Opioid Overdose, Naloxone Administration, and Survival Outcomes in Puerto Rico: A Retrospective Analysis, 2019–2023

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Objective: Puerto Rico has had an alarming increase in opioid distribution, overdose, and opioid-related deaths in the last 2 decades. It is crucial to analyze both the effects of naloxone on mortality in opioid-overdose cases and the current trends in naloxone administration to implement strategies to reduce deaths from opioid-related overdoses.

Methods: This retrospective study analyzed opioid overdoses and naloxone administration in Puerto Rico from 2019 to 2023. The data was obtained from the Puerto Rico Mental Health and Anti-Addiction Services Administration and included findings on the spatial and temporal patterns of naloxone administration and a demographic description of the affected populations. Additionally, the study provided an overview of naloxone's role in fatality reduction in cases of opioid overdose.

Results: The key findings indicate a higher prevalence of naloxone administration in public spaces, with peaks occurring during afternoon hours; middle-aged men were the predominant group experiencing opioid overdoses. Additionally, the results demonstrated significantly higher mortality among individuals who did not receive naloxone. Those who received a single dose had a survival rate of 76%, compared to 56% for those who received no naloxone. Furthermore, individuals who received multiple doses of naloxone had an even higher probability of survival.

Conclusions: The findings present an effective approach to enhance the targeted geographic distribution of naloxone. Our findings indicated that increasing access to naloxone and strengthening overall community engagement could contribute to mitigating the ongoing public health crisis in Puerto Rico.

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Key words: Naloxone, Opioid Crisis, Puerto Rico, Overdose Prevention, Community Outreach

Epidemic Context in Puerto Rico

Puerto Rico is experiencing an opioid epidemic of alarming proportions. From 1999 through 2013, the island experienced more than a 100% increase in the distributions of fentanyl, oxycodone, methadone, and hydromorphone (1). This surge in opioid availability and use was later reflected in a 7.5-fold increase in non-fatal opioid overdoses from 2009 through 2018 (2). Unfortunately, the overall trends in opioid-related outcomes have not improved so far in the 2020s. The island experienced a steady increase in opioid-related deaths from 2018 through 2022. However, encouragingly, there was a 26.1% decline in the number of deaths from 2022 through 2023 (3).

This trajectory parallels that of the continental United States, where increased opioid availability has fueled a growing crisis of overdose mortality, which experts have characterized as occurring in 4 distinct waves. Lead by prescription opioids (1999–2017), heroin (2010–2017), illicit fentanyl (2013–present), and most recently polysubstance overdoses involving fentanyl with stimulants such as cocaine and methamphetamine (4).

Naloxone as a Critical response tool

Naloxone is a well-established opioid antagonist used to treat overdose. Initially restricted to hospitals, it is now widely utilized by medical and law enforcement personnel. As a high-affinity mu-opioid receptor competitive antagonist, naloxone rapidly reverses opioid-induced respiratory depression. It is a life-saving intervention that counteracts toxicity from opioids such as heroin, fentanyl, hydrocodone, and oxycodone (5). Its effectiveness in reducing fatalities is well documented, with studies showing that individuals who received naloxone during an overdose had 11 times greater odds of survival compared to those who did not (6). Survival is further improved when naloxone is administered by trained individuals in overdose recognition and response (7). In March 2019, Puerto Rico's Department of Health approved the purchase of intranasal naloxone without a prescription, highlighting the need for easy access (8). However, experts argue it should also be free of charge, given the economic barriers many Puerto Ricans face (9).

