subregion continued to be reported by China, which accounted for 72 per cent of all such seizures in the subregion in 2017.

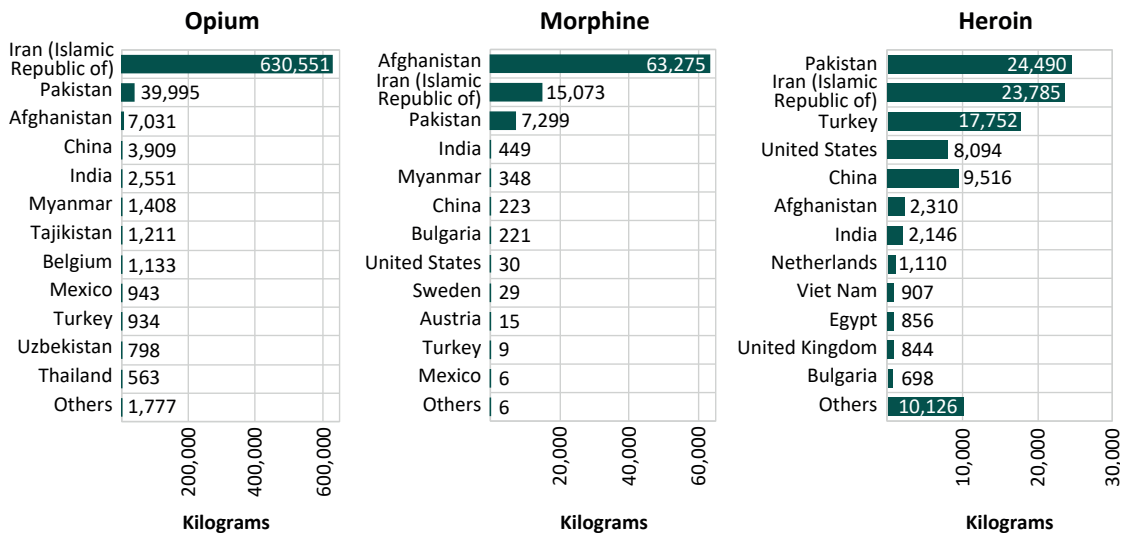
In South Asia, a marked increase, most notably in India, in the quantities of heroin and morphine seized has been reported in recent years. With increases of 34 per cent in 2016 and 51 per cent in 2017, the subregion now accounts for almost 2 per cent of the global total quantities of heroin and morphine seized.

The largest quantities of heroin and morphine seized outside Asia are reported in Europe (13 per cent of the global total), followed by the Americas (5 per cent), two important markets for heroin.

In Europe, the quantities of heroin and morphine seized more than doubled in 2017, to 24 tons, back to the level reported in the first decade of the new millennium. The increase in Europe was primarily the consequence of a tripling in the quantities of heroin and morphine seized in South-East Europe, notably in Turkey and, to a lesser extent, Bulgaria and other countries along the Balkan route.

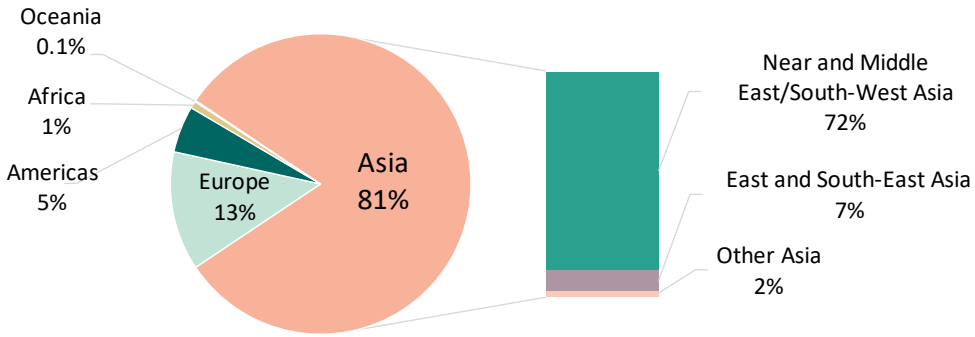
Quantities of heroin and morphine seized in West and Central Europe rose by 29 per cent in 2017

FIG. 20 Countries reporting the largest quantities of opiates seized, 2017



Source: UNODC, responses to the annual report questionnaire and other Government sources.

FIG. 21 Distribution of global quantities of heroin and morphine seized in 2017 (total = 190 tons)



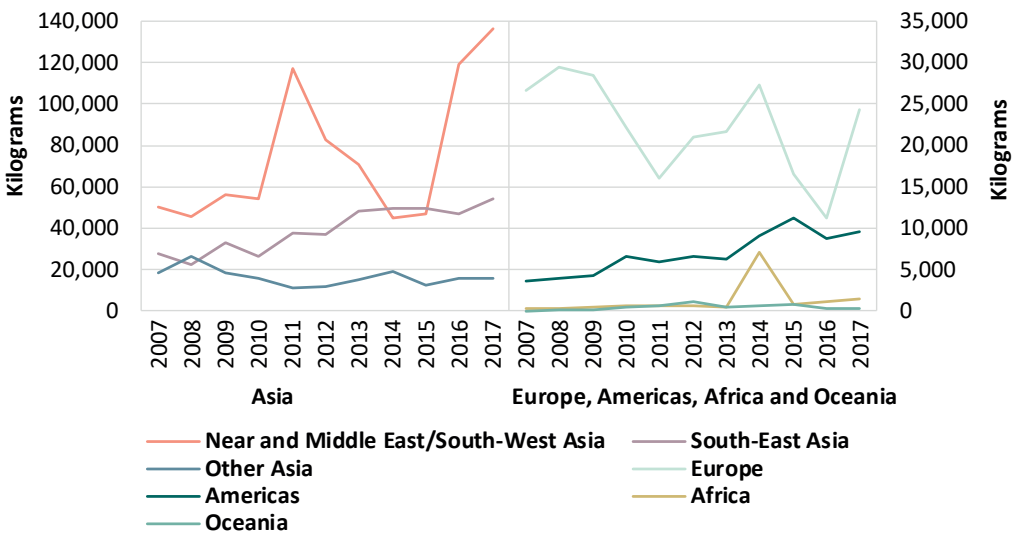
Source: UNODC, responses to the annual report questionnaire, and other Government sources

from the previous year, with increases reported by most countries. Seizures in the subregion nonetheless remained clearly below the annual average reported over the past decade. The largest seizures in the subregion in 2017 were reported by the Netherlands, followed by the United Kingdom, France, Italy and Spain.

By contrast, the quantities of heroin and morphine seized continued to decline in Eastern Europe for the third year in a row, falling by 48 per cent in 2017 (or by 85 per cent since 2014), mainly as a result of a decline in the quantities seized in the Russian Federation. This is in line with the ongoing decline, by 64 per cent in 2017 (or by 78 per cent since 2014), reported in the quantities of heroin and morphine seized in Central Asia and Transcaucasia, the main transit area for heroin shipments to the market in the Russian Federation.

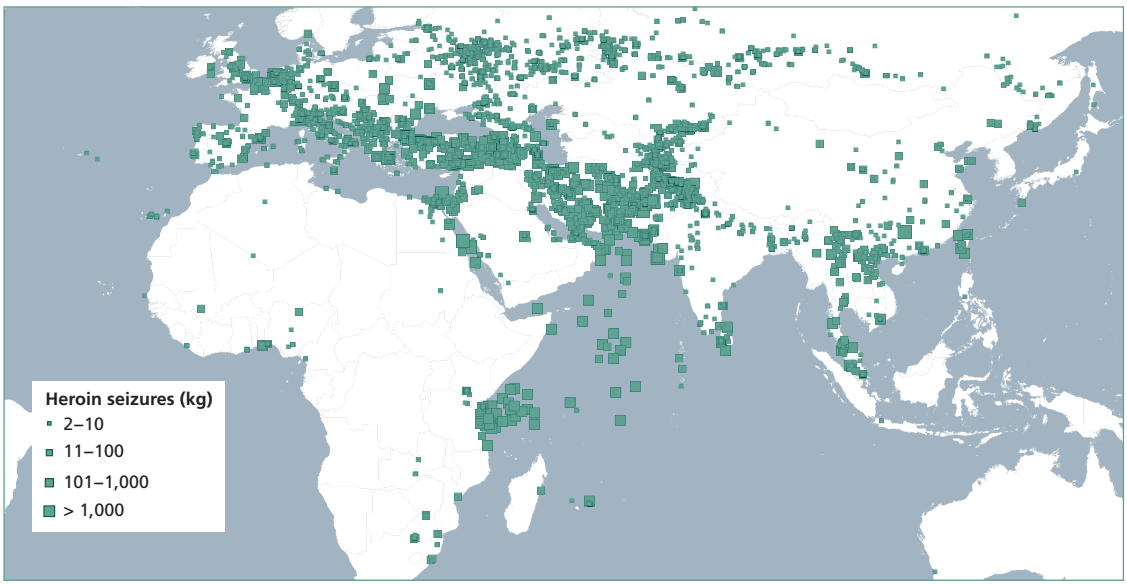
The quantities of heroin and morphine seized in the Americas rose by 9 per cent in 2017, to 9.5 tons, almost three times the quantity seized a decade earlier. Seizures made in North America accounted for 90 per cent of all the heroin and morphine intercepted in the Americas, with 85 per cent being seized

FIG. 22 Quantities of heroin and morphine seized, by region, 2007–2017



Source: UNODC, responses to the annual report questionnaire data and other Government sources.

MAP 6 Significant individual heroin seizures, January 2013–April 2019



Source: UNODC and Paris Pact, Drugs Monitoring Platform.

The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.

in the United States, followed by Colombia, Ecuador, Mexico, Canada and Guatemala.

Despite a 31 per cent increase in 2017 and a fourfold increase compared with a decade ago, the quantities of heroin and morphine seized in Africa remained comparatively low, at 1.5 tons, in 2017. Most seizures continue to be reported in North Africa, which accounted for nearly two thirds of all quantities of heroin and morphine seized in Africa in 2017, and in East Africa (21 per cent). Egypt is the country where most such seizures have been reported in Africa, reflecting the trafficking of opiates via the Red Sea and Suez Canal, followed by the United Republic of Tanzania, South Africa, Kenya and Nigeria.

The quantities of heroin and morphine seized in Oceania decreased in 2017 for the second year in a row, to the lowest level since 2009, with more than 99 per cent being seized in Australia.

Trafficking in opiates continues to be dominated by opiates originating in Afghanistan

Reflecting the increasing dominance of opium production in Afghanistan, most opiates worldwide are trafficked from Afghanistan to markets in neighbouring countries (in particular the Islamic Republic of Iran, Pakistan, Central Asian countries and India), to Europe, the Near and Middle East, South Asia, Africa and, to a lesser extent, South-East Asia, North America and Oceania. Some 88 per cent of the global total of heroin and morphine seized in 2017 was related to Afghan opiate production, up from 73 per cent in 2015. Nearly all opiates seized in Europe, Central Asia and Africa are derived from opium originating in Afghanistan; that country accounted for 100 per cent of all mentions of the "country of origin" of opiates seized in Central Asia, 96 per cent of mentions by authorities in Europe and 84 per cent of mentions in Africa over the period 2013–2017.[124]

Heroin is also trafficked from production areas in South-East Asia (Myanmar and, to a lesser extent, the Lao People's Democratic Republic) to markets in East and South-East Asia and Oceania. In the Americas, heroin manufactured in Latin America (notably Mexico, and, to a far lesser extent, Colombia and Guatemala) accounts for most of the heroin

124 For details of calculation, see the online methodology section.

supply to the United States and also supplies the comparatively limited heroin market in South America.

Most opiates continue to be trafficked from Afghanistan along the Balkan route and its various branches

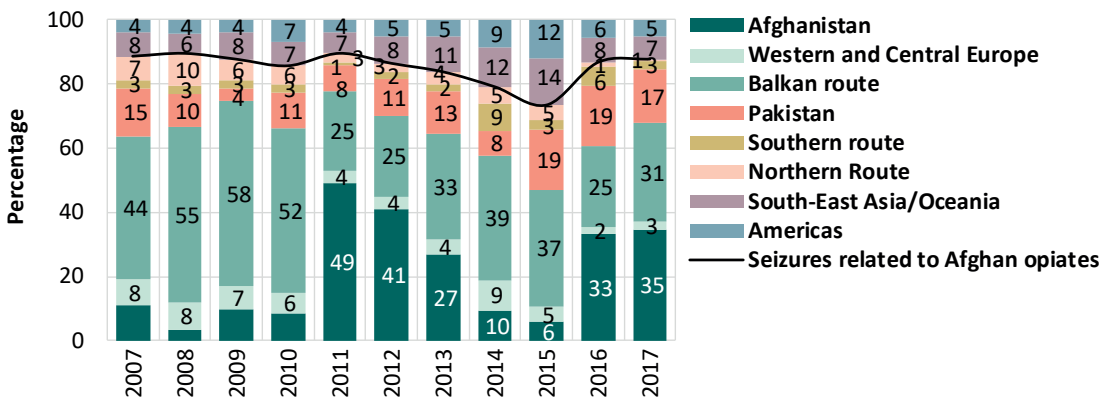
Based on seizures, the world's single largest heroin trafficking route continues to be the Balkan route, along which opiates are smuggled from Afghanistan to the Islamic Republic of Iran, Turkey, and the Balkan countries to various destinations in Western and Central Europe. Excluding seizures made in Afghanistan, countries along the Balkan route accounted for 47 per cent of the global quantities of heroin and morphine seized in 2017, with a further 4 per cent reported by countries in Western and Central Europe.

Opiates are either trafficked along the eastern branch of the Balkan route from Turkey to Bulgaria and then onward to Romania and Hungary, or along the western branch from Bulgaria to various western Balkan countries and from there to Western and Central Europe. More than three quarters of the mentions of countries of origin, departure and transit of heroin in the annual report questionnaire submitted by countries in Western and Central Europe over the period 2013–2017 referred to trafficking via countries along the Balkan route, while 7 per cent referred to shipments via Pakistan.

Although some heroin may transit Pakistan for subsequent trafficking along the Balkan route, some heroin is also trafficked directly from Pakistan, either by air or sea to Europe; this has been mainly reported by the United Kingdom, Denmark and Italy and, to a lesser extent, by Greece, Spain, France and Belgium in recent years. Pakistan reported 32 tons seized in 2017, up from a low of 4 tons (4 per cent of the global total) in 2009. The main destination countries, based on seizures made by the Pakistani authorities in 2017, were, in Europe, the United Kingdom and, on the Arabian Peninsula, the United Arab Emirates and Saudi Arabia. In addition, opiates are smuggled via Pakistan and via the Islamic Republic of Iran for onward trafficking along the Balkan route. The Islamic Republic of Iran reported that 80 per cent of the morphine and 85 per cent of the heroin seized on its territory in 2017 had been smuggled into the country via Pakistan, with only the remainder having been smuggled directly from Afghanistan into the Islamic Republic of Iran.

Smaller amounts of heroin were also seized on the "Caucasus route" and along the Black Sea. This deviation of the Balkan route goes from the Islamic

FIG. 23 Distribution of global quantities of heroin and morphine seized, by main trafficking routes, 2007–2017[a]



Source: UNODC, responses to the annual report questionnaire.

[a] *The Balkan route: Islamic Republic of Iran, half of Transcaucasia, South-Eastern Europe; the southern route: South Asia, Gulf countries and other countries in the Near and Middle East and Africa; the northern route: Central Asia, Eastern Europe and half of Transcaucasia. Heroin seized in Transcaucasia was partly attributed to the Balkan route and partly to the northern route as it may supply both routes.*

Republic of Iran to the Caucasus countries (Azerbaijan, Armenia and Georgia) across the Black Sea to Ukraine and then by land to Romania for onward trafficking along the eastern branch of the Balkan route to Central and Western Europe. This route increased in importance for several years, with seizures of heroin and morphine rising from 0.7 tons in 2007 to 1.8 tons in 2014, before falling to 1.3 tons in 2016 and 0.4 tons in 2017, compared with 18 tons of heroin and morphine seized in Turkey, 0.9 tons seized in Bulgaria and 0.4 tons seized in Greece in 2017. While seizures in Turkey, Bulgaria and Greece increased in 2017, they decreased in countries affected by trafficking via the Black Sea. The decrease in 2017 resulted from a marked reduction in seizures reported by Azerbaijan and Georgia, which was not offset by the increase in seizures reported by Armenia, Ukraine, Romania and the Republic of Moldova.

The "Caucasus route" has also been used to supply heroin to markets in the Russian Federation, although to a lesser extent than the northern route (via Central Asia).[125]

Heroin continues to be trafficked along a complex array of routes running south from Afghanistan

The southern route encompasses an array of different routes along which opiates are smuggled from Afghanistan via Pakistan or the Islamic Republic of Iran for onward trafficking to the Near and Middle East, Africa and Europe, to India for onward trafficking to neighbouring countries (Sri Lanka and Bangladesh) and to North America (notably Canada), as well as to South-East Asia and Oceania. Countries along the southern route accounted for, on average, 4 per cent of global heroin and morphine seizures (excluding seizures made in Afghanistan) over the period 2013–2017, including in 2017.

Trafficking of heroin along the southern route has been referred to in 9 per cent of mentions of countries of origin, departure or transit by countries in Western and Central Europe. The latest data reported suggest that in 2017 trafficking via the southern route played a key role for only one European country, Belgium, which reported a fifth of its "heroin imports" smuggled via Uganda and another fifth via Ethiopia. Italy reported limited trafficking of heroin via Qatar, Oman and South Africa, while Spain and Portugal reported some trafficking via Mozambique.

Some of the heroin trafficked along the southern route is also destined for domestic consumption in various countries located along the route, in particular Pakistan, as well as countries on the Arabian Peninsula and in East and Southern Africa.

While there is some domestic production of opiates in India for the illicit market, India reported that 53 per cent of all the heroin seized on its territory in 2017 came from Pakistan and just 0.4 per cent originated in Myanmar. India also reported an almost sixfold increase in the quantity of heroin seized that originated in South-West Asia, which was linked to an increase in maritime trafficking. The bulk of the heroin smuggled into India in 2017 arrived by boat (88 per cent) with smaller amounts smuggled across land borders (12 per cent), often by heroin parcels being thrown over border fences along the border between Pakistan and India or being hidden in farming equipment transported to India on trucks. Heroin of South-West Asian origin seized in India was reported to be of higher purity (54 per cent on average) than other heroin seized in the country in 2017.

Countries in South-West Asia and South Asia (Pakistan, followed by Afghanistan, India and the Islamic Republic of Iran) were also the most frequently mentioned countries of origin, departure and transit of heroin shipped to Africa (as mentioned by African countries). The above-mentioned Asian countries accounted for 91 per cent of all such mentions of Asian countries over the period 2013–2017, with the remaining 9 per cent accounted for by countries in South-East Asia (Thailand, the Lao People's Democratic Republic and Myanmar). Transit via the United Republic of Tanzania, followed by Nigeria and Kenya, was the most frequently mentioned transit route through Africa over the period 2013–2017 at the global level, though African countries also mentioned trans-shipment through Uganda, Ethiopia, Madagascar and South Africa.

While heroin is often smuggled to East Africa by sea (80 per cent of the total reported by Kenya in

125 UNODC and Afghan Opiate Trade Project, "Short update: the Caucasus route" (Vienna, 2019) (forthcoming).

Recent heroin seizures in Africa

Overall, seizures suggest that the trafficking of heroin via Africa appears to have increased between 2013, when less than 0.5 tons of heroin was seized, and 2017, when almost 1.5 tons were seized, with 2018 seizures suggesting that it may have increased further since then. The Egyptian authorities seized 1,350 kg of heroin in the exclusive economic zone of the Red Sea in April 2018 and 2,147 kg (including 99 kg of crystal methamphetamine) in April 2019.[a] In May 2018, the Combined Maritime Forces seized 260 kg of heroin on a dhow in the exclusive economic zone of the United Republic of Tanzania; overall, 1.63 tons of heroin were seized over the period July 2017–June 2018 by the Combined Maritime Task Force in various operations in the Indian Ocean when searching ships bound for, or planning to transit, the United Republic of Tanzania.[b] Moreover, in October 2018, the National Coast Guard of Mauritius seized 125 kg of heroin in Coin de Mire, Mauritius. A number of smaller heroin seizures were also reported by Kenya in 2018, most notably on the coast near Mombasa, and by the Seychelles, Madagascar, Zambia and Mozambique.[c] The authorities of Mozambique reported frequent trafficking of heroin from Pakistan to Kenya and from there to Mozambique, most notably Maputo, for onward trafficking to Johannesburg in South Africa.[d] A number of reports suggest that heroin trafficking activities to Mozambique for onward trafficking to South Africa may have gained in importance in recent years.[e]

[a] UNODC and Paris Pact, Drugs Monitoring Platform.

[b] Twenty-eighth Meeting of Heads of National Drug Law Enforcement Agencies, Africa, "Country report: United Republic of Tanzania", UNODC/HONLA 28 CRP.16, Dar es Salaam, (17-21 September 2018).

[c] UNODC and Paris Pact, Drugs Monitoring Platform.

[d] Twenty-eighth Meeting of Heads of National Drug Law Enforcement Agencies, Africa. "Country report: Mozambique: Situation of Illicit Drug Trafficking in Mozambique", UNODC/HONLA 28 CRP.7, Dar es Salaam, (17-21 September 2018).

[e] Joseph Hanlon, "The Uberization of Mozambique's heroin trade", *London School of Economics* (Working Paper Series 2018, No. 18-190, July 2018); Nampula, Africa is heroin's new highway to the West, The Economist, (31 January 2019).

2014 and 50 per cent by Madagascar in 2016), heroin trafficking to countries in Southern and West Africa seems to be more common by air (75 per cent of the total in South Africa in 2017, 99 per cent of the total in Nigeria in 2017 and 100 per cent of the total in Ghana in 2016). Similarly, most outbound heroin trafficking by countries in Southern and West Africa seems to be by air.

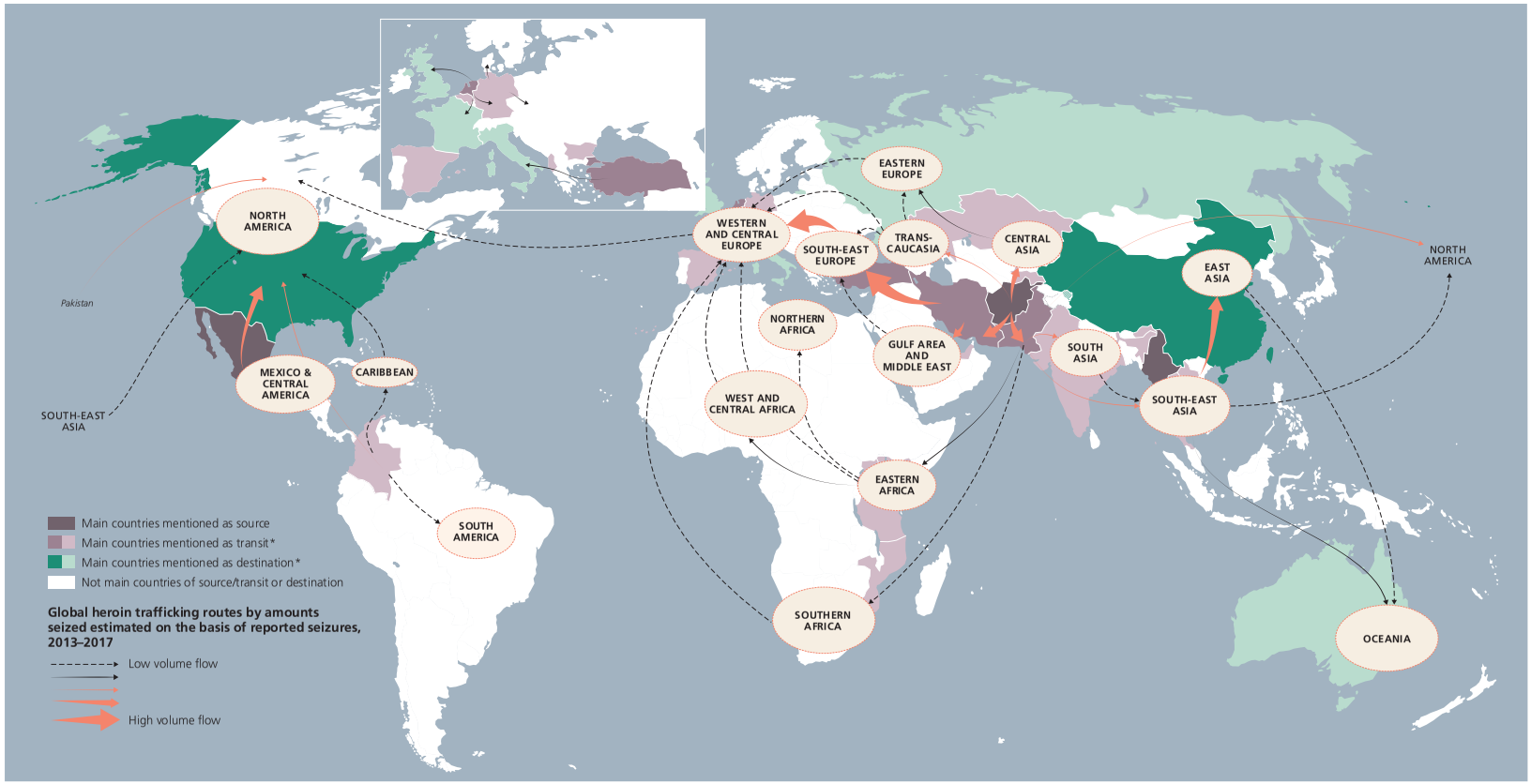
The main heroin trans-shipment countries on the Arabian Peninsula, both globally and for countries in Africa, were the United Arab Emirates and Qatar over the period 2013–2017.

