Coping With Addictive Opioid Markets

12

Amir A. Afkhami and Javad John Fatollahi

Introduction

Opioid dependence is a significant contributor to the global disease burden. Over the past generation, both the range of opiates and markets for the drugs have expanded to unprecedented levels. On the supply side, opioid drug markets have seen record levels of production and manufacture. On the demand side, nonmedical use of opioids and their synthetic analogues have reached epidemic proportions in parts of the world. Opioid dependence is a chronic disorder that prompts users to persist in using the drug despite the negative downstream effects of its consumption including imprisonment, exposure to infectious diseases, and possible fatal overdose. Social, political, geographical factors are important determinants of opiate dependence rates, morbidity, and mortality in a population. Drugs also play an important role in eroding stability and governance, particularly in low- and middle-income nations, through conflict, criminality, and corruption fueled by the profits of the opiate trade. Globally, there is increasing realization that combating opioid dependence is an essential component of a healthy and stable society. Despite this recognition, most individuals struggling with addiction do not receive appropriate care. The prevailing stigma across cultures and the criminalization of the disorder have largely shifted the opioid-dependent population into prisons instead of clinics, which has worsened the impact of opioid misuse.

A. A. Afkhami (✉) · J. J. Fatollahi
Department of Psychiatry and Behavioral Sciences, The George Washington University, Washington, DC, USA
e-mail: aafkhami@mfa.gwu.edu; jfatollahi@gwu.edu

A. R. Dyer et al. (eds.), *Global Mental Health Ethics*,
https://doi.org/10.1007/978-3-030-66296-7_12

Population Health and the Opiate Drug Market

Economic/Social/Legal Impacts

The economic burden of opioids was estimated to have cost the US $55.7 billion in 2007. Lost workplace productivity contributed $25.6 billion, healthcare costs contributed $25 billion, and criminal justice costs accounted for the remaining $5.1 billion [3]. In 2013, the CDC estimated that the cost had risen to $78.5 billion per year [11], and in 2015, The White House Council of Economic Advisers estimated that the cost of the opioid epidemic exceeded $500 billion, largely because of lost productivity from premature death [17]. Since the start of the war on drugs campaign led by the US federal government in the early 1970s, the number of addicts incarcerated in American prisons has increased exponentially. Other countries that have adopted similar strict interdiction and criminalization drug policies have also witnessed a dramatic increase in their prison populations. Besides an increase in incarcerations, opioid dependence has been shown to correlate with a higher proportion of criminal activity outside of crimes specific to drug use and possession. Typically the more the addict uses, the more crime they are likely to commit. The cause for this is likely twofold; increased risk-taking behaviors coupled with the strength of addiction which causes addicts to be motivated to procure their next dose by any means necessary.

Global Burden of Opioid Use

The contribution of opioid use to premature mortality varies across the globe, with North America, Eastern Europe, and Southern Sub-Saharan Africa being the regions most affected by this growing epidemic. Nearly two-thirds of the deaths attributed to drug use disorders in 2017 were due to opioids [8]. In 1990, there were an estimated 10.4 million people globally who were opioid-dependent. That number skyrocketed to 15.5 million people in 2010, resulting in 9.2 million disability-adjusted life years (DALYs) lost to opioid-related ill health and premature mortality (approximately 7 million years lived with disability (YLD) and 2 million years of life lost (YLL)) [5]. There is also a geographic variation in the contribution of YLD versus YLL due to opioid dependence. For example, in the majority of regions, burden was mainly due to YLD, but in North America, Eastern Europe, and Southern Sub-Saharan Africa, there was a higher burden (>50%) due to YLL [6]. By 2016, there were an estimated 34.3 million past-year users of opioids which corresponded to roughly 0.7 percent of the global population (aged 15–64 year). The prevalence of past-year opioid users in 2016 was especially high in regions like North America (4.2 percent) and Oceania (2.2 percent) [12].

