Critical Overview of Current Drug Abuse in Puerto Rico based on Governmental Data

Christian D. Del Valle-Colón, MS*; Julienn Torres-Rodríguez, BS*; Mallerie Carrasquillo-Rivera, BS; Esteban Fernández-Rodríguez, BS; Alejandra Beltrán-Rivera, BS; Patricia Pujols, BS; Carmen S. Maldonado-Vlaar, PhD

The abuse of psychoactive substances poses a critical public health challenge in Puerto Rico, with farreaching implications for both individuals and society as a whole. This article provides a comprehensive overview of the patterns and trends associated with drug abuse in Puerto Rico, focusing on alcohol, tobacco, cannabis, benzodiazepines, opioids, and methadone. Recent statistics reveal a concerning increase in substance abuse, particularly among young adults. Long-standing problems with alcohol and tobacco continue to drive chronic health conditions, while the legalization of medical cannabis has influenced its usage patterns. The abuse of prescription medications, especially benzodiazepines and opioids, has intensified, contributing to an expanding opioid crisis on the island. This review critically examines the current scientific literature, highlighting the urgent need for comprehensive, evidence-based strategies for prevention, intervention, and regulation. It also underlines the importance of continued research efforts and the development of tailored approaches to effectively address drug abuse in Puerto Rico. By shedding light on these complex challenges, the article provides valuable insights that can inform future initiatives aimed at curbing substance abuse and promoting the well-being of Puerto Rico's population.

[P R Health Sci J 2024;43(4):177-185]

Key words: Alcohol, Tobacco, Cannabis, Benzodiazepines, Opioids

The use and abuse of psychoactive substances in Puerto Rico is of increasing concern, having significant implications for public health and society as a whole. In recent years, the island population has sustained a notable rise in the consumption of substances such as alcohol (1), tobacco (2), cannabis (3), benzodiazepines (4), and opioids (5), as evidenced by alarming statistics. This escalating trend has raised significant concerns among health authorities and the scientific community, highlighting the need for an in-depth and evidence-based understanding of the issue.

This article addresses this challenge through a comprehensive review of current scientific literature. Its primary objective is to examine and synthesize key statistical data and research findings related to substance use in Puerto Rico. Through this analysis, we seek to provide a clear understanding of the scope of the problem and its impact on public health on the island. This evidence-based approach will serve as a foundation for guiding future research, prevention, and intervention strategies at a critical time for public health in Puerto Rico.

Methods.

The articles included in this review were identified through bibliographic searches in PubMed and several other reliable databases relevant to the topics. Additionally, statistics were obtained from the Mental Health and Addiction Services Administration (ASSMCA, by its Spanish acronym) of Puerto Rico through a formal request, along with reports from the Puerto Rico Medicinal Cannabis Regulatory Board (Junta Reglamentadora del Cannabis Medicinal: JRCM). The data were analyzed based on variables such as age, sex, and region to provide a comprehensive understanding of drug abuse patterns of the past 25 years. Data visualization was performed using GraphPad software, version 10.0.2 (171).

Alcohol

Alcohol abuse in Puerto Rico is deeply rooted in the island's historical narrative and has intricately shaped the collective idiosyncrasy of the island population. The thesis, titled Alcohol, economía y cultura: los problemas del ron en Puerto Rico (1949–1976) (Alcohol, Economy, and Culture: The Challenges of Rum in Puerto Rico [1949–1976]) (6), provides a historical chronicle of the role of rum in Puerto Rico. The origins of the rum industry in Puerto Rico are tied to a blend of Spanish and American cultural influences. A key moment in its development came with the opening of the Caribe Hilton Hotel, which marked Puerto Rico's emergence as a tourist destination and attracted significant American investment. As the industry gained momentum, it experienced multifaceted growth, including in the area of scientific research, through the establishment of rum distilleries, legislative adaptations prompted by rum smuggling facilitated by the arrival

University of Puerto Rico, Río Piedras Campus, San Juan, Puerto Rico

The authors have no conflict of interest to disclose. *Students that contributed equally to this article

Address correspondence to: Carmen S. Maldonado-Vlaar, PhD, University of Puerto Rico, Río Piedras Campus, Department of Biology, University of Puerto Rico, Río Piedras Campus, PO Box 23360, San Juan, PR 00926. Email: carmen. maldonado7@upr.edu

of vehicles at island ports, and the intricate relationship between the state and the industry, which resulted in regulatory measures governing sales and consumption. Moreover, advertising promoted rum consumption, foreign investments drove the industry's growth, and wartime initiatives increased rum production, making it more accessible to Puerto Rican soldiers.

Understanding the historical evolution of rum in Puerto Rico is essential for analyzing the island population's patterns of alcohol consumption. As revealed by the needs assessment report from the Behavioral Sciences Research Institute, by 2001 (7), roughly 1 in 100 individuals in Puerto Rico from the ages of 18 to 64 years met the criteria for Alcohol Use Disorder (AUD). The highest prevalence was detected within the 26 to 45 years age group, with 2.4% of its members affected by AUD. A more recent study

(mentioned in Medicina y Salud Pública) (8) revealed that 16.9% of the adults on the island—approximately 1 in 6—suffer from alcohol abuse or dependence. Unfortunately, the largest statistical sources are treatment centers such as ASSMCA, and their data are now outdated. This underscores the need for conducting a comprehensive census to ascertain the prevalence of alcohol-related disorders in the population.