Relative importance of the northern route continues to decline

The northern route continues to be used to smuggle heroin from Afghanistan via Central Asia to markets in that subregion as well as to the Russian Federation, the main destination market. There are also reports of heroin trafficking, although to a very small extent, to countries neighbouring the Russian Federation such as Belarus, Lithuania, Latvia and Ukraine, as well as of small amounts of heroin smuggled into the Russian Federation, in particular the Kaliningrad Oblast (an exclave between Poland and Lithuania), via countries in the European Union.

The trafficking of heroin to the Russian Federation is carried out predominantly via the northern route. Its importance seems to have been declining, however: 10 per cent of global quantities of heroin and morphine were seized along the route in 2008, whereas the proportion decreased to 1 per cent in 2017; it is noteworthy that over the past decade there has also been a decline in the number of registered opiate users in Central Asia and the Russian Federation. In 2015, the Russian Federation estimated that 80 per cent of the heroin seized in the country had originated in Afghanistan and had been trafficked via Central Asia into the Russian Federation, while 20 per cent had departed from Pakistan and was probably trafficked via the Islamic Republic

MAP 7 Main heroin trafficking routes as described by reported seizures, 2013–2017



Sources: UNODC, responses to the annual report questionnaire and individual drug seizure database.

**A darker shade indicates a larger amount of heroin being seized with the country as transit/destination.*

The size of the route is based on the total amount seized on that route, according to the information on trafficking routes provided by Member States in the annual report questionnaire, individual drug seizures and other official documents, over the period 2013–2017. The routes are determined on the basis of reported country of departure/transit and destination in these sources. As such, they need to be considered as broadly indicative of existing trafficking routes while several secondary routes may not be reflected. Route arrows represent the direction of trafficking: origins of the arrows indicate either the area of departure or the one of last provenance, end points of arrows indicate either the area of consumption or the one of next destination of trafficking. Therefore, the trafficking origin does not reflect the country in which the substance was produced.

The main countries mentioned as transit or destination were identified on the basis of both the number of times they were identified by other Member States as departure/transit or destination of seizures, and the annual average amount that these seizures represent during the period 2013–2017. For more details on the criteria used, please see the Methodology section of this document.

The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.The dotted line represents approximately the Line of Control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties.

of Iran and Azerbaijan into the Russian Federation. In subsequent years, however, Pakistan was no longer reported to be a major country of departure for heroin shipments intercepted in the Russian Federation. The main transit countries for heroin found in the Russian Federation in 2016 were in Central Asia (notably Tajikistan and Kazakhstan) and the Caucasus (notably Azerbaijan), with reports in 2017 suggesting that, in the context of ongoing decreases in heroin shipments to the Russian Federation, there may have been an overall decrease in trafficking along the northern route and a concentration via Central Asia, notably via Kazakhstan (50 per cent of all identified shipments in transit) and Uzbekistan (30 per cent).

Decline in heroin trafficking linked to a decline in opium production in East and South-East Asia, but the subregion remains the main source of opiates for Oceania

On the basis of seized amounts, the largest non-Afghan-related opiate trafficking activities are of opiates produced in South-East Asia (mostly Myanmar), which are trafficked to other markets in East and South-East Asia (mostly China and Thailand) and to Oceania (mostly Australia). Seizures made in those countries accounted for 11 per cent of the total global quantities of heroin and morphine seized (excluding seizures reported by Afghanistan) in 2017. This represents a decrease from 2015 when the share was 15 per cent. The decrease went in parallel with a reported decline in opium production in Myanmar of 37 per cent over the period 2013–2017.[126]

Despite the recent decline in opium production in Myanmar, the Australian authorities, based on a detailed analysis of bulk weight border seizures, reported that the proportion of heroin of South-East Asian origin seized increased from a low of 26 per cent in 2008 to more than 99 per cent over the period January–June 2017.[127] Nonetheless, in line with the reported decline in opium production in Myanmar, heroin seizures made at the Australian border turned out to be smaller in 2016–2017 than in 2014–2015, both in terms of quantity and number of seizure cases.[128] The main embarkation points for heroin seized at the Australian border in 2016–2017 were, by weight, Malaysia, followed by the Lao People's Democratic Republic, Thailand, Cambodia and Viet Nam, i.e., all countries located in South-East Asia.[129]

Most of the heroin trafficked in the Americas continues to originate in the region

Based on quantities seized, heroin trafficking within the Americas, towards the United States in particular, has shown a clear upward trend over the past decade. Most of this trafficking takes place within North America, i.e., from Mexico to the United States and, to a far lesser extent, from Colombia and Guatemala (typically via Mexico) to the United States.

Analysis of wholesale seizures of heroin in the United States has shown the increasing predominance of heroin originating in Mexico over the past decade, which accounted for over 80 per cent of the heroin samples analysed in 2016. This does not include the 14 per cent that was classified as "inconclusive South American", i.e., consisting of white powder heroin processed using the "South American method", with no means of linking the samples to heroin originating either in Colombia or Mexico. In parallel, the proportion of heroin originating in South America (mostly Colombia), which appears to have been predominant until 2010, has since been decreasing (4 per cent in 2016). Data on retail trafficking in metropolitan areas confirm the shift to the predominance of heroin from Mexico, not only in the western areas of the country but also in the eastern areas, which until 2014 appear to have been dominated by heroin originating in South America.[130] In the United States market, the presence of heroin from Asia has become minimal: heroin from South-West Asia was identified in less than 1 per cent of samples in 2016, while heroin from South-East Asia,

126 This is based on changes in opium production reported from Shan and Kachin States (UNODC and Central Committee for Drug Abuse Control, *Myanmar Opium Survey 2017* (December 2017, p. iv).

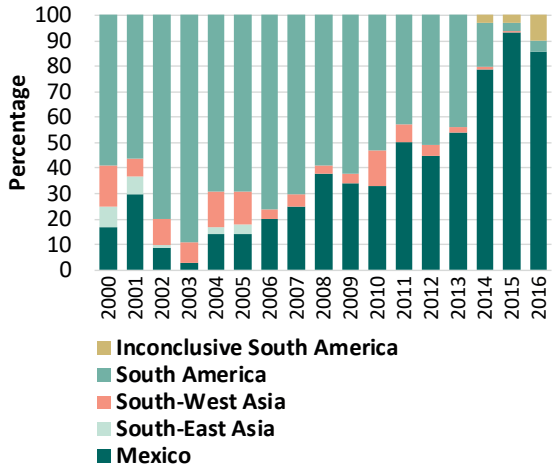
127 Australian Criminal Intelligence Commission, *Illicit Drug Data Report* 2016-17 (Canberra, 2018).

128 Ibid.

129 Ibid.

130 *2018 National Drug Threat Assessment*.

FIG. 24 Origin of heroin seized at the wholesale level in the United States, 2000–2016



Source: United States, DEA, *2018 National Drug Threat Assessment 2018.*

the main source of heroin over the period 1988–1994,[131] is likely to have disappeared from the United States market. The last shipment of heroin in the United States found to have originated in South-East Asia was in 2005, with no sample of heroin originating in that subregion having been identified since then in wholesale-level seizures.[132]

By contrast, heroin found in Canada is mostly of Afghan origin, with transit through Pakistan and India, and also through the Islamic Republic of Iran and the United Arab Emirates. In addition, transit through Africa (South Africa and United Republic of Tanzania) and Europe (Belgium, Netherlands and Germany) were reported over the period 2013–2017.

In South America, Central America and the Caribbean, heroin markets continue to be supplied mainly with heroin from Colombia, with transits through a number of countries within those subregions (2013–2017). However, a number of indicators suggest that those heroin markets remain relatively small.

131 United States, DEA, *2014 National Drug Threat Assessment* (November 2014).

132 *2018 National Drug Threat Assessment.*

Supply of pharmaceutical opioids

Licit and illicit manufacture of pharmaceutical opioids

The supply of pharmaceutical opioids to illicit drug markets for non-medical use may occur in the form of diversion from licit sources and from illicit production. Diversion can take place in various ways: the purchase of pharmaceutical opioids – often in preparations (such as cough syrups containing codeine) – for non-medical purposes in drug stores and pharmacies, which are subsequently re-sold on the black market; theft from hospitals or pharmacy stocks; the diversion of shipments from the licit trade at the wholesale level or at the import/export level when crossing borders mainly by means of false declarations;individuals can also access the licit supply of pharmaceuticals to obtain substances through doctor shopping, that is, obtaining prescriptions from several different doctors.

The most widely manufactured licit opioids at the global level in 2017, in descending order, were the three main opium alkaloids directly derived from the poppy plant: morphine, codeine and thebaine.[133, 134]

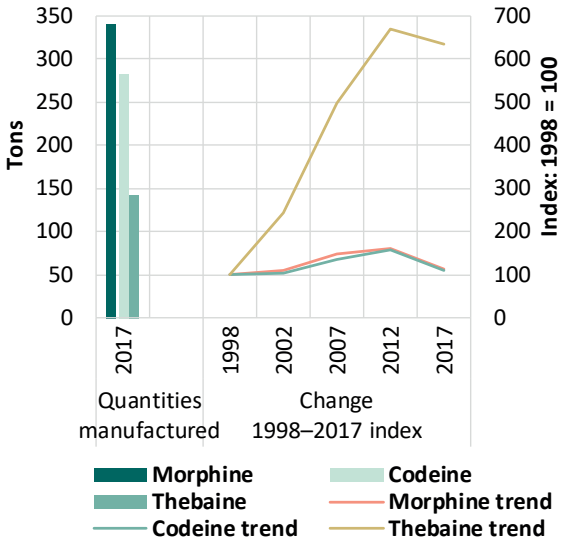
The global production of morphine and codeine has remained largely stable over the past two decades; however, production of thebaine has risen sixfold and increased demand for thebaine-rich poppy plant material has been reported. Although thebaine is not used for therapeutic purposes, it is required as a starting material in the manufacture of a number of semi-synthetic opioids, including oxycodone, oxymorphone and buprenorphine. In most years, the United States has been the main manufacturer of oxycodone, hydrocodone and of the other thebaine-related substances, except for buprenorphine.[135]

133 *Narcotic Drugs: Estimated World Requirements for 2019.*

134 Although all of these substances are directly extracted from opium or from poppy straw, codeine is also manufactured from morphine or thebaine, while thebaine is also partly manufactured from oripavine, another alkaloid of the poppy plant (see, INCB, *Narcotic Drugs: Estimated World Requirements for 2019*).

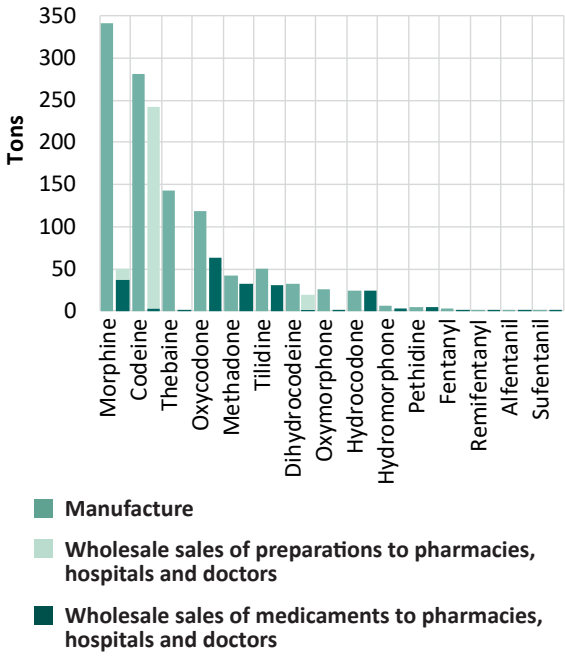
135 *Narcotic Drugs: Estimated World Requirements for 2019*, and previous years.

FIG. 25 Global quantities of the main opium alkaloids manufactured in 2017 and trends over the period 1998–2017



Source: *Narcotic Drugs: Estimated World Requirements for 2019—Statistics for 2017* (E/INCB/2018/2) and previous years.

FIG. 26 Licit manufacture of selected opioids and amounts available for consumption, 2017



Source: *Narcotic Drugs: Estimated World Requirements for 2019–Statistics for 2017* (E/INCB/2018/2).

Note: The large differences in the manufacture of morphine and the amounts of morphine available for consumption result from the fact that roughly 88 per cent of the morphine manufactured globally is converted into other narcotic drugs, mostly codeine, which is in turn used for the manufacture of various preparations, notably cough medication (89 per cent), or into substances not covered by the 1961 Convention. The remaining morphine is used directly for medical purposes, mainly for palliative care.

Given the role of the main natural opium alkaloids in the manufacture of various semi-synthetic opioids –including of hydrocodone, dihydrocodeine and desomorphine from codeine, while codeine and a large number of semi-synthetic opioids (including heroin) are also manufactured from morphine – wholesale quantities of those alkaloids sold to pharmacies, hospitals and medical doctors, i.e. opioids available for consumption, are far smaller than the actual quantities manufactured. It should also be noted that in a few cases, in particular of codeine and dihydrocodeine, amounts available for consumption have been dominated by the sale of preparations of these substances,[136] which are subject to less strict controls at the international level, and thus usually at the national level.

The licit manufacture of heroin takes place, mainly in Switzerland and the United Kingdom, to supply people enrolled in heroin-assisted treatment programmes in those countries as well as in a number of other countries, including Canada, Denmark, Germany and the Netherlands. During the period 2013–2017, the quantity manufactured globally per year amounted, on average, to less than 1 ton (929 kg in 2017),[137] which is only a minor fraction of the average total quantity of heroin estimated to have been illicitly manufactured (540 tons per year)[138] and seized (88 tons per year) over that period. This adds weight to the hypothesis that diversions from the licit market, if occurring, are a negligible contributor to the supply of heroin to illicit markets.

136 *Narcotic Drugs: Estimated World Requirements for 2019.*

137 Ibid.

138 UNODC estimate based on UNODC opium poppy cultivation surveys.

Likewise, most of the morphine found on illicit markets originates from illicitly produced opium, and only small quantities of morphine are likely to be diverted from licit manufacture to illicit markets. In fact, there is no evidence of large-scale diversion. Over the period 2013–2017, 4,417 cases of diversion of morphine (665,000 units, or 67 kg) were reported, while the overall number of reported seizure cases of "illicit morphine" was almost twice that figure (8,135 seizures of 221 tons). Moreover, while the majority of the licit manufacture of morphine takes place in France, followed by the United Kingdom and Australia,[139] nearly all of the morphine seized has been intercepted in South-West Asia, which is also the subregion where most of the opium destined for illegal markets is produced and where most clandestine morphine and heroin laboratories have been dismantled.

Compared with the 234 clandestine heroin laboratories (most of them in Afghanistan) reported by 14 countries over the period 2013–2017, only a few clandestine laboratories manufacturing other opioids were dismantled over the same period, including a few laboratories manufacturing morphine (India and Mexico), methadone (Belarus, Latvia and the Russian Federation), desomorphine (Russian Federation), codeine (Czechia) and monoacetylmorphine (Austria).

Data that can help explain whether other pharmaceutical opioids are diverted from the licit to the illicit market or are illicitly produced at source are limited, although this varies depending on the substance and region. In the case of fentanyl, for example, evidence suggests that the bulk of the substance found on the illicit market comes from illicit manufacture, although some small diversions of fentanyl have been reported in the United States. The clandestine manufacture of pharmaceutical opioids concerns fentanyl and its analogues. A number of laboratories have been found manufacturing fentanyl and analogues in recent years in Australia, Canada, the Dominican Republic, Germany, Mexico, the Russian Federation, Slovakia, Sweden and the United States. At the same time, most of the illicit supply, based on reports by Member States, appears to have originated in illicitly operating laboratories in China. However, as the United States is also the largest manufacturer country of licit fentanyl worldwide (2017 and previous years),[140] some diversion of fentanyl from domestic licit manufacture also seems to occur, mostly for personal use and street sales in the country.[141]

The large market for tramadol of non-medical use in North Africa and the Near and Middle East also seems to be supplied by tramadol specifically manufactured and trafficked for the illegal market, but information remains limited. The diversion of pharmaceutical opioids such as codeine and oxycodone from the licit to the illicit market is evident in North America. Outside that subregion diversions of pharmaceutical opioids are not reported in large quantities, but that could be the result of underreporting or the limited capacity of law enforcement authorities to detect diversions. There is a gap in knowledge about the supply chain of codeine that is reportedly being used non-medically across many subregions. The fact that the global quantities of codeine seized are far smaller than those licitly manufactured at the global level, coupled with a lack of evidence of the existence of illicit laboratories for codeine manufacture, suggests that the non-medical use of codeine is largely supplied by the legal market. It is unclear, however, how and at what stage the supply of codeine for medical use is diverted for non-medical use. There may be a combination of scenarios, with some codeine preparations being easy to access for non-medical use in pharmacies or other types of outlet and diversion taking place before the drug reaches the retail market, resulting in a large proportion of the licit supply been diverted to the illicit market.

Amounts of pharmaceutical opioids available for consumption

Amounts of opiates and synthetic opioids (expressed in daily doses) available for consumption globally more than doubled over the period 1998–2010, followed by a period of stabilization and a decline over the period 2014–2017. This sharp increase mainly reflected an increase in the United States, where the increase over the period 1998–2010 was a consequence of initial reports suggesting that there had been insufficient access to pain medication for

139 *Narcotic Drugs: Estimated World Requirements for 2019.*

140 Ibid.

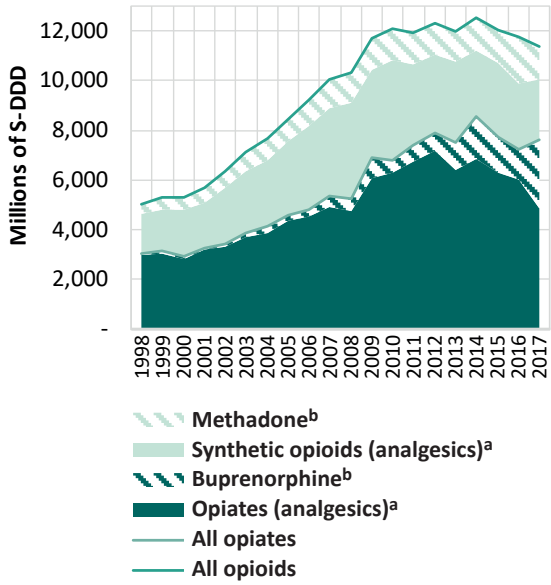
141 *2018 National Drug Threat Assessment.*

patients suffering from severe pain, and the view that few people would develop dependence on that type of medication if taken in a medical environment,[142, 143] together with the broadening of applications and an increase in the demand for some opioids, including fentanyl.[144]

Most of the increase in the amounts of pharmaceutical opioids available for consumption over the period 1998–2010 was not, however, of "traditional" opiates such as codeine and morphine; they increased in line with overall growth in opioid wholesale sales. The bulk of that increase was in the United States in wholesale sales of "new opiates"[145] marketed in the past as having less potential for addiction, substances used in substitution treatment and some synthetic opioids, notably fentanyl.[146] The strong increases in the amounts available for consumption included oxycodone (which experienced tenfold growth over the period), hydromorphone (fivefold growth), hydrocodone (threefold growth) and oxymorphone (46,000-fold growth). Substances used in substitution treatment for heroin-dependent people also saw strong increases in the amounts available for consumption. This applied to both methadone (threefold growth) and buprenorphine (11-fold growth). Amounts available for consumption of fentanyl rose ninefold over the period 1998–2010.[147]

While most of the increase in the availability of opioids for consumption over this period reflected increases in North America, some increases – starting from far lower levels – were also observed in most other regions, except Africa.[148]

FIG. 27 Global amounts available for consumption of pharmaceutical opioids for medical use under international control, number of daily doses, 1998–2017



Source: *Narcotic Drugs: Estimated World Requirements for 2019–Statistics for 2017* (E/INCB/2018/2)

Note: S-DDD refers to "defined daily doses for statistical purposes" as defined by INCB. S-DDDs are "technical units of measurement" for the purposes of statistical analysis and are not recommended daily prescription doses; actual doses may differ based on treatments required and medical practices. The statistics exclude preparations of opioids listed in Schedule III of the 1961 Convention. Details of S-DDDs used for these calculations will be provided in the methodological annex.

[a] *Substances used as analgesics, i.e. excluding substances used in substitution treatment;*

[b] *Substances used in substitution treatment and as analgesics.*

The initial strategy of marketing "new opiates" as having very low addiction potential, however, turned out to be harmful.[149, 150, 151] Reports of an increase in the non-medical use of pharmaceutical opioids as well as in related drug use disorders and health

142 Russell Portenoy and Kathleen Foley, "Chronic use of opioid analgesics in non-malignant pain: report of 38 cases", *Pain*, vol. 25, No. 2 (May 1986), pp. 171–186.

143 Gary M. Franklin, "Opioids for chronic, non-cancer pain", St. Luke's Rehab Institute and COHEs, 7 November 2007.

144 *Narcotics Drugs: Estimated World Requirements for 2018*.

145 Most "new opiates" are not, in fact, really new. Their development mostly dates back to the first or second decade of the 20th century. However, several of these substances had their names and formulas changed successfully for marketing purposes (see, Arzneimittelkommission der deutschen Ärzteschaft: Oxycodon (Oxygesic®) – Missbrauch, Abhängigkeit und tödliche Folgen durch Injektion zerstoßener Retardtabletten, *Deutsches Ärzteblatt*, vol. 100, No. 36 (2003); Patrick Radden Keefe, "The family that built an empire of pain", *The New Yorker* (New York, 23 October 2017).

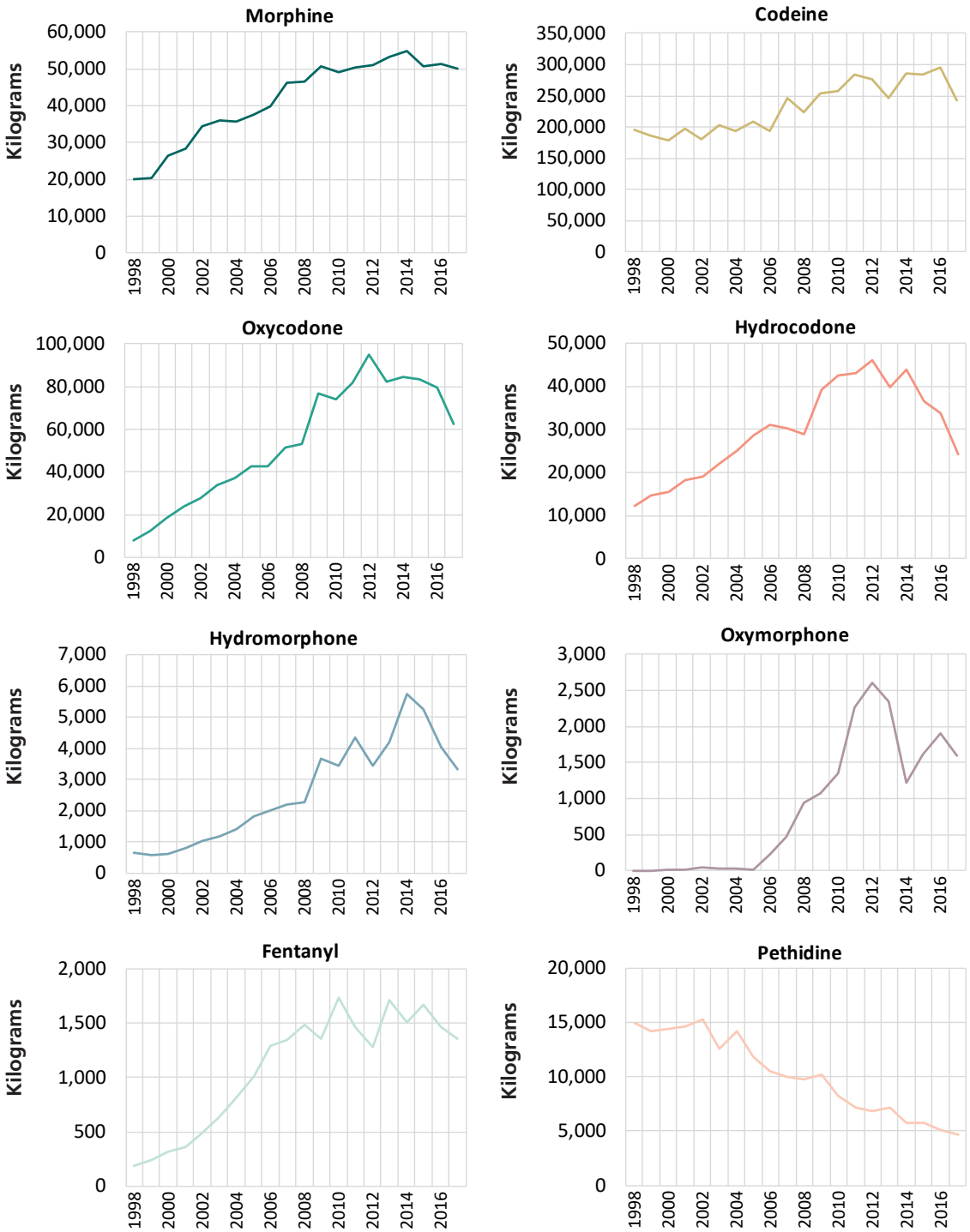
146 Gary M. Franklin, "Opioids for chronic, non-cancer pain", St. Luke's Rehab Institute and COHEs, 7 November, 2007.