The rise of synthetic opioids is also a cause for concern in today's drug climate. Fentanyl, which was first synthesized in 1959, was approved initially for use as an anesthetic in the USA in 1972. With a potency of 50–100 times that of morphine, it is produced using inexpensive and readily available chemical precursors. This surge in potency, coupled with Fentanyl's ease in traversing across the blood-brain barrier,

narrows the therapeutic window of the drug, with small dosage increases resulting in fatal respiratory depression [17]. The rate of overdose deaths in the USA due to synthetic opioids, like fentanyl, increased from 1 per 100,000 people in 2013 to 9 per 100,000 in 2017. This was approximately double the corresponding 2017 rates for heroin (4.9 per 100,000) or prescription opioids (4.4 per 100,000) giving rise to the concern that inexpensive, readily accessible, and mass-produced synthetic opioids were changing the morbidity and mortality patterns of opioid dependence in the USA [14].

Associated Medical Comorbidities

One of the major downstream consequences of opioid dependence is the surge of blood-borne infectious diseases associated with their use, including higher rates of Acquired Immune Deficiency Syndrome (AIDS) caused by the human immunodeficiency virus (HIV), viral hepatitis, infective endocarditis, and other skin and soft tissue diseases. This creates a converging public health concern that requires a coordinated effort by both infectious disease specialists and substance use disorder providers to address. Most of these infections are spread via intravenous injection through the sharing of needles [19]. According to WHO data, injecting drug use is reported in 136 countries, of which 93 reported HIV infection among those who are injecting [4]. Injecting drug use as a global risk factor for HIV accounted for 2.1 million DALYs and as a global risk factor for hepatitis C accounted for 0.5 million DALYs in 2010. In 2017, there was an estimated 11 million people worldwide who inject drugs and more than half of them live with Hepatitis C and close to one in eight live with HIV [8].

According to the US National Institute of Drug Abuse (NIDA), roughly 30–60% of individuals with a diagnosis of substance use disorder met the criteria for post-traumatic stress disorder (PTSD) as well. The most prominent example of this dual diagnosis phenomenon can be found among American veterans of the Vietnam War. A study found that 75% of combat Vietnam veterans with diagnosed PTSD also met criteria for a substance use disorder (mainly due to heroin addiction). These same veterans also faced a higher risk of fatal overdose when compared to the general population. Similarly, American veterans of the Iraq/Afghanistan War shared an increased prevalence of opioid dependency. But unlike their predecessors, these soldiers were becoming addicted to prescription opioids. A veterans affairs healthcare study showed that roughly 11% of veterans who served in operations in Iraq and Afghanistan were diagnosed with a substance use disorder and 22% of the veterans diagnosed with PTSD had a comorbid substance use disorder.

Addiction in Humanitarian Settings

While growing addiction rates and its burden on the developing world have been cause for concern, the prevalence of opioid dependence in humanitarian settings

