THE GROWING COMPLEXITY OF THE OPIOID CRISIS
About the SMART Update

Synthetic drugs constitute one of the most significant drug problems worldwide. Along with synthetic drugs, the emergence of the new psychoactive substances (NPS) market over the last years has become a policy challenge and a major international concern. A growing interplay between these new substances and traditional illicit drug markets is being observed, and the synthetic drugs market continues to evolve rapidly.

The Global SMART Updates (GSU)* are biannual publications of the UNODC Global Synthetics Monitoring: Analyses, Reporting and Trends (SMART) Programme, implemented by the UNODC Laboratory and Scientific Section. The GSU is published in English, Spanish and Russian. The Global SMART Programme enhances the capacity of Member States in priority regions to generate, manage, analyse, report and use synthetic drugs information to design effective policy and programme interventions.

The main products and services of the Global SMART Programme include capacity building workshops, online drug data collection, national, regional and global assessment reports, and the UNODC Early Warning Advisory (EWA) on NPS. The EWA is a web portal that provides access to information on NPS, including on latest developments, emergence of NPS, global trends, chemical analysis, toxicology, pharmacology and legislative response. (available at: www.unodc.org/nps and www.unodc.org/tox).

Previous issues
- An expanding synthetic drugs market – Implications for precursor control (GSU 23, March 2020)
- The ATS market – 10 years after the 2009 Plan of Action (GSU 22, October 2019)
- Understanding the global opioid crisis (GSU 21, March 2019)
- Methamphetamine continues to dominate synthetic drug markets (GSU 20, September 2018)

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A. INTRODUCTION

The current opioid crisis is a far-reaching drug and public health policy issue affecting several geographical regions. Since its appearance, endeavours have been undertaken both at the national and international level to develop integrated policy responses to address the crisis. Yet, despite some progress, the crisis continues both to expand geographically and to deepen in complexity with the emergence of a new generation of new psychoactive substances (NPS) with opioid effects, including substances belonging to chemical structural classes which were not significantly present on illicit drug markets previously. This evolution in chemical structural groups signals the potential development of similar new substances which may exacerbate the already significant challenges faced by public health and drug control systems. Additionally, the onset of the COVID-19 pandemic in late 2019 and early 2020 may further complicate and reshape existing trends in the crisis.

This issue of the Global SMART Update provides an overview of the multi-faceted opioid crisis and highlights major international and domestic policy responses to date. The Update also presents key developments related to NPS with opioid effects and examines how these developments are influenced by existing control measures. It also outlines possible policy responses and assesses how the COVID-19 pandemic may affect the ongoing opioid crisis.

"...despite some progress, the crisis continues both to expand geographically and to deepen in complexity with the emergence of a new generation of new psychoactive substances (NPS) with opioid effects,..."
The global tragedy of unnecessary pain and suffering – insufficient access to internationally controlled opioids for medical use

