Brazilian Journal of Psychiatry
bjp
Revista Brasileira de Psiquiatria

Braz J Psychiatry. 2023 Sep-Oct;45(5):405-413
doi:10.47626/1516-4446-2022-3023
Brazilian Psychiatric Association

ORIGINAL ARTICLE

Drug overdose deaths in Brazil between 2000 and 2020: an analysis of sociodemographics and intentionality

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Objectives: To examine drug overdose records in Brazil from 2000 to 2020, analyzing trends over time in overdoses and overall sociodemographic characteristics of the deceased.
Methods: Using data from the Brazilian Mortality Information System (Sistema de Informações sobre Mortalidade), we identified records from 2000-2020 in which the underlying cause-of-death was one of the following codes: X40-X45 (accidental poisoning), X60-X65 (intentional poisoning), or Y10-Y15 (undetermined intentionality poisoning). The Brazilian dataset included 21,410 deaths. We used joinpoint regression analysis to assess changes in trends over time.
Results: People who died of drug overdoses in Brazil between 2000 and 2020 had a mean age of 38.91 years; 38.45% were women, and 44.01% were identified as White. Of the overdose deaths, 44.70% were classified as intentional and 32.12% were classified as unintentional. Among the identified drugs, stimulants were the most common class. However, most records did not report which drug was responsible for death.
Conclusion: Sociodemographic trends in overdose deaths in Brazil must guide country-specific policies. Nevertheless, data collection protocols must be improved, particularly regarding the drug used in overdoses.

Keywords: Drug overdose; substance-related disorders; central nervous system stimulants

Introduction

Drug use and drug overdose mortality is a public health crisis in many countries worldwide. Drug abuse is prevalent in Brazil: 3.9, 2.9, and 1.4% of benzodiazepine, opioid, and amphetamine users, respectively, report non-prescription use or prescription misuse during their lifetime.[1]

Stimulants are the leading drug involved in overdoses in Brazil.[2] Nevertheless, literature about drug overdose mortality in Brazil is scarce. In 1999, Mesquita et al.[3] conducted a cross-sectional survey in the metropolitan region of Santos, São Paulo regarding fatal and non-fatal overdoses among of 396 cocaine users. Although a few studies have been conducted on the topic, none have use nationwide data or focused on fatal overdoses. This study aimed to investigate the patterns and trends in drug overdose deaths in Brazil from 2000 to 2020.

Methods

Data source

Drug overdose data from Brazil were obtained from the Brazilian Unified Health System (Departamento de Informática do Sistema Único de Saúde) through the Mortality Information System (Sistema de Informações sobre Mortalidade) online database.[4] In Brazil, physicians must issue death certificates and fill out all relevant forms.[5] For deaths due to natural causes, such as disease, the death certificate can be issued by the attending physician or, when untreated, it is issued by a physician from the Death Verification Service (Serviço de Verificação de ＝bito). However, when the death is due to external causes or involves suspicious circumstances, the Legal Medical Institute (Instituto de Medicina Legal [IML]) must investigate.[6] The IML is a branch of the Department

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Submitted Dec 23 2022, accepted Jul 19 2023.

How to cite this article: Bianco MCM, Tardelli VS, Brooks ER, Areco KCN, Tardelli AO, Bandiera-Paiva P, et al. Drug overdose deaths in Brazil between 2000 and 2020: an analysis of sociodemographics and intentionality. Braz J Psychiatry. 2023;45:405-413. http://doi.org/10.47626/1516-4446-2022-3023

of Scientific and Technical Police (Departamento de Polícia Técnico-Científica) and is responsible for the autopsy and forensic procedures.[7]

Drug overdose deaths were identified using ICD-10 codes. We selected the underlying cause-of-death codes X40-X45, which refer to accidental poisoning and exposure to drugs (unintentional overdose), X60-X65, which refer to intentional self-poisoning and exposure (intentional overdose), and Y10-Y15, which refer to poisoning and exposure events with undetermined intent (undetermined intent overdose). The ICD code selection followed U.S. Centers for Disease Control recommendations for overdose analysis.[8-10] We excluded code X85, which refers to assault by drugs, medications, or biological substances. Since all reports with ICD codes V-Y are considered external causes of death, they must be assessed by the IML. It is important to note that there are no objective criteria for establishing intent in an overdose; it is determined through the doctor's assessment.

Drug use was only confirmed through laboratory analysis when the corpse underwent autopsy. In all other cases, the physician determined the involved drug according to the decedent's previous history and clinical evaluation. Furthermore, no specific ICD code exists for overdoses involving multiple drugs. To evaluate polydrug use, we searched for records with more than one ICD code for the drug of interest.