147 *Narcotic Drugs: Estimated World Requirements for 2019* and previous years.

148 *Progress in Ensuring Adequate Access to Internationally Controlled Substances for Medical and Scientific Purposes* (E/INCB/2018/1/Supp.1).

149 National Academies of Sciences, Engineering, and Medicine, *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use* (Washington, D. C., The National Academies Press, 2017).

FIG. 28 Global amounts available for consumption of selected opioids (including preparations) for medical use, 1998–2017 (kilograms)



Source: INCB, *Narcotic Drugs: Estimated World Requirements for 2019–Statistics for 2017* (E/INCB/2018/2) and previous years.
Note: all these substances are controlled under the 1961 Convention.

consequences prompted authorities in North America to gradually strengthen the overall control system and warn medical doctors of the dependence potential of these substances and against overprescribing in order to avoid diversion.

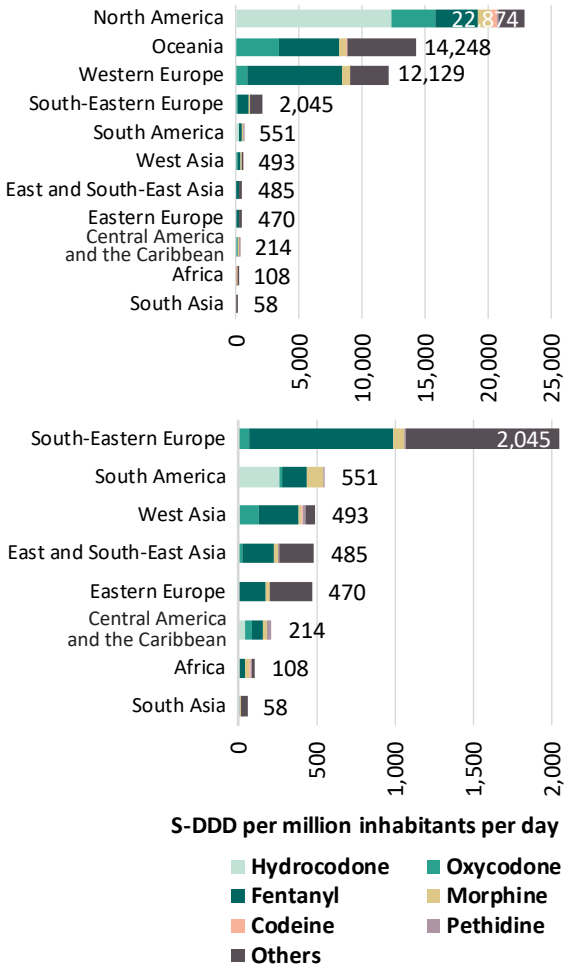
This in turn led to a period of stabilization, at a high level, of the licit manufacture and availability for consumption of internationally controlled pharmaceutical opioids over the period 2010–2014, followed by a period of moderate decline (around 10 per cent) at the global level over the period 2014–2017, as opioid-related harm continued to worsen and controls were further tightened in North America. The recent decline at the global level was mostly prompted by reductions in amounts of opioids available for consumption reported in North America, although declines in 2017 from the previous year were also reported from South America, East and South-East Asia, West and Central Europe and Africa.[152]

Since 2014, the decline in the amounts of opiates available for consumption has been particularly pronounced in the case of opiates, such as oxycodone, hydrocodone and hydromorphone, which had found their way on to the illicit markets, particularly in North America. Despite this decline, North America continued to account in 2017 for a major share of global amounts available for consumption of hydromorphone (72 per cent), oxycodone (73 per cent) and hydromorphone (99 per cent).[153]

Some of the other synthetic opioids, such as pethidine, continued declining (69 per cent over the period 1998–2017) and amounts available for consumption of dextropropoxyphene, which was very popular in the 1990s, fell by more than 99 per cent over the past two decades following requests by the United States authorities not to prescribe it any longer,[154] while in other countries the substance was banned owing to concerns over serious side effects.[155]

By contrast, amounts of buprenorphine available for consumption, which, like methadone, is used to treat drug-dependent people, continued to increase, by 65 per cent over the period 2014–2017. This

FIG. 29 Amounts available for consumption of codeine, fentanyl, morphine, pethidine and other opioids, by region, expressed in standard defined daily doses per million inhabitants, 2017



Source: *Narcotics Drugs: Estimated World Requirement for 2019–Statistics for 2017* (E/INCB/2018/2), p. 49.

150 Wilson M. Compton and others, "Relationship between nonmedical prescription opioid use and heroin use", *The New England Journal of Medicine*, vol. 374 (2016), pp 154–163.

151 Brigid Huey, "Mother's postpartum oxycodone use: no safer for breastfed infants than codeine", *Journal of Pediatrics* (Elsevier, 6 September 2011).

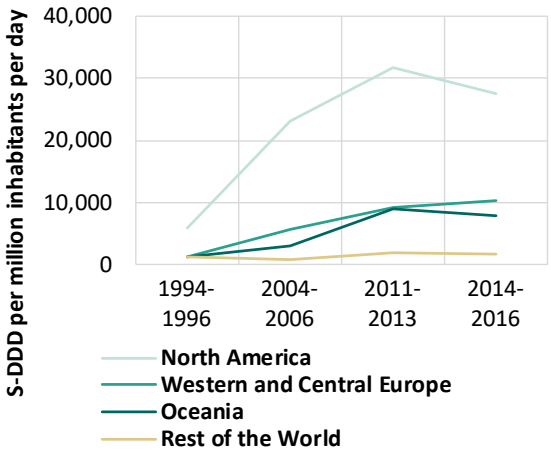
152 INCB database on the amounts available for consumption of opioids, expressed in S-DDD per million inhabitants per day, to hospitals, pharmacies and medical doctors.

153 Ibid.

154 United States, Food and Drug Administration, Drug Safety and Availability, "FDA drug safety communication: FDA recommends against the continued use of propoxyphene", 19 November 2010.

155 INCB, *Narcotics Report 2018*, (New York, 2019).

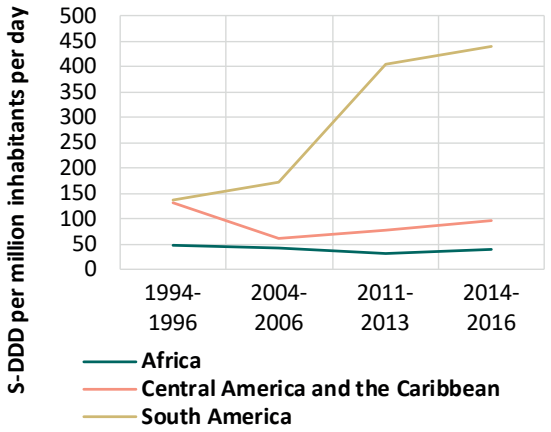
FIG. 30 Trends in availability of opioid analgesics for consumption, by region, 1994–2016



Source: Progress in Ensuring Adequate Access to Internationally Controlled Substances for Medical and Scientific Purposes (E/INCB/2018/1/Supp.1).

Note: S-DDD per million inhabitants per day, by total regional population.

FIG. 31 Trends in availability of opioid analgesics for consumption, selected subregions, 1994–2016



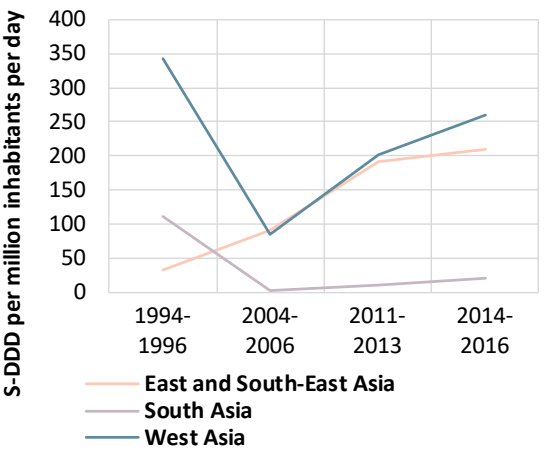
Source: Progress in Ensuring Adequate Access to Internationally Controlled Substances for Medical and Scientific Purposes (E/INCB/2018/1/Supp.1).

Note: S-DDD per million inhabitants per day, by total regional population.

resulted in a substantial increase in amounts of buprenorphine and methadone available for consumption, which, taken together, increased by 34 per cent over that period. However, as with other pharmaceutical opioids, there are large differences in the global consumption patterns of buprenorphine and methadone for medical purposes, as seen in the coverage of opioid-agonist treatment for people with opioid use disorders.[156]

In more general terms, although they have declined in recent years, amounts of pharmaceutical opioids available for consumption remain at a very high level – expressed in standard defined daily doses (S-DDD) per million inhabitants – in North America, followed by Oceania and Europe. By contrast, the level continues to be extremely low in most developing countries, notably in South Asia and in Africa.[157] While the comparatively high level of sales and the availability of pharmaceutical opioids in North America may point to over-prescription practices in the subregion, data indicate that a number of countries in the developing world continue to face a severe lack of access to pharmaceutical opioids as pain medication, despite an increase in their availability in subregions such as South America, East and South-East Asia and South-West Asia. Subregions of Africa and Central America and the

FIG. 32 Trends in availability of opioid analgesics for consumption, Asia, 1994–2016

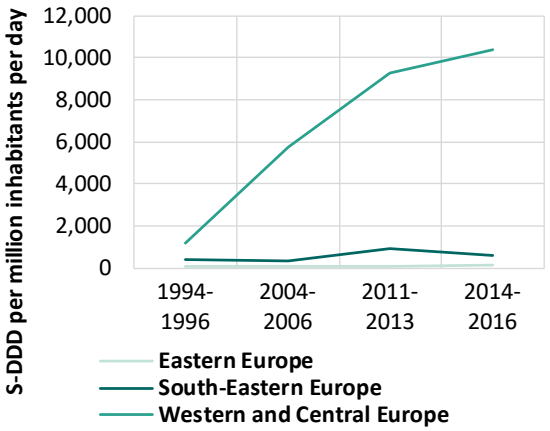


Source: INCB, *Progress in Ensuring Adequate Access to Internationally Controlled Substances for Medical and Scientific Purposes* (E/INCB/2018/1/Supp.1).

156 See, for example, *World Drug Report 2018*.

157 *Narcotics Drugs: Estimated World Requirements for 2019*.

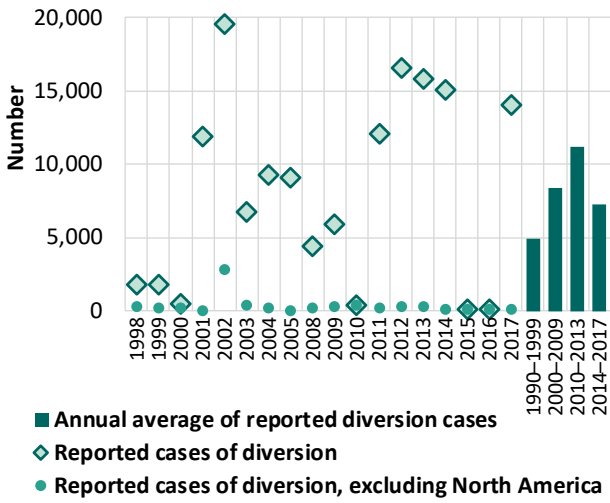
FIG. 33 Trends in availability of opioid analgesics for consumption, Europe, 1994–2016



Source: Progress in Ensuring Adequate Access to Internationally Controlled Substances for Medical and Scientific Purposes (E/INCB/2018/1/Supp.1).

Note: S-DDD per million inhabitants per day, by total regional population.

FIG. 34 Reported cases of diversion of pharmaceutical opioids, 1990–2017



Source: UNODC, responses to the annual report questionnaire.

Caribbean, starting from low levels, even faced a decline in availability.[158, 159]

Diversion of pharmaceutical opioids from licit sources

Over the period 1998–2017, 71 countries reported cases of diversion of pharmaceutical opioids from licit sources, including 44 countries reporting cases within their national borders. This includes thefts from manufacturing laboratories and wholesalers, sales of prescriptions to unauthorized persons, thefts from hospitals and doctor's surgeries, and diversion from international trade. The diversion of pharmaceutical opioids from licit sources was reported in all five regions, but the majority of cases (90 per cent) over the past two decades were reported by countries in North America, a subregion where availability for consumption of pharmaceutical opioids is at the highest per-capita level.[160] The number of reported diversions of pharmaceutical opioids fluctuated greatly over the period, mostly because of reporting practices, in particular in North America, rather than year-on-year changes in the number of diversions.

A total of 63 different pharmaceutical opioids have been reported in diversions since 1998. In terms of the number of cases in which each substance is involved, which mainly reflects diversions reported by countries in North America over the past two decades, oxycodone tops the list, followed by hydrocodone, morphine, hydromorphone and codeine. In 2017, however, reflecting a number of indicators that suggest growth in the illegal market for fentanyl in North America, most reported diversions were of fentanyl, followed by morphine and tramadol.

For most substances, reported seizures are far more important than reported diversions, both in terms of cases and even more so in terms of quantities seized.

Seizures of pharmaceutical opioids

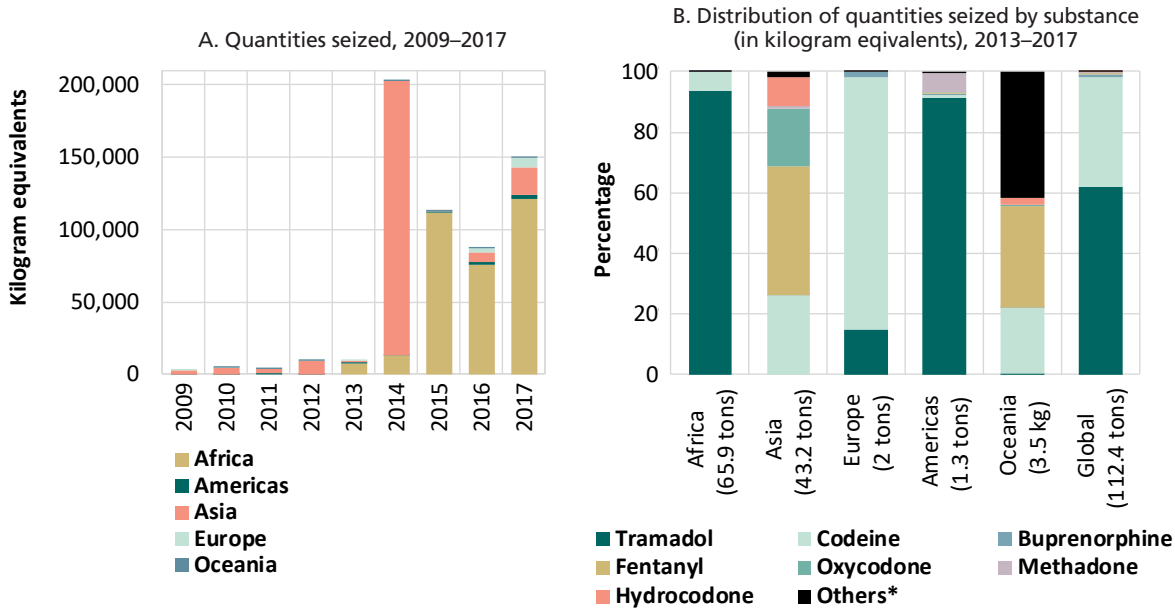
Seizure data show the distinct problems that each region faces in relation to the non-medical use of opioids: the illicit market for non-medical use of opioids is dominated by tramadol in Africa, codeine in Asia and fentanyl in North America. Those regions also experience different challenges in

158 Regions as defined by INCB.

159 *Progress in Ensuring Adequate Access to Internationally Controlled Substances for Medical and Scientific Purposes* (E/INCB/2018/1/Supp.1).

160 *Narcotic Drugs: Estimated World Requirements for 2019.*

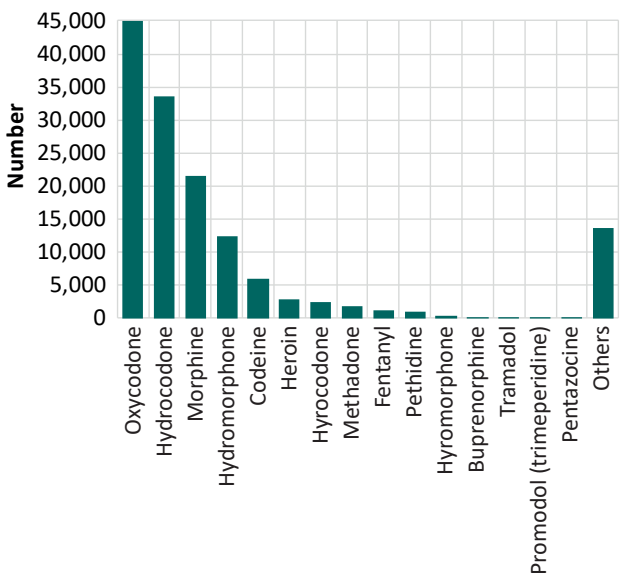
FIG. 35 Global quantities of pharmaceutical opioids seized



Source: UNODC, responses to the annual report questionnaire.

**Others include diphenoxylate, thebaine, hydromorphone, morphine, phenazocine, novahistex, pentazocine, carfentanil, alpha-methylacetylfentanyl, ocfentanil, furanylfentanyl, pethidine, Percocet® methyldihydromorphine, tapentadol, trimeperidine, Oxycocet®, Apo-oxycodone®, dihydrocodeine, M-Eslon®, Oxyneo® and U-47700.*

FIG. 36 Main pharmaceutical opioids reported to have been diverted, number of cases, 1998–2017

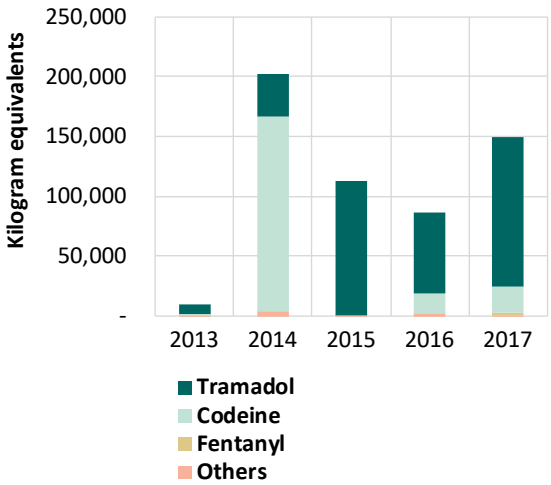


Source: UNODC, responses to the annual report questionnaire.

relation to the availability of opioids for medical use, with North America having the highest availability of opioids for medical purposes and Africa and Asia the lowest.

Until 2009, only small quantities of pharmaceutical opioids were seized each year at the global level (an average of 116 kg per year over the period 1998–2008). Those quantities increased, however, to an annual average of 6.3 tons over the period 2009–2013. In 2014, the amount seized reached a record high of 203 tons; since then, despite fluctuations, the amount seized has remained at a high level, exceeding global seizures of heroin every year, except in 2016. In 2017, 150 tons of pharmaceutical opioids were intercepted worldwide, more than 1,000 times the quantity of opioids reported in diversion cases, which accounted for 47 kg, 72 litres and 61,000 units of different opioids. In 2017, the increase, compared with that in 2016, was particularly marked in the case of fentanyl (sixfold increase) and methadone (fivefold increase). By contrast, global quantities of oxycodone and hydrocodone seized in 2017 decreased by 92 per cent and 47 per

FIG. 37 Global quantities of pharmaceutical opioids seized, 2013–2017



Source: UNODC, responses to the annual report questionnaire.

Note: others include methadone, hydrocodone, oxycodone, dextropropoxyphene, diphenoxylate, hydromorphone, buprenorphine, thebaine, hydromorphone, morphine, phenazocine, novahistex, pentazocine, penazocine, carfentanil, -alpha-methylacetylfentanyl, cfentanil, furanylfentanyl, pethidine, Percocet®,methyldihydromorphine, tapentadol, trimeperidine, Oxycocet®, Apo-oxycodone®, dihydrocodeine M-Eslon®, Oxyneo® and U-47700.

cent, respectively, from the previous year. That might have been linked to a number of factors that mainly affected the United States market, including a decline in the licit manufacture and the amounts of those substances available for consumption,[161, 162] and reduced demand (see page 16 of the present booklet) – for example, the implementation of prescription drug monitoring programmes, which track the prescription and dispensation of controlled prescription drugs to patients[163] – which resulted in fewer opportunities for trafficking and, consequently, for diversion and seizures.

In recent years, 59 per cent of the total quantity of pharmaceutical opioids seized over the period 2013–2017 was intercepted in Africa, where it was mostly destined for local markets in the region, and 38 per cent was intercepted in Asia. In Africa, those seizures were mostly of tramadol in West and North Africa; in Asia they were of codeine, mainly in East and South-East Asia, South Asia and the Caucasus.

Accounting for 62 and 36 per cent, respectively, of the total quantity seized, tramadol and codeine dominated global seizures of pharmaceutical opioids over the period 2013–2017. Expressed in S-DDD, as defined by INCB,[164] seizures of pharmaceutical opioids were, however, dominated by fentanyl and its analogues in both 2016 and 2017 (over 80 per cent in 2017), followed by tramadol (11 per cent). This reflects the fact that fentanyl is about 100 times more potent than morphine.[165] Such comparisons may be misleading, however, as the purity of the various substances may differ. While some of the products diverted from licit channels may be completely pure, like any licit pharmaceutical drug, fentanyl(s) seized in the United States were found to have been heavily adulterated (average purity of 5.1 per cent in 2017).[166]

Trafficking in tramadol continues to grow in importance

Tramadol is not under international control, even though it is under national control in many countries in Africa, the Middle East, Europe and North America. It has been considered for critical review by the Expert Committee on Drug Dependence six times over the past three decades: in 1992, 2000, 2002, 2006, 2014 and 2018.[167]

Tramadol is widely used in medicine and was originally manufactured in Germany in 1977 then, some 20 years later, in other industrialized countries, including Australia, the United Kingdom and the United States.[168] It is not clear if, and to what extent, tramadol found in the illicit markets has been diverted from licit channels or to what extent is has been illicitly manufactured. Some high dosage packaging found on illicit markets in Africa[169] suggest that there is specialized manufacturing to supply the illegal market, but more extensive research is required to improve understanding of

161 *Narcotic Drugs: Estimated World Requirements for 2019.*

162 INCB database on the amounts available for consumption of opioids.

163 *2018 National Drug Threat Assessment.*

164 *Narcotic Drugs: Estimated World Requirements for 2019.*

165 Ibid.

166 *2018 National Drug Threat Assessment.*

167 WHO, "Annex 1: extract from the report of the forty-first meeting of the Expert Committee on Drug Dependence".

168 *World Drug Report 2018.*

169 Ibid.

Tramadol trafficking to and within West Africa: early findings from an ongoing study

Based on data from investigations and interviews with both officials and key informants in West Africa, it seems that most tramadol available for the non-medical market in West Africa has been imported from India, by boat or plane. A number of different methods of concealment have been used, including: false declarations claiming legitimate transport of items and falsification of legal documentation such as import licences; fraudulent packaging (for example, illicitly manufactured tramadol tablets have been discovered in boxes bearing the United Nations symbol); concealment of illicitly sourced tramadol among legally imported pharmaceutical drugs, medical equipment and other goods. Criminal networks also exploit some West African countries' structural vulnerabilities, such as limited knowledge of pharmaceutical drugs among law enforcement agencies and corruption.

