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Article

Psychoactive Substance Use and Violent Death: Toxicological and Geospatial Evidence from a Four-Region Cross-Sectional Study in Brazil

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Abstract

External causes of death contribute to over four million annual global fatalities, with drug use representing a significant risk factor. However, the true national impact and regional variations of psychoactive substance use in these deaths remains undefined in Brazil. To address this critical knowledge gap, this pioneering four-region study sought to elucidate the influence of alcohol and drug use on external cause mortality. We collected post-mortem blood from 3,577 victims of violent death across four distinct Brazilian regions using a standardized protocol to identify alcohol, illicit drugs, and psychoactive medicines. Analysis revealed a predominantly male cohort (89.7%; 56.0% aged 30 years or more), with homicide as the primary manner of death (67.3%). Critically, over half of the victims (53.0%) were positive for at least one psychoactive substance prior to death, most commonly cocaine (29.6%) and alcohol (27.7%). Substance consumption was highest among homicide victims (55.7%), predominantly cocaine (36.0%), and in self-harm cases (26.4%), which showed high benzodiazepine rates (20.0%). Consumption patterns varied regionally: alcohol-related deaths were more common in the Northeast, drug-only deaths concentrated in the Southeast and North, and the South showed a higher prevalence of alcohol use versus drug use. This widespread, regionally heterogeneous prevalence underscores the urgent need for targeted, region-specific interventions. By critically linking psychoactive substance use to various modes of violent death, these data provide crucial forensic and public health insights to inform tailored preventive strategies.

Keywords: post-mortem; violent deaths; illicit drugs; homicides

1. Introduction

External causes of mortality refer to all circumstances of unnatural deaths—that is, deaths not involving diseases or pathological conditions—as defined in chapter 23 of the 11th revision of the International Classification of Diseases (ICD-11). These deaths typically result from injuries caused by external agents, which the World Health Organization (WHO) classifies into categories: unintentional (accidental), intentional, interpersonal, self-inflicted, legal intervention, war, civil unrest, and undetermined intent [1] and are typically addressed as violent deaths.

In 2021, external causes accounted for over 4.4 million deaths globally, with traffic crashes leading at more than 1.1 million fatalities [1]. In Brazil, these causes resulted in 158,250 deaths in 2024, ranking fourth after circulatory system diseases, neoplasms, and respiratory diseases. Mortality rates from external causes have remained relatively stable from 2012 to 2023, with approximately 75 deaths

per 100,000 inhabitants in the latest year [2] (DATASUS, 2024). According to the Pan American Health Organization (PAHO, 2021), traffic crashes combined with interpersonal violence prematurely cost Brazil 2,649.1 years of life and accounted for a loss of 91.9 Disability-Adjusted Life Years (DALYs) [3].

External causes remain a major public health concern in Brazil, with an age-adjusted mortality rate of approximately 70.8 per 100,000 population in 2023, reflecting significant losses due to homicides (31.6/100,000), traffic crashes (15.1/100,000), and suicides (6.4/100,000) (WHO, 2024). Mortality disproportionately affects men and young adults, while regional disparities show higher risks in the North, Northeast, and Central-West regions [2]. These deaths not only cause premature mortality but also contribute substantially to the nation’s economic and social burden

Multiple complex factors influence injury occurrence from external causes, often making their elucidation challenging. Alcohol and drug use stand out as significant risk factors for such injuries and deaths. Goldstein (1985) proposed a triadic framework to understand the violence-drug nexus: psychopharmacological effects of substances (e.g., alcohol, cocaine, stimulants) that may provoke violent behavior; economic-compulsive motives driven by drug-seeking; and systemic factors related to the illegal drug market, which primarily victimizes users. These systemic factors stem from the illicit nature of drugs, rendering violence endemic to their context [4].

Victimization from external causes may also be linked to drug consumption, since the use of psychoactive substances (PSA) impairs cognitive and motor functions, potentially leading to involvement in accidents or acts that put the physical safety of the user or others at risk. These effects are generally associated with the pharmacological classes of the PSAs (stimulants, depressants, or central nervous system—CNS—disturbing agents) and the dose consumed [5].