The American Psychiatric Association (9) defines AUD as a complex condition characterized by persistent substance use despite the presence of detrimental consequences. Alcohol is an intrinsically addictive substance that leads individuals to develop tolerance and experience pleasure due to the release of neurotransmitters such as dopamine in specific brain circuits associated with reward, promoting chronic and excessive alcohol abuse (10). Prolonged alcohol consumption increases exposure to acetaldehyde, a toxic metabolic byproduct (11).

Figure 1 illustrates treatment patterns (categorized by region, sex, and age [Fig. 1A]) at ASSMCA (12) treatment centers, the prevalence of treated patients based on sex and region (Fig. 1B), and the overall number of cases across the island from 2015 to 2021 (Fig. 1C).

A significant disparity exists between the individuals meeting the criteria for AUD and those who seek treatment. This incongruity underscores the urgent need for concerted efforts aimed at addressing the issue of AUD. Such endeavors require a healthcare system that prioritizes, first, the prevention and, lacking that, the management of alcohol-related issues. To achieve this goal, the acquisition of more precise, current statistical data is of paramount importance. Alcohol stands as a major contributor to

Figure 1. Use and consumption of alcohol in Puerto Rico. A) Cases of patients treated in ASSMCA treatment centers, organized by region and age from 2019 through 2021. B) Prevalence of treated patients by sex and region. C) Total island cases from 2015 through 2021.



fatalities resulting from vehicular accidents, elevated crime rates, incidents of violence, and a spectrum of health-related problems (Centers for Disease Control and Prevention) (13), all of which have profound ramifications in society.

Tobacco

Throughout history, tobacco has played a significant role in Puerto Rican culture. In the last century, its increasing commercial value placed Puerto Rico as one of the leading exporters of this product to the US, positively impacting the local economy (14). Consequently, tobacco became popular among Puerto Ricans and, along with alcohol, emerged as a leading contributor to drug-related mental health conditions—such as substance use disorder although its consumption has decreased during the past decades (Fig. 2A). Recent studies have shown alarming trends regarding tobacco use among adolescents, with many of these individuals reporting having consumed nicotine-containing products at least once during the year prior to their having taken the survey (15).

Among Latino populations, nicotine consumption is high among adolescents, although cigarette smoking prevalence is lower in the prior group compared to non-Hispanic groups. This trend pattern is observed mainly among groups of young females and is commonly attributed to acculturation, while the opposite is observed in young males, depending on their country of origin (16). Overall, Latino males have a higher tendency to consume tobacco than do their female counterparts (Fig. 2B) and are more prone to develop tobacco-related diseases due to limited healthcare access, a lack of smoking-cessation campaigns directly targeting Latinos, and the effective marketing strategies used by the tobacco industry. Despite the global decline in tobacco use, its prevalence in Puerto Ricans living on the US mainland has remained unchanged over the past 2 decades. Moreover, compared to Hispanics from Central and South America, this group has a higher prevalence of active smokers, and they appear to be less influenced by such sociodemographic factors as education, employment, and social status. However, recent studies have demonstrated that low education levels are associated with a higher likelihood of smoking. It is strongly suggested that peer influence is the driving force for not only the smoking behavior of this group but also its early onset. Furthermore, other predictors of nicotine dependence in Puerto Rican adults include illegal drug use, personality attributes (such as risk-taking, depression, and disinhibition), and environmental domain factors (17).

Tobacco consumption has steadily declined due to widespread efforts to raise awareness about its detrimental effects (18), accounting for approximately a 10% decrease in the early 21st century. In response, global manufacturers have developed unconventional nicotine delivery methods, including electronic systems commonly known as vapes or e-cigarettes, heated tobacco products, and smokeless forms such as gums and patches. These newer products have grown popular over the last decade, causing a major impact on younger generations. Smoking prevalence remains a major public health issue as it is one of the main causes of death because of health risks associated with chronic exposure to nicotine. Moreover, the development of the previously named delivery technologies has also increased nicotine use among younger populations. The Puerto Rico Health Department has raised awareness concerning

this matter, hosting campaigns in schools, sharing infographics, and implementing restrictive laws regarding tobacco consumption in public areas, while also increasing sales tax and prices (2).

According to statistics provided by the ASSMCA, the regions with higher percentages of tobacco consumption in individuals aged 12 to 19 years correspond to cities rather than rural regions, with San Juan having the highest prevalence (approximately 11%). These results were not expected because cigarette smoking prevalence is usually higher in rural areas, suggesting that environmental triggers may not be the main factor for developing nicotine dependency among adolescents in Puerto Rico. There is a strong association between mental health disorders and the emergence of nicotine addiction in adolescents living in San Juan, Puerto Rico (19). A complex relationship exists between mental health disorders and smoking, especially among individuals who suffer from

attention deficit hyperactivity disorder, anxiety, and/or depression. Another factor influencing smoking behavior is peer/parental interaction dynamics, particularly in households where adults are drug-dependent. This is further confirmed by a survey published by the ASSMCA, which reported that elementary and secondary school students claimed that they acquired cigarettes from peers (31.0%), by asking someone (24.1%), or at stores (21.9%) (15).

Despite an overall decrease in smoking prevalence among adolescents since 2001, there was a notable increase from 2019 to 2020, especially in male students from 15 to 19 years old (Fig. 2C). This spike could be attributed to stress factors related to the COVID-19 pandemic, as most students reported having experienced negative feelings, including nervousness, solitude, depression, and fear, all of which are known risk factors for dependency development (15).