Criminal groups from West Africa that are based in Asia and Asian criminal groups play a role in the trafficking of tramadol to West Africa. West African importers usually develop their supply chain by making contact with an exporter or an intermediary located in Asia, or directly with a manufacturer or a pharmaceutical trading company.[a] Importers often rely on their local contacts in the country of production for picking, buying and delivering the drugs. Importers of illicitly sourced tramadol may work in tandem with importers of licitly supplied pharmaceutical products who provide their expertise, blurring the frontier between the legal and the illegal markets. There is no evidence of clandestine laboratories manufacturing tramadol in West Africa, but a number of interviewees shared their concern about the likelihood of tramadol manufacture emerging in the subregion.

The smuggling of tramadol across West Africa appears to involve a range of actors. On the one hand, "big men" with the capacity to buy significant quantities of the drug control overall aspects of trafficking on a certain route; on the other hand, there are individuals who buy small quantities from retailers in, for example, street markets, organize transport from one country to another by taxi, motorcycle or bus, and resell the merchandise to users or to small-scale dealers.

Source: UNODC, Tramadol Trafficking in West Africa (provisional title), forthcoming.

[a] See for example: UNODC Transnational organized crime in West Africa: A Threat Assessment, Vienna, 2013; TOCTA, 2013; Gernot Klantschnig, "Négocier les profits et la facticité : Le commerce des produits pharmaceutiques entre la Chine et le Nigeria", Politique africaine, 2014/2 (N° 134), p. 89-110.

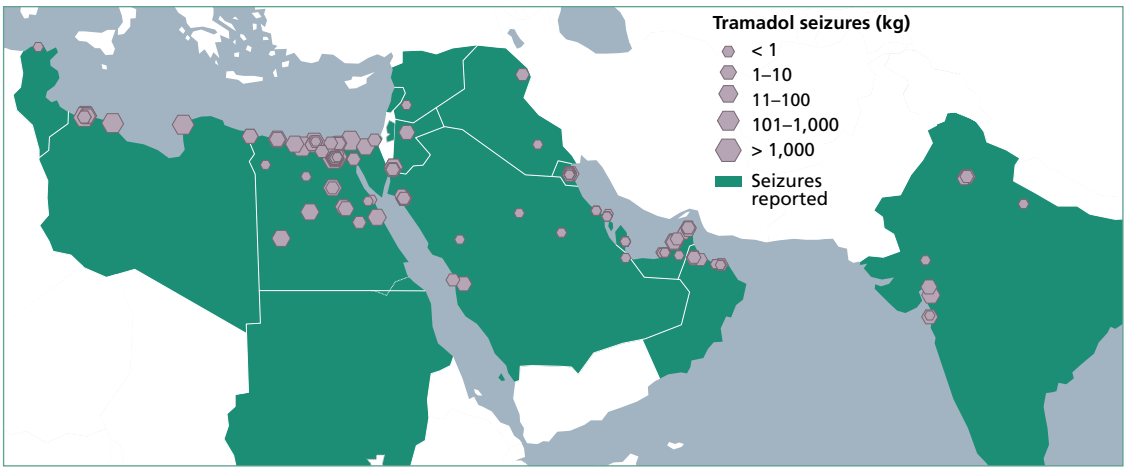
these dynamics. Most tramadol seized worldwide over the period 2013–2017 seems to have originated in India. In 2017, only India was reported to have been a country of origin of internationally trafficked tramadol.

Global seizures of tramadol increased from less than 10 kg in 2010 to almost 9 tons in 2013; they reached a record high of 125 tons in 2017. The largest quantities of tramadol seized over the period 2013–2017 were reported by Nigeria, followed by Benin, Egypt, Jordan, the United Arab Emirates and the Islamic Republic of Iran. In 2017, Nigeria intercepted the largest quantity worldwide (96 tons), followed by Egypt (12 tons in weight equivalents) and the United Arab Emirates (9 tons in weight equivalents).

Based on recent seizure data, the main destinations of illegal tramadol shipments are countries in West and Central Africa (including Benin, Cameroon, the Central African Republic, Chad, Côte d'Ivoire, Ghana, Guinea, the Niger, Senegal, Sierra Leone and the Sudan) and Northern Africa (mostly Egypt and, to a lesser extent, Libya), from which some tramadol is further smuggled to countries in the Near and Middle East (including Jordan and Lebanon). In addition, significant shipments in terms of quantity have been intercepted, originating in India and destined for countries in the Near and Middle East, such as the United Arab Emirates, both for use in the region and onward trafficking.

The fact that tramadol has been intercepted in areas close to where Islamic State and some of its

MAP 8 Significant seizures of tramadol in South Asia, North Africa and the Near and Middle East, January 2013–January 2019



Sources: Source: UNODC and Paris Pact, Drugs Monitoring Platform.

The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.

associated groups have been active (including in parts of Libya, Nigeria and the Syrian Arab Republic, as well as in the Sahel) has given rise to additional concerns that tramadol trafficking may be used by those groups to finance terrorist activities and that it may also be used non-medically by their fighters to suppress pain caused by injury, to increase endurance and their potential for violence while altering their senses.[170, 171, 172] Shipments to those groups have allegedly been sent from South Asia to countries in West Africa, North Africa and the Middle East, sometimes via Europe.

The largest tramadol seizures in Europe in recent years concerned tramadol shipments to final destinations in North Africa. Malta reported 36 million tramadol tablets seized in three seizure cases in 2016, all originating in India and destined for Libya, as well as a further 117 million tablets seized in four seizure cases in 2017. Another major seizure of tramadol tablets took place in Genoa, Italy, in May 2017. The seizure consisted of 37 million tablets, which had originated in India and been sold to an importer based in Dubai, United Arab Emirates. The importer sent the tablets to Sri Lanka before shipping them by sea to Italy en route to the cities of Misrata and Tobruk in Libya, possibly destined for Islamic State groups operating in that country.[173] Greece reported the seizure of 26 million tramadol tablets in two seizure cases in 2016; the tablets had originated in India, with Libya as the final destination.

Those seizures are modest in comparison with the quantities of tramadol intercepted by some countries in North Africa and the Middle East. For example, Egypt reported the seizure of 252 million tramadol tablets in 2016 and 236 million in 2017, while the United Arab Emirates seized 175 million in 2017. In addition, for the first time, Morocco reported the seizure of 40 million units of tramadol in 2017, which had been shipped into the country from India by sea in containers; they were destined for Guinea and other countries in West Africa.

Most of the tramadol seizures reported by Libya since 2013 have been made along the country's

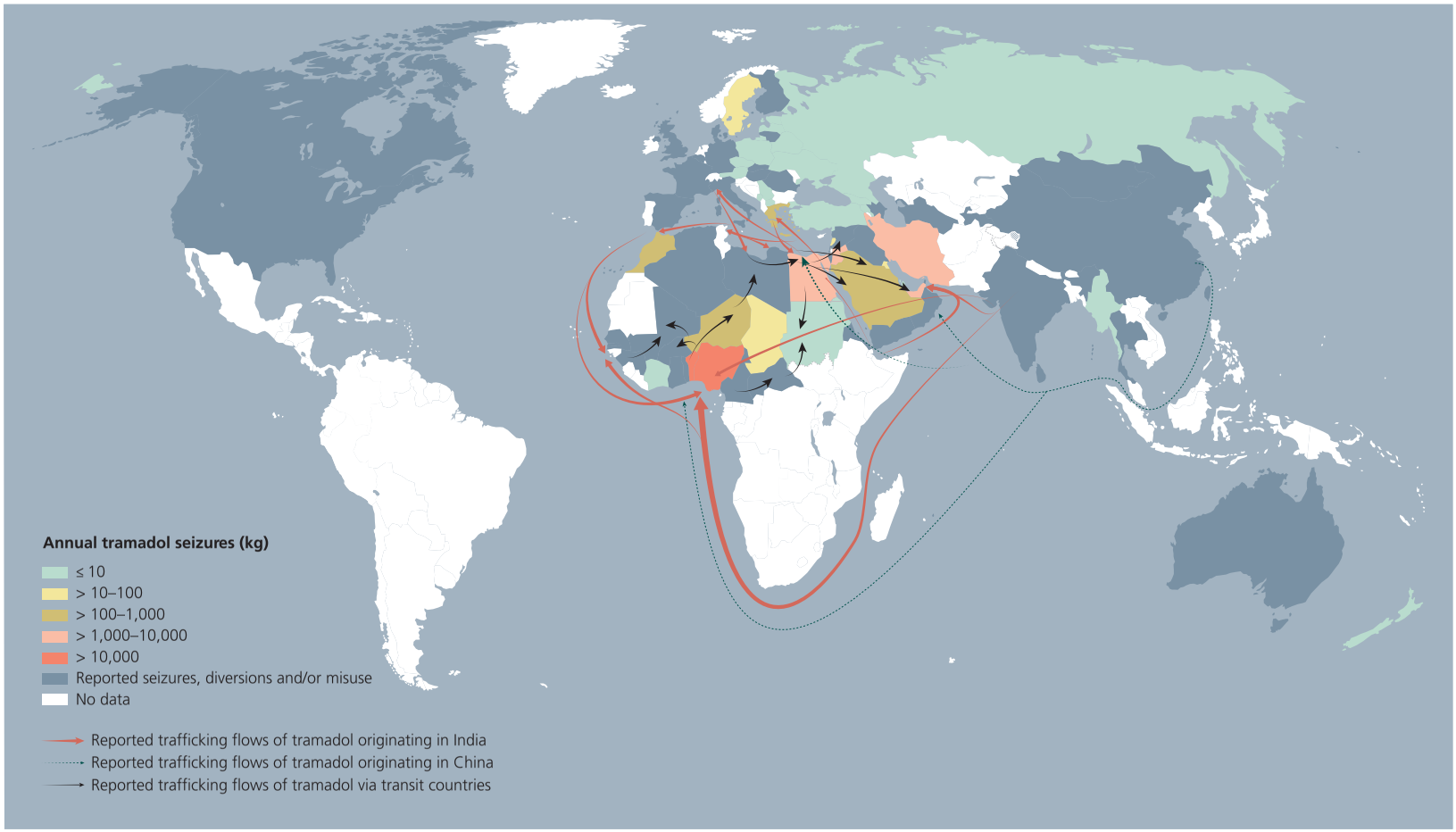
170 INCB, "Tramadol: review of the global situation".

171 Rita Santacroce and others, "The new drugs and the sea: the phenomenon of narco-terrorism", *International Journal of Drug Policy, January*, vol. 51 (January 2018), pp. 67–68.

172 Florence Gaub and Annelies Pauwels, *In-depth Analysis: Counter-Terrorism Cooperation with the Southern Neighbourhood* (Brussels, European Parliament, Directorate-General for External Policies, Policy Department, 2017).

173 Guardia di Finanza, reported in UNODC, Drugs Monitoring Platform; Santacroce and others, "The new drugs and the sea", pp. 67–68.

MAP 9 Reported seizures, diversion and trafficking routes of tramadol (based on reported seizures), 2013–2017



Sources: UNODC, annual report questionnaire data; International Narcotics Control Board, Report 2018 (and previous years); Heads of National Law Enforcement Agency report 2018 (and previous years); World Health Organization, Expert Committee on Drug Dependence, Thirty-sixth Meeting, Geneva, 16–20 June 2014; Bureau for International Narcotics and Law Enforcement Affairs, *International Narcotics Control Strategy Report 2019* (and previous years).

The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations. Dashed lines represent undetermined boundaries. The dotted line represents approximately the Line of Control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. The final boundary between the Republic of Sudan and the Republic of South Sudan has not yet been determined. A dispute exists between the Governments of Argentina and the United Kingdom of Great Britain and Northern Ireland concerning sovereignty over the Falkland Islands (Malvinas).

Mediterranean coast. A cluster of tramadol seizures occurred in the Middle East in various countries in the Gulf region, from Kuwait to Oman, most notably along the coast of the United Arab Emirates. Most of the tramadol seizures in India in 2017 and 2018 were reported in the western part of the country, in particular in three locations: the State of Gujarat, India, which accounts for a third of the total turnover of that country's pharmaceutical sector;[174] in locations near the coast and in the city of Mumbai (suggesting substantial trafficking in tramadol by sea); and in New Delhi, in particular at its airport.[175]

There have also been reports of non-medical use of tramadol in North America, Europe, East and South-East Asia, and Oceania, where diversion from licit sources has been reported in a number of countries.

The overall trafficking patterns of tramadol seen to date may change in the near future, however. As of April 2018, under its Narcotics and Drugs and Psychotropic Substances Act of 1985, India introduced more restrictive control measures for tramadol.[176] Control under the Act gives more powers to law enforcement and, in particular, enables authorities to enter the premises of tramadol laboratories and prosecute those who manufacture tramadol without permission.

Trafficking in fentanyl and its analogues on the increase

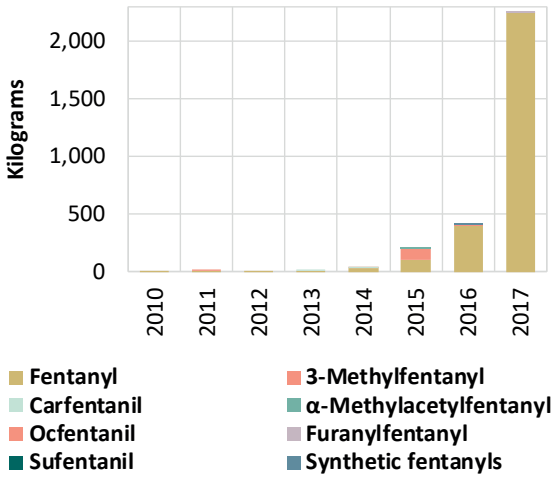
Accounting for more than 80 per cent of all quantities of pharmaceutical opioids seized in 2017, when expressed in S-DDD, the global quantity of fentanyl and analogues seized has grown markedly in the past few years: year-on-year increases were fourfold in both 2015 and 2016 and almost sixfold in 2017. While the number of countries reporting seizures of fentanyls has increased over the past few years, the illicit market for fentanyls remains highly concentrated in North America, accounting for 99 per cent of all global quantities of fentanyls seized in 2017.

174 India, Government of Gujarat, "Pharmaceuticals: sector profile" (Gujarat, 2017).

175 UNODC and Paris Pact, Drugs Monitoring Platform.

176 "Tramadol: review of the global situation".

FIG. 38 Global quantities of fentanyl and its analogues seized, 2010–2017



Source: UNODC, responses to the annual report questionnaire.

While a number of fentanyl analogues have been intercepted recently, fentanyl remains the most seized fentanyl-type substance (in terms of quantities) in all the regions, with the exception of Europe in 2015, when the Russian Federation reported several hundred seizure cases involving over 98 kg of 3-methylfentanyl.

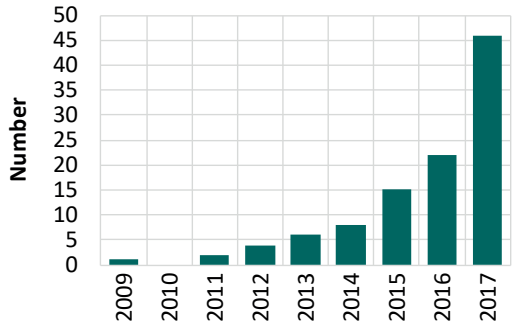
New synthetic opioid receptor agonists not under international control are dominated by newly emerging fentanyl analogues. Their number has risen markedly in recent data provided by Member States. Out of 78 NPS identified at the global level for the first time in 2017, forensic laboratories reported 22 new synthetic opioids receptor agonists, of which 19 were fentanyl analogues.[177]

In the European Union in 2016, only 2 per cent of the total number of seizures of new substances reported to the European early warning system were new opioids; however, around 70 per cent of those 2 per cent (1,600 seizure cases of new opioids) were fentanyl analogues.[178]

177 UNODC, early warning advisory on new psychoactive substances (January 2019).

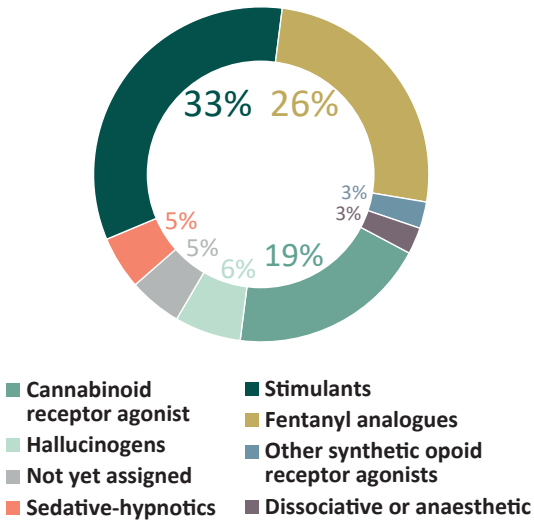
178 EMCDDA, *Fentanyls and Synthetic Cannabinoids: Driving Greater Complexity into the Drug Situation–An Update from the EU Early Warning System* (Luxembourg, Publications Office of the European Union, 2018).

FIG. 39 Identified new synthetic opioid receptor agonists, 2009–2017



Source: UNODC, early warning advisory on new psychoactive substances.

FIG. 40 New psychoactive substances reported for the first time in 2017 (N = 78)

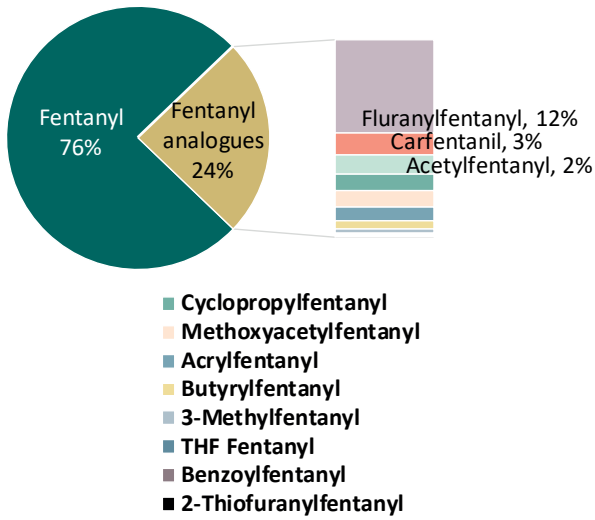


Source: UNODC, early warning advisory on new psychoactive substances.

In the United States, the single largest market for fentanyl and its analogues, in 2016, 85 per cent of more than 40,000 samples of seized fentanyl-type substances were fentanyl. Making up the other 15 per cent of the total sample, 16 different fentanyl analogues were identified, including furanylfentanyl (6 per cent), acetylfentanyl (4 per cent), carfentanil (3 per cent) and 3-methylfentanyl (1 per cent).[179]

Another analysis, based on a smaller sample of substances seized by the DEA of the United States in

FIG. 41 Distribution by substance of fentanyl and its analogues identified in the United States, 2017 (N = 2,475)



Source: United States Department of Justice, DEA, *2018 National Drug Threat Assessment*, October 2018, p. 22.

2017, pointed to the growing importance of the fentanyl analogues, which accounted for a quarter of the samples analysed. However, fentanyl remained the main substance in this group, accounting for 76 per cent of all fentanyls analysed, followed by furanylfentanyl, carfentanil and acetylfentanyl.[180]

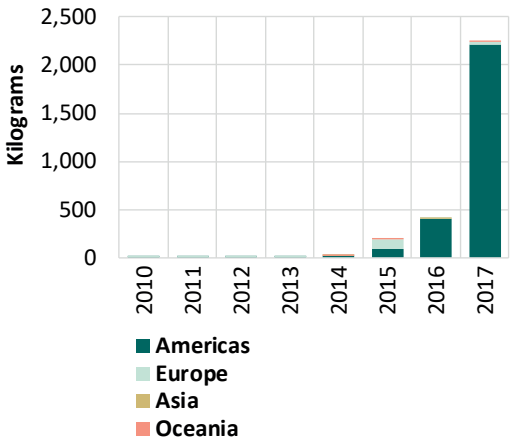
Overall, 21 countries in the Americas, Asia, Europe and Oceania reported seizures of fentanyls over the period 2013–2017. The number rose from just 4 countries in 2013 to 12 countries in 2016 and 16 countries in 2017, pointing at the global spread of trafficking in fentanyl-type substances.

Nonetheless, based on seizures, trafficking in fentanyl and its analogues appears to be mainly concentrated in the Americas (mostly in North America), which accounted for 95 per cent of the total quantities of fentanyls seized worldwide over the period 2013–2017. In the same period, seizures of fentanyls in Europe totalled 4.8 per cent; countries in Oceania and Asia reported minimal seizures and Africa reported none. The largest seizures of fentanyls in 2017 (expressed in kg equivalents) were reported by the United States (2,158 kg), Canada (61 kg), Estonia (10 kg) and Sweden (4 kg).

179 *2018 National Drug Threat Assessment.*

180 Ibid.

FIG. 42 Global quantities of fentanyl and its analogues seized, by region, 2010–2017



Source: UNODC, responses to the annual report questionnaire.

In 2017, the total quantity of fentanyl seized amounted to 2.2 tons. For comparison, global licit manufacture of fentanyl was 2.7 tons and the amount of fentanyl available for medical consumption was 1.4 tons.[181] As it is unlikely that more than 80 per cent of the global licit manufacture of fentanyl in 2017 was seized and/or that more fentanyl was diverted than was available for consumption, fentanyl seizures suggest the existence of significant clandestine manufacture of the drug at the global level to supply illicit drug markets. In addition, there may be significant adulteration of the fentanyl products on the illicit markets, resulting in large quantities of fentanyl of low purity seized (as reported by the United States).

Rapidly growing market for fentanyl and its analogues in North America – supplied mainly with substances produced in East Asia

According to United States authorities, the bulk of fentanyls trafficked to the United States (the principal market for the drugs) for the illegal market, seems to originate in China.[182] Fentanyls are imported either by mail directly to the United States or they are trafficked into the country via Mexico, often in the form of diluted powders or falsified prescription tablets containing fentanyls. Having been ordered on the darknet, some also enter the United States via Canada, where powders containing fentanyl substances are processed further by, for example, being pressed into tablets, mixed with heroin and sometimes sold as heroin, both for consumption in that country as well as for onward smuggling into the United States, in particular the north-eastern states.[183] The main "departure" country for shipments (which may be different from the country of "origin") of fentanyls to the United States in 2017 appears to have been Mexico, followed by China.[184]

Smuggling patterns can be even more complex. While the main final destination of fentanyls seized in the United States was the domestic market, some shipments were also meant for destinations abroad, notably Mexico (4 per cent) and Canada (1 per cent) in 2017. It has been speculated that some of these "exports" from the United States might have been intended for pressing into falsified pharmaceutical opioid tablets, such as falsified oxycodone tablets, in Mexico for subsequent "re-imports" into the

Top five fentanyl analogues identified by law enforcement in the European Union, 2016

Powders: valerylfentanyl, ocfentanil, carfentanil, 4-fluoro-isobutyrylfentanyl, furanylfentanyl

Liquids: acryloylfentanyl, furanylfentanyl, tetrahydro furanylfentanyl, 4-fluoro-isobutyrylfentanyl, cyclopentylfentanyl.

Tablets: acryloylfentanyl, 4-fluoro-isobutyrylfentanyl acetylfentanyl, cyclopentylfentanyl, furanylfentanyl.

Source: EMCDDA, Fentanyls and Synthetic Cannabinoids: Driving Greater Complexity into the Drug Situation–An Update from the EU Early Warning System (Luxembourg, Publications Office of the European Union, 2018).

181 *Narcotic Drugs: Estimated World Requirements for 2019.*

182 *2018 National Drug Threat Assessment.*

183 United States Department of Justice, DEA, *2017 National Drug Threat Assessment*, October 2017.

184 *2018 National Drug Threat Assessment.*

United States.[185] Moreover, the discovery of clandestine laboratories in both Canada and the United States suggests that illicit production of fentanyl (and analogues) has also been taking place in the two countries.

Although the diversion of fentanyl from the pharmaceutical industry takes place, it appears to be no more than a minor contribution to the supply of fentanyl and analogues to the North American illicit market. In the United States, the largest licit producer of fentanyl worldwide,[186] diversion of fentanyl mainly seems to take place on a small scale, mostly for personal use and/or street sale.[187] In Canada, 391 identified cases of fentanyl diversion from licit sources were reported in 2017, but there were more than four times as many identified trafficking cases involving fentanyl (1,626 cases). The differences are even more pronounced when the quantities intercepted are considered. The aggregate amounts of fentanyl identified in diversion cases in Canada amounted to less than 0.1 kg in 2017 while the quantity of fentanyl seized, resulting from trafficking activities, amounted to 61 kg in the same year.