In the face of the need for international control of the trafficking and non-medical use of opioids, there is a global divide regarding access to internationally controlled opioid analogues for pain management and palliative care. Whilst an estimated 1.2 per cent of the global population used opioids for non-medical purposes in the past year, an estimated 80 per cent of the global population has limited or no access to controlled medicines, especially for the treatment of pain.\(^4\)\(^,\)\(^5\)\(^,\)\(^6\)\(^,\)\(^7\) Despite a global increase in the availability of controlled pharmaceutical opioids for medical use in the last 20 years, the growth is imbalanced and skewed towards higher-income (sub)regions especially in North America, Oceania and Western and Central Europe (see Figure 2).\(^8\)\(^,\)\(^9\) Furthermore, the increase is largely driven by the greater availability of expensive synthetic analogues (e.g. fentanyl and oxycodone) concentrated in high-income countries, which is not matched by an increase in the availability of more affordable opiate analogues such as morphine.\(^10\)\(^,\)\(^11\) The Lancet Commission on Palliative Care and Pain Relief found that of the average amount of 298.5 tonnes of morphine-equivalent opioids distributed in the world annually between 2010 and 2013, 287.7 tonnes were distributed to high-income countries, representing an excess of 233 per cent of their projected need for 86.4 tonnes, whilst only 0.1 tonnes was distributed to low-income countries, which is 99.7 per cent short of their projected need for 37.2 tonnes. Similarly, the distribution of morphine-equivalent opioids to upper-middle- and low-middle-income countries fell short of their projected needs by 96.7 per cent and 99.3 per cent respectively.\(^12\)\(^,\)\(^13\) Another significant issue identified is that on average 88 per cent of the morphine manufactured between 1997 and 2016 was converted by pharmaceutical companies to codeine or other related substances instead of being used in morphine preparations for palliative care. This is in part a result of the marketing and supply of more expensive opioids by pharmaceutical companies which has lowered the availability of opiates among all opioid analogues over the years and ultimately the capacity of health services to treat pain, especially in low- and middle-income countries.\(^14\)\(^,\)\(^15\) The imbalance in access to opioid analogues for medical use and the rising non-medical use of synthetic opioids demonstrates the duality of the opioid crisis and the conflicting objectives, i.e. access versus control, faced by international and national drug control systems.

![FIG. 2: Average consumption of selected opioids, by region, expressed in defined daily doses for statistical purposes (S-DDD) per million inhabitants per day, 2016-2018](image)

Substances with opioid effects are one of the fastest growing groups of NPS

The rapidly growing number of NPS with opioid effects on the illicit drug market represents a further serious challenge faced by the international community. Over the last decade, the number of such substances reported annually to the UNODC Early Warning Advisory (EWA) on NPS increased significantly from just one...
in 2009 to 55 in 2018 (see Figure 3). Additionally, between 2015 and 2019, the number of synthetic opioids as a proportion of all synthetic NPS reported quadrupled from 2 per cent to 8 per cent.

As a result of the rapid emergence and increasing prevalence of opioid NPS, coupled with substantial public health risks, the number of such substances placed under international control has also increased. Despite representing only a small fraction of the total synthetic NPS reported to the UNODC EWA (8 per cent), almost a third, or 17 out of 60, of the NPS scheduled from 2015 to 2020 into either the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol (“1961 Convention”) or the Convention on Psychotropic Substances of 1971 (“1971 Convention”) were substances with opioid effects. In comparison, only 18 synthetic cannabinoids and 17 stimulant NPS were put under international control during the same period despite these pharmacological effect groups accounting for around 30 per cent of synthetic NPS reported to the UNODC EWA.

### FIG. 3: Number of different synthetic NPS with opioid effects reported each year, by chemical structural class, 2009 – 2019

![Graph showing number of different synthetic NPS with opioid effects reported each year, by chemical structural class, 2009 – 2019](image-url)

**Source:** UNODC Early Warning Advisory on NPS, 2020

**Note:** A total of 77 different synthetic NPS with opioid effects were reported to UNODC between 2009 and 2019 (but not all of them were reported each year). Plant-based substances were excluded from the analysis as they usually contain a large number of different substances some of which may not be known and their effects and interactions not fully understood. Data for 2019 are preliminary.

### B. INTERNATIONAL AND NATIONAL POLICY RESPONSES TO THE OPIOID CRISIS

Despite these challenges, the international community has taken major steps towards developing a set of balanced international and domestic responses to address various aspects of the growing opioid crisis (see Figure 4). In 2018, the 61st Session of the Commission on Narcotic Drugs (CND) for the first time adopted a resolution with direct reference to enhancing and strengthening international and regional cooperation to address the threats posed by the non-medical use of synthetic opioids. In the same year, UNODC launched an integrated strategy based on an overarching set of complementary principles to support Member States and coordinate the international response to the opioid crisis. Furthermore, between 2018 and 2020, the CND scheduled 12 fentanyl analogues under the 1961 Convention.