Brazil’s vast territorial extent comprises diverse social, economic, cultural, and health landscapes, leading to regional variations in psychoactive substance use patterns and their impact on deaths from external causes. Regional differences also affect drug availability and pricing, influencing consumer profiles [6]. Despite the significance of substance use in external cause mortality, Brazil lacks nationwide studies correlating psychoactive substance consumption with deaths from traffic crashes, homicides, and suicides. Amid varying consumption patterns and drug availability across Brazil, a nationwide study correlating psychoactive substance use to these violent deaths remains crucial but methodologically challenging. This study aims to fill this knowledge gap by pioneering a comprehensive assessment across four macro-regions.

2. Materials and Methods

2.1. Study Design and Sample Collection

External causes deceased victims were included in a cross-sectional study among four Brazilian regions. In each geographical region, one state capital was selected as target based upon mortality rate and for being located along drug trafficking routes. Belém/PA, Recife/PE, Vitória/ES and Curitiba/PR were involved in sample collection representing the North, Northeast, Southeast and South regions respectively. In addition to the capital cities, satellite cities from each metropolitan region were also included. The selected cities exhibit significant differences in cultural, economic, social, and sanitary aspects, with human development indices (HDI) comparable to those of different countries, such as Tunisia (0.746), South Africa (0.741), Qatar (0.886), and Portugal (0.890) (Table 1). Sampling occurred during autopsies at the Institutes of Legal Medicine (ILM), that are official public forensic institutions responsible for autopsies in criminal cases.

Table 1. Cities included at the study and its social characteristics.

City	State	Brazilian geographical region	HDI*	External causes mortality rate/100,000*
Belém	Pará (PA)	North	0.746	43.5
Recife	Pernambuco (PE)	Northeast	0.772	143.8
Vitória	Espírito Santo (ES)	Southeast	0.845	197.0
Curitiba	Paraná (PR)	South	0.885	80.4

*data from 2021.

A representative sample of all violent death cases in each city was achieved by adopting a probabilistic sampling strategy [7]. All days and hours were included proportionally, allowing a population-based sample from each city to be achieved. Sample collection occurred in the four cities simultaneously and continuously from March 2022 to June 2024. All victims older than 18 years who were autopsied within eight hours of death were included. Decomposed corpses and victims who received six or more hours of medical treatment were excluded.

Data from the victim (age and sex) and information about the fatal injuries (i.e. day, time, cause and manner of death) were obtained from police records. Only closed cases with definitively determined causes of death were included.

2.2. Toxicological Analysis

Cardiac blood samples were collected during autopsies, using vacuum tubes containing sodium fluoride and ethylenediamine tetraacetic acid (EDTA) and stored at -20°C until transportation to the Toxicology Laboratory at the University of Sao Paulo Medical School. In cases where the cardiac chamber was not intact and sample risked contamination with stomach contents or other biological fluids or if there was insufficient blood available due to the extent of the injuries, peripheral (femoral) blood was collected.

All blood samples were analyzed at the Toxicological Laboratory from the University of Sao Paulo Medical School in Sao Paulo. Blood Alcohol Concentration – BAC was analyzed by headspace gas chromatography with flame ionization detector (HS-GC-FID) whilst drugs were detected by liquid chromatography with tandem mass spectrometry (LC-MS/MS). All analyzed substances and their respective cut-offs are presented in Table 2. Analytes were chosen given its importance at a Brazilian setting. Benzoylecgonine, major cocaine metabolite, was used to identify cocaine consumption.

Table 2. Analyzed substances and their analytical cutoffs limits.

Analyte	Cutoff (ng/mL)
Alcohol (g/L)	0.2
Cannabis	
Δ9-tetrahydrocannabinol (THC)	1
Cocaine and metabolites	
Cocaine	20
Benzoylecgonine	40
Cocaethylene	20
Anhydroecgonine methyl ester (AEME – crack cocaine)	20
Amphetamines	
Amphetamine	20
Methamphetamine	20
MDMA (3,4-methylenedioxymethamphetamine - ecstasy)	20
MDA (3,4-methylenedioxyamphetamine)	20
Benzodiazepines	
Clonazepam	5
7-aminoclonazepam	5
Alprazolam	5
Diazepam	10
Bromazepam	20
Oxazepam	10

Substance use was categorized into five groups (1) Any alcohol presence - detection of alcohol (2) at least one substance - confirmed positivity for alcohol and/or other drugs (3) only alcohol - positive BAC but negative for all other drugs (4) only other drugs - negative BAC but positive for at

least one other drug (5) two or more substances - positive for at least two different substances (which may include alcohol).