According to United States authorities, in both 2016 and 2017, about 97 per cent of all fentanyls intercepted in international mail in the United States originated in China. However, imports of fentanyls by mail are estimated to represent just a fraction (12 per cent) of total illegal fentanyl imports into the United States, as the bulk of the fentanyls found on the United States market is estimated to have entered the country via land borders.[188] Most people arrested for trafficking in fentanyls in the United States were citizens of the United States, and, to a lesser extent, Mexico.

Fentanyl profiling in the United States[189] shows that, although typically seized in small quantities, fentanyl shipped directly from China is of high purity. In almost 80 per cent of such cases of direct shipment, purity was over 50 per cent; in half of those cases, it was actually over 90 per cent. This compares with an overall average purity of fentanyl of 5.1 per cent found on the United States market in 2017. This also seems to confirm the thesis that most fentanyl found on the United States market, in gross weight terms at least, has been trafficked overland from Mexico into the United States, which typically results in seizures of larger bulk quantities but of a far lower purity than fentanyl shipped by mail directly to the United States. It also supports the hypothesis that the bulk of the fentanyls found on the United States market is not diverted from the licit sector, which would be of almost 100 per cent purity.

Most of the fentanyls seized and most of the increase in the quantities seized along the border between Mexico and the United States in 2017 were observed in Tucson and San Diego, – that is, at the western end of the border, which is an area largely controlled by the Sinaloa cartel.[190] While the Sinaloa cartel controls most of the northern Pacific ports of Mexico, most of the country's southern Pacific ports, which are also key for imports of fentanyl and/or its precursors from South Asia, are controlled by the Cartel de Jalisco Nueva Generación.[191] Investigations in the United States have shown that the two cartels are the primary groups involved in the trafficking of fentanyl into the United States via its southwestern border,[192] although both cartels have also been heavily involved in the smuggling of a number of other drugs into the United States.[193]

According to United States authorities, shipments of fentanyls from Mexico to the United States include fentanyls manufactured in China and adulterated in Mexico, as well as fentanyls manufactured and adulterated in Mexico. The hypothesis that there may be also significant illicit manufacture of fentanyls in Mexico was confirmed in 2017 when a Mexican army patrol, operating in some remote areas of the State of Sinaloa, discovered a major fentanyl manufacturing facility, which was subsequently dismantled.[194]

As reported by the United States, precursor chemicals used in the manufacture of fentanyls in

185 *2017 National Drug Threat Assessment.*

186 *Narcotic Drugs: Estimated World Requirements for 2019.*

187 *2018 National Drug Threat Assessment.*

188 Ibid.

189 Ibid.

190 *2017 National Drug Threat Assessment.*

191 Scott Stewart, "Mexico's cartels find another game changer in fentanyl", *Stratfor*, 3 August 2017.

192 *2018 National Drug Threat Assessment.*

193 *2017 National Drug Threat Assessment.*

194 *2018 National Drug Threat Assessment.*

clandestine laboratories in North America appear to originate in China and are trafficked to the United States, partly via Mexico and Canada, while some are also smuggled from the United States into Mexico for subsequent "re-imports" of fentanyls into the United States. The main chemical used in the clandestine manufacture of fentanyls intercepted in the United States in recent years is 4-ANPP, suggesting that the less sophisticated "Siegfried method" is popular among operators of clandestine laboratories in both Mexico and the United States. This method can also use NPP as the starting material for its synthesis into 4-ANPP and then into fentanyl.[195]

Growing market for fentanyl and its analogues in Europe

A far smaller, though also growing market for fentanyl and its analogues is found in Europe. Fentanyl seizures and/or the non-medical use of fentanyl have been reported in most countries in Europe. Quantities of fentanyl and analogues seized have shown a clear upward trend in Western and Central Europe, rising from 1 kg in 2013 to 5 kg in 2016 and 17 kg in 2017. In parallel, the European early warning system also has shown a clear increase in the number of seizures involving fentanyls in recent years, as well as in the quantities of powder and tablets seized.[196]

Most shipments of new fentanyls arriving in Europe reportedly originated in China.[197] Reports received by UNODC from a number of countries in Europe – Estonia (2017), Poland (2017), Sweden (2016) and the United Kingdom (2017) – also seem to confirm that China is the main source of fentanyl and its analogues found on the markets in Europe.

Like many other new substances, most new fentanyl analogues are not controlled under the international drug control conventions, which means that they can be manufactured in many countries and traded relatively freely. This situation has been exploited by organized crime groups in Europe that use companies to manufacture fentanyl analogues, which are then typically shipped to Europe by express mail and courier services. Once in Europe, the new fentanyls are sold as "legal" replacements for controlled opioids on the surface web as well as on the darknet. Similar to the situation in the United States, the new fentanyls may be sold as heroin, or mixed with heroin and other controlled opioids. They may then be found in falsified medical products, although to a lesser extent than in the United States.[198]

Although fentanyls are often injected, their high potency and ease of use mean that nasal sprays containing diluted solutions have also appeared in some illicit markets in Europe in recent years. In Sweden, for example, unlabelled nasal sprays filled with acryloylfentanyl were offered for sale online until the

Recent international control of fentanyls and related precursor chemicals

The international scheduling of ANPP and its direct precursor, NPP, in Table I of the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988 was decided by the Commission on Narcotic Drugs in March 2017 and went into effect in October 2017. All parties to the 1988 Convention are requested to place those substances, the two main precursors for manufacturing fentanyl, under national control.

In the past few years, the Commission on Narcotic Drugs has also approved the placing of a number of fentanyl analogues under international control. The substances include: carfentanil, acrylofentanyl, furanylfentanyl, tetrahydrofuranylfentanyl, ocfentanil and 4-fluoroisobutyrylfentanyl (all controlled in 2018), butyrfentanyl (2017) and acetylfentanyl (2016). Following the scheduling of 116 NPS by China in October 2015, the country also placed carfentanil, furanylfentanyl, acryloylfentanyl and valerylfentanyl under control in March 2017.[a]

[a] *2017 National Drug Threat Assessment.*

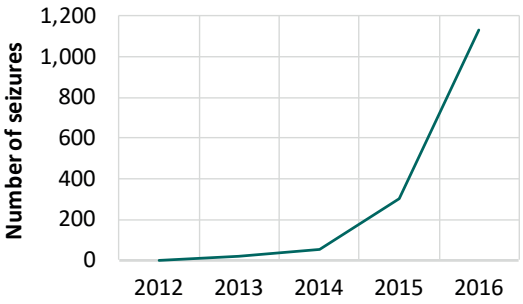
195 *2017 National Drug Threat Assessment.*

196 EMCDDA, *Fentanyls and Synthetic Cannabinoids: Driving Greater Complexity into the Drug Situation.*

197 Ibid.

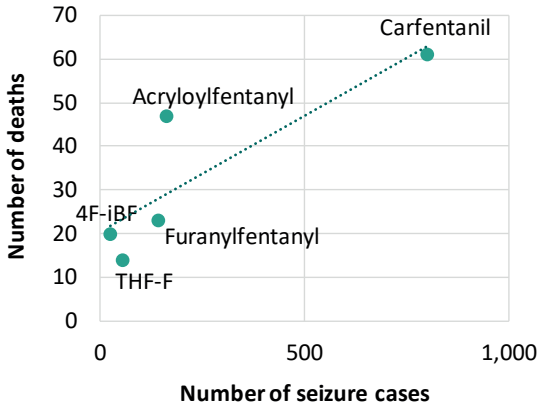
198 Ibid.

FIG. 43 Seizures of fentanyls reported to the European early warning system, 2012–2016



Source: EMCDDA, *Fentanyls and Synthetic Cannabinoids: Driving Greater Complexity into the Drug Situation*, p. 10.

FIG. 44 Number of deaths and seizure cases involving fentanyl analogues in the European Union (based on key findings from risk assessments of fentanyl analogues, conducted between 2013 and 2017)



Source: EMCDDA, *Fentanyls and Synthetic Cannabinoids: Driving Greater Complexity into the Drug Situation*, p. 13.

company was dismantled in 2016; nasal sprays of this type were involved in 47 deaths in Europe that year. There have also been reports of the emergence of e-liquids containing fentanyls that can be vaped using electronic cigarettes.[199]

Given the increasing problems related to a number of fentanyl analogues in Europe in recent years, EMCDDA and Europol conducted joint investigations and research on the following: acetylfentanyl in 2015; acryloylfentanyl and furanylfentanyl in 2016; and 4-fluoroisobutyrylfentanyl (4F-iBF), tetrahydrofuranylfentanyl (THF-F), carfentanil, methoxyacetylfentanyl and cyclopropylfentanyl in 2017. They resulted in the preparation of five risk assessments in 2017 and revealed that the largest numbers of both seizure cases and substance abuse-related deaths in Europe among the five substances investigated were related to carfentanil, followed by acrylofentanyl and furanylfentanyl.[200]

The diversion of fentanyl from licit sources prior to 2013 was reported by several countries in Europe (Bulgaria, Croatia, Germany, Hungary, the Russian Federation and the United Kingdom). No such cases have been reported to UNODC since then.

In addition, there have been sporadic reports of fentanyls produced in clandestine laboratories in Europe,[201] mostly destined for local distribution and consumption. The only exception involved laboratories operating in the Russian Federation that may also have supplied fentanyl to neighbouring countries. In particular, Estonia reported for years that the Russian Federation was the main source of fentanyl found on its territory, but this appears to have changed in 2017 following the dismantling of an organized crime group and the disappearance from the market in Estonia of fentanyls trafficked from the Russian Federation within a period of several weeks. This has since been largely substituted by fentanyls trafficked by mail from China, according to reports from Estonia.

Most of the significant seizures of fentanyl and its analogues in the Russian Federation over the period 2013–2017 were reported in the part of the country that is located in Europe, notably in the area around Saint Petersburg and other cities in the north of the country. The substances reported in significant seizures were mostly 3-methylfentanyl, fentanyl and carfentanil.[202]

199 Ibid.

200 Ibid.

201 EMCDDA, *Fentanyls and Synthetic Cannabinoids: Driving Greater Complexity into the Drug Situation*.

202 UNODC and Paris Pact, Drugs Monitoring Platform.

OTHER CENTRAL NERVOUS SYSTEM DEPRESSANTS

Introduction

After opioids, the groups of depressants that are seized in the largest quantities are sedatives and tranquillizers. In contrast to opioids, most sedatives and tranquillizers are diverted from legal sources rather than being illegally produced. Whereas most opioids are controlled under the 1961 Convention, sedatives and tranquillizers are controlled under the 1971 Convention. While benzodiazepines and barbiturates are controlled under the less strict Schedules III and IV of the 1971 Convention, methaqualone and GHB are controlled under Schedule II of the 1971 Convention.

Different benzodiazepines may vary in potency and are widely used in medicine as anticonvulsants, anxiolytics, hypnotics, sedatives, skeletal muscle relaxants and tranquillizers. Many benzodiazepines are currently under international control in the 1971 Convention.

Barbiturates represent another group of synthetic central nervous system depressants that were once widely used medically as hypnotics and sedatives. Their medical use today is limited to anti-epileptics, adjuncts to anaesthesia in surgical procedures and, less commonly, as anti-anxiety drugs. Some of the common pharmaceutical barbiturates include amobarbital, pentobarbital, phenobarbital and secobarbital. As with benzodiazepines, individual barbiturates differ in the onset and duration of their action and potency. Since barbiturates have a low therapeutic index – that is, the quantity that produces a therapeutic effect and may result in toxicity – an overdose of barbiturates can prove fatal.[203] As a result, they have been largely replaced on both the licit and illicit markets by benzodiazepines. Nevertheless, in 2016 and 2017, some 18 countries, mainly located in Europe and Asia, ranked the non-medical use of barbiturates higher than the non-medical use of benzodiazepines on their territory.

Methaqualone is another synthetic central nervous system depressant with sedative-hypnotic, anticonvulsant, antispasmodic and local anaesthetic properties. As with other depressants in this class, the sedative-hypnotic properties of methaqualone are mediated through its effect on the GABA receptors.[204]

GHB is another central nervous system depressant that produces sedation and anaesthesia; it is mainly associated with drug-facilitated sexual assault. The effects of GHB on the body are mediated through a specific GHB receptor, its activation of the GABA receptors, as well as through the dopamine system.[205] GBL, a natural precursor of GHB that generates GHB in the body after ingestion, is also available in some countries as an industrial solvent for cleaning metal and removing spray paint. GBL is sold on the illicit market as a substitute for GHB in some countries.

Gabapanthinoids, such as gabapentin and pregabalin, are another group of central nervous system depressants that are considered to be derivatives of the neurotransmitter GABA or its analogues. Gabapentionoids have been traditionally used to treat epilepsy and generalized anxiety disorder; as non-opioid analgesics, they are also effective in treatment of neuropathic pain.[206] Gabapentin and pregabalin are neither on the WHO Model List of essential medicines nor under control in the international conventions, but there are reports of their non-medical use, especially among opioid users.

Non-medical use of sedatives and tranquillizers

The non-medical use of sedatives and tranquillizers as a group of substances remains quite widespread and is reported in all regions. In 2017, 40 Member States ranked the non-medical use of sedatives and tranquillizers among the three most commonly used substances in their countries, while the non-medical use of benzodiazepines was ranked number one within the broader category of sedatives and

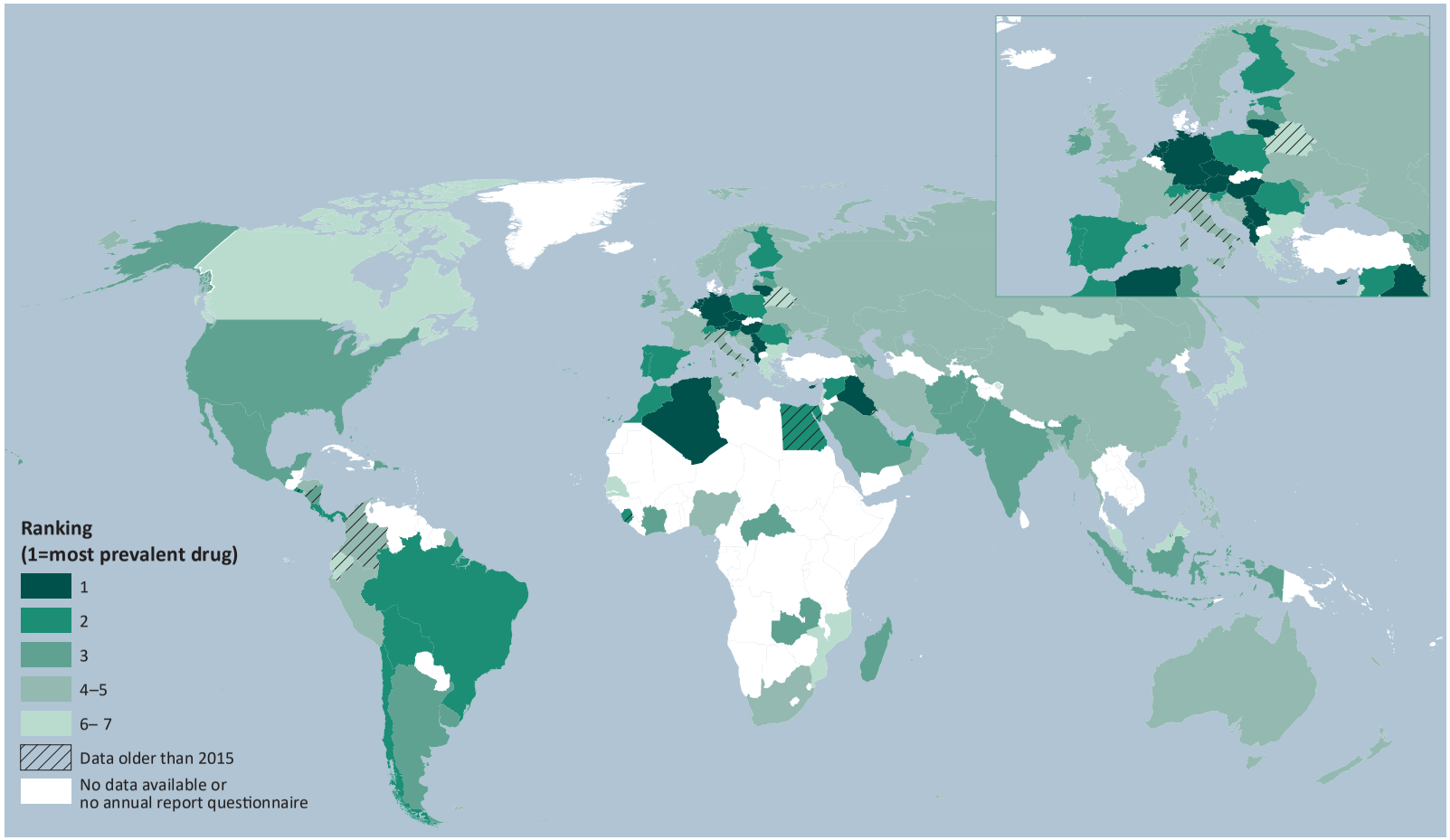
203 *Terminology and Information on Drugs*, 3rd ed. (United Nations publication, Sales No. E.16.XI.8).

204 Ibid.

205 Ibid.

206 WHO, Expert Committee on Drug Dependence "Pregabalin: pre-review report–agenda item 5.1" (Geneva, November 2017).

MAP 10 Ranking of sedatives and tranquillizers in order of prevalence (based on national qualitative information, 2017)



Source: UNODC.

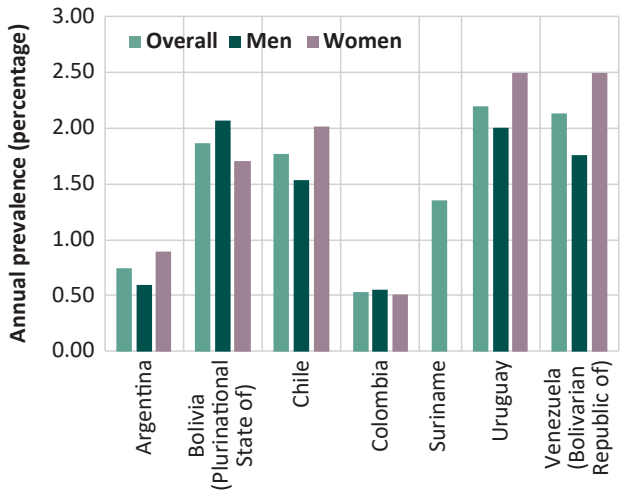
The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations.
Dotted line represents approximately the Line of Control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. A dispute exists between the Governments of Argentina and the United Kingdom of Great Britain and Northern Ireland concerning sovereignty over the Falkland Islands (Malvinas).

tranquillizers. Women seem to be particularly affected by the non-medical use of sedatives and tranquillizers, with past-year prevalence in some countries reported as being higher among women than among men, or at least at comparable levels.[207] The non-medical use of benzodiazepines also figures quite prominently within polydrug use patterns, especially among opioids users.[208] Opioid users typically use benzodiazepines to self-medicate in order to increase or potentiate the effects of opioids, as well as to deal with the negative effects of opioid use, such as negative emotional states, dealing with anxiety or depression and even dealing with opioid withdrawal.[209] Individuals in long-term opioid agonist treatment are particularly prone to using benzodiazepines in order to increase the effects of opioid medication and to achieve a more potent "euphoric effect".[210] Benzodiazepines are also commonly reported among overdose deaths attributed to the use of opioids.[211, 212]

Extent of non-medical use of sedatives and tranquilizers

Among the countries that have reported recent survey data on the non-medical use of sedatives and tranquillizers in South and Central America, the annual prevalence of non-medical use of tranquillizers in most of them is more than 2 per cent of the general population and the non-medical use of tranquillizers is higher among women than among men. The non-medical use of tranquillizers is also quite commonly reported in school surveys in those subregions. For example, El Salvador reported an annual prevalence of the non-medical use of tranquillizers of 1.9 per cent among students aged 13 to17 in 2016, Chile reported a rate of 10 per cent among those aged 15 to 16 in 2015, and Colombia reported a rate of 2.3 per cent among those aged 15 to 16 in 2016.

FIG. 45 Non-medical use of tranquillizers and sedatives among the general population in Central America and South America



Source: UNODC, responses to annual report questionnaire.

Note: The reference year for Argentina is 2017; Bolivia (Plurinational State of), 2014; Chile, 2016; Suriname, 2013; Uruguay, 2014; and Venezuela (Bolivarian Republic of), 2011.

In North America, the past year non-medical use of tranquillizers in 2017 was reported to be 0.2 per cent of the population aged 15 and older in Canada[213] and 2.2 per cent of the population aged 12 and older in the United States. The non-medical use of tranquillizers in the United States was reported to be at similar levels among men and women, and to be highest among young people aged 18-25.[214]

The non-medical use of tranquillizers is quite common in Western and Central Europe, where it ranges from 19.5 per cent among the adult population in Czechia to less than 1 per cent in Portugal. In eight of the 14 countries that reported recent estimates, non-medical use of tranquillizers was greater than the use of cannabis; in all 14 countries

207 See, for example, *World Drug Report 2018: Women and Drugs–Drug Use, Drug Supply and Their Consequences* (United Nations publication, Sales No. E.18.XI.9 (Booklet 5)).

208 Jermaine D. Jones, Shanthi Mogali and Sandra D. Comer, "Polydrug abuse: a review of opioid and benzodiazepines combination use", *Drug and Alcohol Dependence,* vol. 125, Nos. 1–2 (September 2012), pp. 8–18.

209 EMCDDA, "Perspectives on drugs: the misuse of benzodiazepines among high-risk opioid users in Europe" (Lisbon, 2018).

210 Jones, Mogali and Comer, "Polydrug abuse".

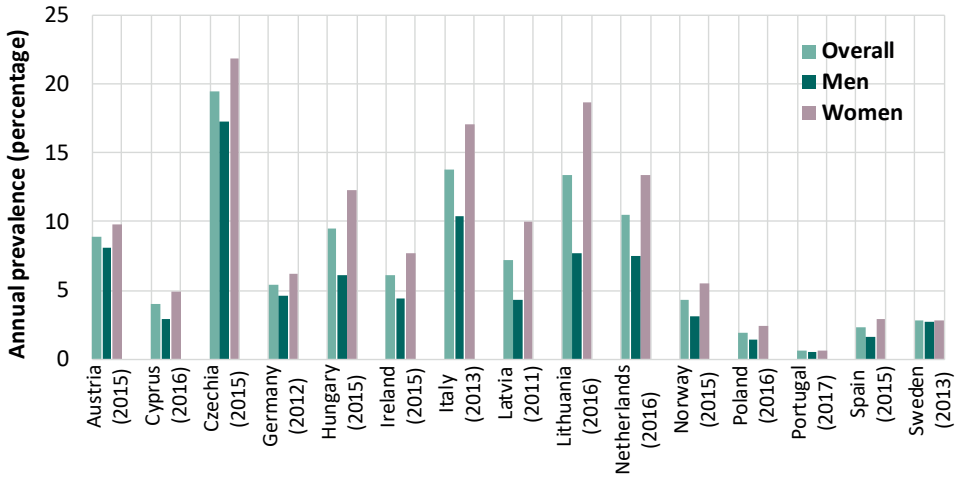
211 EMCDDA, "The misuse of benzodiazepines among high-risk opioid users in Europe".

212 UNODC, "Non-medical use of benzodiazepines: a growing threat to public health", Global SMART Update, vol. 18 (September 2018).

213 Health Canada, "Canadian Tobacco, Alcohol and Drugs Survey (CTADS): summary of results for 2017", December 2017.

214 *Results from the 2017 National Survey on Drug Use and Health: Detailed Tables.*

FIG. 46 Non-medical use of tranquillizers among the adult population aged 15–64 in Western and Central Europe



Source: UNODC, responses to the annual report questionnaire.

the non-medical use of tranquilizers was higher among women than men. The non-medical use of tranquillizers and sedatives was also quite common among students aged 15 and 16 in Europe. In 2015, lifetime prevalence was reported to be 6 per cent, the highest rates being reported in Poland (17 per cent) and Czechia (16 per cent) and the lowest in Demark and Romania (between 1 and 2 per cent). Students who had used alcohol also reported the use of other substances, including cigarettes (54 per cent), cannabis (19 per cent), inhalants (9 per cent), tranquillizers or sedatives (7 per cent) and NPS or other controlled drugs (5 per cent or less). Since 2016, falsified Rivotril®, a benzodiazepine containing clonazepam and classified as a narcotic substance in Finland, has been reported as having been trafficked from Central Europe to Finland, among other Nordic countries.[215]

The non-medical use of sedatives and tranquillizers was also reported in Africa, although survey data are limited in the region. In the 2018 drug use survey in Nigeria, the past-year prevalence of the non-medical use of tranquillizers was estimated at roughly 0.5 per cent of the adult population: 0.4 per cent among women and 0.5 per cent among men.[216] The non-medical use of tranquillizers was also prevalent in North Africa: for example, in Algeria in 2010, the annual prevalence of the non-medical use of tranquillizers among the population aged 12 and older (0.6 per cent) was at a comparable level to that of cannabis (0.5 per cent). Recent school surveys among secondary school students measured the past-year prevalence of the non-medical use of tranquillizers – mainly benzodiazepines. Among students aged 15–19 in Egypt, the prevalence was 1.7 per cent in 2016;[217] among students aged 15–17 in Morocco, the prevalence was 2.3 per cent in 2017.[218]

In Asia, where survey data are also limited, the annual prevalence of the non-medical use of tranquillizers reported in the most recent drug use survey in Pakistan, conducted in 2013, was 1.5 per cent among women and 1.3 per cent among men.[219] In India in 2018, around 1 per cent of people aged 10–75 were current users of sedatives and tranquillizers for non-medical reasons.The non-medical use of sedatives and tranquillizers was also reported in South-East Asia, including in Brunei Darussalam; Hong Kong, China; Indonesia; Malaysia; the Philippines; Singapore; and Taiwan Province of China. Prevalence estimates are not available, however.