We examined data from 2000 to 2020, excluding all records identifying decedents aged $\leqslant$ 9 years or of undetermined age (323 records). The final dataset included 21,410 records including the following variables: i) year of death, ii) sex, iii) race, iv) age, v) place of death, vi) education, vii) marital status, viii) circumstance of death, ix) autopsy, x) underlying cause of death, and xi) other codes on the death certificate, such as T codes, which represent groups of drugs involved in the death.

Exposure variables

The following exposure variables were included: age (in years); sex (male or female), education level (incomplete high school, complete high school, at least some college, unknown/missing), race (White, non-White, or missing), marital status (single, married, divorced/widowed, unknown, or missing), autopsy (yes, no, unknown, or missing), circumstance of death (accident, suicide, homicide, unknown, other, or missing), intentionality (intentional, unintentional, or undetermined), T code recorded in the death certificate (yes or no), and T code type.

Indigenous people and Asians represented less than 1% of the population. Although *pardos* (mixed race) and Blacks represent a significant percentage of the population (nearly 45% and 8%, respectively), they are a minoritized group that faces oppression and marginalization. Considering this, we chose to classify race as White or non-White.

We did not perform a trend analysis for T code type due to the poor quality of the data: 76.72% of the records did not state the drug/s involved in the overdose.

To assess the intentionality of the overdoses, we considered two different sources of information in each record: intentionality in the ICD code for underlying cause of death and the circumstances of the death. The variable "circumstance of death" is reserved for deaths due to external causes.[11] It reflects intentionality in the cause of death, whether suicide, homicide, accident, or unclear. When the ICD code for "cause of death" was undetermined, the "manner of death" indicated whether it was intentional (suicide) or not (homicide or accident); we used this information to determine intentionality.

Analytical strategy

For all above-mentioned exposure categories, we computed summary statistics, mean, and SD for continuous variables and percentages for categorical variables using STATA SE 16.1 for Windows. We also used joinpoint regression analyses to assess changing trends over time. Joinpoint analysis fits a trend curve into a regression model that describes the data as parsimoniously as possible. This technique fits joinpoints to this curve to show significantly different trend lines. The ideal number of joinpoints is calculated using a permutation test. The program compares models with zero to three joinpoints with at least two observations between the joinpoints and indicates the model that parsimoniously describes the data. The point estimates for each trend line are the proportional variations provided with p-values, following an equation for a linear model. Our choice of "proportion" as the variable type assumed homoscedasticity, as has been done in other studies.[12,13] We used Joinpoint Regression Program 4.9.0.0 for these analyses. Statistical significance was set at $p < 0.05$.

Results

Descriptive analysis

Our analyses included 21,410 drug overdose deaths in Brazil between 2000 and 2020 (Table 1). The overall mean age of the victims was 38.91 (SD 16.49) years; the mean age did not vary significantly during the study period. Of all overdose deaths, 38.45% were women, 21.07% had not completed high school, and 30.92% had at least some college education. The proportions of unknown and missing education level were 12.86 and 7.99%, respectively. A total of 52.45% were identified as non-White. Autopsies were performed in 52.19% of the deaths, not performed in 25.01% of the deaths, and this information was missing in 20.63% of the reports.

Of the overdose deaths, 32.12% were reported as unintentional (X40-45) and 44.70% as intentional (X60-65). However, according to the circumstance of death, 31.84% were considered accidental and 37.68% as suicide.

Most records (76.72%) did not state the drug/s involved in the overdose. In the 4,985 records with drug information, cocaine was indicated in 47.12% (2,349), alcohol in 21.36% (1,065), benzodiazepines in 13.76% (686), and opioids in 5.36% (267). More than one drug was reported in 6.02% (300) of the records.

Table 1 Sociodemographic data of all individuals who died by overdose between 2000 and 2020 in Brazil (n=21,410)

Variable	Results
Age, mean (SD) years	38.91 (16.49)
Sex, total (%)	
Female	8,232 (38.45)
Male	13,178 (61.55)
Education, total (%)	
Incomplete high school or less	4,512 (21.07)
High school graduate	5,815 (27.16)
Some college or more	6,620 (30.92)
Unknown	2,753 (12.86)
Missing	1,710 (7.99)
Race, total (%)	
White	9,423 (44.01)
Non-White	11,230 (52.45)
Missing	757 (3.54)
Marital status, total (%)	
Single	12,702 (59.33)
Married†	4,975 (23.24)
Widowed or divorced	2,350 (10.98)
Unknown	845 (3.95)
Missing	538 (2.51)
Autopsy, total (%)	
Yes	11,174 (52.19)
No	5,354 (25.01)
Unknown	465 (2.17)
Missing	4,417 (20.63)
Circumstance of death, total (%)	
Accident	6,816 (31.84)
Suicide	8,068 (37.68)
Homicide	4 (0.02)
Other	1,052 (4.91)
Unknown	5,109 (23.86)
Missing	361 (1.69)
Intentionality, total (%)	
Intentional (X60-65)	9,570 (44.70)
Unintentional (X40-45)	6,877 (32.12)
Undetermined (Y10-15)	4,963 (23.18)
T code present, total (%)	
Yes	4,985 (23.28)
No	16,425 (76.72)
T code prevalence, total (%)‡	
Cocaine (T40.5)	2,349 (47.12)
Alcohol (T51)	1,065 (21.36)
Benzodiazepines (T42.4)	686 (13.76)
Other narcotics and psychodysleptics (T40.9)	419 (8.41)
Opioids (T40.0-4 and T40.6)	267 (5.36)
Presence of at least two T codes	300 (6,02)