There have also been responses to the crisis at the national level. In April 2018, India scheduled tramadol in its Narcotics Drug and Psychotropic Substances Act to regulate and increase law enforcement of the manufacturing, import, export and sale of tramadol, and to impose criminal penalties for breaches of these regulations, effectively increasing controls over tramadol beyond existing prescription controls contained in its Drugs and Cosmetics Act of 1940 and the Drugs and Cosmetics Rules of 1945. This change appears to have had an impact on the supply of tramadol in West Africa with reports from Ghana and Nigeria indicating a significant decrease in border seizures of the drug as well as reduced availability and increases in prices of tramadol on illicit markets in those countries. This impact has not been felt consistently across West Africa however with countries such as Benin still reporting large seizures of tramadol in the first half of 2019, suggesting that large-scale tramadol trafficking remains active in the region. Likewise, despite the substance being under stricter national control since 2012, Egypt continues to seize large quantities of diverted, falsified and sub-standard tramadol (more than 231 million tablets in 2017), some of which contains a wide range of impurities.

Countries including Canada, China and the United States have extended their national controls over fentanyl analogues and/or fentanyl precursors, and have increased cooperation with international and domestic partners to tackle illicit activities relating to these substances. Early signs following China’s 2019 extension of national control to include all fentanyl analogues suggest that less of this class of substances is being smuggled from China to North America, although attempts to manufacture these substances inside the region, especially in Mexico, using precursor chemicals from East and South Asia, are increasing. Countries such as the United States have also stepped up their public health responses to promote the rational prescribing of opioids and to widen access to prevention and treatment services.
Despite having similar pharmacological effects, opioids occur in a variety of chemical structural classes ranging from morphinans to phenethylpiperidines. About 83 per cent of opioids in the Schedules of the 1961 Convention fall into four main structural classes: morphinans (including heroin, hydrocodone and oxycodone); phenethylpiperidines (including fentanyl and fentanyl analogues); phenylpiperidines (including pethidine and ketobemidone); and diphenylheptanes (including methadone and acetylmethadol). The remaining 17 per cent belong to a variety of smaller structural classes including diphenylmorphinines, thiambutenes and diphenylheptanones (see Figure 5). For the purpose of this publication, non-fentanyl-related synthetic opioids are defined as opioids belonging to dissimilar chemical structural classes to fentanyl and fentanyl analogues (i.e. phenethylpiperidines).

## Trends in non-fentanyl related synthetic opioids

The number of non-fentanyl-related synthetic opioids reported has increased steadily over the last decade from an average of two substances per year between 2009 and 2014, to ten substances in 2018 alone. An analysis of NPS with opioid effects according to their chemical structural class reveals trends in the structural diversity and popularity of certain chemical classes in the NPS opioid market. In 2009, only one chemical class of NPS with opioid effects was reported to the UNODC EWA. This number had grown to five by 2015 and eight by 2019, indicating a proliferation in the diversity of chemical classes of NPS with opioid effects in the global market (see Figure 6). Interestingly, substances belonging to four of the eight chemical classes including cyclohexylbenzamides (e.g. U-47700, AH-7921), diphenylpiperazines (e.g. MT-45), cinnamonylpiperazines (e.g. 2-methyl-AP-237) and cyclohexylphenols (e.g. O-desmethyramidol) were not included in the schedules of the 1961 Convention prior to 2015. In addition, substances in three chemical classes of opioids, cinnamonylpiperazines, thiambutenes...
Advancing effective and innovative approaches, through national, regional and international action, to address the multifaceted challenges posed by the non-medical use of synthetic drugs, particularly synthetic opioids.

Inclusion of cyclopropylfentanyl, methoxyacetylfentanyl, ortho-fluoroantifentanil and para-fluoroantifentanil in the 1961 Convention.