215 EMCDDA, "Finland country report 2018".

216 UNODC, *Drug Use in Nigeria 2018*.

217 MedSPAD 2016 in Egypt.

218 Jallal Toufiq, National Centre for Drug Abuse Prevention and Research of Morocco, presentation on "Drug use among Moroccan youth: MedSPAD surveys", Lisbon, October 2017.

219 UNODC and Pakistan, Ministry of Interior and Narcotics Control, *Drug Use in Pakistan 2013*.

NPS benzodiazepines

The number of reported NPS with a sedative-hypnotic effect remains low: they numbered 25 among the 492 NPS reported in 2017. Of the 79 NPS reported for the first time to the UNODC early warning advisory in 2017, only four were NPS with a sedative-hypnotic effect. Most such NPS are benzodiazepines, some of which have been patented, but many have never been marketed for medical use. The majority, as in the case of NPS opioids, have never undergone clinical trials.[220] They are sold as "legal benzodiazepines", "designer benzodiazepines" or "research chemicals".[221]

There are also a number of NPS benzodiazepines that have been approved for medical use in a few countries, but their use is largely unknown elsewhere. Phenazepam is one such example; it was developed in the former Soviet Union in the 1970s and was licensed for medical use in the Russian Federation and parts of the Commonwealth of Independent States.[222] Along with nimetazepam, phenazepam was the first NPS benzodiazepine to be identified in Europe, in 2007, on the illicit market.[223] Following a large number of reports about its non-medical use and fatalities associated with its use, especially in Europe, phenazepam was put under international control in the 1971 Convention in 2016. Since then, small numbers of NPS benzodiazepines – including adinazolam, cloniprazepam, flunitrazolam, metizolam and nitrazolam – continue to be reported, mainly in Europe.[224]

Many NPS benzodiazepines have also been found mixed with other NPS, including synthetic cannabinoids and synthetic opioids.[225] NPS benzodiazepines may also provide an alternative to prescribed benzodiazepines as they are readily available via the internet or sold on the illicit market.[226] As the pharmacology and toxicology of NPS benzodiazepines is largely unknown, they may pose a high risk to users and in some cases have resulted in acute emergencies and deaths. NPS benzodiazepines and thienodiazepines were implicated in nine drug-related deaths in England and Wales in the period 2013–2014, as either the cause of death or having contributed to death.[227]

Methaqualone

Methaqualone is a potent quinazoline within the class of sedatives, which has hypnotic, anticonvulsant, antispasmodic and local anaesthetic properties. Formerly sold under the brand names Quaalude® and Mandrax®, methaqualone became popular as a club drug in the late 1960s and 1970s, but its use had waned in Western countries by the mid-1980s. Withdrawn from the pharmaceutical market around the same time in many countries as a result of problems of abuse, methaqualone is controlled under Schedule II of the 1971 Convention.[228] One of the few countries that currently reports the non-medical use of methaqualone is South Africa, where the mixed use of cannabis and methaqualone (also known as "smoking white pipe") is reported in some regions as being the primary or secondary substance of use among people in treatment for drug use disorders and is seen as serious public health problem.[229, 230]

gamma-Hydroxybutyrate

GHB, another depressant, is used medically as an adjunct in anaesthesia and is also used to treat insomnia and clinical depression. The non-medical use of GHB is not common, with only a few countries worldwide reporting such use among the general population. The past-year prevalence of GHB ranges from 0.1 per cent reported in Israel

220 Kieran R. Manchester and others, "The emergence of new psychoactive substances (NPS) benzodiazepines: a review", Drug Testing and Analysis, vol. 10, No. 1 (January 2018), pp. 37–53.

221 See also *World Drug Report 2018: Analysis of Drug Markets–Opiates, Cocaine, Cannabis, Synthetic Drugs* (United Nations publication, Sales No. E.18.XI.9 (Booklet 3)).

222 "Non-medical use of benzodiazepines: a growing threat to public health".

223 Ibid.

224 Manchester and others, "The emergence of new psychoactive substances (NPS) benzodiazepines".

225 EMCDDA, "The misuse of benzodiazepines among high-risk opioid users in Europe".

226 Ibid.

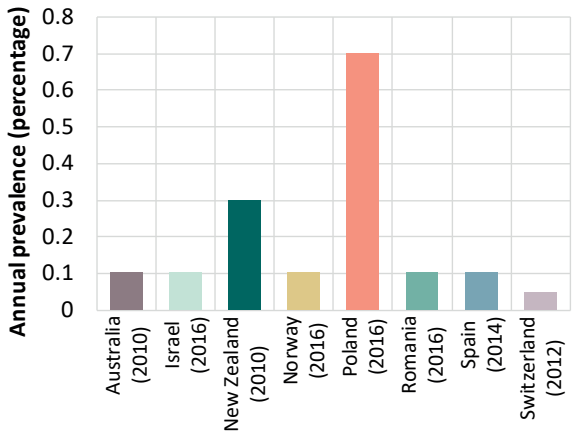
227 Manchester and others, "The emergence of new psychoactive substances (NPS) benzodiazepines".

228 *Terminology and Information on Drugs*.

229 Siphokazi Dada and others, *Monitoring Alcohol, Tobacco and Other Drug Use Trends in South Africa*: *Phase 43* (Cape Town, South Africa, South African Community Epidemiology Network on Drug Use, October 2018).

230 Greg McCarthy, Bronwyn Myers and Nandi Siegfried, "Treatment for methaqualone dependence in adults", *Cochrane Database of Systematic Review* (April 2005).

FIG. 47 GHB use among the general population in selected countries



Source: UNODC, responses to the annual report questionnaire.

Note: In the case of Norway, Romania and Switzerland, the prevalence is reported for both GBL and GHB.

and Spain to 0.7 per cent reported in Poland. The use of GBL, a natural precursor to GHB, has also been reported among the general population in Norway, Romania and Switzerland. Yet, in 2016, GHB ranked fourth in the top 20 drugs recorded in emergency presentations in 19 sentinel hospitals in 13 European Union member countries.[231]

GHB acts on the central nervous system in a biphasic time profile, i.e. induces an initial stimulant-like effect with a disinhibiting action and a subsequent sedative effect. This makes GHB one of the most used substances in drug-facilitated sexual assaults and in settings in which men have sex with men, with an associated risk of sexually transmitted infections, including HIV.[232]

The use of GHB, GBL and benzodiazepines such as flunitrazepam has been associated with drug-facilitated sexual assault, which occurs when alcohol or drugs are used to compromise an individual's ability to consent to sexual activity. It has been reported across the regions.[233, 234, 235] The use of GHB and GBL has also been reported over the past two decades among subgroups of drug users such as those attending dance events[236, 237] and in lesbian communities in Australia, Europe and North America.[238, 239, 240] The use of GHB, along with methamphetamine and mephedrone, is also frequently reported among people who participate in "chemsex".[241, 242, 243]

Different qualitative studies have shown that people engaging in chemsex report that these drugs "reduce their inhibitions, increase pleasure, facilitate sustained arousal and induce a feeling of instant rapport with sexual partners".[244] "Chemsex", or sexualized drug use, in particular has emerged as a marker of high-risk sexual activity and poor sexual health among gay, bisexual and other men who have sex with other men.[245] Several sociosexual factors associated with the practice of chemsex have been

231 EMCDDA, *European Drug Report 2018*.

232 Giorgetti and others, "When 'Chems' meet sex".

233 United States, Department of Justice, Department Enforcement Administration, Community Outreach and Prevention Support Section, Victim Witness Assistance Program, "Drug-facilitated sexual assault" (April 2017).

234 EMCDDA, "Sexual assaults facilitated by drugs or alcohol" (Lisbon, 2008).

235 Nancy S. Harper, "Drug-facilitated sexual assault", in *Child Abuse and Neglect: Diagnosis, Treatment, and Evidence*, Carole Jenny, ed. (Philadelphia, United States, Saunders, 2010).

236 Judith C. Barker, Shana L. Harris and Jo E. Dyer, "Experiences of gamma hydroxybutyrate (GHB) ingestion: a focus group study", *Journal of Psychoactive Drugs*, vol. 39, No. 2 (June 2007), pp. 115–129.

237 Mark A. Bells and others, "The role of an international nightlife resort in the proliferation of recreational drugs", *Addiction*, vol. 98, No. 12 (December 2003), pp. 1713–1721.

238 EMCDDA, *European Drug Report 2018*.

239 EMCDDA, *GHB and its Precursor GBL: An Emerging Trend Case Study* (Lisbon, 2008).

240 Raffaele Giorgetti and others, "When 'Chems' meet sex: a rising phenomenon called "ChemSex"", *Current Neuropharmacology*, vol. 15, No. 5 (2017), pp. 762–770.

241 The term "chemsex" was first coined on the London gay scene and rapidly spread, to indicate the voluntary intake of psychoactive and other drugs in the context of sex parties and sexual intercourse with the intention of facilitating or enhancing sexual encounters, mostly among men who have sex with other men.

242 Hannah McCall and others, "What is chemsex and why does it matter", *British Medical Journal,* vol. 351 (2015).

243 Claire Edmundson and others, "Sexualized drug use in the United Kingdom (UK): A review of literature", *International Journal of Drug Policy,* vol. 55 (May 2018), pp. 131–148.

244 McCall and others, "What is chemsex and why does it matter".

245 Isabelle Giraudon, Axel Jeremias Schmidt and Hamish Mohammed, "Surveillance of sexualised drug use: the challenges and the opportunities", *International Journal of Drug Policy,* vol. 55 (May 2018), pp. 149–154.

identified by a number of studies. Those factors are HIV-positive status; social engagement with gay men who use drugs; a high number of sexual partners; and participation in group sex and unprotected sex with casual partners.[246, 247, 248]

Pregabalin and gabapentin

Pregabalin and gabapentin, the two gabapentinoids that are also GABA analogues, respectively marketed under the brand names Lyrica® and Neurontin,®, are used in medicine to treat epilepsy, neuropathic pain, fibromyalgia and generalized anxiety syndromes.[249] Systematic reviews of the scientific literature on the misuse of pregabalin and gabapentin have shown that an increasing number of patients, in Europe in particular, self-administer higher doses than the recommended therapeutic dose to achieve euphoria.[250, 251] The majority of case reports concerning the non-medical use of pregabalin involved people with a history of substance use disorders, especially opioid users: between 15 and 22 per cent of opioid users had used gabapentin non-medically and between 3 and 68 per cent had used pregabalin non-medically concomitantly with opioids.[252]

In Europe, out of the total adverse drug reaction reports of non-medical use and substance use disorders over the period 2004–2015, around 7 per cent of cases were associated with the non-medical use of pregabalin and 5 per cent with the non-medical use of gabapentin.[253, 254] In a 2013 online survey of people aged 16–59 in the United Kingdom, self-reported lifetime prevalence of the non-medical use of gabapentin was 1.1 per cent and of pregabalin was 0.5 per cent.[255] The survey also revealed that the provenance of most of the pregabalin used non-medically was from sources other than legitimately prescribed medication.[256]

The non-medical use of pregabalin has also been reported in countries in the Near and Middle East. In Saudi Arabia, 7 per cent of people in drug treatment were reportedly in treatment for disorders related to the non-medical use of pregabalin. In a 2015 study in the United Arab Emirates, more than 80 per cent of people in treatment were polydrug users, of whom the majority had used four or more substances either sequentially or concomitantly.[257] While tramadol and heroin remained the main opioids used among this group, more than 60 per cent reported concurrent use of pregabalin.[258] In Gaza, Palestine, in 2016, nearly all high-risk male drug users reported current use of tramadol, and more than half also reported the concurrent use of pregabalin.[259]

The concomitant use of gabapentin with opioids

246 Mohammad A Hammoud and others, "Intensive sex partying with gamma-hydroxybutyrate: factors associated with using gamma-hydroxybutyrate for chemsex among Australian gay and bisexual men–results from the Flux Study", *Sexual Health*, vol. 15, No. 2 (December 2017), pp. 123–134.

247 G. J. Melendez-Torres and others, "Typology of drug use in United Kingdom men who have sex with men and associations with socio-sexual characteristics", *International Journal of Drug Policy,* vol. 55 (May 2018), pp. 183–186.

248 Kathleen E. Ryan and others, "Implications of survey labels and categorisations for understanding drug use in the context of sex among gay and bisexual men in Melbourne Australia", *International Journal of Drug Policy,* vol. 55 (May 2018), pp. 149–154.

249 James E. Framptom, "Pregabalin: a review of its use in adults with generalized anxiety disorder", *CNS Drugs,* vol. 28, No. 9 (September 2014), pp. 835–854.

250 Kirk E. Evoy, Megan D. Morrison and Stephen R. Saklad, "Abuse and misuse of pregabalin and gabapentin", *Drugs,* vol. 77, No. 4 (March 2017), pp. 403–426.

251 Ole Schjerning and others, "Abuse potential of pregabalin: a systematic review", *CNS Drugs,* vol. 30, No. 1 (January 2016), pp. 9–25.

252 Evoy, Morrison and Saklad, "Abuse and misuse of pregabalin and gabapentin".

253 EudraVigilance, the database of European Medicines Agency.

254 Stefania Chiappini and Fabrizio Schifano, "A decade of gabapentinoid misuse: an analysis of the European Medicine Agency's 'Suspected Adverse Drug Reactions' database", *CNS Drugs,* vol. 30, No. 7 (July 2016), pp. 647–654.

255 Vikas Kapil and others, "Misuse of the gamma-aminobutyric acid analogues baclofen, gabapentin and pregabalin in the UK", *British Journal of Clinical Pharmacology*, vol. 78, No. 1 (July 2014), pp. 190–191.

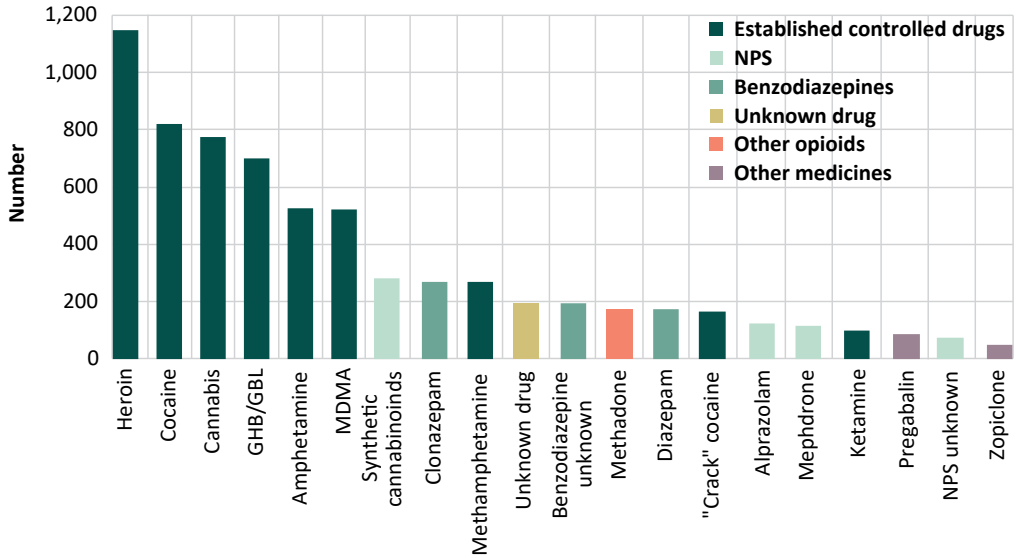
256 Ibid.

257 Hiba Alblooshi and others, "The pattern of substance use disorder in the United Arab Emirates in 2015: results of a National Rehabilitation Centre cohort study", *Substance Abuse Treatment, Prevention, and Policy* (May 2016), pp. 11–19.

258 See also Amneh Al-Husseini, Mayyada Wazaify and Marie Claire Van Hout, "Pregabalin misuse and abuse in Jordan: a qualitative study of user experiences", *International Journal of Mental Health and Addiction*, vol. 16, No. 3 (June 2018) pp. 642–654.

259 Ministry of Health of the State of Palestine and Palestinian National Institute of Public Health, *Estimating the Extent of Illicit Drug Use in Palestine* (Ramallah, 2017).

FIG. 48 Emergency presentations in sentinel hospitals, by top 10 drugs recorded in Europe, 2016



Source: EMCDDA, *European Drug Report, 2018.*

has been associated with a substantial increase in the risk of opioid overdose, probably reflecting both additive respiratory depression and increased gabapentin concentrations when used with opioids.[260] In 13 countries in the European Union, pregabalin is listed among the top 20 drugs reported in 2016 among drug-related toxicity presentations in 19 sentinel hospitals, although not in the same numbers or proportions as drugs such a heroin, cocaine, cannabis and GHB.[261]

Supply of sedatives and tranquillizers

In terms of quantity, methaqualone has been the substance most seized among sedatives and tranquillizers over the past two decades, other than during the period 2010–2015 when benzodiazepines were dominant. Overall, 133 countries reported seizures of sedatives and tranquillizers to UNODC over the period 1998–2017, including 91 countries over the period 2013–2017. The largest quantities of sedatives and tranquillizers seized in the period 2013–2017 were reported by countries in Asia (47 per cent), Africa (25 per cent) and the Americas (21 per cent), most notably by India, the United States, South Africa, Nigeria and Thailand (in descending order of quantities).

Methaqualone

The geographical scope of trafficking in methaqualone appears to be quite limited at present, except for ongoing trafficking flows from India to East and Southern Africa. Almost the entire quantity of methaqualone (99 per cent) seized over the period 2013–2017 was intercepted in just three countries: 75 per cent of it in India and the remainder in Mozambique and South Africa. This reflects the fact that the majority of the illicit manufacture of methaqualone worldwide takes place in India and its main illicit markets are located in Southern Africa. The lack of data on the use of methaqualone for non-medical purposes, however, makes it difficult to assess the overall extent of the market for the drug.

Data indicate that a limited amount of very large shipments of methaqualone – that is, seizures weighing several kg to several tons — are intercepted in India, which are mainly destined for export. In addition, a large number of small seizures, destined for trafficking and distribution on the local market, are made in South Africa. The average methaqualone seizure in South Africa was 0.14 kg in both 2016

260 Tara Gomes and others, "Gabapentin, opioids, and the risk of opioid related death: a population-based nested case–control study", *PLoS Medicine*, vol. 14, No. 10 (October 2017).

261 EMCCDA, *European Drug Report 2018.*

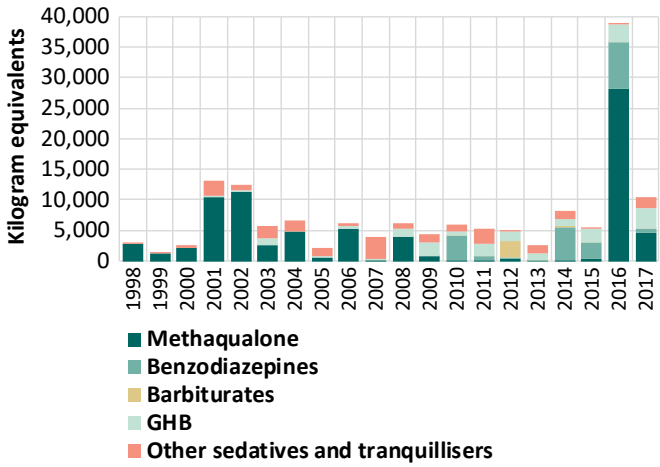
and 2017, while in India it was 3 tons in 2016 and 5 kg in 2017. This may be an indication of a supply chain originating in India, from where methaqualone is exported at wholesale level to South Africa, where it is distributed on the retail market, although little is known about detailed trafficking patterns and routes. Seizures of methaqualone have also been reported by other countries in Southern Africa (Namibia) and in East Africa (Kenya and the United Republic of Tanzania) in the past decade. However, given the limited capacity of some countries in Africa to undertake and report seizures, it is also possible that some trafficking goes undetected in that region.

A few other countries also reported seizures of methaqualone over the period 2013–2017, including countries in the Americas (notably the United States and, to a lesser extent, Canada and Argentina), Europe (Spain, Italy and Belgium) and Oceania (Australia).

While methaqualone used to have a global reach – 70 countries reported seizures over the period 1982–2017 across all regions – only 11 countries reported seizures of the drug in the past five years. The presence of methaqualone in international drug markets and in drug shipments intercepted appears to have declined since its widespread use as a recreational drug in the club scene in North America and Europe in the late 1960s and 1970s. The decline in the 1990s followed the rescheduling of methaqualone from a Schedule IV to a Schedule II substance in 1979, given reports of its limited medical usefulness and of abuse potential.[262, 263] The declining use was prompted by subsequent recommendations in 1989 to have its production and its international trade stopped.[264]

However, there has been a recent surge in the quantities of methaqualone seized, owing primarily to large quantities intercepted in India in 2016 (24 tons). This resulted in a global total of 28 tons seized

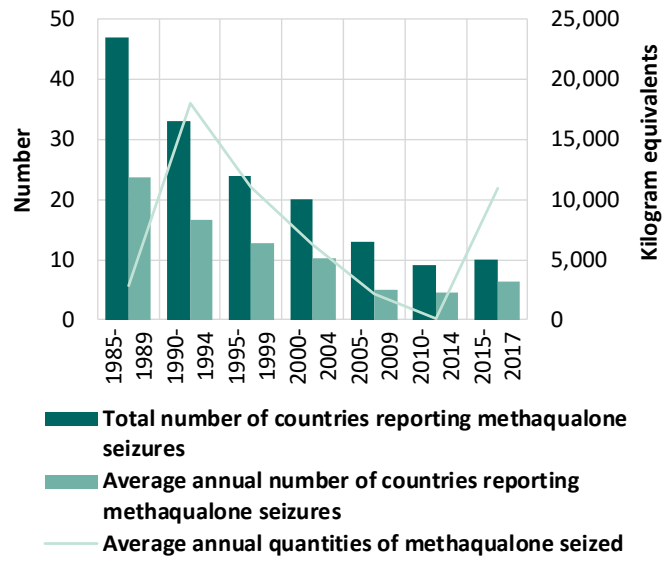
FIG. 49 Global quantities of sedatives and tranquillisers seized, 1998–2017



Source: UNODC, responses to the annual report questionnaire.

Note: GHB has been reported explicitly in the annual report questionnaire since 2003, benzodiazepines since 2007 and barbiturates since 2010. Prior to that, seizures of such substances were included under "other depressants".

FIG. 50 Countries reporting methaqualone seizures and quantities of methaqualone seized, 1985–2017



Source: UNODC, responses to the annual report questionnaire.

that year, the third-largest annual quantity ever reported. Annual methaqualone seizures in 2017 fell back to 4.5 tons, although that was still above the average over the period 2007–2016 (3.4 tons).

The licit manufacture of only very limited amounts

262 *WHO Expert Committee on Drug Dependence: Twenty-fifth Report*, WHO Technical Report Series, No. 775 (Geneva, World Health Organization, 1989).

263 *Psychotropic Substances: Statistics for 2016–Assessments of Annual Medical and Scientific Requirements for Substances in Schedules II, III and IV of the Convention on Psychotropic Substances of 1971* (E/INCB/2017/3), para. 27.

264 *WHO Expert Committee on Drug Dependence: Twenty-fifth Report*.

of methaqualone has been reported in recent years:[265] 10 g in the United States, and 2 g in Japan in 2017; 20 g in Switzerland in 2016; and 30 g in Canada in 2014.[266] As a result, it can be assumed that, in contrast to most other sedatives and tranquillizers, practically all of the methaqualone trafficked and seized in recent years has been illicitly manufactured.