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Legislative and Community response

In Puerto Rico, local lawmakers enacted legislation to ensure the continuity of care for patients with opioid use disorder, an effort that demonstrates a multi-faceted approach to tackling the issue. In 2016, the United States government published the "Grants to Prevent Prescription Drug/Opioid Overdose-Related Deaths" (PDO) (10). Through this grant, Puerto Rico launched Proyecto PR PDO, a program aimed at strengthening efforts to prevent opioid overdose deaths by expanding community outreach, improving treatment referral pathways, and implementing a surveillance system to monitor naloxone use and overdose incidents, thus enabling earlier and more effective interventions. The project's initiatives involve distributing intranasal naloxone and fentanyl test strips, along with providing targeted training on naloxone administration for individuals who are likely to witness an overdose and be in a position to respond. The initial training efforts focused on local officials, including police officers and other first responders, former inmates, correctional officers, peer facilitators, and staff from community-based organizations (11). Community organizations and clinics have developed responses to Puerto Rico's opioid crisis; however, persistent barriers, such as delays in implementation and a lack of training in managing co-occurring mental health conditions, continue to hinder their effectiveness (12).

This paper aims to examine opioid overdose rates and patterns of naloxone use in Puerto Rico from 2019 through 2023, with a particular focus on survival outcomes following naloxone administration. By analyzing demographic, temporal, spatial, and situational variables, the study sought to identify key factors associated with fatal and non-fatal overdose events. Special attention was given to the impact of the number of naloxone doses on survival probabilities.

Materials and Methods

This retrospective analytical study provided a demographic description of the population affected by opioid overdoses in Puerto Rico spanning from June 2019 through March 2023. The Institutional Review Board at the San Juan Bautista School of Medicine granted this study ethical approval (EMSSJBIRB-5-2023).

Participants and procedures

The dataset was supplied directly to the senior investigator by the Puerto Rico Mental Health and Anti-Addiction Services Administration (Administración de Servicios de Salud y Contra la Adicción [ASSMCA]). *ASSMCA* translates to "Mental Health and Anti-Addiction Services Administration;" this organization is responsible for overseeing programs and services related to mental health and substance addiction, as well as data gathering, in Puerto Rico. Naloxone use was documented through field reports submitted by personnel affiliated with the ASSMCA, including individuals from community organizations, treatment centers, and emergency medical entities in Puerto Rico. The dataset included a range of variables, such as demographic information (e.g., age, reported sex/gender identity, and pregnancy status), as well as overdose-related details, including the date and time of the event and the specific location (e.g., public space, private residence) and municipality in Puerto Rico where the event occurred. Additional variables captured whether naloxone was administered, the number of doses given when it was, the individual who administered the naloxone (including citizens, emergency personnel, friends or acquaintances of the individual who overdosed, and unknown responders), and the substance suspected to be involved in the overdose (e.g., heroin, fentanyl, or a combination of these or other substances). Naloxone administration was defined as any documented delivery of naloxone (intranasal or intravenous) during a suspected opioid overdose event. A "dose" was defined as 1 unit of administration, such as a single nasal spray or injection, either of which would contain 4 milligrams of naloxone. A primary outcome was survival, defined as the individual being alive following the overdose event. Fatality was defined as any overdose event explicitly documented as having resulted in death in the field report(s) submitted by ASSMCA-affiliated personnel at the time of said event. All the cases were analyzed except for 12 duplicates, which were excluded. The data were anonymized to safeguard participant privacy. Strict privacy protocols were adhered to by the principal investigators throughout the handling of the data.

Data analysis

Descriptive statistics were used to summarize demographic and overdose-related variables. To evaluate whether women or men were more likely to be administered naloxone, we used chi-square tests. To assess whether the number of doses administered impacted individual survival, we used a logistic regression model (with a binomial response variable). In addition, to evaluate the changes in the temporal pattern of opioid use, we used a generalized linear model with a Poisson distribution, as the response variable consisted of counts (i.e., number of individuals). All the significance levels were set at the threshold of $P < 0.05$. All the analyses used data collected from June 2019 through March 2023, except for the demographic analysis presented in Figure 1, which excluded data from the partial collection periods in 2019 and 2023 (due to the mid-year start and early end of data collection, respectively). All the analyses were performed using R (version 4.2.2, R Core Team, 2024) (13), using the following packages: tidyverse for data wrangling (14), janitor for data variable cleaning (15), pois.exact from the epitools package to calculate Poisson confidence intervals (16), BinomCI from the DescTools package to calculate binomial confidence intervals (17), and chisq.test from the stats package (13,17), and for visualization, we used ggplot2 (14) and ggsci (18); for mapping, we used tigris (19).