Cannabis

In the US, including Puerto Rico, cannabis is categorized as a Schedule I drug by the Food and Drug Administration, meaning that it is considered to have no accepted medical use at the federal level and a high potential for abuse. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, has replaced the term "cannabis abuse" with "Cannabis Use Disorder," which encompasses patterns of impaired control, social dysfunction, risky behavior, and physiological adaptation associated with cannabis use (20, 21). The changing legal landscape surrounding cannabis, with a growing number of states favoring legalization, has led to its increased

Figure 2. Smoking prevalence of Puerto Rican adolescents. Cases (reported from 2001 through 2020) of individuals aged from less than 10 to 24 years. These individuals reported consistent tobacco consumption throughout the year prior to having taken the survey. A) Total cases reported by surveyed year. B) Reports divided by sex within a given year group . C) Data about tobacco use by those aged (less than) 10 to 24 years in 2020.



cultivation, the development of more potent strains, and a competitive marketplace. These shifts are often driven by perceived health benefits and a lack of wellsubstantiated health concerns. Cannabis use has been on the rise globally, including in Puerto Rico, with evolving laws influencing its availability and consumption and demographics and social contexts playing pivotal roles in shaping usage patterns (22).

In Puerto Rico, the use of cannabis is regulated by specific laws addressing both medicinal and recreational use. The first law, enacted in 2015, legalizes medicinal-cannabis use under certain conditions, establishing comprehensive regulations for its cultivation, processing, distribution, and utilization for medical purposes. This law also introduced the Medicinal Cannabis Program, which outlines requirements for patients, doctors, and authorized dispensaries. The

second law, passed in 2020, permits recreational cannabis use and possession for adults over 21, while extensively regulating the production, distribution, sales, and taxation of recreational cannabis (23). These laws represent a multifaceted approach to cannabis regulation in Puerto Rico, addressing both medical and recreational uses with the goal of ensuring safe, legal access to cannabis-based treatments for various medical conditions, while also regulating the broader recreational cannabis industry.

The use of medicinal cannabis in Puerto Rico has exhibited a consistent upward trend over the years. Recent data from the JRCM reveal that the age group with the highest consumption is the 21 to 30 years group (Fig. 3A), with males exhibiting a higher prevalence of medicinal-cannabis consumption than females (Fig. 3B). Over the past 3 years, a discernible consumption pattern has emerged concerning age and sex.

As of July 2023, however, the data indicate a nearly consistent level of consumption in both male and female populations compared to the figures from July 2021 and 2022. While it is important to note that this dataset may not represent the entire demographic spectrum of Puerto Rico, it nevertheless suggests that cannabis consumption has been stable over a period of time.

Conversely, when examining the age group engaging in recreational cannabis consumption, it becomes evident that this behavior is most prevalent among individuals aged 25 to 64 years, a trend seen across both users and non-users (individuals who do not report cannabis as their primary drug of use) (Fig. 3C). In alignment with the findings related to medicinal cannabis, males tend to dominate the demographic of recreational cannabis consumers (Fig. 3D).

Figure 3. Use and consumption of cannabis in Puerto Rico. A & B) The number of medicinal cannabis users by age (A) and sex (B) from 2021–2023. C & D) The number of recreational cannabis users by age (C) and sex (D) for 2022. These data are not representative of Puerto Rico.



It is imperative to note that the available data pertain to clients with specific sociodemographic characteristics who are utilizing recreational cannabis within the framework of the mental health and substance use treatment programs provided by ASSMCA in 2022 (24). These statistics exclusively reflect the clientele served under the purview of ASSMCA treatment programs and do not represent the broader population of Puerto Rico. Regrettably, no pre-pandemic data are available for comparison, rendering it challenging to draw definitive conclusions about the full impact of the pandemic on both recreational and medicinal cannabis consumption patterns.

Benzodiazepines (BZDs)

Since ancient times, natural and synthetic products have been used as pharmacological treatments against anxiety and insomnia. It was not until 1950 that the first 2 benzodiazepines (BZDs) were synthesized: chlordiazepoxide (Librium) and diazepam (Valium). Once introduced to the market as safe anxiolytics, their use increased rapidly. However, cases of the misuse and mishandling of these drugs soon followed, leading to a BZD addiction crisis in the 1980s. The primary effect of BZDs is sedation, which occurs through the activation of the gamma-aminobutyric acid (GABA) receptor complex. The interaction of BZDs with the GABA complex causes the opening of chloride channels, allowing the entry of more negative charges into the cytosol. This hyperpolarizes the membrane and reduces the excitability of neurons that regulate vigilance, emotions, cognition, and muscle tension (25). As a result, the activation of these inhibitory complexes produces a relaxing and sedative effect.

The routes of administration of BZDs include oral, intramuscular, and intravenous methods. It is important to emphasize that while doses of BZD produce relaxing effects, high doses can lead to hypnosis or coma. The biggest risk currently being faced in Puerto Rico is that people are taking high doses of BZDs combined with alcohol, which leads to a 90% fatality rate when both are ingested in large quantities. The common adverse side effects of BZDs include extreme sedation, a slowing of reaction time, and the impairment of memory and psychomotor function (26); a tolerance to sedation also occurs frequently. Since most anxiety disorders are chronic or relapsing, long-term treatment is often necessary. Many studies postulate that if a patient's dosage is increased, it is usually the result of attempts to eradicate all symptoms, manage withdrawal and rebound effects between doses, and/or address poor communication between doctor and patient. These increases are not necessarily due to the development of tolerance or attempts to achieve the anxiolytic effects or euphoria.

