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OUTPATIENT DISPENSATION OF OPIOIDS BY THE UNIFIED HEALTH SYSTEM IN BRAZIL AND MINAS GERAIS FROM 2018 TO 2023: AN ECOLOGICAL STUDY

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ABSTRACT

Background: Opioid use in Brazil remains low, despite international recommendations and growing demand for effective pain treatment. Objective: To analyze trends in the outpatient dispensation of selected opioids - codeine, morphine, and methadone - by the Unified Health System (SUS) in Brazil and in the state of Minas Gerais between 2018 and 2023. Methods: A descriptive and ecological study using secondary data from the health information systems of the SUS. Amounts in milligrams, equivalent in milligrams of morphine (MME) and defined daily doses (S-DDD per million inhabitants) were evaluated. Results: The most commonly dispensed presentations were codeine 30 mg and methadone 10 mg. Codeine was the most consumed opioid, followed by morphine and methadone. Between 2018 and 2023, a moderate upward trend was observed in Brazil (5.36% per year) and a sharper increase in Minas Gerais (56% per year). However, consumption levels remained very inadequate (<100 S-DDD), with significant fluctuations and a sharp decline in 2019. In 2023, Brazil reached 42.5 S-DDD/million inhabitants. Conclusions: The findings highlight the persistent underuse of opioids in Brazil and Minas Gerais, with structural, regulatory, and educational barriers hindering adequate access, especially among SUS users. There is an urgent need to strengthen public policies, improve the training of health workers, and ensure equitable access to essential medicines for pain relief.

Keywords: Opioids. Pain management. Pharmaceutical dispensing. Unified Health System. Brazil.

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INTRODUCTION

Chronic pain is an important complaint, associated or not with chronic comorbidities and with a prevalence that is difficult to measure. According to the 2019 National Health Survey of the Brazilian Institute of Geography and Statistics, half of the population of Brazil has at least one Chronic Non-Communicable Disease (IBGE, 2019). Among these, diabetes, rheumatic and oncological diseases, depression, musculoskeletal disorders, and back pain can course with chronic pain (MALTA et al., 2022).

The prevalence of pain in Brazil is 45.59%, affecting the population with lower income and less education, the elderly, the unemployed, and women (AGUIAR et al., 2021). The most affected sites were dorsal and lumbar regions, legs, head, knees, shoulders, and feet (MALTA et al., 2022; POSSO et al., 2018; VASCONCELOS et al., 2018), with the most frequent cause being disorders of the locomotor system (POSSO et al., 2018). The prevalence of chronic pain increases from adulthood onwards, with a peak around the seventh decade of life (MALTA et al., 2022).

The pharmacological treatment of pain was guided by the World Health Organization (WHO), which proposed the analgesic pain ladder based on the intensity of this symptom (COSTA et al., 2022; SOBRAMANIAN, et al., 2019). It is recommended that the use of opioids be gradually escalated with other categories of adjuvant medications, in order to increase the potency of the treatment, envisioning a synergistic effect between the modalities and a reduction in undesirable effects. The WHO advises the use of the oral route as the main form of drug administration and its continuous use at fixed times and, preferably, with controlled release for the continuity of treatment. Adjuvant medications can be represented by antidepressants, anti-inflammatories, anticonvulsants, corticosteroids, among others (SOBRAMANIAN, et al., 2019). In the category of opioids, they range from the weakest such as codeine to the strongest such as fentanyl and morphine, the latter being widely used in the medical field (COSTA et al., 2022; SOBRAMANIAN, et al., 2019).

The history of the use of these substances in Brazil deserves attention. While there has always been a concern about excessive and illicit use, health consumption can still be considered low. For example, in 2005, the household survey carried out by the Brazilian Center for Information on Psychotropic Drugs (CEBRID) showed that the share of the population that used opioids in their lifetime was 1.3%, with women, between 18 and 34 years of age, being the largest users of codeine syrups (1.9%). As a result, at that time, the country was the largest consumer of opioid painkillers in South America. In another study,

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with data from 2014 to 2018, opioid consumption was still low when compared to the entire Brazilian population, with no trend towards increases (CASTRO et al., 2022). However, despite indicators that point to low use, the consumption of opioids in Brazil has been gaining strength. Based on data extracted from the National System for the Management of Controlled Products (SNGPC), between 2009 and 2015, it was shown that the prescription of opioids in Brazil increased almost fourfold, with the main products being codeine-based (KRAWCZYK et al., 2018; BRAZIL, 2012).

In view of this scenario, the present study aims to describe the release profile of opioids as substances related to the reduction of suffering in the final stages of life and, at the same time, as a substance capable of providing increased mortality with complications of abusive use, focusing on the state of Minas Gerais and in comparison with the Brazilian reality.