Description of the population

The dataset covered the period from June 2019 through March 2023, as data collection by the ASSMCA began and ended within that period. The demographic characteristics of the population, as provided by the ASSMCA, are presented in Table 1. No significant association between reported sex/gender identity and naloxone administration was noted ($N = 1{,}428$, $\chi 2 = 0.001$, degrees of freedom [df] = 1, $P \leq .98$). Women were not more likely to have received naloxone than men; respondents who identified as transgender or elected not to provide information regarding either sex or gender were excluded from the analysis due to small sample

Table 1. Demographic characteristics of individuals who experienced suspected opioid overdose events reported to ASSMCA (2019–2023)

Demographic descriptors		
Variable	**Level**	**No. of Patients (%) (n = 1,428)**
Reported Sex/Gender	Men	1287 (90.15%)
	Woman	129 (9.04%)
	Transgender	2 (0.14%)
	Unknown	10 (10.70%)
Age, years	15–24	89 (6.23%)
	25–34	321 (22.48%)
	35–44	446 (31.25%)
	45–54	258 (18.07%)
	55–64	163 (11.42%)
	65+	43 (3.01%)
	Unknown	108 (7.56%)
Municipality	San Juan	196 (13.73%)
	Caguas	172 (12.05%)
	Vega Baja	145 (10.16%)
	Arecibo	100 (7.01%)
	Bayamón	67 (4.69%)
	Carolina	64 (4.48%)
	Ponce	61 (4.27%)
	Mayagüez	61 (4.27%)
	Manatí	47(3.29%)
	Fajardo	39 (2.73%)

Abbreviation: ASSMCA, Administración de Servicios de Salud Mental y Contra la Adicción

size. Most of the individuals who received naloxone were men, primarily aged 25 to 54 years (31.6%); among women, the 25- to 34-year age range was the most common (28.68%). Most naloxone administrations were carried out by emergency medical service personnel (737 [53.4%]), friends of the individual who overdosed (294 [21.4%]), or unspecified citizens (201 [16.6%]). Other reported administrators included family members of the individual who overdosed (11 [0.79%]), police officers (5 [0.4%]), and correctional officers (4 [0.3%]).

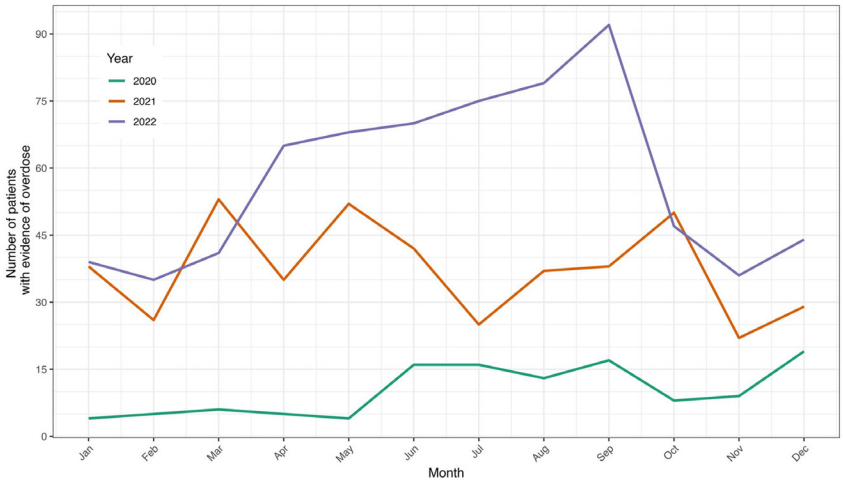
Temporal patterns: years, days of the month, weekdays, and times