(zones of conflict, natural disasters, and displaced populations) is just as glaring. In these settings, addiction has been linked to issues ranging from organized crime, to gender violence, to the unfortunate neglect of small children. Like soldiers returning from war, refugees have shown a similar trend in increasing addiction rates. Refugees are at a higher risk for dependence when compared to the general population due to higher levels of stress, unemployment, and difficulties adapting to a new environment. Lack of access to treatment services along with cultural, economic, and language barriers can increase the risk of developing a drug habit or create barriers to accessing appropriate addiction treatment. Dependence can develop in the country of origin, while in transit, or in the setting of temporary or permanent residence. Risk factors in these settings include male gender, exposure to combat, and coexisting mental health problems. The Assimilation/Acculturation Model postulates that refugees tend to adopt the social norms of their new environment, including harmful behaviors such as substance misuse. The Acculturative Stress Model, on the other hand, theorizes that difficulties in managing new cultural and societal norms result in drug use as a coping mechanism [13]. The Syrian refugee crisis has brought a resurgence of interest in this topic. There are approximately 6.6 million Syrian refugees that have fled their country and another 6.1 million that have been displaced from their homes with in Syria. Of those, 12 million people, 90% of them live outside of camps in makeshift shelters, which are often overcrowded. What is even more disheartening is that roughly 50% of all registered Syrian refugees are under the age of 18 meaning millions have spent their formative years experiencing high levels of poverty, malnutrition, and conflict [20]. While opioid dependence is considered a public health issue in humanitarian settings, it is an area that has been overlooked given the lack of relevant literature on the matter. The challenges of collecting data in emergency settings and stigma are major barriers to empirical studies that can shed light on supporting a correlation between humanitarian emergencies and increased addiction rates. However, the Acculturative Stress Model and the know significant traumas of conflict, deprivation, and displacement make it very plausible that illicit opioid use in these regions may increase as more individuals seek to self-medicate and treat mental/physical pain or to alleviate the stress of adapting to a new lifestyle and environment. There are also instances where during or following a national emergency, supply of medications used for the treatment of opioid use disorders (like methadone and buprenorphine) can abruptly be discontinued. The Ukrainian revolution in 2014 was a prime example as to how discontinuation of medication-assisted treatment (MAT) can cause sudden withdrawal and return to illicit opioid use among dependent users. Even more cause for concern is the dangerous shift in how opioids are being consumed. Afghanistan, for example, has had a shift from its traditional smoking of opium to more high-risk use via intravenous injection of heroin. This shift can be attributed to a combination of outdated drug policies and a war that destabilized an already fragile nation. This instability led to a lack of proper border control, which in turn increased trafficking and access to drugs. Libya, a country that had back-to-back civil wars in less than a decade, experienced a similar shift of increasing intravenous opioid use, which was also coupled with an HIV epidemic that nearly crippled the entire country's health system [13].

Impact on National Security and Stability

The transnational trade and domestic trade in illicit opioids are significant threats to public health, law enforcement, and overall stability throughout the world. The actors involved in the production and trade of this illegal commodity include civilian farmers and manufacturers; criminal groups such as drug trafficking organizations and mafias; belligerent actors, such as terrorist, insurgent, and paramilitary groups; and corrupt government and law enforcement officials. Mexican transnational criminal organizations, including the Sinaloa Cartel and Jalisco New Generation Cartel, are the principal suppliers, traffickers, and distributors of opioid drugs in the USA. They work closely with US-based actors to distribute the drugs on a local level [16]. National and neighborhood-based street gangs and prison gangs continue to dominate the market for the street sales and distribution of illicit drugs in their respective territories. The profit from this trade fuels the criminality, violence, and disruptions to the social fabric across both rural and urban communities in the USA. The adulteration of heroin with fentanyl and the increased purity of opioids by cartels to maximize profits have been the primary drivers of rising overdose deaths in the USA in the last 4 years.

Terrorist or insurgent actors involved in the global illicit opioid market represent a particularly significant threat to nations and regional stability since these groups often seek to disrupt or eliminate the existing sovereign governing structures of a state. In Afghanistan, the world's largest opium producer, most of the poppy cultivation tends to take place in areas and villages controlled by insurgent and other non-state actors, compared with just 26 percent for non-poppy villages. Insurgent groups such as the Taliban enforce a variety of taxes on the production and sale of the agricultural product, earning them tens of millions yearly, which fuels the armed conflict in the country. Moreover, poppy-producing villages controlled by insurgents have worst access to med medical and educational facilities, especially for girls and women. The United Nations estimates that in villages not under state control only 13 percent of women have access to culturally sanctioned female providers, resulting in higher maternal and child mortality and morbidity figures [1].

Case Examples

The Portuguese Case

Background

The location of Portugal on the southwest border of Europe makes it the perfect gateway for drug trafficking. Despite this, the lifetime prevalence of illicit drug use in the country has been historically low. However, in the 1990s there was a significant increase of intravenous (IV) drug users within the country, which increased the rates of infectious diseases like HIV, AIDS, Hepatitis B, and Hepatitis C. By the turn of the century, Portugal had the highest rate of

drug-related AIDS and the second highest rate of HIV among IV drug users in the European Union [2]. Drug-related deaths also peaked within the country and drug users were slowly becoming marginalized and socially excluded. Drug-related offenders made up 44% of the Portuguese prison population, and overcrowding was becoming an issue [15]. It was around this time that law enforcement and health sectors within the country started viewing criminalization of drug use more as a problem than a real solution.