Data presented as n (%), unless otherwise specified.
† We merged married and stable union in the same category, as they are similar.
‡ We presented the five most prevalent T codes; the percentage is of the total number of records with any T code.

Trends over time in total overdose deaths

There was an increasing trend in drug overdose deaths in Brazil between 2000 and 2020. Two joinpoint were identified: 2009 and 2012. There was a significant annual increase of 7.97 (CI 6.4-9.6, p < 0.001) percentage points between 2000 and 2009, followed by a significant annual increase of 22.20 (CI 4.0-43.7, p = 0.019) percentage points between 2009 and 2012. After 2012, there was a significant annual increase of 3.94 (CI 2.1-5.8, p < 0.001) percentage points (Figure 1).

Trends over time in drug overdose deaths by sex

Women

Regarding the percentage of women who died from an overdose (Figure 2), joinpoints were identified in 2010 and 2013. There was a significant annual decline of 1.31 (CI -0.3 to – 2.8, p = 0.015) percentage points for female victims between 2000 and 2010, followed by a non-significant annual decrease of 8.57 (CI -19.7 to 4.1, p = 0.161) percentage points between 2010 and 2013, and then by a significant annual increase of 2.71 (CI 0.9-4.5, p = 0.005) percentage points after 2013.

Trends over time in drug overdose deaths by race

Non-Whites

We observed three joinpoints (2004, 2007, and 2013) (Figure 3), starting with a significant annual increase of 5.26 (CI 2.1-8.5, p = 0.004) percentage points among

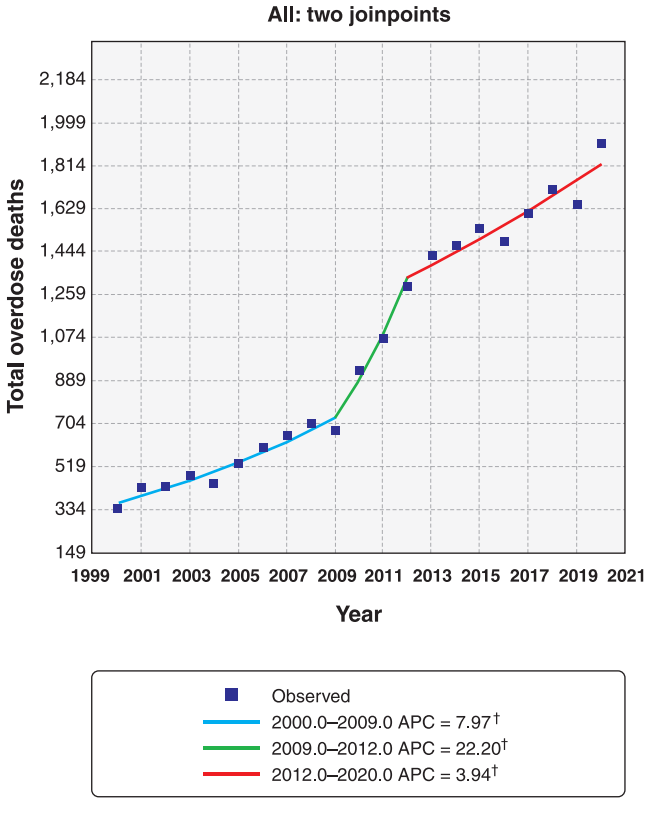

Figure 1 Joinpoint regression model with trends in drug overdose death counts from 2000 to 2020 in Brazil. Final selected model: two joinpoints. † Annual percent change (APC) was significantly different form zero at an alpha level of 0.05.