The number of overdose cases documented by the ASSMCA increased steadily from 2020 through 2022, with the highest number of cases being reported in 2022 (n = 713), followed by 2021 (n = 477) and 2020 (n = 132) (Figure 1). In 2022, the monthly variation in the number of overdose cases was greater than in the other years in the dataset. Data from 2019 and 2023 were excluded from this analysis due to limited coverage, as data collection began in June of 2019 and ended in March of 2023. The probability of death varied from 2020 to 2023, with an approximate 50% reduction by 2023 compared to 2020. Notably, this probability of death was highest in the first year and declined consistently in the years that followed, reaching 6.5% in 2020, 4.9% in 2021, 4.6% in 2022, and 3.3% in 2023. Naloxone administration events did not differ significantly by the day of the week (generalized linear model with a Poisson distribution; all $p > 0.08$). However, Figure 2A shows a pattern of reduced instances of naloxone administration on Thursdays and Fridays. The distribution of naloxone administration varied significantly across different times of day. The period with the lowest median number of cases ranged from midnight to 5:59 a.m., while the highest ranged from noon to 5:59 p.m. (Figure 2B).

Impact of the number of naloxone doses on survival

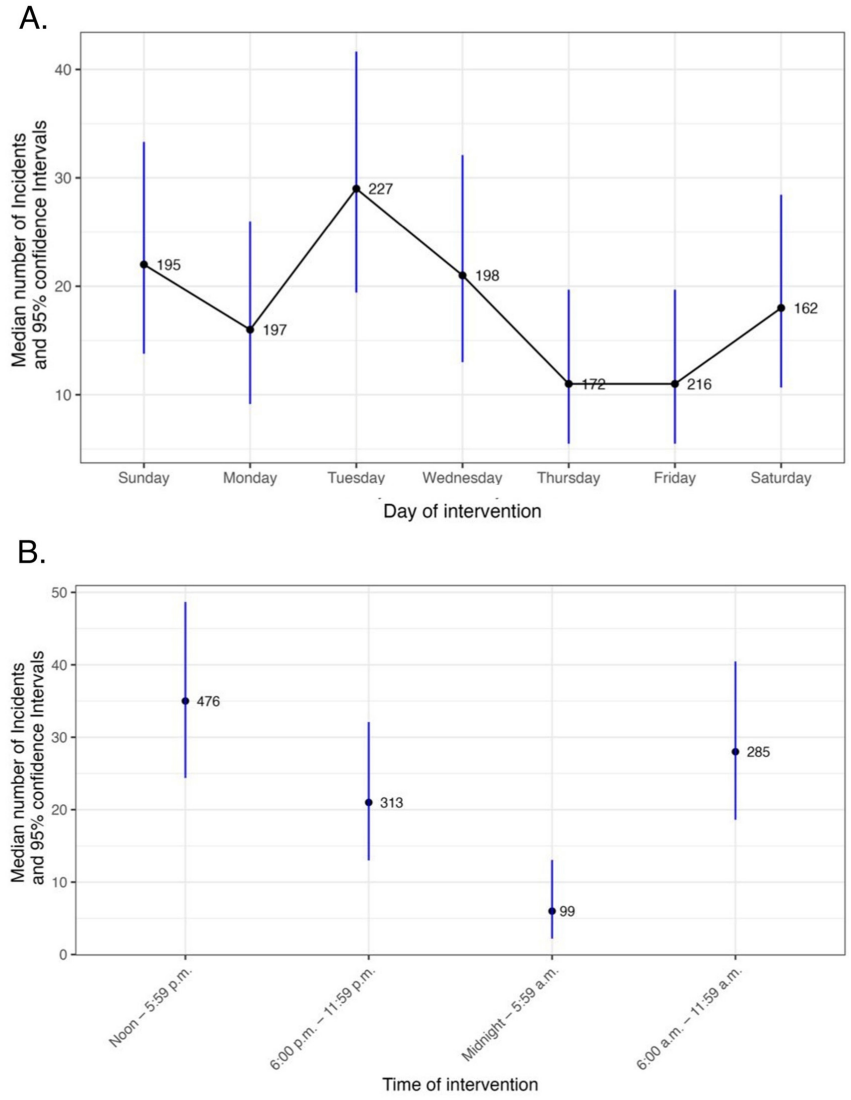
Survival was significantly associated with using naloxone ($\chi 2 = 20.49$, df = 3, $p = 0.0001$). The highest fatality rates occurred in cases in which no naloxone was administered—59%—compared to 2.5% with intranasal naloxone and fewer than 1% with intramuscular/intravenous naloxone. The administration of naloxone and the number of doses administered greatly impacted the probability of survival (logistic regression model coefficient = -2.344, $p < 0.0001$) (Figure 3). Consequently, a single dose had a substantial impact on survival. Individuals who did not receive naloxone had the lowest probability of survival (39.8%), while those who received 1, 2, or 3+ doses had higher survival probabilities (76.0%, 66.7%, 100%, respectively). None of the individuals who received 3 or more doses died (n = 47). Individuals who received more than 3 doses were excluded from figure 3 but not from the statistical analysis. The number of doses administered did not show significant differences by reported sex/gender identity (Poisson regression: $p > 0.85$) or age group (all p values > 0.043, df = 1233).