Promoting awareness-raising, education and training as part of a comprehensive approach to ensuring access to and the availability of internationally controlled substances for medical and scientific purposes.

Enhancing the capacity of Member States to adequately estimate and assess the need for internationally controlled substances for medical and scientific purposes.

Enhancing and strengthening international and regional cooperation and domestic efforts to address international threats posed by the non-medical use of synthetic opioids.

Enhancing the capacity of Member States to adequately estimate and assess the need for internationally controlled substances for medical and scientific purposes.

Enhancing international acâ©on, to ensure access to and the availability of internationally controlled substances for medical and scientific purposes.

India introduced more restrictive control measures for the manufacturing, import, export and sale of tramadol by scheduling it into its Narcotics Drug and Psychotropic Substance Act.

China listed NPP and 4-AP in the Schedule to the “Regulation on the Administration of Precursor Chemicals”.

China introduced drug controls based on generic legislation with regards to fentanyl, which effectively placed more than 1,400 known fentanyl analogues in the “Supplementary List of Controlled Narcotic Drugs and Psychotropic Substances with Non-medical Use”.

FIG. 5: Distribution of opioids in the 1961 Convention, 1961-2020


Note: Based on analysis of 124 opioids in the Schedules of the 1961 Convention, excluding opiates.
Developed through successive modifications of opioids from either of these two categories, other "new" opioids are typically analogues where they are not approved for medical use. Pharmaceuticals that are sold in countries or are falsified or unregistered/unlicensed (also known as "failed pharmaceuticals"), agents but were never commercialized that were originally developed as therapeutic is recent. The majority of these "new" opioids are neither new nor recent inventions, however, but rather, their appearance in the illicit market... are falling outside the typical scope of generic legislation for fentanyl analogues.50

These trends in NPS with opioid effects indicate a shift in the synthetic opioid market towards newer and more varied chemical classes of opioids to quickly replace "older generations" of substances once they are in general) remain the dominant and fastest growing chemical class of opioids among NPS with opioid effects, followed by cyclohexylbenzamides (see Figure 3).

Brophine (1-(1-[1-(4-bromophenyl)ethyl] piperidin-4-yl)-1,3-dihydro-2H-benzimidazol-2-one) is an instance of a recently emerging non-fentanyl-related synthetic opioid that has been increasingly detected in seized drug samples and forensic casework since 2019, especially after the temporary scheduling of isotonitazene by the United States Drug Enforcement Administration in June 2020.49 Despite having structural similarities to fentanyl, brophine differs in key aspects with the additional presence of the 4-bromo and 1,3-dihydro-2H-benzimidazol-2-one groups (or the phenethylpiperidine-benzimidazolone sub-class), therefore falling outside the typical scope of their chemical structures to circumvent existing legislation. Although the potency and pharmacological effects of these non-fentanyl-related synthetic opioids may differ significant from fentanyl, they can still be highly dependence producing and dangerous, as opioids in general have a narrow therapeutic index, wide interindividual response variability and potentially life-threatening toxicity. For these reasons, a very small variability in dosage can lead to serious therapeutic failures and/or adverse drug reactions resulting in significant incapacity or even death.51 In common with fentanyl and its analogues, non-fentanyl-related opioids may be sold as stand-alone products or used as adulterants or constituents of drugs such as heroin or falsified pain medication, and can be bought from a variety of sources including both the Internet and the Dark Web.52,53

Failed pharmaceutical opioids: from potential medicines to public health threats

Many "new" non-fentanyl-related opioids were originally developed by the pharmaceutical industry over the past five decades in attempts to search for better and safer opioid analgesics.55,56,57 Two isotonitazene analogues, etonitazene and clonitzene, are included in Schedule I of the 1961 Convention because of their ability to produce morphine-like effects and sustain and suppress abstinence phenomena from morphine dependence.58