Additionally, proportions for alcohol-positive cases and drug-positive cases are reported, along with other combinations. These proportions indicate positivity for each respective group of substances and do not mutually exclude the concurrent use of other substances.

2.3. Geospatial Analysis

A geospatial analysis based on the macro region within the state capital was conducted to study the influence of alcohol and other drug use according to the place of the fatal injury. Death densities were calculated for each of the 4 macro regions based on the population rate for 2021 (per 100,000 population).

A map of Brazil divided into all states was used to input data on death densities by states according to drug and alcohol use positivity. A color gradient was used to illustrate death density rates across all four included states, with darker tones representing higher densities than lighter ones. The grouping of density rates across maps was reached using a Jerks algorithm, which makes an approximation of the intervals to the closest possible value of the median for each rate reported. MapInfo Professional software, version 10.0 was used.

Additionally, a ratio was created between mean death densities obtained for drug and alcohol positivity (q drug positivity / q alcohol positivity) grouped according to the four Brazilian regions involved in the study (North, Northeast, Southeast and South). A region with a “drug problem ratio” (DPR) greater than 1 indicates a higher density of drug positivity compared to alcohol, whereas rate values less than 1 indicate the opposite. DPR I is based on any results of alcohol and drugs, whereas DPR II considers findings of alcohol alone and drugs alone.

2.4. Statistical Analysis

Absolute and relative frequencies (%) are presented for categorical variables. Associations between categorical variables were analyzed using bivariate cross-tabulation and Pearson’s chi-square test. Crude odds ratios (ORs) and adjusted odds ratios (aORs), adjusting for sex, alcohol, cocaine, cannabis, and benzodiazepines use, were calculated using multivariable logistic regression. Variables for each logistic regression model were selected based upon statistical significance derived from Pearson’s chi-square test. Significance levels were set at $p < 0.05$. All analyses were conducted using STATA statistical software, version 16.1 (College Station, Texas, USA).

3. Results

A total of 3,577 victims were included. The vast majority were males (89.7%), aged 30 years or older (56.0%), and non-white (80.8%). Homicides were the main manner of death (67.3%), followed by traffic crashes (14.7%) and suicides (9.2%). More than half of the victims (53.0%) had consumed at least one substance before death, with cocaine being the most common (29.6%), followed by alcohol (27.7%), benzodiazepines (6.8%), and cannabis (2.2%). Homicide victims had the highest prevalence of alcohol/drug use (55.7%; 95% CI: 53.7-57.7), mainly cocaine use (36.0%; 95% CI: 34.1-38.0). Self-harm victims had the second-highest prevalence of substance use, with alcohol being the main substance (29.4%; 95% CI: 24.7-34.6). Those victims also presented very high rates of benzodiazepine consumption; one-fifth of the sample tested positive in toxicological analysis. While more than two in five traffic-related victims had consumed substances, this was driven especially by alcohol (38%; 95% CI: 33.9-42.2) (Table 3).

Table 3. Substance use confirmed among victims by manner of death.

	All deaths		Traffic-related		Homicides		Suicides		Poisoning		All others	
	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
n	3,577		524		2,406		330		52		265	
General positivity												
At least one	53.0	(51.3-54.6)	46.0	(41.8-50.2)	55.7	(53.7-57.7)	54.6	(49.1-60.0)	65.4	(51.3-77.2)	37.7	(32.1-43.7)