Figure 1. The total number of overdose cases in Puerto Rico from 2020 through 2022, by month



Legend: Reported opioid overdose cases from the years 2020–2022, as reported by ASSMCA. Years 2019 and 2023 were excluded due to the mid-year start and early end of data collection, respectively.

Figure 2. Temporal patterns of naloxone administration in Puerto Rico (2019–2023)



Legend: Figure 2A) The median number of cases per weekday, shown with 95% Poisson confidence intervals. Values displayed next to each median are the total number of cases for that day. Figure 2B) The time distribution of when individuals intervened and the 95% Poisson confidence intervals. Values displayed next to each median are the total number of individuals per time interval.

Site of intervention

Regarding the locations where naloxone was administered, they most frequently were public/open spaces ($\chi 2 = 1127$, df = 3, $p < 0.001$; n = 884 [62.6%]), followed by closed public spaces (n = 143 [10.0%]), private residences (n = 285 [20.0%]), and unknown/unidentified locations (n = 106 [7.4%]) (Figure 4).

Spatial distribution across Puerto Rico

The distribution of opioid overdose cases varied over the years. A noticeable trend emerged from 2020 through 2022, characterized by increasing numbers of cases (Figure 1) and broader geographic dispersion across municipalities, particularly in the final 2 years (Figure 5). Generally, higher numbers of cases were reported in larger municipalities, including those within the San Juan metropolitan area—San Juan, Bayamón, Carolina, and Caguas—as well as in the distinct metropolitan areas of Mayagüez, Arecibo, and Ponce (Figure 5), although cases were also present in municipalities with smaller populations.

Discussion

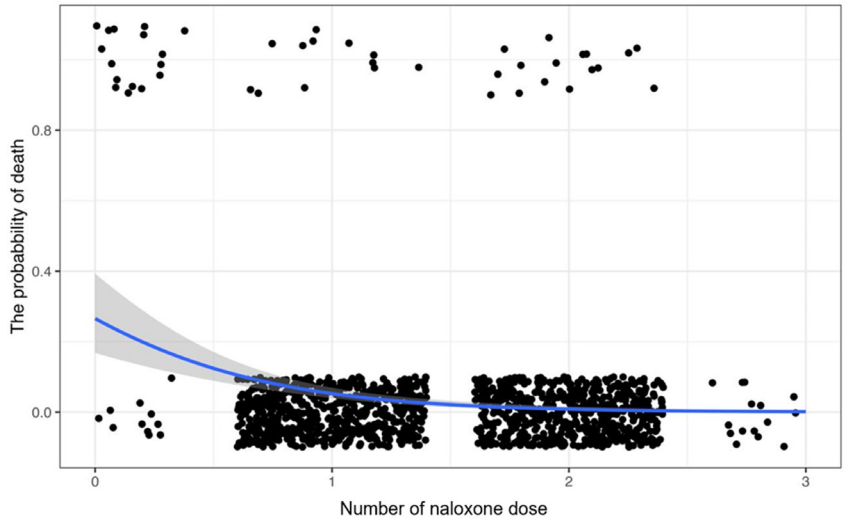
Demographic profiles and arguments for more targeted interventions