Model Intervention

Efforts at harm reduction could be seen in Lisbon as early as the 1990s, when Odette Ferreira, an experienced pharmacist and pioneering HIV researcher, started an unofficial needle exchange program to address the growing HIV epidemic. Ferreira, whose fieriness made up for her small stature, began giving away clean syringes in the middle of Europe's biggest open-air drug market, in the Casal Ventoso neighbourhood of Lisbon. She also collected donations of clothing, soap, razors, condoms, fruit, and sandwiches, and distributed them to users. Her efforts were met with death threats from drug dealers and legal threats from politicians. Not one to back down easily, she eventually convinced the Portuguese Association of Pharmacies into running the country's—and arguably the world's—first national needle exchange program [9].

Along with harm reduction programs, the Portuguese government eventually appointed an expert commission that proposed decriminalization of all illicit drugs for personal use as its first national drug strategy. Their goal was to provide a more evidence-based approach to drug use and decriminalization aimed to create a more humane legal framework [7]. Decriminalization of illicit drugs ultimately went into full effect in Portugal on July 1, 2001. Prior to this reform, drug possession or cultivation was punishable by up to 1 year of imprisonment, but with decriminalization, these minor drug offenders were now being funneled through the drug treatment system rather than the criminal justice system [15].

Results

While decriminalization caused a slight increase in apparent drug use within Portugal, its effects on the criminal justice system, drug treatment, mortality, and infectious disease were considerably profound. The number of people arrested for criminal drug offences reduced from over 14,000 offenders in 2000 to an average of 5000 per year after decriminalization went into effect. The number of drug-related offenders in the Portuguese prison population decreased from 44% in 1999 to 21% in 2008. As the number of incarcerated drug users decreased, so did the rate of drug use within prisons. Between 1998 and 2008, the overall number of drug users in treatment expanded from 23,654 to 38,532 [18]. The proportion of drug-related deaths due to opioids decreased from 95% in 1999 to 59% in 2008 [15]. From 2000 to 2008, the number of new HIV cases decreased among drug users from 907 to 267 and the number of new AIDS cases decreased from 506 to 108 [18].

The Iranian Case

Background

For much of the twentieth century, the Iranian government's strategy for curbing the country's growing problem with opiate misuse was one of interdiction, by stopping the flow of opium products, banning, and destroying the poppy crop, and increasingly draconian criminal justice laws against trafficking and possessing narcotics. When, in the late 1960s, it became clear that this approach was not working due to a rising heroin epidemic, Iranian authorities adopted policies that focused more on prevention and treatment, with promising results. The Iranian government allowed the resumption of opium cultivation and use, increased access to overdose management, detoxification services, and pilot MAT programs. But the country returned to strict zero-tolerance narcotics laws after the 1979 revolution that overthrew the secular monarchy. Iran's new Islamic government saw drug use not as a medical or public health issue but as a moral shortcoming, believing that addiction and abuse could be addressed through religiously sanctioned punitive measures. Penalties for addicts included fining, imprisonment, and physical punishment; drug dealers and smugglers were often considered to be "at war with God" were either imprisoned or executed. But by the late 1980s, the rising number of incarcerated addicts had become a burden on the prison system, and a boot camp approach, led by the Ministry of Justice but administered by The Ministry of Welfare and Social Security, was adopted to address the increasing opioid-dependent population. Tehran began sending thousands of addicts to these camps, where they were supposed to abruptly detoxify without medical assistance and atone for their sins through forced labor and minimal social work approach to supporting the process. As expected, many relapsed after release from the camps.