Specific positivity	Only alcohol	16.6	(15.4-17.9)	30.9	(27.1-35.0)	14.5	(13.2-16.0)	14.5	(11.1-18.8)	5.8	(1.8-16.8)	12.5	(8.9-17.0)
	Only drugs	21.6	(20.3-23.0)	5.5	(3.9-7.9)	27.3	(25.5-29.1)	10.9	(7.9-14.8)	32.7	(21.2-46.8)	12.8	(9.3-17.5)
	Two or more	10.9	(9.9-12.0)	7.1	(5.2-9.6)	11.7	(10.5-13.1)	14.8	(11.4-19.1)	13.5	(6.4-26.0)	6.0	(3.7-9.6)
	Alcohol	27.7	(26.2-29.2)	38.0	(33.9-42.2)	26.4	(24.7-28.2)	29.4	(24.7-34.6)	19.2	(10.5-32.5)	18.5	(14.2-23.7)
	Cocaine	29.6	(28.1-31.1)	9.9	(7.6-12.8)	36.0	(34.1-38.0)	21.2	(17.1-26.0)	44.2	(31.2-58.1)	17.7	(13.6-22.8)
	Cannabis	2.2	(1.2-2.7)	0		3.2	(2.5-4.0)	-	-	0		-	-
	Benzodiazepines	6.8	(6.0-7.7)	4.4	(2.9-6.5)	4.8	(4.0-5.8)	20.3	(16.3-25.0)	25.0	(14.9-38.8)	9.0	(6.1-13.2)
	Alcohol + Cocaine	9.8	(8.8-10.7)	5.2	(3.6-7.4)	10.9	(9.7-12.2)	11.5	(8.5-15.4)	13.5	(6.4-26.0)	5.3	(3.1-8.7)
	Alcohol + Cannabis	-	-	0		-	-	0		0		0	
	Alcohol + Benzodiazepines	1.7	(1.4-2.2)	1.9	(1.0-3.5)	1.3	(1.0-1.9)	4.2	(2.5-7.0)	3.9	(1.0-14.5)	1.5	(1.0-4.0)

Note: - = <0.01.

Men were more likely to have consumed substances (OR = 1.52; 95% CI: 1.24-1.89), specially drugs (OR=1.92; 95%CI: 1.42-2.61) or a combination of substances. Young victims (less than 30 years old) consumed more drugs (OR=1.89; 95% CI: 1.59-2.22) while those aged 30 or more were more likely to have consumed alcohol alone (OR = 1.94; 95% CI: 1.59-2.36). Alcohol alone was strongly associated with traffic-related deaths, drug use associated with homicides and combination of substances with homicides and suicides. Alcohol use was associated with deaths occurring at nighttime and at weekends, used alone or in combination with other substances (Table 4).

Table 4. Substance use according to each substance group by demographic and fatal event characteristics (n = 3,577).

		All victims		At least one		Any alcohol		Only alcohol		Only drugs		Two or more	
		%	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)	OR	(95% CI)
Sex	Women	10.9	(9.9-11.9)	1.0		1.0		1.0		1.0		1.0	
	Men	89.1	(88.1-90.1)	1.52	(1.24-1.89)*	1.06	(0.85-1.31)	1.16	(0.87-1.57)	1.92	(1.42-2.61)*	1.52	(1.04-2.25)*
Age	Less than 30	44.0	(42.3-45.7)	1.0		1.0		1.0		1.0		1.0	
	More than 30 or equal	56.0	(54.3-57.8)	1.09	(0.95-1.26)	1.42	(1.23-1.63)*	1.94	(1.59-2.36)*	0.53	(0.45-0.63)*	1.11	(0.89-1.39)
Race	Non-white	80.8	(79.4-82.0)	1.0		1.0		1.0		1.0		1.0	
	White	19.2	(18.0-20.6)	1.17	(0.98-1.40)	2.52	(2.12-3.03)*	0.92	(0.72-1.16)	0.82	(0.65-1.03)	1.64	(1.27-2.12)*
Injury type	All others	7.4	(6.6-8.3)	1.0		1.0		1.0		1.0		1.0	
	Homicides	67.3	(65.7-68.8)	2.00	(1.51-2.66)*	1.42	(1.06-1.91)*	1.38	(0.93-2.08)	1.98	(1.32-2.95)*	2.18	(1.24-3.83)*
	Traffic-related	14.7	(13.5-15.9)	1.31	(0.96-1.80)	2.30	(1.66-3.19)*	3.27	(2.13-5.02)*	0.32	(0.19-0.56)*	1.22	(0.64-2.32)
	Suicide	9.2	(8.3-10.2)	1.81	(1.28-2.56)*	2.12	(1.49-3.02)*	1.08	(0.65-1.78)	0.76	(0.45-1.28)	2.70	(1.43-5.06)*
	Poisoning	1.4	(1.1-1.9)	2.78	(1.40-5.51)*	1.04	(0.52-2.09)	1.14	(1.07-1.22)	3.71	(1.77-7.75)*	2.62	(0.94-7.27)
Death time	Day	46.1	(44.3-47.9)	1.0		1.0		1.0		1.0		1.0	
	Night	53.9	(52.1-55.7)	1.75	(1.50-2.04)*	1.36	(1.17-1.59)	2.00	(1.61-2.48)*	1.12	(0.93-1.35)	1.64	(1.28-2.10)*
Death day	Weekday	62.6	(61.0-64.2)	1.0		1.0		1.0		1.0		1.0	
	Weekend	37.4	(35.8-39.0)	1.52	(1.32-1.76)	1.52	(1.31-1.76)*	2.28	(1.89-2.76)*	0.84	(0.70-1.01)	1.41	(1.13-1.78)*