While India appears to have been the main source of methaqualone destined for international illicit markets, a number of clandestine methaqualone laboratories have been dismantled in recent years in South Africa (eight in 2013 and eight in 2016). Authorities in Mozambique also reported the dismantling of a clandestine methaqualone laboratory in 2017.[267] This is a contrast to the period 2006–2009, when South Africa regularly reported that most of the methaqualone found on its market originated in China and, to a lesser extent, in India. No mentions of China, either by South Africa or any other country, were reported in subsequent years. Pertaining to 2015, the latest detailed report received from India confirmed that most of the methaqualone seized in that country continued to be destined for markets in East and Southern Africa. The United Republic of Tanzania accounted for 35 per cent of the total, and Zambia for another 8 per cent of all known destination countries. Almost a third of it was reported as destined for markets in South-East Asia (Malaysia, 30 per cent).

Benzodiazepines

The use of benzodiazepines for non-medical purposes as well as trafficking in benzodiazepines appear to be far more widespread than for methaqualone at the global level, even though the overall reported quantity seized was smaller than that of methaqualone in both 2016 and 2017.

A total of 36 benzodiazepines were under international control in 2018, of which 28 had a significant presence on the licit market in 2017.[268] Most benzodiazepines are listed in Schedule IV of the 1971 Convention. The licit manufacture of benzodiazepines was reported by 21 countries in 2016;[269] Italy, India, China and Brazil, in descending order of amounts manufactured, together accounted for more than 85 per cent of the total global manufacture of benzodiazepines in 2017.[270]

The largest licit manufacture of benzodiazepines in 2017 was of diazepam (47 tons), followed by chlordiazepoxide (19 tons) and oxazepam (14 tons). Expressed in S-DDD, the largest production was of alprazolam (9.5 billion S-DDD in 2017), followed by diazepam (4.8 billion S-DDD) and lorazepam (3.7 billion S-DDD).[271, 272] Those three substances are the most consumed benzodiazepines in the context of medical use,[273] and alprazolam and diazepam are the benzodiazepines most frequently found on illicit markets. In 2017, the most traded benzodiazepines worldwide, in terms of number of countries reporting their licit import, were diazepam, midazolam, clonazepam, alprazolam and lorazepam in 2017.[274]

Global licit manufacture of and trade in benzodiazepines decreased significantly in 2017. Manufacture of bromazepam and midazolam, for example, decreased by more than 70 and 25 per cent, respectively, from the previous year. Global stocks of diazepam and alprazolam decreased by 50 per cent each, while stocks of midazolam and clonazepam decreased by 18 and 30 per cent, respectively. As a result, the volume of imports and exports also decreased, with imports of diazepam decreasing by more than 40 per cent and midazolam by 50 per cent in 2017.[275]

In parallel to the reduction in the licit manufacture and trade in benzodiazepines, seizures of benzodiazepines also declined by more than 90 per cent from the previous year, following marked

265 *Psychotropic Substances: Statistics for 2017–Assessments of Annual Medical and Scientific Requirements for Substances in Schedules II, III and IV of the Convention on Psychotropic Substances of 1971* (E/INCB/2018/3), para. 177.

266 E/INCB/2017/3.

267 Country report submitted by Mozambique to the Twenty-eighth Meeting of Heads of National Drug Law Enforcement Agencies, Africa (UNODC/HONLAF/28/CRP.7).

268 E/INCB/2018/3.

269 E/INCB/2017/3.

270 E/INCB/2018/3.

271 Ibid.

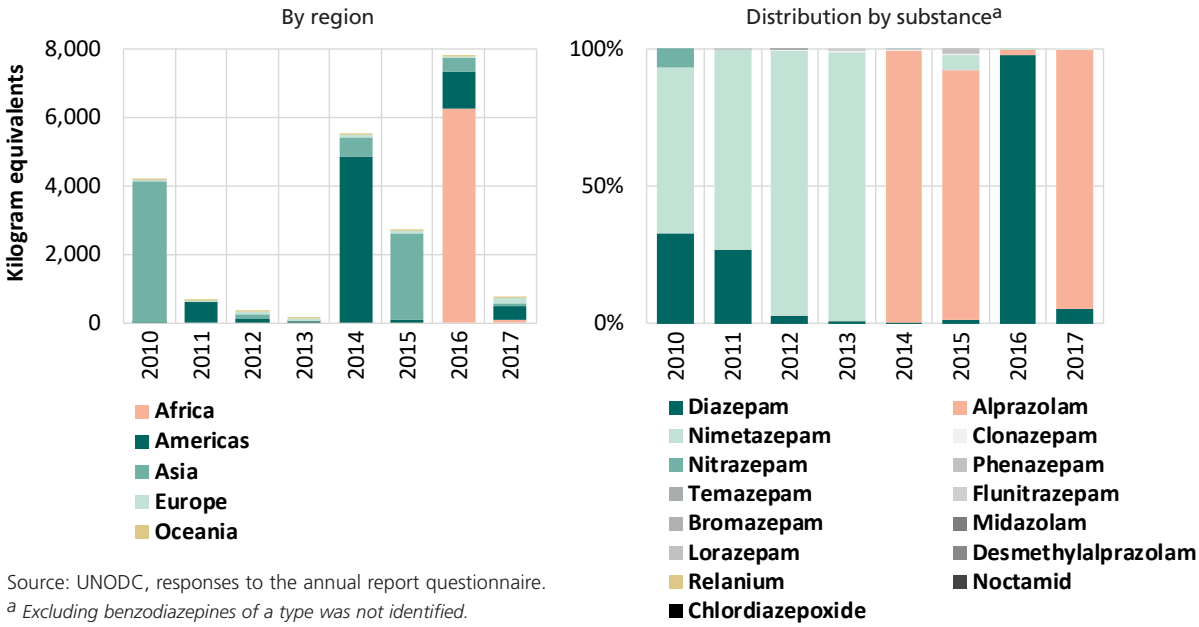
272 Ibid. E/INCB/2017/3.

273 Ibid.

274 E/INCB/2018/3.

275 Ibid.

FIG. 51 Global quantities of benzodiazepines seized, 2010–2017



Source: UNODC, responses to the annual report questionnaire.

[a] *Excluding benzodiazepines of a type was not identified.*

fluctuations over the years. The regions where most quantities seized were reported have also shifted over time. In 2010 and 2015, most seizures (measured in kg equivalents) were reported in Asia; in 2016, most quantities seized were reported in Africa; and in 2011, 2013 and 2017, in the Americas.

Record highs in quantities of specific benzodiazepines seized have been reported in recent years, including 4.8 tons of alprazolam (e.g. Xanax®) in 2014 and 6.3 tons of diazepam (e.g. Valium®) in 2016. For comparison, in 2016 the global licit manufacture of alprazolam and diazepam totalled 12.1 tons and 46.5 tons, respectively.[276] Overall, the licit manufacture of benzodiazepines (some 150 tons in 2017)[277] is substantially greater than global seizures of benzodiazepines (8 tons in 2016 and 0.7 tons in 2017). Since 2010, diazepam has been seized in larger quantities than any other benzodiazepine, although large quantities of alprazolam have also been intercepted in recent years.

One of the key benzodiazepines on illicit drug markets in the 1980s and the 1990s, flunitrazepam (e.g. Rohypnol®) is often used by heroin-dependent persons and as a drug facilitating sexual assault. It was transferred from Schedule IV to Schedule III of the 1971 Convention in 1995,[278] and remains the only benzodiazepine found in this schedule. In parallel, owing to its potential for abuse, several countries, including major manufacturers and importers of the substance, adopted strict control policies for it, in close cooperation with the pharmaceutical industry.[279]

Licit manufacture and diversions of the substance have declined markedly of late: global licit manufacture of flunitrazepam amounted to 590 kg in 2016 and 205 kg in 2017, down from nearly 2 tons in 2015.[280] Meanwhile, global flunitrazepam seizures fell from some 60 g in 2013 to just 0.2 g in 2017. Seizures of flunitrazepam were reported only by Canada, Taiwan Province of China and Kenya. France was the only country to report diversions of the substance over the period 2013–2017, suggesting that only small amounts of this benzodiazepine still enter global clandestine drug markets.

276 E/INCB/2017/3.

277 E/INCB/2018/3.

278 *WHO Expert Committee on Drug Dependence: Twenty-ninth Report*, WHO Technical Report Series, No. 856 (Geneva, World Health Organization, 1995).

279 E/INCB/2018/3 and previous years.

280 E/INCB/2017/3.

TABLE 2 Examples of trafficking routes of benzodiazepines with provenance or transit from abroad, 2013–2017

Substance	Country where the substance was seized	Countries mentioned as being of provenance or transit	Countries mentioned as destination
alprazolam	Indonesia	Malaysia, Thailand, United Arab Emirates and United States	Indonesia
phenazepam	Ukraine	Belarus, Bulgaria, Republic of Moldova and Russian Federation	Belarus, Republic of Moldova, Russian Federation and Ukraine
clonazepam	Azerbaijan	Georgia, Iran (Islamic Republic of) and Russian Federation	*n.a.*
	Finland	Estonia, Hungary and Sweden	Finland
	Latvia	Netherlands	Latvia and Sweden
nitrazepam	Bhutan	China	Bhutan
nimetazepam	Malaysia	Taiwan Province of China and Myanmar	Indonesia, Malaysia, Singapore and Thailand
	Indonesia	Taiwan Province of China and Malaysia	Indonesia
	Singapore	Malaysia	Singapore
	Brunei Darussalam	Malaysia	Brunei Darussalam
flunitrazepam	Belgium	Netherlands, Spain	*n.a.*
benzodiazepines (undistinguished)	Australia	China; Hong Kong, China; and Republic of Korea	*n.a.*
	Indonesia	China, and Hong Kong, China	Indonesia
	Sweden	China and India	Sweden
	Norway	Hungary, Spain and Thailand	Norway
	Romania	Serbia	Norway and Sweden

PSource: UNODC, responses to the annual report questionnaire.

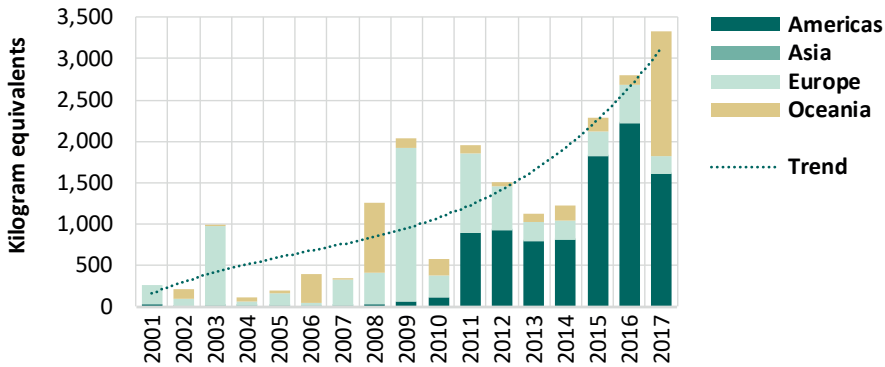
Note: n.a. information not available

The majority of benzodiazepines seized over the period 2013–2017 consisted of diazepam (in Africa), alprazolam (in the Americas and Asia) and clonazepam, followed by diazepam (in Europe). In total, five countries accounted for 92 per cent of the global quantity of benzodiazepines seized over that period: Nigeria and the United States, followed by Thailand, India and Canada.

In contrast to most other drugs, no clear trafficking patterns emerge from seizures of benzodiazepines. Most countries could not provide information about the origin of the benzodiazepines seized on their territory. When countries did identify a country of origin, it was often their country itself. Only a small number of countries identified other countries of provenance or transit of benzodiazepines over the period 2013–2017.

Although most seizures of benzodiazepines result from the diversion from licit manufacture, a small number of clandestine laboratories illicitly manufacturing benzodiazepines have been detected in recent years. In 2011 and 2015, Malaysia reported the dismantling of clandestine laboratories manufacturing nimetazepam. Canada, India and Sweden reported the dismantling of a total of six clandestine laboratories involved in the manufacture of alprazolam in the period 2013–2017. Sweden also reported the dismantling of a laboratory manufacturing flunitrazolam (a NPS benzodizepine) in 2017.

FIG. 52 Global quantities of GHB seized, by region, 2001–2017



Source: UNODC, responses to the annual report questionnaire.

gamma-Hydroxybutyric acid

GHB, also known on the street as "liquid ecstasy", was put under international control in 2001 and transferred from Schedule IV to Schedule II of the 1971 Convention in 2013[281] on the basis of a growing number of countries reporting problems,[282] in particular deaths linked to respiratory depression involving GHB, especially when taken together with alcohol,[283] as well as the use of GHB as a drug facilitating sexual assault.[284] There was also evidence that dependence on GHB exists in humans and withdrawal syndromes, including withdrawal seizures, have been reported. The non-medical use of GHB was reported mainly in the United States of America, Europe and Australia. [285]

The licit manufacture of GHB, which is used in the pharmaceutical industry and in the production of a variety of industrial polymers, has been increasing for some time, in particular since 2012, and reached a record high of 72 tons in 2016 (68 tons in 2017). International trade in GHB has continued to increase: in 2017, total reported imports of GHB amounted to 71 tons at the global level, up from 20 tons in 2015,[286] although it should also be noted that the reported global imports (71 tons in 2017) and exports (34 tons) do not match.[287]

At the same time, illicitly supplied GHB appears to have increased and seizures of GHB have shown a marked upward trend over the past 15 years, in particular since 2015, with the total quantity of GHB seized exceeding 3 tons in 2017. Over the period 2013–2017, countries in the Americas accounted for more than two thirds of the total global quantity of GHB seized, followed by countries in Oceania (19 per cent) and Europe (13 per cent), while seizures in Asia were comparatively small (0.1 per cent). No GHB seizures were reported in Africa.

A total of 32 countries reported seizures of GHB over the period 2013–2017, with the largest quantities seized reported in the Americas: the United States (also the leading licit manufacturer of GHB worldwide in 2016 and previous years), followed by Canada and Argentina. In Oceania, the largest quantity of GHB was intercepted in Australia, followed by New Zealand. In Europe, the largest quantities seized were reported by Norway, followed by Poland, Belgium, Sweden and Switzerland.

281 *WHO Expert Committee on Drug Dependence: Thirty-fifth Report*, WHO Technical Report Series, No. 973 (Geneva, World Health Organization, 2012).

282 Ibid.

283 E/INCB/2017/3, para. 27.

284 Lawrence P. Carter and others, "Illicit gamma-hydroxybutyrate (GHB) and pharmaceutical sodium oxybate (Xyrem®): differences in characteristics and misuse, *Drug and Alcohol Dependence*, vol. 104, Nos. 1–2 (September 2009), pp. 1–10.

285 *WHO Expert Committee on Drug Dependence: Thirty-fifth Report*.

286 E/INCB/2017/3, para. 28.

287 E/INCB/2018/3.

Barbiturates

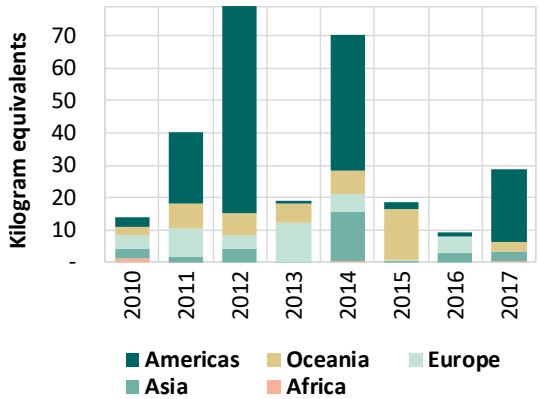
Overall, 12 different barbiturates are under international control, under schedules II, III and IV of the 1971 Convention.[288]

Quantities of barbiturates seized, although fluctuating, have been substantially smaller than those of benzodiazepines, which reflects the fact that far more benzodiazepines than barbiturates are manufactured and traded at the global level. While an annual average of 3.4 tons of benzodiazepines were seized over the period 2013–2017, seizures of barbiturates amounted to less than 600 kg per year.

Over the period 2013–2017, most data on barbiturates seized do not specify the substance involved, except in the case of phenobarbital. In the period 2010–2012, phenobarbital, barbital, pentobarbital, pentobarbitone and secobarbital were also explicitly mentioned among the substances seized. This seems to be in line with the licit manufacture of barbiturates: in 2017, phenobarbital accounted for 73 per cent of global manufacture of all barbiturates, followed by barbital (11 per cent) and pentobarbital (8 per cent).[289] Global licit manufacture of the seven barbiturates most commonly seen on international markets amounted to 356 tons in 2017.

Of the barbiturates seized over the period 2013–2017, 47 per cent of the total quantity was reported in the Americas (mostly the United States, followed by Canada and Argentina), 22 per cent in Oceania (mostly Australia), 16 per cent in Europe (mostly Portugal and the Russian Federation), 15 per cent in Asia (mostly India, followed by Indonesia, Tajikistan, Myanmar and Japan) and 1 per cent in Africa (mostly Zambia, followed by Senegal).

FIG. 53 Quantities of barbiturates seized, by region, 2010–2017



Source: UNODC, responses to the annual report questionnaire.

Not much is known about the trafficking routes for barbiturates, with the Russian Federation being the only country to report information: in 2016, most of the barbiturates (that is, phenobarbital) seized in the Russian Federation had departed from China and Ukraine with the Russian Federation as final destination. According to INCB, China continued to be the leading licit manufacturer of barbiturates, accounting for 49 per cent of total manufacture of the entire group of barbiturates in 2017, followed by India (24 per cent) and the United States (10 per cent).[290]

288 E/INCB/2017/3, para. 141.
289 E/INCB/2018/3, para. 61.
290 E/INCB/2018/3, p. 43.

TABLE 3 Annual prevalence of the use of opioids, by region and globally, 2017

	Number of users annually (best estimate)	Estimated number of users annually (lower)	Estimated number of users annually (upper)	Per cent of population aged 15–64 years (best estimate)	Per cent of population aged 15–64 years (lower)	Per cent of population aged 15–64 years (upper)
Africa	**6,080,000**	**5,000,000**	**7,390,000**	**0.87**	**0.71**	**1.06**
Eastern Africa	-	-	-	-	-	-
Northern Africa	360,000	120,000	660,000 -	0.25	0.08	0.46-
Southern and South-Eastern Africa	-	-	-	-	-	-
West and Central Africa	-	-	-	-	-	-
Americas	**13,600,000**	**11,980,000**	**16,320,000**	**2.03**	**1.79**	**2.43**
Caribbean	-	-	-	-	-	-
Central America (excluding Mexico)	-	-	-	-	-	-
Northern America (including Mexico)	12,830,000	11,640,000	13,720,000	3.96	3.60	4.24
South America	580,000	250,000	2,180,000	0.20	0.09	0.76
Asia	**29,460,000**	**26,280,000**	**31,910,000**	**0.98**	**0.88**	**1.06**
Central Asia and Transcaucasia	540,000	480,000	600,000	0.93	0.83	1.03-
East and South-East Asia	3,280,000	2,330,000	4,010,000	0.20	0.15	0.25
Near and Middle East/South-West Asia	6,950,000	4,910,000	8,550,000	2.28	1.61	2.81
Southern Asia	18,680,000	-	-	1.81	-	-
Europe	**3,570,000**	**3,330,000**	**3,830,000**	**0.66**	**0.61**	**0.70**
Eastern and South-Eastern Europe (including Turkey)	1,730,000	1,660,000	1,810,000	0.77	0.74	0.80
Western and Central Europe	1,840,000	1,670,000	2,020,000	0.58	0.52	0.63
Oceania	**650,000**	**570,000**	**730,000**	**2.48**	**2.18**	**2.79**
Australia and New Zealand	630,000	570,000	680,000	3.28	2.98	3.58
Melanesia	-	-	-	-	-	-
Micronesia	-	-	-	-	-	-
Polynesia	-	-	-	-	-	-
Global	**53,350,000**	**47,160,000**	**60,180,000**	**1.08**	**0.96**	**1.22**

Source: UNODC estimates based on annual report questionnaire data and other official sources.

TABLE 4 Annual prevalence of the use of opiates, by region and globally, 2017

	Number of users annually (best estimate)	Estimated number of users annually (lower)	Estimated number of users annually (upper)	Per cent of population aged 15–64 years (best estimate)	Per cent of population aged 15–64 years (lower)	Per cent of population aged 15–64 years (upper)
Africa	**1,470,000**	**530,000**	**2,800,000**	**0.21**	**0.08**	**0.40**
Eastern Africa	-	-	-	-	-	-
Northern Africa	360,000	120,000	660,000 -	0.25	0.08	0.46-
Southern and South-Eastern Africa	-	-	-	-	-	-
West and Central Africa	-	-	-	-	-	-
Americas	**2,690,000**	**1,970,000**	**3,480,000**	**0.40**	**0.29**	**0.52**
Caribbean	-	-	-	-	-	-
Central America (excluding Mexico)	-	-	-	-	-	-
Northern America (including Mexico)	2,400,000	1,790,000	2,970,000	0.74	0.55	0.92
South America	240,000	150,000	330,000	0.08	0.05	0.12
Asia	**21,730,000**	**18,970,000**	**24,570,000**	**0.72**	**0.63**	**0.82**
Central Asia and Transcaucasia	520,000	470,000	580,000	0.90	0.80	1.00
East and South-East Asia	3,280,000	2,330,000	4,010,000	0.20	0.14	0.25
Near and Middle East/South-West Asia	4,930,000	3,300,000	6,910,000	1.62	1.08	2.27
Southern Asia	12,990,000	-	-	1.26	-	-
Europe	**3,220,000**	**3,010,000**	**3,600,000**	**0.59**	**0.55**	**0.66**
Eastern and South-Eastern Europe (including Turkey)	1,490,000	1,410,000	1,570,000	0.66	0.63	0.70
Western and Central Europe	1,740,000	1,590,000	2,030,000	0.54	0.50	0.64
Oceania	**40,000**	**40,000**	**70,000**	**0.16**	**0.14**	**0.28**
Australia and New Zealand	35,000	35,000	41,000	0.18	0.18	0.22
Melanesia	-	-	-	-	-	-
Micronesia	-	-	-	-	-	-
Polynesia	-	-	-	-	-	-
Global	**29,160,000**	**24,510,000**	**34,520,000**	**0.59**	**0.50**	**0.70**

Source: UNODC estimates based on annual report questionnaire data and other official sources.

TABLE 5 Illicit cultivation of opium poppy, 2007–2018 (hectares)

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
SOUTH-WEST ASIA												
Afghanistan (best estimate)	193,000	157,000	123,000	123,000	131,000	154,000	209,000	224,000	183,000	201,000	328,000	263,000
lower bound [a]			102,000	104,000	109,000	125,000	173,000	196,000	163,000	182,000	301,000	242,000
upper bound [a]			137,000	145,000	155,000	189,000	238,000	247,000	202,000	221,000	355,000	283,000
SOUTH-EAST ASIA												
Lao People's Democratic Republic (best estimate) [b]	1,500	1,600	1,900	3,000	4,100	6,800	3,900	6,200	5,700	..	..	..
lower bound [a]	1,230	710	1,100	1,900	2,500	3,100	1,900	3,500	3,900			
upper bound [a]	1,860	2,700	2,700	4,000	6,000	11,500	5,800	9,000	7,600			
Myanmar (best estimate) [b]	27,700	28,500	31,700	38,100	43,600	51,000	57,800	57,600[c]	55,500[c]	..	41,000	37,300[c]
lower bound [a]	22,500	17,900	20,500	17,300	29,700	38,249	45,710	41,400	42,800		30,200	29,700
upper bound [a]	32,600	37,000	42,800	58,100	59,600	64,357	69,918	87,300	69,600		51,900	47,200
SOUTH AND CENTRAL AMERICA												
Colombia (best estimate)	715	394	356	341	338	313	298	387	595	462	282	..
Mexico (best estimate) [b, d, f, h]	6,900	15,000	19,500	14,000	12,000	10,500	11,000	17,000	26,100	25,200	30,600	..
lower bound [a]									21,800	20,400	22,800	
upper bound [a]									30,400	30,000	38,400	

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
OTHER												
Other countries [e]	**5,885**	**10,509**	**9,479**	**12,221**	**16,462**	**12,282**	**13,293**	**11,522**	**10,597**	**68,139**	**14,589**	***45,471***
TOTAL (best estimate)	235,700	213,003	185,935	190,662	207,500	234,895	295,291	316,709	281,492	294,801	414,471	*345,771*
lower bound			**152,935**	**149,762**	**170,000**	**189,444**	**245,201**	**269,809**	**242,692**	**256,501**	**367,251**	***307,751[g]***
upper bound			**211,835**	**233,662**	**249,400**	**287,952**	**338,309**	**372,209**	**320,792**	**335,601**	**462,251**	***385,551[g]***
TOTAL (best estimate, rounded)	**235,700**	**213,000**	**185,900**	**190,700**	**207,500**	**234,900**	**295,300**	**316,700**	**281,500**	**294,800**	**414,500**	***345,800[g]***

Sources: Afghanistan, Lao People's Democratic Republic and Myanmar: national illicit crop monitoring system supported by the United Nations Office on Drugs and Crime (UNODC). Colombia: Government of Colombia. Mexico: up to 2014, estimates derived from surveys by the Government of the United States of America (international narcotics control strategy reports); for 2015 and onwards, joint Mexico/UNODC project entitled "Monitoring of the illicit cultivation on Mexican territory".