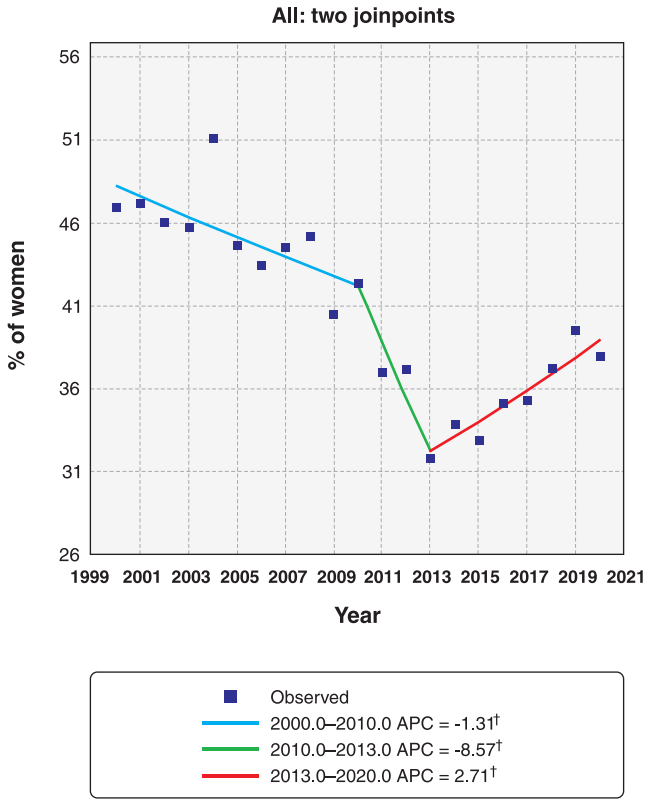

Figure 2 Joinpoint regression model with trends of the percentage of drug overdose deaths among women from 2000 to 2020 in Brazil. Final selected model: two joinpoints. † Annual percent change was significantly different form zero at an alpha level of 0.05.

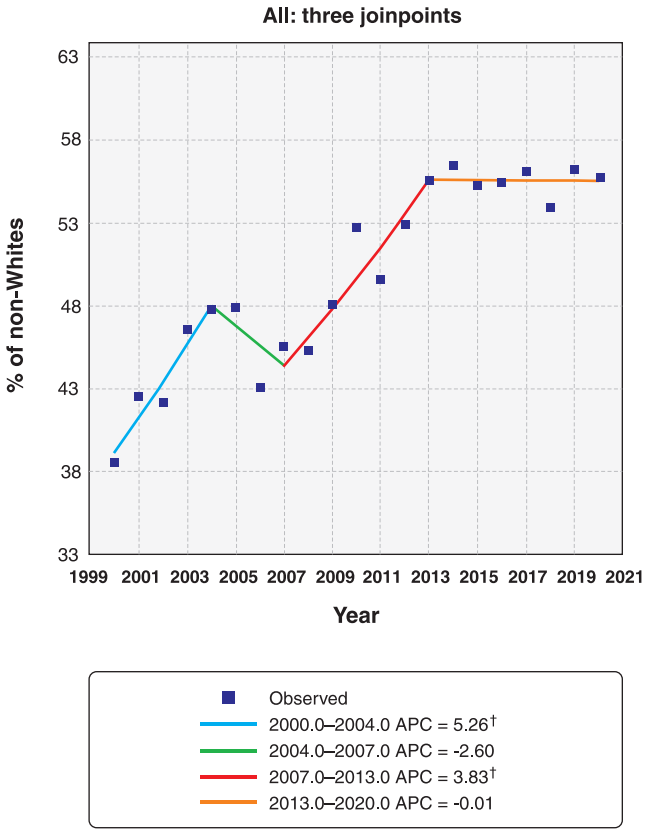

Figure 3 Joinpoint regression model with trends in the percentage of drug overdose deaths among non-Whites from 2000 to 2020 in Brazil. Final selected model: three joinpoints. † Annual percent change (APC) was significantly different form zero at an alpha level of 0.05.

non-Whites between 2000 and 2004, followed by a non-significant annual decrease of 2.60 (CI -11.5 to 7.2, p = 0.553) percentage points between 2004 and 2007, then by a significant annual increase of 3.83 (CI 1.6-6.1, p = 0.003) percentage points between 2007 and 2013, and finally by a non-significant annual decline of 0.01(CI -1.3 to 1.3, p = 0.985) percentage points between 2013 and 2020.

Trends over time in drug overdose deaths by education level

Regarding the education level of those who died from an overdose (Figure 4A), joinpoints were identified in 2008 and 2012 in the percentage of victims with incomplete high school. There was a significant annual decrease of 4.63 (CI -7.1 to -2.0, p = 0.002) percentage points between 2000 and 2008, a non-significant annual increase of 6.86 (CI -5.5 to 20.8, p = 0.263) percentage points between 2008 and 2012, and a significant annual decrease of 5.09 (CI -7.6 to -2.5, p = 0.001) percentage points between 2012 and 2020.