In vitro and in vivo studies have found that isotonitazene is a highly potent mu opioid receptor agonist which may potentially be as potent as fentanyl and is 500 times more potent in mice relative to morphine.59,60 Although there is presently no information about the side effects of consuming isotonitazene, its pharmacological characteristics indicate that the risks would be similar to other opioids, including dependence, respiratory depression, and potentially life-threatening overdose.61 Reports of isotonitazene in seized drug samples and toxicology cases in North America and Europe have been submitted to the UNODC EWA since 2019.62 Significantly, a study found 18 deaths in the Midwestern United States where isotonitazene was identified in biological samples. Other opioids (fentanyl, morphine, tramadol, piperidylthiambutene and U-47700), as well as designer benzodiazepines (flualprazolam and etizolam), were also identified in most of these cases.63 In February 2020, authorities in Canada seized 1,900 falsified hydromorphone tablets that were found to contain isotonitazene.64

Compounds in the phenethylpiperidine-benzimidazolone opioid sub-class including brophine were first developed by Janssen Pharmaceuticals as central nervous system depressants with morphine-like analgesic activity. While structural analogues of...
Structural similarity does not equate to pharmacological activity – the cases of W-18 and benzylfentanyl

An emergent synthetic opioid gaining popularity, W-18 (or 4-chloro-N-[2(E)-1-[2-(4-nitrophenyl)ethyl]piperidin-2-ylidene] benzene-1-sulfonamide) was developed in 1981 at the University of Alberta and belongs to a class of compounds referred to as the “W” series.\(^\text{65}\) Despite being structurally related to fentanyl (see Figure 7), W-18 differs in key chemical aspects with the presence of an aryl sulfonamide group which could potentially lead to differences in pharmacological effects between the substances. Although the original patent indicated that W-18 had an analgesic potency 10,000 times greater than morphine, recent animal and in vitro studies reveal no activity for W-18 or any of its metabolites at the opioid receptors.\(^\text{66,67}\) Another fentanyl analogue, benzylfentanyl, has been found to be “essentially inactive” when assessed for morphine-like activity, dependence liability and analgesic effect.\(^\text{68,69}\) It is likely that its presence in seized drug samples is due to it being used as a precursor in the fentanyl manufacturing process, resulting in a residual amount of the unreacted substance after synthesis.\(^\text{70}\) These examples demonstrate that substances sharing structural similarities with known opioids do not necessarily equate to having similar pharmacological activity. Therefore, additional structure-activity relationship studies are always required for new emerging substances to predict or determine if there is a pharmacological activity that warrants control.

AH-7921 is another popular substance belonging to the cyclohexylbenzamide class of opioids, which shares structural similarities with U-47700. It was developed by Allen & Hanburys Limited in 1974 but was never made available for medical use, possibly due to its highly addictive properties observed in animal studies.\(^\text{91,92}\) Limited animal studies also indicate that AH-7921 has a similar potency and risk of respiratory depression to morphine. Users of this substance have reported opioid side effects including euphoria, mental relaxation, pleasant mood lifts, analgesia, nausea and dependence.\(^\text{93}\) Though less prevalent than U-47700, AH-7921 has been reported to the UNODC EWA by 16 countries\(^\text{94}\) and has been detected in seized samples and cases of acute non-fatal intoxications and deaths in Europe,\(^\text{95}\) East Asia\(^\text{96}\) and North America.\(^\text{97}\) It was placed under international control in 2015.\(^\text{98}\)

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Source: UNODC elaboration.
Availability of falsified and unlicensed pharmaceutical opioids

In addition to failed pharmaceutical opioids, falsified and/or unregistered/unlicensed pharmaceutical opioids have also surfaced in markets where they are not approved for medical use. One such substance is tianeptine, a tricyclic antidepressant and anxiolytic that is also a full mu opioid and delta opioid receptor agonist. Tianeptine does not have the common side effects of most antidepressants, such as sedation, and is prescribed in Europe, Asia and Latin America. There are multiple documented cases of recreational use and dependence related to tianeptine, presumably as a result of its atypical pharmacological profile, ability to induce euphoria at high doses and relatively mild side effects. Case studies and reports of tianeptine dependence found opiate-like euphoria and withdrawal symptoms including myalgia, nausea, vomiting and agitation.