Surprisingly, the available statistical information we have on BZDs is related to non-prescribed purchases of these drugs at pharmacies (27). Nevertheless, there is a wide spectrum of purchasing behavior that is not being considered or monitored to determine the current status of BZD use on the island. For this study, we requested specific data from the ASSMCA (including age, sex, and year of treatment) regarding the use of BZDs in Puerto Rico. The data revealed 215 reported cases of non-prescribed BZD purchases in pharmacies in 2021, these purchases primarily involving females aged 45 to 64 years (see Figure 4A). The age range with the second highest number of purchases was that encompassing 65 to 79 years; once again, women outnumbered men. The data corresponding to 2023 indicate a decrease in the number of cases, with women still outnumbering men. This may suggest that females vulnerable to anxiety or insomnia, leading to increased BZD use. If we compare the dispensing data by sex and age for the year 2023, we observe the same pattern, although the number of cases can be seen to have dropped by more than 50%, with females still comprising the greatest number of users (Fig. 4B). Since the majority of BZD use has been dominated over the years by women (Fig. 4C), treatment efforts should be focused on addressing the specific needs of this population.

Opioids

Opium, extracted from the poppy plant, serves as the origin for a group of drugs referred to as opiates or, at times, opioids. Opioid is a broader term and encompasses not just opiates but also synthetic compounds and naturally occurring peptides that interact with opioid receptors in the body. Humans naturally have opioid receptors that are abundant in the brain and are responsible for releasing endorphins that alleviate pain, generate feelings of pleasure, and create a sense of well-being. However, this mechanism also presents a potential for abuse and the development of addiction.

According to the United Nations Office on Drugs and Crime (UNODC), in 2021, a total of 60 million people worldwide used opioids, with 31 million of them being opiate users, predominantly heroin (UNODC, World Drug Report 2023) (28). The global production of heroin in 2021 was approximately 495 to 755 tons, reflecting a more than 7% increase over the previous year (World Drug Report 2022) (29). About 35% of patients treated for drug abuse reported opioids as being their drug of choice, with approximately 85% of these patients being male and 15% being female. Opioids are the leading cause of drug-related deaths, being responsible for a staggering 77% of fatalities (29). The alarming

experience higher rates of anxiety and, perhaps, are more likely to seek medical treatment that results in the prescription of BZDs.

Additionally, we obtained data regarding BZD use at ASSMCA addiction treatment clinics. When evaluating the sex and age of individuals who were receiving BZDs for the years 2021 and 2023, we observed that females outnumbered males, once again. In Figure 4B, the data clearly show that the highest rate of BZD dispensing in 2021 occurred in individuals aged 45 to 64 years, with 280,599 of them being women and 210,842 being men. That same year, the second highest rate of BZD dispensing occurred in women and men aged 65 to 79 years, with a total of 196,889 and 124,424 dispensed prescriptions, respectively. This suggests that individuals in these age groups, particularly women, are more

Figure 4. Use and consumption of benzodiazepines (BZDs) in Puerto Rico. A) The use of BZDs acquired at addiction treatment clinics. B) The non-prescribed purchase of BZDs in terms of age and sex. C) The general consumption of BZDs by sex and year. These data are not representative of Puerto Rico.



Del Valle-Colón et al

drug abuse situation around the globe underscores the fact that opioids are the most abused drugs for non-medical purposes. In low doses, opioids induce drowsiness and provide analgesic effects, making them valuable for medical treatments. However, at higher doses—especially with fentanyl as one of the ingredients—they become lethal, as highlighted in the World Drug Report 2023 (28). Their euphoric effects can lead to addiction and, ultimately, if left untreated, can result in fatal consequences. In Puerto Rico, opioid addiction is prevalent due to the availability of both medical and illegal opioid products on the market. These products include controlled substances such as morphine, tramadol, codeine, and fentanyl (30).

The basis of opioid addiction can be represented in 3 distinct scenarios. The first one states that when influenced by factors such as cost, purity, perceived effects, and side effects, as well as accessibility and the regulatory measures in place, individuals tend to replace familiar opioids with alternative options or venture into experimenting with new opioids (28). In the second scenario, individuals may switch between different opioids or use them in a particular sequence for various reasons, including managing pain or coping with withdrawal symptoms, even when they are receiving prescribed opioid treatments. The third involves 3 types of individuals: those who are new to using opioids, those who use them often, and, occasionally, those who primarily use non-opioid drugs while unknowingly consuming opioids that have been added as adulterants or diluting agents in substances that are available on the market (29).

Puerto Rico, which is facing a severe drug addiction crisis (particularly with opioids), is known as a significant trafficking of the total reported cases. Although the number of cases varied each year, this trend of drug abuse remained relatively stable. In Figure 5C and Figure 5D, we can see that women consume more opioids than men in Puerto Rico; however, Figure 5A clearly shows that overdose rates in Puerto Rico are predominantly higher in men, with a ratio of 10 to 1 compared to women. This disparity could be attributed to 2 factors. First, nearly 50% of the prescribed opioids in Puerto Rico consist of fentanyl, a substance known for its high potential for both addiction and abuse. This trend (more men overdosing than women) is especially evident within the prison population, in which fentanyl is the opioid of choice. The second factor is that illegal drug consumption in Puerto Rico is male-dominated, which contributes to unregulated doses of opioids and increases the risk of possible overdoses.