Among those who had completed high school (Figure 4B), a joinpoint was identified in 2015, with a significant annual increase of 4.33 (CI 5.2-10.5, p < 0.0011) percentage points between 2000 and 2015 and significant annual decline of 5.45 (CI -9.6 to -1.1, p = 0.019) percentage points between 2015 and 2020.

There was an increasing trend in drug overdose deaths among those with at least some college education. A joinpoint was identified in 2002 (Figure 4C). There was a significant annual increase of 27.11 (CI 6.6- 51.5, p = 0.011) percentage points between 2000 and 2002, followed by a significant annual increase of 5.11 (CI 4.5-5.7, p < 0.001) percentage points between 2002 and 2020.

Trends over time in drug overdose deaths according to intentionality

We found a decreasing trend in intentional overdoses during the study period. Joinpoints (Figure 5A) were identified in 2009 and 2013, with a non-significant annual decrease of 0.03 (CI -1.4 to 1.5, p = 0.969) percentage points between 2000 and 2009, a significant annual decrease of 11.94 (CI -18.8 to -4.5, p = 0.005) percentage points between 2009 and 2013, and a significant annual increase of 4.94 (CI 2.7-7.2, p < 0.001) percentage points between 2013 and 2020.

Joinpoints (Figure 5B) were identified in 2008 and 2014 regarding unintentional drug overdose deaths, with