Our data indicate that the opioid overdose cases documented by the ASSMCA consisted primarily of men in the age range of 25 to 54 years. A consistent predominance of young adult men among overdose cases was also reported in studies conducted in Baltimore (65% men; median age, 46) (20), Australia (75% men; median age, 35) (21), Vermont (67% men; median age, 42) (22), and Rhode Island (53% men; median age, 35) (23). Given this demographic trend, targeted interventions should prioritize outreach and prevention efforts toward this group. For example, implementing community-based naloxone training programs specifically for settings that are predominantly populated by young men—such as nightlife establishments, correctional facilities, or reentry programs for formerly incarcerated individuals—could increase preparedness in overdose scenarios. Notably, our findings did not reveal a significant difference in the rate of naloxone administration to individuals by reported sex/gender identity, which contrasts with other studies, such as the one in Baltimore, in which men were more likely to be administered naloxone during overdose events (20).

Temporal and geographical patterns of use

The significant increase in the number of opioid overdose cases over the years, particularly in 2022, and the concentration of naloxone administration in the afternoon hours provide fundamental insights for resource allocation. Puerto Rico's increase in overdose cases from 2020 through 2022 mirrors a similar trend seen in Texas, where naloxone use steadily increased from 2019 through 2021 (24). The pandemic-related restrictions and lockdowns in 2020 and 2021 may have limited public activity and emergency medical encounters, resulting in the decreased reporting and visibility of overdose events. This could have contributed to an apparent spike in cases in 2022 as both mobility and data documentation returned to more typical levels.

Figure 3. Probability of death as a function of the number of naloxone doses administered



Legend: The probability of death as a function of the number of naloxone doses the individual received. A logistic regression model is shown: the blue line is the mean (best fit) model, while the gray area represents the 95% confidence intervals. Each point represents an individual who received naloxone; data points were jittered in order to observe their frequency, otherwise only 7 points would be observed, as they would overlap.

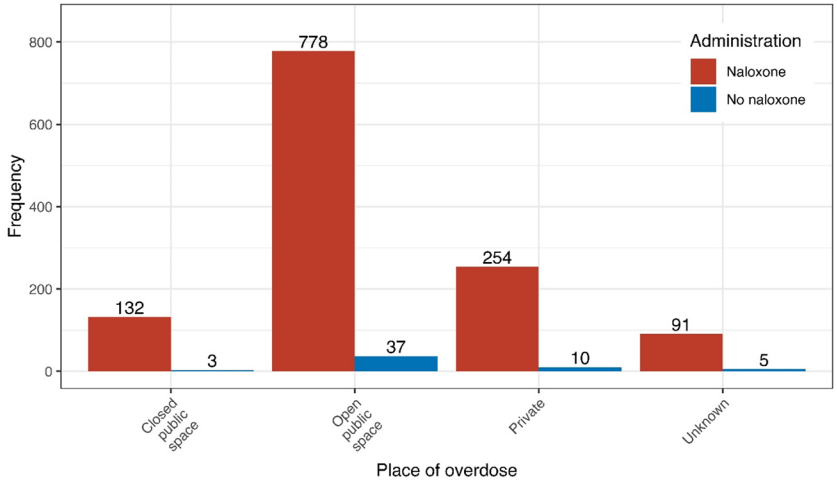
The weekly data showed reduced naloxone administration on Thursdays and Fridays, with most occurring from noon to 5:59 p.m. Although the daily time frame in our study was wider than those used in other studies, it still resulted in patterns similar to those observed in other locations. For example, the time frame of naloxone administration observed in Puerto Rico was comparable those reported in studies in Baltimore (4–5 p.m.) (20) and Australia (3–4 p.m.) (21) but differed from those in Rhode Island (9 p.m.) (23). The spike in overdose cases during the afternoon hours is likely multifactorial. One possibility explaining said spike is that more naloxone administrations occurred during these hours due to the greater availability of emergency medical personnel, who were among the most common administrators of naloxone.