Note: Figures in italics are preliminary and may be revised when updated information becomes available. Two dots indicate that data were unavailable. Information on estimation methodologies and definitions can be found in the online methodology section of the World Drug Report 2019.

[a] *Bound of the statistically derived confidence interval.*
[b] *May include areas that were eradicated after the date of the area survey.*
[c] *Estimates for 2014, 2015 and 2018 included satellite image estimates for Kayah and Chin states. National estimates for these years are therefore not directly comparable with the other years.*
[d] *Up to 2014, the estimates for Mexico are sourced from the Department of State of the United States. The Government of Mexico does not validate the estimates provided by the United States as they are not part of its official figures and it does not have information on the methodology used to calculate them.*
[e] *Includes countries with low levels of cultivation (with less than 400 hectares in at least two of the last three years) and countries with indirect evidence of illicit cultivation (eradication of opium poppy) but no direct measurement. See table "Cultivation of opium poppy and production of opium in other countries, and eradication of opium poppy, 2008–2018".*
In addition, for 2016, 2017 and 2018, best estimates for countries for which data are not available (Lao People's Democratic Republic, Myanmar for 2016 and Mexico and Colombia for 2018) are included in this category.
Starting in 2008, a new methodology was introduced to estimate opium poppy cultivation and opium/heroin production in countries with no data on illicit cultivation of opium poppy. A detailed description of the estimation methodology is available in the online methodology section of the World Drug Report 2019.
[f] *The figures for 2015, as published in the World Drug Report 2016 (United Nations publication, Sales No. E.16.XI.7), have been revised owing to a statistical adjustment processed by UNODC. These figures are based on the estimation period July 2014-June 2015.*
[g] *Preliminary estimates for 2018; they may change as more country estimates will become available.*
[h] *The figures for 2016 and 2017 are based on the estimation periods July 2015–June 2016 and June 2016–July 2017 respectively.*

TABLE 6 Potential production of oven–dry opium, 2007–2018 (tons)

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
SOUTH-WEST ASIA												
Afghanistan (best estimate)	7,400	5,900	4,000	3,600	5,800	3,700	5,500	6,400	3,300	4,800	9,000	6,400
lower bound [a]				3,000	4,800	2,800	4,500	5,100	2,700	4,000	8,000	5,600
upper bound [a]				4,200	6,800	4,200	6,500	7,800	3,900	5,600	10,000	7,200
SOUTH-EAST ASIA												
Lao People's Democratic Republic (best estimate) [b, f]	9	10	11	18	25	41	23	92	..	..	..	..
lower bound [g]	7	4	7	11	15	18	11	51	84			
upper bound [g]	11	16	16	24	36	69	35	133	176			
Myanmar (best estimate) [b]	460	410	330	580	610	690	870	670[h]	647	..	550	520
lower bound			213	350	420	520	630	481	500		395	410
upper bound			445	820	830	870	1,100	916	820		706	664
LATIN AMERICA												
Colombia (best estimate)	14	10	9	8	8	8	11	12	17	13	7	..
Mexico (best estimate) [c, e]	150	325	425	300	250	220	225	360	*499*	*482*	*586*	..
lower bound									*279*	*261*	*292*	
upper bound									*693*	*684*	*876*	
OTHER												
Other countries (best estimate) [d]	58	187	178	224	290	172	182	198	178	888	272	*870*

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
TOTAL (best estimate)	8,091	6,841	4,953	4,730	6,983	4,831	6,810	7,732	4,771	6,184	10,415	*7,790*
lower bound				**3,894**	**5,783**	**3,738**	**5,558**	**6,202**	**3,758**	**4,973**	**8,920**	***6,540***
upper bound				**5,576**	**8,214**	**5,539**	**8,052**	**9,419**	**5,784**	**7,391**	**11,907**	***9,070***
TOTAL best estimate (rounded)	**8,090**	**6,840**	**4,950**	**4,730**	**6,980**	**4,830**	**6,810**	**7,730**	**4,770**	**6,180**	**10,410**	***7,790***

Sources: Afghanistan, Lao People's Democratic Republic and Myanmar: national illicit crop monitoring system supported by the United Nations Office on Drugs and Crime (UNODC). Colombia: National illicit crop monitoring system supported by UNODC. Since 2008, production was calculated based on updated regional yield figures and conversion ratios from the Department of State and the Drug Enforcement Administration of the United States of America. Mexico: up to 2014, estimates derived from surveys by the United States Government; for 2015 and onwards, UNODC estimate.

Note: Figures in italics are preliminary and may be revised when updated information becomes available. Two dots indicate that data were unavailable. Information on estimation methodologies and definitions can be found in the online methodology section of the World Drug Report 2019.

[a] *Bound of the statistically derived confidence interval.*

[b] *Based on cultivation figures which may include areas eradicated after the date of the area survey.*

[c] *Up to 2014, the estimates are sourced from the Department of State of the United States. The Government of Mexico does not validate the estimates provided by the United States as they are not part of its official figures and it does not have information on the methodology used to calculate them.*

[d] *Includes countries with low levels of cultivation and countries with indirect evidence of illicit cultivation (eradication of opium poppy) but no direct measurement.* See table "Cultivation of opium poppy and production of opium in other countries, and eradication of opium poppy, 2008–2018".

In addition, for 2016, 2017 and 2018, best estimates for countries for which data are not available (Lao People's Democratic Republic, Myanmar for 2016 and Mexico and Colombia for 2018) are included in this category.

Starting in 2008, a new methodology was introduced to estimate opium poppy cultivation and opium/heroin production in countries with no data on illicit cultivation of opium poppy. These estimates are higher than the previous figures but have a similar order of magnitude. A detailed description of the estimation methodology is available in the online methodology section of the World Drug Report 2019.

[e] *The figures for 2015, as published in the World Drug Report 2016 (United Nations publication, Sales No. E.16.XI.7), have been revised owing to a statistical adjustment processed by UNODC. The Government of Mexico does not validate any opium production estimates. The production figures will be presented once yield data from the joint Mexico/UNODC project entitled "Monitoring of the illicit cultivation on Mexican territory" become available. Opium production figures estimated by UNODC for 2015–2017 are based on: (a) the area under cultivation, established by the joint project of the Government of Mexico and UNODC; (b) yield data, based on yield studies conducted by the United States in Mexico over the period 2001–2003. The opium production figures shown for 2015–2017 are preliminary and, for methodological reasons, are not comparable with the production figures over the period 1998–2014.*

[f] *Owing to the late timing of the monitoring activities in 2013, the survey may not have captured illicit cultivation in this year in its entirety.*

[g] *Bound of the statistically derived confidence interval, with the exception of 2015. The figures for 2015 represent independently derived upper and lower estimates; the midpoint was used for the calculation of the global total.*

[h] *Estimates for 2014, 2015 and 2018 include estimates for Kayah and Chin states. National estimates for these years are therefore not directly comparable with the other years.*

TABLE 7 Cultivation of opium poppy and production of opium in other countries, and eradication of opium poppy, 2008–2018

Country	Indicator	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Guatemala	Cultivation (hectares)					220	310	640	260	310	700	
Guatemala	Production (tons)					4	6	14	6	6	15	
Pakistan	Cultivation (hectares)	1,909	1,779	1,721	362	382	493	217	372	130	90	
Pakistan	Production (tons)	48	44	43	9	9	12	5	9	3	2	
Thailand	Cultivation (hectares)	288	211	289	289	209	265			399		
Thailand	Production (tons)	5	3	5	6	3	4					
Afghanistan	Eradication (hectares)	5,480	5,351	2,316	3,810	9,672	7,348	2,692	3,760	355	750	406
Algeria	Eradication (plants)			868	340	204	2,721	7,470				
Algeria	Seizure poppy plants (in kg equivalents)	7,761	962	87	34	20.4	272.1			106		
Argentina	Seizure poppy plants (in kg equivalents)									0.2		
Armenia	Seizure poppy plants (in kg equivalents)							0.18	0.13	60		
Australia	Seizure poppy plants (in kg equivalents)									37	264	
Austria	Seizure poppy plants (in kg equivalents)	8.76	13.83		4.60	1.91	2.07	1.41		0.05	0.2	
Azerbaijan	Eradication (hectares)				2.26	0.21	0.40	0.45				
Azerbaijan	Eradication (plants)				201	2,628	34	284			49,154	
Bangladesh	Eradication (hectares)			8	22							

Country	Indicator	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Bangladesh	Seizure poppy plants (in kg equivalents)		145,021									
Belarus	Eradication (hectares)			14	52	26				92	157	
Belarus	Seizure poppy plants (in kg equivalents)				59		81	51		94	119	
Canada	Eradication (hectares)			7	7							
Canada	Eradication (plants)			60,000	60,000							
Canada	Seizure poppy plants (in kg equivalents)			6,600	9.3		7.3			85.9		
China	Eradication (hectares)									6		
Colombia	Eradication (hectares)	381	546	712	294	320	514	813	613	450	397	
Cyprus	Seizure poppy plants (in kg equivalents)								6			
Czechia	Seizure poppy plants (in kg equivalents)								40			
Ecuador	Eradication (plants)	74,555	115,580	128,653	22,100	2,170,900	1,797,966	2,023,385	183,573	1,207,147	279,074	
Ecuador	Seizure poppy plants (in kg equivalents)	7,456	11,558	12,865	2,210	185,490	75,765					
Egypt	Eradication (hectares)	121	98	222	1		3		98	105	60	
Georgia	Seizure poppy plants (in kg equivalents)							8		9		
Greece	Eradication (plants)					192	60	144	145	624	44	
Guatemala	Eradication (hectares)	536	1,345	918	1,490	590	2,568	1,197	430	45	803	
Guatemala	Eradication (plants)									17,643,447	417,004,278	

Country	Indicator	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Guatemala	Seizure poppy plants (in kg equivalents)	27,880,441	69,228,416	54,612,442			10,935,532	864,150				
Hungary	Seizure poppy plants (in kg equivalents)					1,502	2,152			1917		
India	Eradication (hectares)	624	2,420	3,052	5,746	1,332	865	1,636	3,461	2,875	3,076	
India	Seizure poppy plants (in kg equivalents)							3,770				
Iran (Islamic Republic of)	Eradication (hectares)			2		1	1	1		1	0.5	
Iran (Islamic Republic of)	Eradication (plants)					140,000	100,000	120,000		90,000	90,000	
Italy	Eradication (plants)			1,797	2,007	6,717						
Italy	Seizure poppy plants (in kg equivalents)					716	375	168	30	1,098		
Japan	Seizure poppy plants (in kg equivalents)	535	104	90	26	20	11					
Kazakhstan	Eradication (hectares)									0.2		
Kazakhstan	Eradication (plants)				1,692			2,254	19,510	15,515		
Kazakhstan	Seizure poppy plants (in kg equivalents)	68	127	105	90	30	2	8	298			
Kyrgyzstan	Seizure poppy plants (in kg equivalents)	102	344	58	200	399	147	63	55			
Lao PDR	Eradication (hectares)	575	651	579	662	707	397		809			
Latvia	Seizure poppy plants (in kg equivalents)	23	31		1	12	7	9	43			
Lebanon	Eradication (hectares)		21	14	4		6	1				

Country	Indicator	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Lithuania	Seizure poppy plants (in kg equivalents)	45	16									
Mexico	Eradication (hectares)	13,095	14,753	15,491	16,389	15,726	14,662	21,644	26,426	22,437	29,692	
Mexico	Seizure poppy plants (in kg equivalents)	7,263	7,964	9,335	10,101	9,572	10,209	14,812	17,948	16,401	20,187	
Myanmar	Eradication (hectares)	4,820	4,087	8,267	7,058	23,718	12,288	15,188	13,450	7,561	3,533	2,605
Nepal	Eradication (hectares)	21	35									
New Zealand	Seizure poppy plants (in kg equivalents)										0.2	
Oman	Eradication (hectares)						6					
Pakistan	Eradication (hectares)	0	105	68	1,053	592	568	1,010	605	1,470	169	
Pakistan	Seizure poppy plants (in kg equivalents)	81,675	25,550				4,650	5,976	4,576	1,023	4,789	
Peru	Eradication (hectares)	23	32	21								
Poland	Eradication (hectares)		9									
Portugal	Seizure poppy plants (in kg equivalents)				164		1.6	9.4			0.4	
Republic of Korea	Eradication (plants)						25,369					
Republic of Korea	Seizure poppy plants (in kg equivalents)			3,855					8,013	9,771	10,040	
Republic of Moldova	Eradication (plants)				32,413	11,255						
Republic of Moldova	Seizure poppy plants (in kg equivalents)	79	26,075									
Russian Federation	Eradication (hectares)		3.3		1.4	0.6	0.9	1.1	0.6	0.8	2.4	

Country	Indicator	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Russian Federation	Eradication (plants)							645				
Russian Federation	Seizure poppy plants (in kg equivalents)	2,799	2,807	2,575	4,273	3,196	2,216	1,438	1,043	270	375	
Spain	Seizure poppy plants (in kg equivalents)			13		10	30	219		0.02	0.5	
State of Palestine	Seizure poppy plants (in kg equivalents)				4.2	5.8	1.2	17.8				
Tajikistan	Eradication (plants)				13	5,400	103					
Thailand	Eradication (hectares)	285	201	278	208	205	264			319		
Ukraine	Eradication (hectares)	28		436			39		48	164		
Ukraine	Eradication (plants)			1,185,118		474,000	22,800,000					
Ukraine	Seizure poppy plants (in kg equivalents)	164,000		4,162		7.4		384	930			
Uzbekistan	Eradication (hectares)				1		1	0.3	0.3	0.3	0.3	
Uzbekistan	Seizure poppy plants (in kg equivalents)	138	687	896	413	330	336	406	205	863	188	
Viet Nam	Eradication (hectares)	99	31		38	35	25	19	18			

Source: United Nations Office on Drugs and Crime annual report questionnaire, government reports, reports of regional bodies, and international narcotics control strategy reports of the United States of America.

TABLE 8 Global manufacture of heroin from global illicit opium production, 2007–2018 (tons)

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Total potential opium production	8,091	6,841	4,953	4,730	6,983	4,831	6,810	7,723	4,771	6,180	*10,420*	*7,790*
Potential opium not processed into heroin	3,078	2,360	1,680	1,728	3,400	1,850	2,600	2,450	1,360	2,510	*1,100-1,400*	*1,225-1,525*
Potential opium processed into heroin	5,012	4,481	3,273	3,002	3,583	2,981	4,210	5,273	3,411	3,670	*9,020-9,320*	*6,265-6,565*
Total potential heroin manufacture	686	600	427	383	467	377	555	542	327	388	*692-1042*	*487-737*

Notes: The calculation shows the potential amount of heroin that could have been manufactured out of the opium produced in a given year; it does not take into account changes in opium inventories, which may add to or reduce the amount of heroin entering the market in that year. Afghanistan and Myanmar are the only countries for which the proportion of potential opium production not converted into heroin within the country is estimated. For all other countries, for the purposes of this table, it is assumed that all opium produced is converted into heroin.

The amount of heroin produced from Afghan opium is calculated using two parameters that may change: (a) the amounts of opium consumed as raw opium in the region; and (b) the conversion ratio into heroin. The first parameter's estimate is based on consumption data in Afghanistan and neighbouring countries. For the second parameter, from 2005 to 2013, a conversion ratio of opium to morphine/heroin of 7:1 was used, based on interviews conducted with Afghan morphine/heroin "cooks", on an actual heroin production exercise conducted by two (illiterate) Afghan heroin "cooks", documented by the German Bundeskriminalamt in Afghanistan in 2003 (published in Bulletin on Narcotics, vol. LVII, Nos. 1 and 2, 2005, pp. 11-31), and United Nations Office on Drugs and Crime (UNODC) studies on the morphine content of Afghan opium (12.3 per cent over the period 2010-2012, down from 15 per cent over the period 2000-2003). Starting from 2014, a different approach to the conversion was adopted, reflecting updated information on morphine content and a different method for taking purity into account. The revised approach uses a ratio of 18.5 kg of opium for 1 kg of 100 per cent pure heroin base (see Afghanistan Opium Survey 2014, UNODC, November 2014). This translates into a ratio of 9.2-12.9 kg (range: 9-14 kg) of opium for 1 kg of export-quality heroin of 50 – 70 per cent purity. For more details, see "Afghanistan Opium Survey 2017 – Challenges to sustainable development, peace and security" (UNODC, May 2018).

The amount of heroin produced in Myanmar in 2018 was calculated by subtracting the estimated unprocessed opium for consumption from the total opium production and using a conversion factor of 10:1. The unprocessed opium in Myanmar was estimated to be 125 tons in 2018, based on the total unprocessed opium in East Asia (TOCTA EAP report, 2013) and considering the relative cultivation levels of Lao PDR and Myanmar. For further information, please refer to the Methodology chapter (section 4.3) of the Myanmar Opium Survey 2018 (UNODC, January 2019).

For countries other than Afghanistan, a "traditional" conversion ratio of opium to heroin of 10:1 is used. The ratios will be adjusted when improved information becomes available. Figures in italics are preliminary and may be revised when updated information becomes available.

GLOSSARY

amphetamine-type stimulants — a group of substances composed of synthetic stimulants controlled under the Convention on Psychotropic Substances of 1971 and from the group of substances called amphetamines, which includes amphetamine, methamphetamine, methcathinone and the "ecstasy"-group substances (3,4-methylenedioxymethamphetamine (MDMA) and its analogues).

amphetamines — a group of amphetamine-type stimulants that includes amphetamine and methamphetamine.

annual prevalence — the total number of people of a given age range who have used a given drug at least once in the past year, divided by the number of people of the given age range, and expressed as a percentage.

coca paste (or coca base) — an extract of the leaves of the coca bush. Purification of coca paste yields cocaine (base and hydrochloride).

"crack" cocaine — cocaine base obtained from cocaine hydrochloride through conversion processes to make it suitable for smoking.

cocaine salt — cocaine hydrochloride.

drug use — use of controlled psychoactive substances for non-medical and non-scientific purposes, unless otherwise specified.

fentanyls — fentanyl and its analogues.

new psychoactive substances — substances of abuse, either in a pure form or a preparation, that are not controlled under the Single Convention on Narcotic Drugs of 1961 or the 1971 Convention, but that may pose a public health threat. In this context, the term "new" does not necessarily refer to new inventions but to substances that have recently become available.

opiates — a subset of opioids comprising the various products derived from the opium poppy plant, including opium, morphine and heroin.

opioids — a generic term that refers both to opiates and their synthetic analogues (mainly prescription or pharmaceutical opioids) and compounds synthesized in the body.

problem drug users — people who engage in the high-risk consumption of drugs. For example, people who inject drugs, people who use drugs on a daily basis and/or people diagnosed with drug use disorders (harmful use or drug dependence), based on clinical criteria as contained in the *Diagnostic and Statistical Manual of Mental Disorders* (fifth edition) of the American Psychiatric Association, or the *International Classification of Diseases and Related Health Problems* (tenth revision) of WHO.

people who suffer from drug use disorders/people with drug use disorders — a subset of people who use drugs. Harmful use of substances and dependence are features of drug use disorders. People with drug use disorders need treatment, health and social care and rehabilitation.

harmful use of substances — defined in the *International Statistical Classification of Diseases and Related Health Problems* (tenth revision) as a pattern of use that causes damage to physical or mental health.

dependence — defined in the *International Statistical Classification of Diseases and Related Health Problems* (tenth revision) as a cluster of physiological, behavioural and cognitive phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state.

substance or drug use disorders — referred to in the *Diagnostic and Statistical Manual of Mental Disorders* (fifth edition) as patterns of symptoms resulting from the repeated use of a substance despite experiencing problems or impairment in daily life as a result of using substances. Depending on the number of symptoms identified, substance use disorder may be mild, moderate or severe.

prevention of drug use and treatment of drug use disorders — the aim of "prevention of drug use" is to prevent or delay the initiation of drug use, as well as the transition to drug use disorders. Once a person develops a drug use disorder, treatment, care and rehabilitation are needed.

REGIONAL GROUPING

The *World Drug Report* uses a number of regional and subregional designations. These are not official designations, and are defined as follows:

- East Africa: Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Mauritius, Rwanda, Seychelles, Somalia, South Sudan, Uganda, United Republic of Tanzania and Mayotte
- North Africa: Algeria, Egypt, Libya, Morocco, Sudan and Tunisia
- Southern Africa: Angola, Botswana, Eswatini, Lesotho, Malawi, Mozambique, Namibia, South Africa, Zambia, Zimbabwe and Reunion
- West and Central Africa: Benin, Burkina Faso, Cabo Verde, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Sao Tome and Principe, Senegal, Sierra Leone, Togo and Saint Helena
- Caribbean: Antigua and Barbuda, Bahamas, Barbados, Cuba, Dominica, Dominican Republic, Grenada, Haiti, Jamaica, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Trinidad and Tobago, Anguilla, Aruba, Bonaire, Netherlands, British Virgin Islands, Cayman Islands, Curaçao, Guadeloupe, Martinique, Montserrat, Puerto Rico, Saba, Netherlands, Sint Eustatius, Netherlands, Sint Maarten, Turks and Caicos Islands and United States Virgin Islands
- Central America: Belize, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua and Panama
- North America: Canada, Mexico, United States of America, Bermuda, Greenland and Saint-Pierre and Miquelon
- South America: Argentina, Bolivia (Plurinational State of), Brazil, Chile, Colombia, Ecuador, Guyana, Paraguay, Peru, Suriname, Uruguay, Venezuela (Bolivarian Republic of) and Falkland Islands (Malvinas)
- Central Asia and Transcaucasia: Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan and Uzbekistan
- East and South-East Asia: Brunei Darussalam, Cambodia, China, Democratic People's Republic of Korea, Indonesia, Japan, Lao People's Democratic Republic, Malaysia, Mongolia, Myanmar, Philippines, Republic of Korea, Singapore, Thailand, Timor-Leste, Viet Nam, Hong Kong, China, Macao, China, and Taiwan Province of China
- South-West Asia: Afghanistan, Iran (Islamic Republic of) and Pakistan
- Near and Middle East: Bahrain, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, State of Palestine, Syrian Arab Republic, United Arab Emirates and Yemen
- South Asia: Bangladesh, Bhutan, India, Maldives, Nepal and Sri Lanka
- Eastern Europe: Belarus, Republic of Moldova, Russian Federation and Ukraine
- South-Eastern Europe: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Montenegro, North Macedonia, Romania, Serbia, Turkey and Kosovo
- Western and Central Europe: Andorra, Austria, Belgium, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Monaco, Netherlands, Norway, Poland, Portugal, San Marino, Slovakia, Slovenia, Spain, Sweden, Switzerland, United Kingdom of Great Britain and Northern Ireland, Faroe Islands, Gibraltar and Holy See

Oceania (comprising four subregions):

- Australia and New Zealand: Australia and New Zealand
- Polynesia: Cook Islands, Niue, Samoa, Tonga, Tuvalu, French Polynesia, Tokelau and Wallis and Futuna Islands
- Melanesia: Fiji, Papua New Guinea, Solomon Islands, Vanuatu and New Caledonia
- Micronesia: Kiribati, Marshall Islands, Micronesia (Federated States of), Nauru, Palau, Guam and Northern Mariana Islands

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UNODC Research

The *World Drug Report 2019* is again presented in five separate parts that divide the wealth of information and analysis contained in the report into individual reader-friendly booklets in which drugs are grouped by their psychopharmacological effect for the first time in the report's history.

Booklet 1 provides a summary of the four subsequent booklets by reviewing their key findings and highlighting policy implications based on their conclusions. Booklet 2 contains a global overview of the latest estimates of and trends in the supply, use and health consequences of drugs. Booklet 3 looks at recent trends in the market for depressants (including opioids, sedatives, tranquillizers and hypnotics), while Booklet 4 deals with recent trends in the market for stimulants (including cocaine, amphetamine-type stimulants and new psychoactive substances). Booklet 5 contains a review of recent trends in the market for cannabis and for hallucinogens. The section on cannabis also includes a review of the latest developments in the jurisdictions that have adopted measures allowing the non-medical use of cannabis.

As in previous years, the *World Drug Report 2019* is aimed at improving the understanding of the world drug problem and contributing towards fostering greater international cooperation for countering its impact on health, governance and security.

The statistical annex is published on the UNODC website: https://www.unodc.org/wdr2019

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