While opioid abuse appeared to stabilize in 2020, there remains a pressing challenge in the development of effective drug-related treatments to combat and ultimately end this pervasive problem of opioid addiction.

Methadone as an Opiate Treatment

The development of methadone dates back to World War II when the drug became a substitute during a shortage of opium derivatives such as morphine and was used as a painkiller (31, 32). Methadone was first synthesized in 1939 at the laboratories of IG Farben, a large pharmaceutical company in Germany. By 1947, after the war, the patent rights were no longer protected, allowing the formula to be available for commercial production. The US company Eli-Lilly introduced its first version at reproduction under the trade name of Dolophine (from the

sharp increase in opioid overdoses was observed; starting in 2015, the increase peaked around 2018 with 1,836 recorded cases of opioid abuse-1,632 of which were males and 191 females. These numbers declined from 2018 to 2023 (ASSMCA) (Fig. 5A). The data provided by the ASSMCA indicate that most cases of opioid abuse are found in 2 age groups: 25 to 44 and 45 to 64 years, with these age groups consistently containing 81% to 85% of all the cases treated for opioid abuse over the years, as seen in Figure 5B. Among these, the 25 to 44 years age group has the highest rate of overdoses and abuse, by a large margin. The group with the third highest number of cases is the age group 20 to 24 years, which had its highest number of reported cases in 2017 (136 cases, representing about 7.5% of the total cases). Combined, all the other groups in

that same year had fewer than 12%

route to the US for illegal drugs. A

Figure 5. Opioid abuse statistics in Puerto Rico A) The number of overdoses and (opioid) abuse cases in Puerto Rico (registered by the ASSMCA). B) The distribution, by age group and year, of opioid abuse cases in Puerto Rico. C) Statistics gathered from the ASSMCA that illustrate how opioids were dispensed, by age and sex (2023). D) How prescription opioids were dispensed, by sex (2018–2023).



Latin words dolor, pain, and finis, end (from the French words dolo, pain, and fin, end) (33, 34) The formula eventually spread to different countries with the drug being formulated under different trade names, and in the 1950s and 60s, methadone became a key aspect of the medical treatment of patients who suffered from heroin addiction and other opiate addictions (35–37) because it was an effective medication for alleviating withdrawal symptoms (38).

Besides to its pharmacological mechanism of action in the brain, several factors make methadone an ideal treatment for drug addiction: By mimicking the effects of endorphins and enkephalins (endogenous opioids), methadone is involved in pain signal modulation (39). In addition, it acts as an N-methyld-aspartate (NMDA) receptor antagonist and as a μ -opioid receptor (mu) agonist, targeting the same receptors as heroin

(40-42), which is one of the most abused opioids worldwide. Methadone's antagonistic effect on NMDA receptors contributes to its analgesic properties by modulating central pain pathways and mitigating the development of opioid tolerance. Meanwhile, its agonistic action at mu receptors mediates its therapeutic effects, including analgesia, and the attenuation of withdrawal symptoms in individuals with opioid use disorder. This mechanism not only supports pain management but also helps in stabilizing opioid dependence and reducing the risk of overdose, ultimately enhancing overall well-being. Its effectiveness extends to individuals addicted to a range of opioids, from natural opiates such as heroin to synthetic opioids that have infiltrated illicit markets. The long-lasting duration of the drug helps to mitigate cravings, allowing the body's endogenous opioid system to adapt to more controlled and personalized dosages based on the specific needs of the patient. While heroin is a short-acting drug with a duration of 2 to 4 hours, methadone is a long-acting one that usually lasts from 24 to 36 hours (43), providing sustained relief and preventing early withdrawal symptoms. Additionally, methadone treatment carries a lower risk of drug overdose and death than treatments with other opioids or opiates. This reduced risk is partly due to its long-lasting effects, which allow for more stable dosing; the fact that it is administered in a controlled environment by medical institutions further mitigates risk.

In Puerto Rico, different institutions, including the ASSMCA, have been using methadone as an alternative treatment to combat opioid addiction. Unfortunately, the various programs have faced challenges in their efforts, as statistics indicate a concerning

Figure 6. Methadone treatment trends in Puerto Rico. A) The total number of admissions to a methadone treatment program, per region. B) The ratio of sexes of the patients admitted to a methadone treatment program, by region. C) The ages of patients who received treatment. D) Number of patients enrolled in a methadone treatment facility, by year. These data are not representative of Puerto Rico.



trend: a significant number of individuals who initially enter these programs ultimately discontinue their participation. Regarding patients admitted to the program, data from 2020 and 2021 show a decrease in the regions of Aguadilla, Bayamón, Caguas, and Cayey. Meanwhile, in the area of San Juan, the number of patients admitted increased, doubling the number of cases from 2019 (Fig. 6A).

Statistics from the ASSMCA have revealed a higher prevalence of opioid addiction among males compared to females (Fig. 6B). However, it is important to note that the underlying factors contributing to substance addiction remain underexplored for both sexes. In this context, individuals aged 25 to 34 years constitute a substantial portion of opioid addiction cases, representing a significant proportion of the total cases (Fig. 6C). In contrast, when examining the usage of other synthetic opioids, such as Tramadol, Oxycodone, and Fentanyl, a distinct pattern emerges. Users of these synthetic opioids are disproportionately concentrated within the age range of 45 to 65 years according to data from the Puerto Rico Opioids Dashboard. This underscores the demographic disparities in opioid consumption, although sex distribution remains relatively consistent.