Though tianeptine is not approved for medical use in the United States of America, it has recently been encountered by law enforcement in the country in various forms including bulk powder, falsified hydrocodone and oxycodone tablets, and in individual stamp bags commonly used to distribute heroin. The United States Centers for Disease Control and Prevention reported a marked increase in tianeptine exposure calls to the National Poison Data Systems, from 11 cases between 2000 and 2013 to five in 2014 and 81 in 2017, suggesting an increase in the non-medical use of the substance which the United States Drug Enforcement Administration termed an "extreme public health concern" in the context of the country's current opioid crisis. A 2018 study also identified two fatalities in the United States associated with the use of tianeptine purchased on the Internet. More recently, tianeptine was identified in eight seized materials and toxicology cases in the United States from the fourth quarter of 2019 to the first quarter of 2020, including three toxicity cases in 2020.

AP-237 (or bucinnazine) and its structural analogues (2-methyl AP-237 and para-methyl AP-237) are further examples of illicitly manufactured pharmaceutical opioids appearing in seized materials in several countries. The parent compound, AP-237, was originally developed in Japan in the late 1960s as an opioid analgesic belonging to the cinnamylpiperazines class and is prescribed for medical use. One such substance is AP-237 (or bucinnazine) and its structural analogues (2-methyl AP-237 and para-methyl AP-237) appearing in seized materials in several countries. The parent compound, AP-237, was originally developed in Japan in the late 1960s as an opioid analgesic belonging to the cinnamylpiperazines class and is prescribed for medical use.

D. RESPONDING TO AN INCREASINGLY COMPLEX OPIOID CRISIS

The emergence of new non-fentanyl-related synthetic opioids can be seen as an unintended consequence of the efficacy of existing control measures in reducing product life cycles and minimising the adverse public health effects of existing synthetic opioids. The displacement/replacement effect is a by-product of a complex cyclic interaction between the imposition and circumvention of novel control measures amid changing market dynamics. As governments introduce new regulatory responses and enhanced forensic tools to detect, identify and interdict existing substances, so organized crime groups respond by identifying, manipulating, manufacturing and distributing new synthetic substances to exploit the limitations of current forensic technologies as well as chemical analogue/generic loopholes in the law. This interaction is further driven by the preferences and behaviours of users being influenced by factors such as the substitution and adulteration of new substances in existing drug supplies.

Without existing control measures however, extremely potent opioids such as fentanyl and its analogues would become entrenched on illicit drug markets with potentially devastating effects. There is some limited evidence to date indicating some degree of success of existing control responses in reducing the availability, use and rate of accidental overdose deaths associated with the existing generation of synthetic opioids. It is therefore essential to continue engaging in this cyclic interaction to prevent synthetic opioids from gaining the firm foothold in illicit markets that certain established drugs already have. The question is how policymakers can address the growing complexity of the opioid crisis and further shorten the product life cycles of emergent synthetic substances of abuse by influencing this complex cycle.

Improving access to opioids for medical use

The dual nature of the opioid crisis calls for an informed approach that balances stemming the non-medical use of internationally controlled opioids with improving access to them for pain management and palliative care. Competent national authorities may wish to refer to guidelines on estimating national requirements of controlled substances and adopt the use of online and electronic systems developed by various international organisations to reassess their current estimates and simplify the import and export process of controlled medicines. Nationally, governments may wish to introduce changes to their health systems in order to improve access and the availability of controlled medicines for both pain management and palliative care whilst maintaining proper oversight such as allowing electronic prescribing, especially in remote areas, permitting a larger base of trained health-care professionals to prescribe opioid analogues and instituting national health insurance and price-setting systems for essential medicines. In addition, international organisations and national authorities alike may wish to promote ethical approaches among pharmaceutical companies and physicians, rational prescribing practices and overcoming stigma associated with opioid use as well as to extend training in pain management and palliative care to more health-care professionals.