These draconian measures were matched with similarly aggressive operations to prevent the flow of opiates across the border from Afghanistan. By the late 1980s, an estimated 50 percent of Afghan opiate production was passing through Iranian territory, and the Iranian markets were flooded with Afghan opium, heroin, and morphine. Starting in the early 1990s, Tehran constructed more than 260 kilometers of static defenses—including concrete dams that blocked mountain passes, antivehicle berms, trenches, minefields, forts, and mountain towers— at a cost of over $80 million. By the late 1990s, more than 100,000 police officers, army troops, and Revolutionary Guardsmen were committed to antinarcotic operations. Yet both the social policies and the border fortifications were fruitless. Although the Iranian authorities seized nearly eight times the amount of narcotics in 1999 than they had in 1990, they could not keep up with the expansion of Afghan opium production, which rose in those years from approximately 1500 metric tons to roughly 4500. Iran also found that the number of intravenous drug users was growing. Ironically, the prisons and camps where addicts were expected to kick their habits became epicenters of drug use, in which people learned how to inject heroin and shared primitive infection-prone needles. The rise in malignant drug use brought with it more deaths, more cases of addiction, and most embarrassingly for Iran's leaders, a full-blown HIV/AIDS epidemic.

Model Intervention

These setbacks prompted a turnaround in Iran's approach to fighting narcotics in 1994 when the Iranian government began focusing on primary prevention programs against opiate misuse for the first time since the revolution. By 2002, over 50 percent of the country's drug-control budget was dedicated to preventive public health campaigns, such as advertisement and education. In 1996, the Iranian government amended its criminal justice codes on opiate misuse, acknowledging the legality of medical and nonmedical interventions for treating opiate dependence. This opened the way for outpatient treatment centers and abstinence-based residential centers to start operating in Tehran and the provinces. The Islamic Republic also began to allow nongovernmental organizations to launch their own prevention and treatment efforts. The government began to implicitly support needle exchange programs, going so far as to encourage the distribution of clean needles in the Iranian prison system. Gradually, the road was paved for methadone maintenance treatment centers and clinics that dispensed locally produced opium pills, in a bid to turn injection drug users into medicated patients.

Results

In making this shift, Iran sought not only to halt the growing HIV/AIDS epidemic but also to reduce the demand for illicit narcotics and to reintegrate drug users back into the economy. These new measures began to show results: The number of new HIV cases among intravenous drug users dropped from a high of 3111 in 2004–1585 in 2010. This trend was particularly notable among Iran's prison population, which witnessed a drop in HIV prevalence from a high of 7.92 percent in 1998 to a low of 1.51 percent in 2007. Additionally, in areas where the country set up harm reduction programs, improvements were observed in addicts' life expectancies and psychological well-being, coupled with an overall reduction in the illicit consumption of opiates.

Analysis

These cases clearly show that strict zero-tolerance criminalization of opiate misuse and interdiction of drug trafficking without a wraparound population health approach not only fail at significantly shifting the opiate drug market, but also can actually worsen health, social, and economic indicators. Effective interventions to change the opiate drug market need to include upstream prevention approaches and a downstream treatment approaches to opiate misuse that improves the overall health outcomes and socioeconomic well-being of the affected population. To succeed, this process requires broad-based coalitions and partnerships across both the healthcare sector, government agencies, including judiciary and criminal justice systems, and communities grappling with opiate addiction. Given the evidence internationally that the incarceration of opiate consumers and sellers is not an effective remedy for opiate use disorder, treatment should be prioritized over

incarceration while making sure that those who are imprisoned receive adequate treatment and care after release, including access to public benefits that will allow them to reintegrate into the social fabric.

Primary Prevention: Education/Public Health Campaigns

Primary prevention should begin by addressing the stigma associated with opiate use disorder by educating stakeholders in the community that opiate addiction is a medical illness, not a moral weakness. In the Iranian case, this involved educating clerics and government officials on the biological underpinnings of opioid dependence, allowing the ratifications to the criminal justice laws that were necessary to establish drug treatment programs in the country.