*p<0.005.

The consumption of substances across Brazilian states was uneven. Deaths involving alcohol, either solely or in combination with drugs, were more prevalent in the Northeast region, while deaths involving only drugs were concentrated in the Southeast and North regions (Figure 1). The calculated DPR further confirmed the prominence of drug-related deaths in these regions. In contrast, the South region exhibited a higher prevalence of alcohol-related deaths compared to drug-related deaths, whereas the Northeast region showed a more similar distribution between alcohol and drug-related deaths (Table 5).

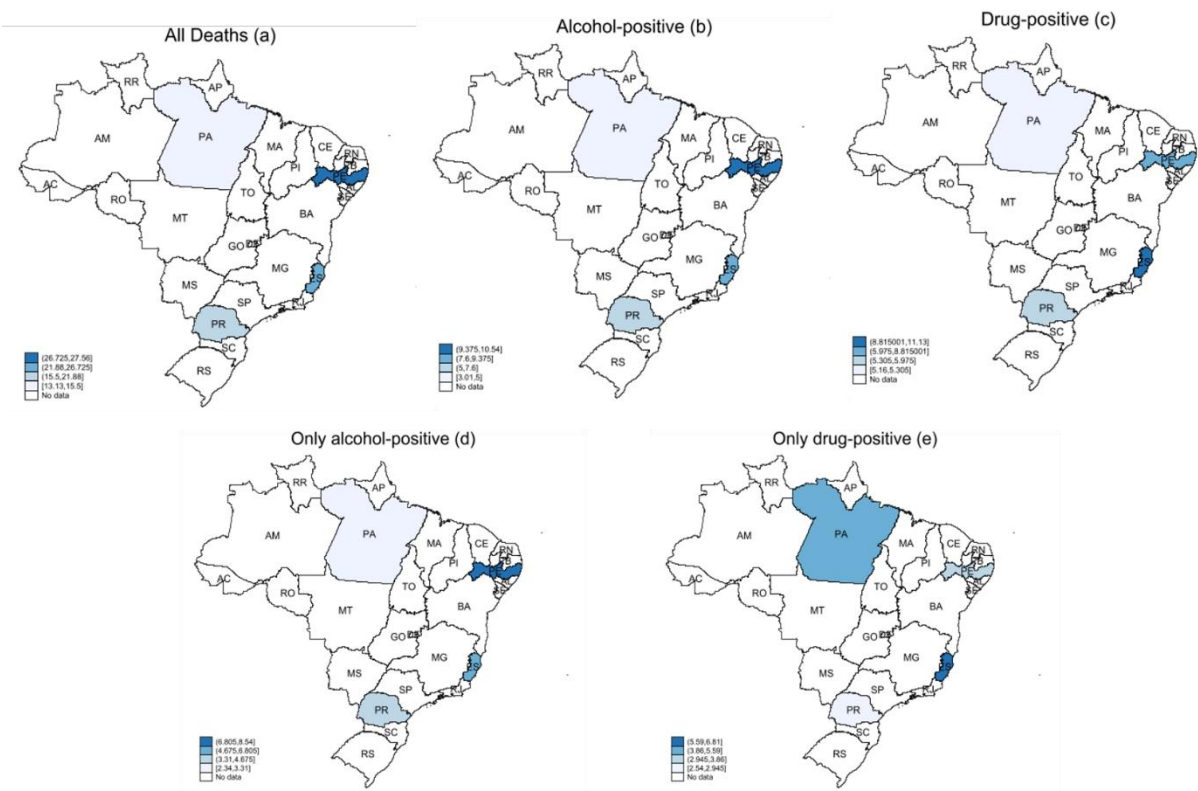


Figure 1. Calculated "drug problem ratio" (DPR) for each city included at the study.

Table 5. Mean death rates according to each positivity group and drug problem ratio (DPR = p drug / alcohol positivity) estimates among major regions in Brazil.

Regions	All deaths		Alcohol-positive		Drug-positive		Only alcohol		Only drugs		DPR I	DPR II
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)		
PA - North	13.13	(5.48-20.78)	3.01	(1.55-4.48)	5.16	(1.12-9.20)	2.34	(1.03-3.66)	4.37	(0.66-8.09)	1.57	1.95
PE - Northeast	27.56	(21.90-33.23)	10.54	(7.92-13.15)	6.50	(4.62-8.38)	8.54	(6.41-10.67)	3.35	(2.26-4.44)	0.80	0.57
ES - Southeast	25.89	(21.77-30.01)	8.21	(6.21-10.21)	11.13	(8.05-14.20)	5.07	(2.51-7.63)	6.81	(3.47-10.16)	1.39	1.39
PR - South	17.87	(13.85-21.88)	6.99	(4.69-9.29)	5.45	(3.50-7.41)	4.28	(2.07-6.49)	2.54	(1.60-3.49)	1.05	1.09

4. Discussion

The present study represents the first investigation among four Brazilian regions to comprehensively examine the association between psychoactive substance use and violent deaths across multiple geographic regions. The finding that over half of violent death victims (53.0%) tested positive for at least one psychoactive