Over time, records of methadone treatment have revealed fluctuating levels of utilization, with certain years indicating higher admission rates than others (Fig. 6D). However, incomplete data from some years creates gaps in our understanding of methadone treatment trends. After Hurricane Maria, in 2017, and later during the pandemic, the cases of opioid addiction in Puerto Rico increased. There was also an alarming increase in the number of overdose cases due to treatment interruptions, as some clinics were unable to operate (44, 45). The low number of patients who have completed the treatment raises concerns about the ASSMCA program's effectiveness; the program's 12-month duration might be making it challenging for patients to complete (46). Another challenge that makes this treatment difficult to complete is the fact that each patient requires a daily oral dosage, which can be obtained only by visiting one of the facilities. These factors underscore the need for a reevaluation of the current methadone treatment program to enhance its accessibility and success rates. The sudden rise in fentanyl-related overdose deaths presents a new threat to public health in Puerto Rico (47). Luckily, naltrexone, an opioid antagonist that acts by blocking the effect of opioids, has proven to be an effective medication in reversing these overdoses due to its rapid pharmacokinetics (48). Unlike methadone, which is a long-acting agonist that helps manage withdrawal symptoms and cravings by activating NMDA and mu receptors, naltrexone functions solely as an antagonist, preventing opioids from binding to these receptors. Its rapid pharmacokinetics make naltrexone particularly effective in reversing overdoses and maintaining abstinence from opioid use. This makes naltrexone a crucial option for those who have achieved abstinence and need to prevent relapse, whereas methadone is more suited to the longterm management of addiction and withdrawal.

Conclusion

The use and abuse of psychoactive substances, such as alcohol, tobacco, cannabis, benzodiazepines, opioids, and methadone, pose a critical challenge to public health in Puerto Rico. These substances have assumed a prominent role in the consumption patterns of the population of Puerto Rico, with alarming trends that indicate an increase in usage prevalence in recent years. The adverse health impacts and social implications of this phenomenon are significant, and the lack of effective interventions could further burden the healthcare system and society at large. Health authorities and local organizations need to continue working on prevention, intervention, and regulation strategies to effectively address this complex issue and improve the well-being of the Puerto Rican population.

Future reviews could gain valuable insights by comparing the approaches of the Substance Abuse and Mental Health Services Administration in the United States with those in Puerto Rico, offering a broader perspective and potentially identifying best practices that could be tailored to Puerto Rico's unique context.

Acknowledgments _

We would like to thank Dr. Carmen Maldonado-Vlaar for encouraging us to do this writing, which is based on what we learned in her course (Biol 6035, Fundamentals of Neuropharmacology at the Department of Biology, University of Puerto Rico, Rio Piedras Campus). We would also like to thank Dr. Cristina Martínez Benito for helping us with the grammatical revision of this review. We appreciate the assistance of the Administración de Servicios de Salud Mental y Contra la Adicción (ASSMCA), as this organization provided us with the information necessary to analyze drug use in Puerto Rico.

Resumen

El abuso de sustancias psicoactivas plantea un importante desafío de salud pública en Puerto Rico, con implicaciones de largo alcance tanto para los individuos como para la sociedad en su conjunto. Este artículo proporciona una visión integral de los patrones y tendencias asociados con el abuso de drogas en Puerto Rico, enfocándose en el alcohol, el tabaco, el cannabis medicinal, las benzodiacepinas, los opioides y la metadona. Estadísticas recientes revelan un aumento preocupante en el abuso de sustancias, particularmente entre los adultos jóvenes. Los problemas de larga data con el alcohol y el tabaco siguen provocando enfermedades crónicas, mientras que la legalización del cannabis medicinal influye en sus patrones de consumo. El abuso de medicamentos recetados, en particular benzodiacepinas y opioides, ha aumentado, contribuyendo a una creciente crisis de opioides en la isla. Esta revisión examina críticamente la literatura científica actual, destacando la necesidad urgente de contar con estrategias integrales de prevención, intervención y regulación basadas en evidencia. El estudio también subraya la importancia de continuar los esfuerzos de investigación y el desarrollo de enfoques personalizados para abordar el abuso de drogas en Puerto Rico de manera efectiva. Al destacar estos complejos desafíos, brindaremos información valiosa para informar futuras iniciativas destinadas a frenar el abuso de sustancias y promover el bienestar de la población de Puerto Rico.