Our study showed that naloxone administration most occurred in open public spaces. Our finding of naloxone use predominating in public settings contrasts with findings from places such as Texas (24), where most administrations occurred in private residences. One possible reason for the higher rates of naloxone administration in public areas rather than private homes may be a lack of naloxone availability within households. Notably, our map of interventions across Puerto Rico (Figure 5) indicates that most overdoses took place in major metropolitan areas, such as San Juan (including Caguas). Previous studies have examined behavioral differences among people who inject drugs in urban and rural regions in Puerto Rico. In urban areas, high-frequency users tend to cluster with others who also use frequently. In contrast, in rural areas, high-frequency users are more likely to be connected with both high- and low-frequency users, suggesting a more heterogeneous network, possibly shaped by close-knit community ties (25). This discrepancy in overdose rates between urban and rural areas may reflect different patterns of opioid use (using as part of a tight-knit community versus not) or drug availability.

Naloxone intervention and accessibility: enhancing survival and overcoming barriers in Puerto Rico

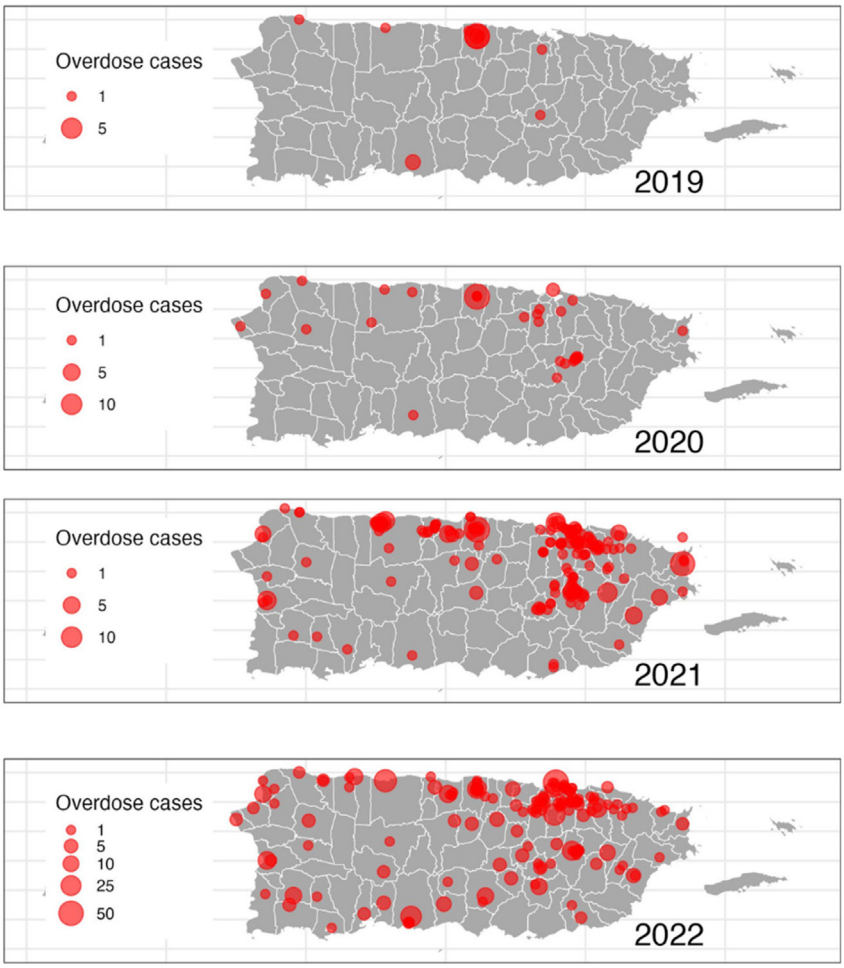
Our findings demonstrate that naloxone administration significantly improved survival among individuals experiencing an opioid overdose. From 2020 through 2023, the probability of death following an overdose decreased by approximately 50%, highlighting the positive impact of expanded naloxone distribution and training initiatives across the island. This reduction in fatality rates underscores the effectiveness of rapid overdose response and increased access to life-saving interventions. Although our study lacks pre-2019 data on fatal overdose outcomes for direct comparison, data from the Forensic Sciences Institute of Puerto Rico indicate a steady rise in opioid-

Figure 4. Distribution of overdose events and naloxone administration across different settings.