substance prior to death underscores the substantial role of substance use in premature mortality from external causes in Brazil. Overall, our findings align with international [8–10] and national [7,11,12] findings regarding postmortem toxicological analysis, while also revealing important regional and substance-specific patterns. Internationally, patterns of substance use vary by region; for example, in Cape Town, South Africa, 61% of assessed victims had consumed drugs, with methamphetamine, methaqualone, and diphenhydramine being the most prevalent [8]. In New South Wales, Australia, among homicide victims, 32.8% tested positive for illicit drugs, with cannabis (21.4%) and opioids (11.2%) being the most common [9]. By contrast, in Milan, Italy, cocaine was the most frequently used substance (27.9%) among postmortem cases, a pattern more closely aligned with our findings [10].

A previous Brazilian study found considerably higher figures for cocaine and cannabis use among homicide victims, 72.2% and 67.7%, respectively. However, in that study toxicological analyses were performed in a non-systematic way, restricted to victims in whom there was already some suspicion of drug use [12], which likely led to an overestimation of drug positivity when compared with the population-based and standardized approach used here.

The demographic characteristics of the victims in our study support the evidence that men are more likely not only to use alcohol and other drugs, but also to be involved in injurious events that result in fatal outcomes [13]. Moreover, given the significant association between exclusive drug use and victims under 30 years of age, there is a clear need to identify and intervene on problematic drug use in youth, since such behaviors can lead both to the perpetration of violence and to victimization [14].