Misapprehensions surrounding harm reduction and medication-assisted treatment of addiction remain a stubborn problem in both low- and high-income countries as evidenced by the position of the US Secretary of Health and Human Services in 2017 that such interventions do little to "move the dial" against opiate use disorders. Educating stakeholders on harm reduction is an important factor in the establishment, expansion, and utilization of programs that focus on reducing the deleterious downstream health and social outcomes of opiate misuse. In the Iranian case, the establishment and widespread use of prison needle exchange programs and its impact on reducing the rate of HIV/AIDS in the Iranian prison system show that investments in harm reduction education pay significant dividends. Such interventions maximize the health of users that are not ready for treatment or face barriers to obtaining care.

Increased community knowledge of risk of opioids, overdose, and overdose prevention strategies through advertisement and education campaigns can have an impact on the both morbidity and mortality associated with opioid misuse in a population.

Secondary Prevention: Focusing on at Risk Populations

This intervention involves screening and more intensive education of the subset of the population more vulnerable to opiate misuse due to increased biological, psychological, or social risk factors. This can include individuals with mental illness, prior substance misuse, and the incarcerated or homeless population. Individuals who screen positive should then receive an in-depth assessment. Self-report questionnaires like the Screener and Opioid Assessment for Patients in Pain (SOAPP) and Opioid Risk Tool (ORT) help assess for the risk of opioid misuse. Preventing initial exposure to opioids should be considered whenever possible and is particularly warranted for minor surgical procedures in which non-opioid modalities can provide effective postsurgical analgesia. Patients with preexisting psychiatric comorbidities or those with family histories of opioid dependence would also

benefit from opioid-sparing analgesic strategies. For the acute care surgical patient, the use of multimodal analgesic regimens, including the use of long-acting local anesthetics, has become an approach for expediting movement away from opioid-centric prescribing practices for postsurgical pain management.

Tertiary Prevention: Interventions

Widespread Naloxone Distribution

Broadly expand access to and training for administering naloxone to prevent overdose deaths. Studies show that in communities where overdose education and naloxone distribution were implemented, there was a 27–46 percent decrease in opioid overdose deaths. High implementation of training and naloxone distribution does not increase rates of riskier opioid use as emergency department visits, and hospitalizations after overdose were equivocal in both high and low implementation communities [21].

Needle and Syringe Programs

Allow injection drug users to access clean hypodermic needles at little to no cost or via exchange of used needles. This harm reduction model intervention can help decrease the spread of communicable blood borne infections and by extension reduce the disease burden of addiction on the individual user and their community. A 2004 World Health Organization study showed that needle and syringe programs markedly decreased the rates of HIV transmission among IV drug users without increasing IV drug use rates at the individual or societal level [23].

Medication-Assisted Treatment (MAT)

The use of FDA-approved medications, in combination with counseling and behavioral therapies, to treat opioid use disorders and prevents overdoses. There are currently 3 FDA-approved medications for treating opioid use disorder: methadone, naltrexone, and buprenorphine. Studies show that a combination of medication and therapy can successfully treat and sustain recovery. Medications work by blocking the euphoric effects of opioids, relieve cravings, and normalizing body functions without the negative effects of opioids [22].

Monitoring and Evaluation Frameworks for MAT for Opioid Dependence

MAT programs for opiate dependence have historically been strictly regulated by political authorities. These top-down regulations and guidelines have unintentionally disincentivized individual programs from monitoring outcomes and implementing innovations that respond to changing local needs. Without outcome evaluations, programs risk not meeting their stated goals, and fail to respond to shifting social, medical, and opiate market conditions over time. Objective

measures of outcomes can be taken in the following way: (I) medical/psychiatric: laboratory analyses, physical examination results, or hospitalizations; (II) relapse: random urinalysis evaluations, record of hospitalizations for overdose, or complications of opiate misuse; (III) employment: verification via pay stub or third party; (IV) crime: arrest records, probation/parole violations. Patient retention and length of time in treatment are also good proxy measures of the ability of a program to engage a patient in rehabilitation. This process can be facilitated through the use of a number of reliable performance tools including the Methadone Treatment Quality Assurance System (MTQAS), Addiction Severity Index, Treatment Services Review, Family Burden Interview/Short Form (SF) Schedule.