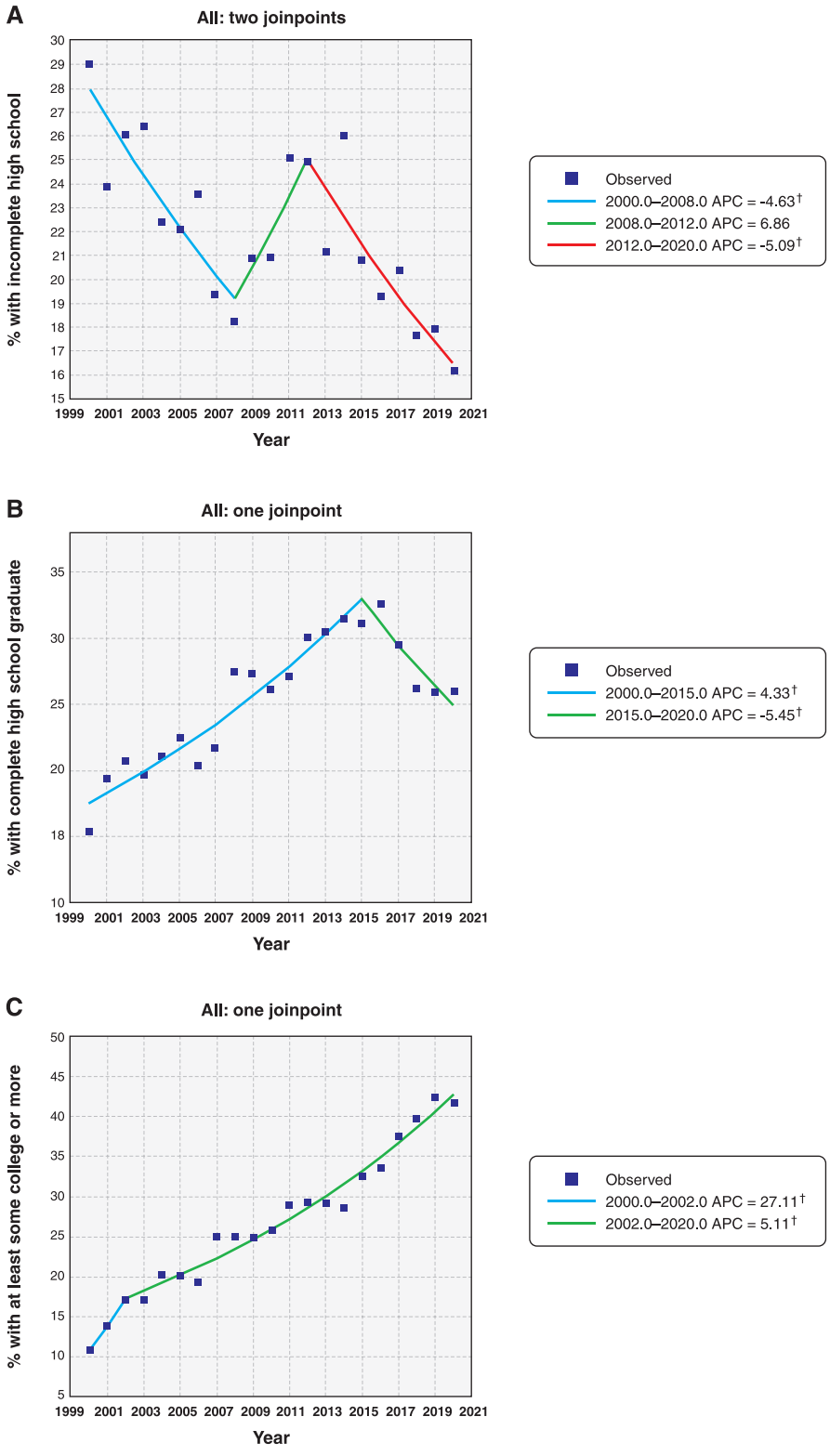

Figure 4 Joinpoint regression model with trends in education level among people who died from a drug overdose between 2000 and 2020. A) Joinpoint regression model with trends in the percentage of victims with incomplete high school or less. B) Joinpoint regression model with trends in the percentage of victims with complete high school. C) Joinpoint regression model with trends in the percentage of victims with at least some college. Final selected model: two, one and one joinpoints in A, B, and C, respectively. † Annual percent change (APC) was significantly different form zero at an alpha level of 0.05.