References

- National Institute on Alcohol Abuse and Alcoholism. Alcohol use disorder (AUD) in the United States: age groups and demographic characteristics. National Institute on Alcohol Abuse and Alcoholism. Updated September 18, 2023. Accessed September 18, 2023. https://www. niaaa.nih.gov/alcohols-effects-health/alcohol-topics/alcohol-factsand-statistics/alcohol-use-disorder-aud-united-states-age-groupsand-demographic-characteristics
- Marrero-Gerena G, Ramírez AL, Ruiz-Serrano K, Felici G, Díaz-García R, Cases-Rosario A. What everyone should know about smoking in Puerto Rico. Tobacco Control Program, Department of Health Chronic Disease Prevention and Control Program. Accessed September 18, 2023. https://www.docs.pr.gov/files/ASSMCA/Estudios/Tabaquismo%20en%20Puerto%20Rico%202021.pdf
- Zehra A, Burns J, Liu CK, et al. Cannabis Addiction and the Brain: a Review. J Neuroimmune Pharmacol. 2018;13(4):438-452. doi:10.1007/s11481-018-9782-9
- Dubovsky SL, Marshall D. Benzodiazepines remain important therapeutic options in psychiatric practice. Psychotherapy and Psychosomatics. 2022;91(5):307-334.
- United Nations Office on Drugs and Crime (UNODC). Global Opioid Usage Data. Accessed September 8, 2023. https://dataunodc.un.org/ dp-drug-use-prevalence-regional
- Hernández López FY. Alcohol, economía y cultura: los problemas del ron en Puerto Rico (1949-1976). Doctoral thesis. University of Puerto Rico, Rio Piedras; 2021.
- Canino G, Vila D, Santiago-Batista K, et al. Need Assessment Study of Mental Health and Substance Use Disorders and Service Utilization Among Adult Population of Puerto Rico: Final Report to ASSCMA. Behavioral Sciences Research Institute, University of Puerto Rico; December 2016.
- Cuellar PF. Exceso de alcohol: un problema de salud pública en Puerto Rico y América Latina. Medicina y Salud Pública. August 26, 2022. Accessed September 9, 2023. https://medicinaysaludpublica.com/ noticias/neurologia/exceso-de-alcohol-un-problema-de-salud-publica-en-puerto-rico-y-america-latina/15254

- American Psychiatric Association. What is a Substance Use Disorder? Accessed September 9, 2023. https://www.psychiatry.org/patientsfamilies/addiction-substance-use-disorders/what-is-a-substanceuse-disorder
- Volkow ND, Michaelides M, Baler R. The Neuroscience of Drug Reward and Addiction. Physiol Rev. 2019;99(4):2115-2140. doi:10.1152/ physrev.00014.2018
- National Institute on Alcohol Abuse and Alcoholism (NIAAA). Alcohol Metabolism. Accessed September 18, 2023. https://www.niaaa.nih. gov/publications/alcohol-metabolism
- Administración de Servicios de Salud Mental y Contra la Adicción. Trastornos de substancias y uso de servicios en Puerto Rico. (Substance Disorders and Service Utilization in Puerto Rico). ASSMCA. 2009:90
- Centers for Disease Control and Prevention. Alcohol Use and Your Health. Accessed September 18, 2023. https://www.cdc.gov/alcohol/about-alcohol-use/.
- 14. Martínez AP, García JJ, Pérez MA. Puerto Rico's foreign trade between two empires, 1879-1923. Am Lat Hist Econ. 2021;28(1):e1118. doi:10.18232/alhe.1118
- Moscoso Álvarez MR, Colón HM, Reyes Pulliza JC, Rodríguez Figueroa L. El uso de substancias en los escolares puertorriqueños: Consulta juvenil VIII, 2020-2022. Administración de Servicios de Salud Mental y Contra la Adicción; 2023. https://docs.pr.gov/files/ASSMCA/Consultas/Informe_CJ_2020-22_ISLA_18%20abr%2023_FINAL.pdf.
- Unger JB, Falcon A. E-cigarette use among Hispanics: Reducing risk or recruiting new tobacco users?. Addict Behav. 2022;125:107149. doi:10.1016/j.addbeh.2021.107149
- Kerner JF, Breen N, Tefft MC, Silsby J. Tobacco use among multi-ethnic Latino populations. Ethn Dis. 1998;8(2):167-183. https://www.jstor. org/stable/45409216
- Polosa R, Casale TB, Tashkin DP. A Close Look at Vaping in Adolescents and Young Adults in the United States. J Allergy Clin Immunol Pract. 2022;10(11):2831-2842. doi:10.1016/j.jaip.2022.06.005
- Dierker LC, Canino G, Merikangas KR. Association between parental and individual psychiatric/substance use disorders and smoking stages among Puerto Rican adolescents. Drug Alcohol Depend. 2006;84(2):144-153. doi:10.1016/j.drugalcdep. 2006.01.008
- Budney AJ, Sofis MJ, Borodovsky JT. An update on cannabis use disorder with comment on the impact of policy related to therapeutic and recreational cannabis use. Eur Arch Psychiatry Clin Neurosci. 2019;269(1):73-86. doi:10.1007/s00406-018-0976-1
- Hasin DS. US Epidemiology of Cannabis Use and Associated Problems. Neuropsychopharmacology. 2018;43(1):195-212. doi:10.1038/ npp.2017.198
- Connor JP, Stjepanović D, Le Foll B, Hoch E, Budney AJ, Hall WD. Cannabis use and cannabis use disorder. Nat Rev Dis Primers. 2021;7(1):16. Published 2021 Feb 25. doi:10.1038/s41572-021-00247-4
- Regulatory Agency for Medicinal Cannabis (JRCM). Department of Health. Accessed May 24, 2023. https://www.salud.gov.pr/CMS/364
- 24. Administración de Servicios de Salud Mental y Contra la Adicción. Sociodemographic profile of clients who are recreational cannabis users served in the Mental Health and Substance Use Treatment Programs of the ASSMCA, calendar year 2022. Bayamón, PR: ASSMCA; May 3, 2023.
- 25. Rudolph U, Moss SJ. Modulating anxiety and activity. Science. 2019;366(6462):185-186. doi:10.1126/science.aaz3176
- 26. Greenblatt DJ, Harmatz JS, Shader RI. Diazepam in the Elderly: Looking Back, Ahead, and at the Evidence. J Clin Psychopharmacol. 2020;40(3):215-219. doi:10.1097/JCP.000000000001213
- Administración de Servicios de Salud Mental y Contra la Adicción (ASSMCA). Benzodiacepinas en Puerto Rico. Accessed March 15, 2023. Available at: Url: https://docs.pr.gov/files/ASSMCA/Material%20Educativo/Informe%20de%20Cosumo%20de%20Benzodiazepinas%20aprobado%2020.7.2023.pdf.
- UNODC. World Drug Report 2023. United Nations Office on Drugs and Crime; 2023. Accessed March 21, 2023. https://www.unodc.org/ unodc/en/data-and-analysis/world-drug-report-2023.html