Ethical Considerations

Patients should be free to choose whether to participate in treatment as prescribed by the ethical principle of autonomy unless a person can no longer care for themselves or poses an imminent risk to self or others as a result of their opiate dependence. It is preferable to offer individuals the option of having their opioid dependence treated in a clinical setting as an alternative to incarceration if they are convicted of crimes related to their opioid use. These diversion programs have shown to have high rates of success in treating addicts and low rates of criminal recidivism once treated [10]. Prisoners should not be denied adequate health care associated with their history of addiction because of their imprisonment. Treatment options available to the non-incarcerated population should be available in prisons, and increased efforts at prevention and harm reduction, such as needle exchange programs, should be implemented in prison systems which have higher rates of blood-borne pathogenic transmission due to intravenous opiate consumption compared to the non-incarcerated population. Opioid withdrawal agonist maintenance and naltrexone treatment should be available in prison settings, and prisoners should not be forced to accept any particular treatment. Patients should have the right to privacy and confidentiality while receiving treatment and when possible, central registration of patients receiving methadone or buprenorphine maintenance treatment should be avoided to reduce the chance of breaching privacy.

Conclusion

Evidence-based methods that focus on preventing and treating opiate misuse and addiction have been shown to be far more effective in reducing demand, mortality, and morbidity associated with addictive markets as compared to punitive tactics, such as criminalization, interdiction, and incarceration. The more progressive aspects of the Iranian and Portuguese experience demonstrate that a more ethical, public-health-oriented, harm reduction approach to opiate misuse holds the best hope of decreasing the impact of addiction on the individual and populations throughout the world. Yet, effective evidence-based gold standard medical

treatments for addiction remain out of reach for most who need it, driven mostly by the prevalence of stigma and sociocultural prejudices in most policy-making bodies and governments. Coping with addictive opiate markets, therefore, demands a renewed effort to raise global public awareness on proven biomedical treatments for addiction and preventive approaches to curb this growing public health crisis.