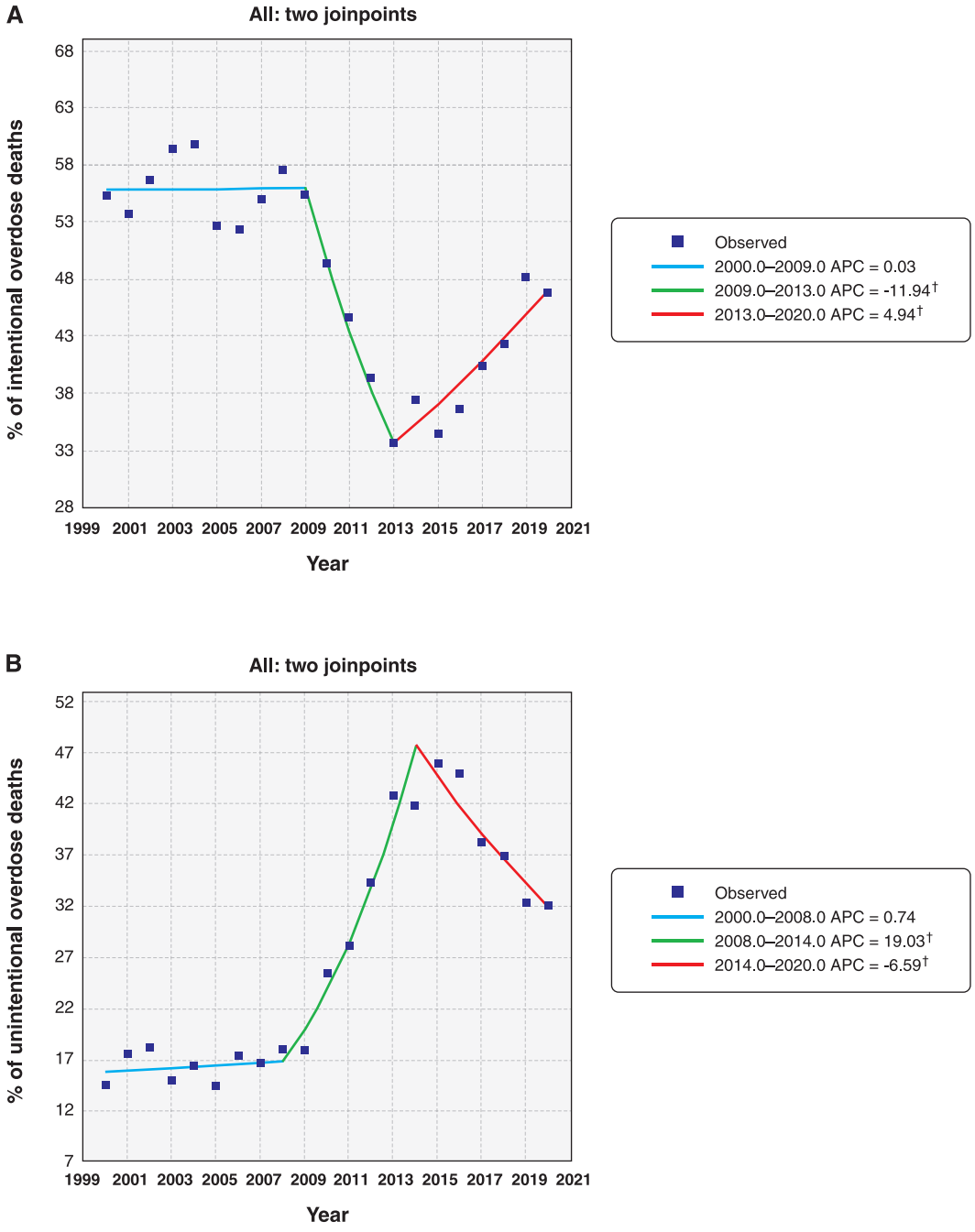

Figure 5 Joinpoint regression models of intentionality trends in drug overdose deaths from 2000 to 2020. A) Joinpoint regression model with trends in the percentage of intentional overdose deaths (ICD X60-65). B) Joinpoint regression model with trends in the percentage of unintentional overdose deaths (ICD X40-45). Final selected model: two joinpoints. † Annual percent change (APC) was significantly different form zero at an alpha level of 0.05.

a non-significant annual increase of 0.74 (CI -1.8 to 3.3, p = 0.545) percentage points between 2000 and 2008, a significant annual increase of 19.03 (CI 13.0-25.4, $p < 0.001$) percentage points between 2008 and 2014, and a significant annual decrease of 6.59 (CI -10.2 to -2.8, p = 0.003) percentage points between 2014 and 2020.

Discussion

This study examined the Brazilian national death certificate registry to characterize trends in drug overdose deaths between 2000 and 2020. During this period, the majority of drug overdose deaths occurred among single

(59.33%) non-White (52.45%) men (61.55%). Many drug overdose deaths were intentional: 44.70% were reported as X60-65 (ICD codes referring to intentional exposure), and the circumstance of death in 37.68% was reported as suicide). An autopsy was performed in 52.19% of the cases, although all records indicated an external cause of death. The involved drug was only identified in 23.28% of the records.

Drug overdose deaths increased during the study period, with the percentage of female and non-White victims decreasing and increasing, respectively. There was a trend toward a better education among victims, given that the percentage of those who had not completed high school decreased and those who had completed high school or had some higher education increased during the period. Regarding intentionality, we found a decreasing trend in intentional overdoses and an increasing trend in unintentional overdoses.

The most common drug associated with overdose deaths in Brazil was cocaine, reported in 47.12% of the records in which a drug was identified. In Brazil, there is little information regarding overdose deaths, but trends in overall drug use can inform this discussion in the absence of more specific data.

The increasing number of drug overdose deaths may be partially due to increased rates of mental health disorders and drug abuse in Brazil. Poor psychiatric health is a strong risk factor for overdose, non-fatal suicide attempts, and suicide. This association is well attested in the literature. A review by Bohnert et al.[14] examined overdose and suicide among drug users, finding that mental distress was a risk for both overdose and suicide. Drug absuse was a risk factor for both outcomes; the heavier the use of opioids, stimulants, sedatives, heroin, and cocaine, the greater the risk.

Bohnert et al.[14] suggested that assessing the intentionality of overdose deaths may be challenging. According to their interviews, many survivors of an overdose classified as intentional did not intend to end their life. Some participants reported wanting to be more intoxicated than usual, while others expressed emotions and stressors that could contribute to overdose, such as fear, anger, and hopelessness. These observations highlight the inconsistency of using an intentional/unintentional dichotomy to classify drug overdose deaths.

It is important to note that the number of both unintentional and intentional overdose deaths increased during the study period. The fluctuation in the percentages of intentional and unintentional overdose deaths represents their proportion of the total of overdose deaths in the corresponding year.

The prevalence of cocaine use can be explained by the proximity of the Andean countries in which it is produced, which affects drug prices. Legislation also plays an important role in the epidemiology of drug overdose deaths. The strict Brazilian regulations for opioid prescription and differences in medical culture have prevented the startling situation seen in North America.[15] A study analyzing the use, regulation, and harm caused by opioids in Brazil concluded that the country's regulations for opioid access are "highly restricted."[16] The Brazilian Ministry of Health and medical associations throughout the nation do not recommend the use of opioids; when they do recommend them, they are considered a second- or third-line strategy for pain management.[17-20] However, recent studies have shown a rising, albeit small, trend in opioid prescriptions.[16,21,22]

A national survey in Brazil that estimated the prevalence of crack/powder cocaine use found a notable sex difference: 78.68% of the users were male.[23] Specifically regarding overdoses, this survey found that 7.82% of the respondents reported having overdosed (i.e., an acute intoxication event) in the past 30 days: 44.72% due to crack, 12.78% due to cocaine, and 22.40% due to alcohol.[23] Although men used more crack/cocaine than women, women were at higher risk of a fatal or nonfatal overdose event.[23] Another study of cocaine users in the metropolitan area of Santos, a 450,000-inhabitant city in the state of São Paulo, found that female sex was associated with having one or more non-fatal overdose episodes.[3]

Crepalde et al.[24] found that mental and behavioral disorders due to cocaine use in Brazil increased between 2009 and 2019. These authors used data from the Global Burden of Disease Study to calculate the prevalence rate of cocaine dependence. This data may explain the increased drug overdose deaths among men, given that a higher proportion of men than women use cocaine.