Although cannabis is the most widely used drug in Brazil and its consumption has increased in the last decade [15], its prevalence in the present study was lower than expected, given that another investigation using the same general study design found a higher percentage of cannabis use (14.0%) among victims of violent deaths in the city of São Paulo [7]. A direct relationship between cannabis use and violence is not firmly established in the scientific literature, and there is ongoing debate about the magnitude of the association between the psychopharmacological effects of cannabis and the occurrence of injuries and deaths. Available data indicate that there may be a moderate increase in the probability of violence among cannabis users, a relationship that seems more evident among those with daily use and some degree of psychosis [16]. The pharmacological effects of cannabis include an altered state of consciousness and changes in time perception; at moderate concentrations, some studies suggest a temporary inhibition of violent behaviors [17]. Our results therefore do not suggest an absence of cannabis use in the population, but rather a low frequency of THC detection among victims of external causes in the studied cities, which may reflect a weaker epidemiological link.

Cocaine, in contrast, emerged as the most frequently detected illicit drug in our sample, particularly among homicide victims. This pattern is consistent with Brazil's role as both a transit corridor and the biggest consumer market for cocaine in South America and with previous studies that identified strong associations between cocaine use, criminal activity, and violent victimization [18]. However, the present study is cross-sectional and cannot establish causality between cocaine use and homicide, and the observed associations should be interpreted in light of psychopharmacological effects, economic-compulsive motives, and systemic violence related to the illegal drug market rather than acute intoxication alone. Even though, the consumption of cocaine has already been associated with increased criminality activities such as robberies [19].

Although alcohol has been regulated in road traffic in Brazil since 1998, it remains the main contributor to traffic crashes. Alcohol is a central nervous system depressant that reduces visual acuity, alertness, and motor and cognitive coordination, all of which are essential abilities for driving [20]. Even at low concentrations, alcohol causes impairments in users, and there is no safe level for driving, since there is a dose-response relationship with an exponential increase in the risk of involvement in traffic crashes [21]. In legal terms, Brazil has one of the strictest frameworks in the world, adopting a zero-tolerance policy for alcohol in drivers. Despite this, alcohol continues to be detected as the main substance among individuals injured [22] and killed [7,23,24] in traffic crashes, and our multicenter *postmortem* data confirm that alcohol remains the primary substance associated with traffic-related deaths. Enforcement of alcohol and other drug use among drivers is one of the most effective ways to reduce consumption of these substances by drivers and, consequently, to reduce deaths resulting from alcohol use. On the other hand, under current Brazilian law drivers may refuse to undergo breathalyzer testing, which, even with administrative sanctions (loss of driver's license and fines), results in a certain degree of impunity for offenders [25]. Thus, to translate Brazil's strict legal framework into greater population impact, it will be necessary to strengthen random testing and police enforcement, reduce the incentive to refuse testing, and integrate roadside enforcement with broader alcohol-control policies.

Regarding the geospatial analysis of alcohol and drug use, the cities located in the North (Belém, PA) and Southeast (Vitória, ES) regions showed the highest drug problem ratio coefficients, indicating greater drug use compared with alcohol. In our study, the drug problem ratio reflected the relationship between death densities with drug positivity and those with alcohol positivity, thereby summarizing whether a region is more "drug-dominant" or "alcohol-dominant" in terms of

substance involvement in violent deaths. Belém lies within the Amazon region and has several river branches used to transport cocaine from neighboring countries such as Peru and Colombia, which may partly explain the higher drug consumption relative to alcohol in this area [26]. By contrast, the cities in the Northeast and South regions (Recife, PE, and Curitiba, PR, respectively) are also located along drug trafficking routes but showed higher alcohol use than drug use [6]. These patterns suggest that, beyond trafficking routes, local drug markets, cultural norms, and social context shape which substances are most involved in fatal events. Therefore, more in-depth studies are needed to understand the dynamics of alcohol and other drug use in these regions, ideally combining toxicological data with information on seizures, prices, treatment demand, and community-level use.

Brazil, with its vast size and diverse landscapes, grapples with significant homicide rates despite a decline in certain states. In 2024, over 39,000 deaths resulted from homicides nationwide. The distribution of homicide rates is uneven throughout the country, with the Northeastern states experiencing the highest rates, while the Southeast and South states have witnessed a decline. Moreover, regions characterized by intense drug trafficking, particularly near international borders, tend to exhibit elevated rates. Beyond drug-trade violence, cocaine consumption itself may contribute to the heightened mortality rates observed in specific Brazilian regions, as our findings substantiate a link between cocaine use and homicides, suggesting that increases in cocaine availability and use may be accompanied by greater levels of lethal violence. A Brazilian study found that victims of violent deaths with a previous criminal record were more likely to have consumed any psychoactive substance before death [7], supporting the hypothesis that substance use, criminal involvement, and victimization form a mutually reinforcing cycle in certain populations.