References

1. Afghanistan opium survey 2018: Challenges to sustainable development, peace and security. (2019). Retrieved from https://www.unodc.org/documents/crop-monitoring/Afghanistan/Afghanistan_opium_survey_2018_socioeconomic_report.pdf
2. Annual report on the state of the drugs problem in the European Union. (2000). Retrieved from http://www.emcdda.europa.eu/system/files/publications/151/ar00_en_69639.pdf
3. Birnbaum, H. G., White, A. G., Schiller, M., Waldman, T., Cleveland, J. M., & Roland, C. L. (2011). Societal costs of prescription opioid abuse, dependence, and misuse in the United States. *Pain Medicine, 12*(4), 657–667. https://doi.org/10.1111/j.1526-4637.2011.01075.x.
4. Data and statistics. (2019). Retrieved from http://www.euro.who.int/en/health-topics/disease-prevention/illicit-drugs/data-and-statistics
5. Degenhardt, L., Charlson, F., Mathers, B., Hall, W. D., Flaxman, A. D., Johns, N., & Vos, T. (2014). The global epidemiology and burden of opioid dependence: Results from the global burden of disease 2010 study. *Addiction, 109*(8), 1320–1333. https://doi.org/10.1111/add.12551.
6. Degenhardt, L., Whiteford, H. A., Ferrari, A. J., Baxter, A. J., Charlson, F. J., Hall, W. D., et al. (2013). Global burden of disease attributable to illicit drug use and dependence: Findings from the Global Burden of Disease Study 2010. *Lancet, 382*(9904), 1564–1574. https://doi.org/10.1016/s0140-6736(13)61530-5.
7. Estratégia Nacional de Luta Contra a Droga: Relatório da Comissão para a Estratégia Nacional de Combate à Droga. (1998). Retrieved from http://www.sicad.pt/BK/Publicacoes/Lists/SICAD_PUBLICACOES/Attachments/48/ENcomissao.pdf
8. Executive summary. (2019). Retrieved from https://wdr.unodc.org/wdr2019/prelaunch/WDR19_Booklet_1_EXECUTIVE_SUMMARY.pdf
9. Ferreira, S. (2017). *Portugal's radical drugs policy is working. Why hasn't the world copied it*?. Retrieved from https://www.theguardian.com/news/2017/dec/05/portugals-radical-drugs-policy-is-working-why-hasnt-the-world-copied-it
10. Fielding, J. E., Tye, G., Ogawa, P. L., Imam, I. J., & Long, A. M. (2002). Los Angeles County drug court programs: Initial results. *Journal of Substance Abuse Treatment, 23*(3), 217–224. https://doi.org/10.1016/s0740-5472(02)00262-3.
11. Florence, C. S., Zhou, C., Luo, F., & Xu, L. (2016). The economic burden of prescription opioid overdose, abuse, and dependence in the United States, 2013. *Medical Care, 54*(10), 901–906. https://doi.org/10.1097/mlr.0000000000000625.
12. Global overview of drug demand and supply. (2018). Retrieved from https://www.unodc.org/wdr2018/prelaunch/WDR18_Booklet_2_GLOBAL.pdf
13. Hanna, F. (2017). Alcohol and substance use in humanitarian and post-conflict situations. *Eastern Mediterranean Health Journal, 23*(3), 231–235. https://doi.org/10.26719/2017.23.3.231.
14. Hedegaard, H., Miniño, A. M., & Warner, M. (2018). *Drug overdose deaths in the United States, 1999–2017*. Hyattsville: National Center for Health Statistics, Centers for Disease Control and Prevention. Data Brief No. 329.
15. Hughes, C. E., & Stevens, A. (2010). What can we learn from the Portuguese decriminalization of illicit drugs? *British Journal of Criminology, 50*(6), 999–1022. https://doi.org/10.1093/bjc/azq038.

16. National drug threat assessment. (2018). Retrieved from https://www.dea.gov/sites/default/files/2018-11/DIR-032-18%202018%20NDTA%20final%20low%20resolution.pdf
17. Pardo, B., Taylor, J., Caulkins, J., Kilmer, B., Reuter, P., & Stein, B. (2019). *The future of fentanyl and other synthetic opioids*. Santa Monica: RAND.
18. Relatório annual 2008: a situação do país em matéria de drogas e toxicodependências, vol. I – Informação estatística. 2009. Lisbon Portugal: Instituto da Droga e da Toxicodependência
19. Schwetz, T. A., Calder, T., Rosenthal, E., Kattakuzhy, S., & Fauci, A. S. (2019). Opioids and infectious diseases: A converging public health crisis. *The Journal of Infectious Diseases, 220*(3), 346–349. https://doi.org/10.1093/infdis/jiz133.
20. Syrian refugee crisis: Aid, statistics and news: USA for UNHCR. (n.d.). Retrieved from https://www.unrefugees.org/emergencies/syria/
21. Walley, A. Y., Xuan, Z., Hackman, H. H., Quinn, E., Doe-Simkins, M., Sorensen-Alawad, A., et al. (2013). Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: Interrupted time series analysis. *BMJ, 346*, f174. https://doi.org/10.1136/bmj.f174.
22. Walsh, L. (2019). *Medication and counseling treatment*. Retrieved from https://www.samhsa.gov/medication-assisted-treatment/treatment#medications-used-in-mat
23. Wodak, A., & Cooney, A. (2004). *Effectiveness of sterile needle and syringe programming in reducing HIV/AIDS among injecting drug users*. Geneva: World Health Organization. Retrieved from https://www.who.int/hiv/pub/prev_care/effectivenesssterileneedle.pdf.