Overdose deaths increased among non-Whites during the study period, which is due in part to the country's racial profile. In 2018, the self-reported racial composition of Brazil was 43.14% White, 46.54% mixed race, and 9.25% Black.[25] Data on racial patterns of drug use and overdose in Brazil are scant and are mainly derived from studies on crack/cocaine and alcohol. A nationwide survey by Bastos & Bertoni[23] showed that a large majority (79.15%) of crack users were non-White.

The prevalence of drug use in Brazil is higher among non-Whites than Whites.[1] Minorities are more likely to be socially vulnerable and have undesirable outcomes, such as overdose deaths. Likewise, Singh et al.,[26] reviewing U.S. data from 1999 to 2017, found substantial disparities in drug overdose mortality and treatment outcomes according to social determinants, such as economic and racial disadvantage. However, they also found that drug overdose deaths increased among those with a higher education level and decreased among those who had not completed high school. This may reflect a better overall education level in the population. In Brazil, educational indexes improved between 2000 and 2020. In 2001, 87.6% of the population $>$ 15 years of age was literate, while in 2017 it had increased to 93.2%.[27]

A national survey by Bastos et al.[1] identified two drug consumption patterns: i) the use of marijuana and similar substances was high among the general population, and ii) the prevalence of crack/cocaine use was low overall but was associated with overdose, accidents, and violence. Other risk factors, such as poor access to health care and social vulnerability (low education, poor social support, etc.), particularly in the latter group, may increase overdose rates.

This is even more concerning due to the increasing prevalence of non-medical opioid use in Brazil in recent

years, as reported by Krawczyk et al.[22] However, the context of opioid use differs greatly between Brazil and the USA: in Brazil, acute and chronic pain is more routinely managed with non-opioid analgesics and non-steroidal anti-inflammatory agents, since it is more difficult to prescribe and obtain opioids.

Our study is limited, first of all, by the incompleteness of the database used to search for death records. Brazil has parallel death reporting systems. The one used in this analysis – the Mortality Information System – is focused on vital and epidemiological statistics. The other system – the civil registry – is used for information about the legal rights of dying individuals. Neither are complete, and some deaths are reported only in one of the systems.[28] The advent of a single death certification number in 2006 enabled analysis of the linked dataset using generalized linear modeling. According to this analysis, the estimated completeness of the Mortality Information System and the civil registry in 2015 was 97% and 94%, respectively.[28]

Mortality-related factors may influence the data, since they can lead to misclassification. Although all records reporting an external cause of death must be processed and investigated by the IML, an autopsy was performed for only 52.19% of the deceased during the study period. The IML is a branch of the Department of Scientific and Technical Police and has state jurisdiction.[7] Thus, different jurisdictions may process death overdose investigations differently based on resource availability. In addition, in municipalities without an IML, a physician may be designated investigate deaths and issue death certificates.[6] All these factors, as well as the expertise of the physician who fills out the death certificate, can lead to bias in the data.

However, the greatest study limitation was the high proportion (76.72%) of unspecified overdoses, i.e., those without a T code in the death certificate. Thus, the drug that caused the overdose was specified in only 23.28% of the records, so although we concluded that cocaine was the most commonly involved drug, we are only referring to a minority of the records (47.12% of 4,985 records). This high percentage of missing data reduces data quality and the strength of the results. Moreover, Brazil is a very heterogeneous country. Regional characteristics may have influenced the data and are not appraised in this study. The lack of laboratory analysis to confirm the drug/s used prior to death is a further limitation.

In conclusion, the leading drug involved in overdose deaths is crack/cocaine; the majority of overdose victims were non-White men. Policymakers must consider these details when developing interventions to reduce overdose deaths, and the identified populations should be targeted in overdose prevention campaigns. Interventions could screen men who live in poorer areas for mental disorders and drug use/abuse.

Moreover, careful data collection is required to adequately substantiate the policy-making process. Data collection in general must be improved, particularly since the drug was unspecified in more than three-quarters of the overdose records (76.72%). These omissions harm the quality of the data and limit the analysis that can be performed. Finally, we recommend more extensive training for coroners, especially the standardization of record-keeping procedures.

Acknowledgements

This study was supported by a pilot grant from the Columbia University President's Global Innovation Fund (PI: SSM). MCMB was supported by the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) during the development of this study.

Disclosure

The authors report no conflicts of interest.

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