The main strength of the study was the use of blood samples for toxicological analysis, since this is one of the best biological matrices to estimate the effect at the moment of death, meaning that at the time of the fatal event the victim was under the influence of the substance. In addition, the systematic and standardized collection of samples provided valuable inter-regional insights from different Brazilian locations, allowing a better understanding of the burden of drugs on violent deaths through a population-based analysis over a 27-month period and across four macro-regions. This multicenter, probabilistic sampling approach enhances the external validity of our estimates and allows for meaningful comparisons between manners of death and regions.

Despite these strengths, the study also has limitations. Because the locations were selected based on mortality rate data, this could introduce selection bias; however, since cities with large social differences were included, it is believed that generalization to other Brazilian locations is still feasible. Moreover, the lack of medical information in suicide cases makes it impossible to assess whether the benzodiazepines identified were being used under medical supervision or deliberately without professional monitoring. Furthermore, the strategy of excluding cases with more than six hours of medical treatment may have contributed, for example, to the low number of cases resulting from traffic accidents. Therefore, this does not indicate that the selected cities have low traffic-related mortality rates.

As noted above, the cross-sectional design of the study also prevents establishing a causal relationship between drug use and deaths, and toxicological positivity cannot be equated with direct cause of the fatal event. Nevertheless, evidence points to a higher probability of victimization after the consumption of psychoactive substances, a fact supported by the present findings. Therefore, drug use is a reality in the Brazilian population that must be approached holistically, so that the associated morbidity and mortality can be effectively controlled, through a combination of prevention, harm reduction, treatment expansion, and criminal-justice reform.

The relationship between deaths from external causes and drug use was evident in the data presented in this study, with more than half of the victims having consumed psychoactive substances, mainly cocaine and alcohol. Despite extensive debate, alcohol remains the main actor in traffic crashes, whereas cocaine is more associated with homicides and benzodiazepines with suicides. The prohibitionist, criminalizing model of drug control creates parallel – and often violent – markets, which can contribute to drug-related mortality [27] and to environments characterized by systemic

and structural violence, in addition to the racial and social injustices intrinsically associated with this perspective. [28]. There is, therefore, an urgent need to address drug consumption from a public health standpoint [29], recognizing that policies which prioritize treatment and social protection over punitive responses are more likely to reduce both substance-related harm and violent deaths. In addition, the geospatial patterns observed in this study, with Belém (PA) and Vitória (ES) showing higher relative involvement of illicit drugs, and Recife (PE) and Curitiba (PR) showing a more prominent role of alcohol, highlight that the burden of psychoactive substances on violent deaths is not homogeneous across the country. These regional differences suggest that prevention and control strategies must be tailored to local profiles of use and market dynamics, rather than relying on a single national model

In summary, the use of psychoactive substances is frequent among victims of violent deaths in Brazil, with more than half of the victims having consumed them, mainly cocaine and alcohol, and the combination of toxicological and geospatial analyses offers a crucial evidence base to guide region-specific, public-health-oriented responses.

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Informed Consent Statement: As this study used an aliquot of blood samples that would be used for police investigation, informed consent was waived.

Data Availability Statement: Since this study used data from police reports, even anonymized, to ensure the integrity of the police data, and given that cases may still be under judicial review, the database will not be publicly available. Any questions related to the presented data can be addressed to the corresponding author (HSB: hbombana@usp.br), who will evaluate the possibility of providing any data that does not interfere with ongoing police investigations.

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Abbreviations

The following abbreviations are used in this manuscript:

BAC	Blood alcohol concentration
DPR	Drug problem ratio
HDI	Human development index
OR	Odds ratio
PSA	Psychoactive substances
THC	Δ 9-tetrahydrocannabinol

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