The importance of early warning systems

The growing complexity of the opioid crisis
...emergence of these substances underscores the importance of strengthening early warning systems, expanding public-private partnerships and enhancing existing legal approaches to respond to the growing complexity of the opioid crisis..."
The onset of the COVID-19 pandemic has brought wide-ranging and profound effects to the world, leading to unprecedented closures of non-essential parts of the economy accompanied by border and movement restrictions on a scale unmatched by past market crises. As was the case in previous major crises, it is likely that the pandemic has affected many aspects of the illicit drug market, in particular the evolving opioid crisis.137

Effects on the trafficking and manufacture of synthetic opioids

Despite early indications of disruption to illicit synthetic opioid manufacture and trafficking in some regions, recent evidence months into the pandemic suggests that these activities have resumed to normal levels and possibly intensified.138 For instance, a year-on-year comparison of fentanyl seizure trends at the borders of the United States indicates that the earlier perceived disruption to the fentanyl trade was extremely short-lived,139,140 with seizures resuming to previous levels as of February 2020, despite temporary restrictions on non-essential travel.141 Similarly, the pandemic seems to have had little impact on tramadol trafficking with large-scale seizures of the drug being reported in Kuwait and India from February to July 2020.142,143 Taken together, these preliminary trends in seizures indicate minimal disruption to illicit synthetic opioid manufacturing and trafficking activities in the wake of the pandemic.

However, the impact of the COVID-19 pandemic on the production and trafficking of opiates remains unclear, affecting in turn the wider market for opioids. At present, there is insufficient or inconclusive information available on the current state of Afghanistan’s opium harvest, which has accounted for approximately 84 per cent of global opium production over the past five years.144,145 In any event, if illicit opiate activities are indeed affected, it would be prudent for governments to closely monitor illicit drug markets for developments such as the adulteration or substitution of opiate supplies with cheaper and potentially more harmful synthetic opioids such as fentanyl and its analogues from illicit sources.146

Effects on the use of synthetic opioids

The COVID-19 pandemic may further expose opioid users to increased vulnerability to problematic drug use and overdose if the economic fallout drives a switch to more efficient methods of administering drugs, such as injecting, in order to compensate for lower purchasing power and maximize the psychoactive effects.147,148 However, this heightens the transmission risks of blood-borne diseases such as HIV/AIDS and hepatitis C, while the sharing of drug paraphernalia e.g. inhalation devices may also increase the spread of COVID-19 itself, further burdening already-strained healthcare systems.149 User behaviour may also shift through abstaining or moving to lower potency or purity opioids, resulting in lower adjusted tolerance and increased risk of opioid overdose as supply and quality improve.150 Possible reductions or suspensions of public health resources and capacities for harm reduction and drug treatment services as a result of the pandemic, especially opioid substitution treatment, may further exacerbate these vulnerabilities.151 The American Medical Association recently cited concerns over increases in opioid-related mortality in more than 35 states during the pandemic and urged flexibility in the provision of harm reduction services.152

The rapidly evolving drug scenario amid the COVID-19 pandemic highlights the need for policymakers and other stakeholders to actively monitor emerging trends and enact suitable policies to respond to changes in drug manufacturing, trafficking and user behaviour. These changes may have a long-term impact on opioid markets and drug use patterns with corresponding implications for future public health and drug control requirements.


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131 Australia, Crimes Legislation Amendment (Psychoactive Substances and Other Measures) Act 2015.

132 Austria, New Psychoactive Substances Act;

133 United Kingdom, Psychoactive Substances Act 2016; United Kingdom, Home Office, Review of the Psychoactive Substances Act 2016;


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