Legend: Frequency distribution of overdose events across multiple locations in Puerto Rico, categorized by naloxone administration and location. The data show a significantly higher frequency of naloxone use in open public spaces compared to other settings.

Figure 5. Geographic distribution and density of overdose cases in Puerto Rico, 2019–2022



Legend: Distribution of overdose cases across the main island of Puerto Rico. Data from 2019 include June and subsequent months. Dot size corresponds to the number of cases—the larger the dot, the greater number of cases. Note that the dots for a given location might vary in size from year to year (see scale).

related deaths from 2018 through 2022, followed by a decline in 2023 (3). These trends support the notion that broader naloxone accessibility and public health interventions may be contributing to recent reductions in mortality.

One of the major limitations of this study was the lack of reporting on xylazine use. Xylazine is a non-opioid muscle relaxant that was first used in the field of veterinary medicine as a horse anesthetic, and its use by injecting drug users—to enhance the effects of the opioids, among other reasons—was first identified in Puerto Rico in the early 2000s (26). Early studies found that xylazine prevalence was as high as 80.7% in injecting drug users in Puerto Rico (27). This finding is significant because naloxone does not directly inhibit the effects of xylazine (28). Furthermore, our data are from individuals who received services from associations affiliated with the ASSMCA and may not fully represent the entire Puerto Rican population. While data collection processes have improved over time, following the program's implementation, it is possible that some cases were underreported during the initial phase due to early documentation challenges. However, overall data quality and reporting consistency strengthened significantly throughout the study period.

Future research should continue to explore the barriers to naloxone use and the potential for broader educational campaigns and policy adjustments to enhance its accessibility in areas with high demands. Future studies should also consider the effect of xylazine on naloxone effectiveness, since it is a substance that is common in Puerto Rico and may interact differently with naloxone.

Overall, our findings underscore the pivotal role of naloxone in reducing opioid-related fatalities, advocating for increased accessibility and continued community engagement to address the ongoing public health challenge on the island. The 50% decline in overdose fatalities from 2020 to 2023 highlights the effectiveness of Puerto Rico's expanded naloxone distribution and public training initiatives in reducing opioid-related mortality. While our research aligns with other studies in key demographic and temporal patterns, it also reveals unique aspects of naloxone use in Puerto Rico. Continued efforts to enhance the data collection quality, building on existing public health strategies, are essential to mitigate the impact of the opioid crisis, effectively.

Resumen

Objetivo: Puerto Rico ha experimentado un alarmante aumento en los índices de sobredosis y muertes relacionadas con el uso de opioides en las últimas dos décadas. Es crucial analizar las tendencias actuales en el uso de naloxona para implementar estrategias para reducir las muertes por sobredosis relacionadas con opioides. Métodos: El estudio retrospectivo analizó la administración de naloxona desde 2019 hasta 2023, proporcionando una visión general de su efectividad en intervenciones por sobredosis. Los datos fueron obtenidos de la Administración de Servicios de Salud y Contra la Adicción de Puerto Rico y destacan los hallazgos sobre patrones de uso, descripción de grupos demográficos y los entornos de administración de naloxona. Resultados: Los resultados indican una mayor prevalencia de administración de naloxona en espacios públicos, con incrementos durante las horas

de la tarde. La población con la tasa de sobredosis más alta fue entre hombres de mediana edad. Además, los resultados demuestran resultados letales significativamente más altos en individuos que no recibieron intervención con naloxona. Aquellos que recibieron una dosis tuvieron una tasa de supervivencia del 76%, en comparación con el 56% de quienes no recibieron naloxona. Asimismo, la administración de múltiples dosis se asoció con una probabilidad aún mayor de supervivencia. Conclusiones: Este estudio confirma que la distribución geográfica de naloxona es una estrategia efectiva para reducir muertes por sobredosis de opioides. Se recomienda ampliar su accesibilidad y fortalecer el compromiso de las comunidades para enfrentar de manera continua el reto de salud pública que enfrenta la isla.

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