- UNODC. World Drug Report 2022. United Nations Office on Drugs and Crime; 2022. Accessed May 12, 2023. https://www.unodc.org/ unodc/en/data-and-analysis/world-drug-report-2022.html
- 30. Colon Rodríguez CJ. Analysis of the Factors Influencing the Level of Opioid Use in the Eligible Adult Population under the Puerto Rico Medicaid Program and Beneficiaries of the Government Health Plan (Vital) during the Years 2019–2020. Dissertation. University of Puerto Rico Medical Sciences; ProQuest Dissertations; 2022.
- Fredheim OM, Moksnes K, Borchgrevink PC, Kaasa S, Dale O. Clinical pharmacology of methadone for pain. Acta Anaesthesiol Scand. 2008;52(7):879-889. doi:10.1111/j.1399-6576.2008.01597.x
- 32. Watanabe S. Methadone: the renaissance. J Palliat Care. 2001;17(2):117-120.
- Scott W, Livingstone HM, Jacoby JJ, Broberg GR. Early clinical experience with dolophine (No.10820). Curr Res Anesth Analg. 1947;26(1):18-21.
- Ball CM, Featherstone PJ. Methadone and buprenorphine: The search for a non-addictive opioid. Anaesth Intensive Care. 2022;50(1-2):4-7. doi:10.1177/0310057X211066706
- Payte JT. Methadone maintenance treatment: The first thirty years. J Psychoactive Drugs. 1997;29(2):149-153. doi:10.1080/02791072.1 997.10400182
- 36. World Health Organization. Clinical guidelines for withdrawal management and treatment of drug dependence in closed settings: methadone maintenance treatment. Accessed May 17, 2023. https://www. ncbi.nlm.nih.gov/books/NBK310658/#
- Judis J. Binding of codeine, morphine, and methadone to human serum proteins. J Pharm Sci. 1977;66(6):802-806. doi:10.1002/ jps.2600660615
- Dole VP. A Medical Treatment for Diacetylmorphine (Heroin) Addiction. JAMA. 1965;193:646-650. doi:10.1001/ jama.1965.03090080008002
- 39. Raehal KM, Schmid CL, Groer CE, Bohn LM. Functional selectivity at the μ-opioid receptor: implications for understanding opioid analgesia and tolerance. Pharmacol Rev. 2011;63(4):1001-1019. doi:10.1124/ pr.111.004598
- 40. Kosten TR, George TP. The neurobiology of opioid dependence: implications for treatment. Sci Pract Perspect. 2002;1(1):13-20. doi:10.1151/spp021113
- 41. Kreek MJ. Methadone-related opioid agonist pharmacotherapy for heroin addiction. History, recent molecular and neurochemical research and future in mainstream medicine. Ann N Y Acad Sci. 2000;909:186-216. doi:10.1111/j.1749-6632.2000.tb06683.x
- Ferrari A, Coccia CP, Bertolini A, Sternieri E. Methadone–metabolism, pharmacokinetics and interactions. Pharmacol Res. 2004;50(6):551-559. doi:10.1016/j.phrs.2004.05.002
- Hachey DL, Kreek MJ, Mattson DH. Quantitative analysis of methadone in biological fluids using deuterium-labeled methadone and GLC-chemical-ionization mass spectrometry. J Pharm Sci. 1977;66(11):1579-1582. doi:10.1002/jps.2600661120
- 44. Burgos-Barreto G, Garcia G, Zanko N, Santiago JG S. Opioid Use and Overdose Patterns in Puerto Rico in 2020-2022: A Retrospective Descriptive Study. Int J Curr Sci Res Rev. 2024;7(1):462-472. https:// ijcsrr.org/wp-content/uploads/2024/01/43-2001-2024.pdf
- 45. Quiñones DS, Melin K, Roman L, Rodriguez F, Alvarado J, Rodríguez-Díaz CE. Treating Opioid Use Disorder in Puerto Rico During the COVID-19 Pandemic: Providers' Leadership Efforts in Unprecedented Times. J Addict Med. 2021;15(4):276-279. doi:10.1097/ ADM.0000000000000764
- Curet E. Methadone maintenance for the treatment of heroin abusers in Puerto Rico. Dissertation. MI: ProQuest LLC; 2004. (Order No. 315600). Accessed May 7, 2023.
- Coto D. Growing opioid crisis adds to Puerto Rico's problems. PBS News Hour. Published January 7, 2019. Accessed March 15, 2023. https://www.pbs.org/newshour/nation/growing-opioid-crisis-adds-topuerto-ricos-problems.
- Ma J, Bao YP, Wang RJ, et al. Effects of medication-assisted treatment on mortality among opioids users: a systematic review and meta-analysis. Mol Psychiatry. 2019;24(12):1868-1883. doi:10.1038/s41380-018-0094-5