LITERATURE REVIEW

PAIN: CONCEPTS AND DEFINITIONS

The IASP, in its 2020 review, defines pain as "an unpleasant emotional sensory experience associated with or related to actual or potential tissue injury" (UN, 2015). For didactic purposes, it is possible to classify pain based on criteria such as intensity, time of onset (acute or chronic), pathogenesis (nociceptive, neuropathic, nociplastic) (MIRANDA et al., 2016; HAUSTEINER-WIEHLE et al., 2022), quality or characteristics, origin or cause (oncological, traumatic, postoperative), and patterns (inflammatory or mechanical). As for the intensity, it can vary from mild to intense. It is considered acute when it occurs in a period of less than three months, usually accompanied by changes in vital signs such as heart rate and blood pressure, corresponding to a warning sign of the body. On the other hand, it is classified as chronic when it persists for more than 3 to 4 months or beyond the expected time for resolution of the problem or injury (DOWELL et al., 2022). The different classifications of pain according to its pathogenesis and duration are fundamental for therapeutic guidance (NICHOLAS et al., 2019). According to the Eleventh International Classification of Diseases (ICD 11), chronic pain can be classified as primary, related to cancer and its treatment, post-surgical and post-traumatic, neuropathic, headache and orofacial, visceral and musculoskeletal pain (NICHOLAS et al., 2019; HAUSTEINER-WIEHLE et al., 2022).

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For a better understanding of the painful process, it is necessary to know the dynamic and complex systems of transmission, transcription and translation of the nervous stimulus, which follows an ascending path to the brain centers and is modulated by a descending inhibitory pathway. This, in turn, is influenced by several connections with brain areas responsible for emotions and mediated by responses that vary according to the culture, gender, ethnicity, socioeconomic condition and life experience of each individual (ROCHA, et al., 2007). Therefore, it should be noted that behavior in the face of pain is an individual, subjective personal experience, influenced by biological, psychological, and social variables (ROCHA et al., 2007; LIMA et al., 2008).

PAIN AND PUBLIC HEALTH

Chronic pain is a serious problem in the field of public health that is widely recognized. Its significant prevalence, combined with a considerable global burden of disease, imposes high costs on society and health systems (POSSO et al., 2018; O'BRIEN et al., 2017). With broad negative social and economic impacts for the individual, their family, and the health system in general, pain can be responsible for high costs in hospitalizations, health problems, and public health burdens (MALTA et al., 2022).

In Brazil, some national conducts favor the improvement of health management, such as free access to comprehensive therapeutic care through the SUS, which is a right guaranteed to citizens according to article 6 of Law No. 8,080/90. The importance of pain treatment in palliative care and for the quality of life of patients with chronic pain is standardized in ordinances such as numbers 19/2002 and 906/2013. These ordinances contemplate the dispensation of specific medicines and treatments.

In addition, opioid drugs are under ANVISA regulation and are dispensed by the Pharmacies of the Health Secretariats of each state of the federation. These are responsible for receiving requests and dispensing medicines from the Specialized Component of Pharmaceutical Services. Releases occur upon medical, dental or veterinary prescription, accompanied by an official prescription form, containing the specifications of the prescriber, the patient, with specification of the disease and its respective International Code of Disease (ICD) for chronic pain and other details.

Addressing chronic pain as a public health problem must consider the limitations of infrastructure and the scarcity of human and financial resources in the health system, in addition to the growing demand in the face of population aging, increased longevity, and

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individual conditions that generate pain. To this end, it is necessary to participate in the community with the help of educational training strategies, through governmental and non-governmental institutions for the implementation and effective insertion and compliance with public policies, as suggested by the WHO.

Thus, public policies that can orchestrate the control and release of opioids are very important to achieve a desired balance between the harms and benefits of their use. Knowledge of the specific demands of the Brazilian territory is fundamental in the promotion of health planning and management strategies and for coping with conditions of inequality, and it is important to study regional realities.

PAIN IMPACT

The WHO, through The World Health Organization Quality Of Live Group, indicates that "quality of life has a multidimensional nature, which includes physical, psychological, social and spiritual dimensions" (WHO, 1995). Thus, the treatment of chronic pain is a crucial part of the quality of life and death of citizens, as it has high rates of mental suffering (depression, anxiety, insomnia), functional impairment, absenteeism, and progressive social and work disability (O'BRIEN et al., 2017).

Studies have shown that chronic pain doubles the incidence of depression, aggravating pain complaints, increasing interference with daily life, and impairing the ability to participate in social activities (PAIVA et al., 2023). Higher unemployment rates and decreased patient satisfaction are observed, associated with losses of social prestige and pleasurable activities, isolation (LIMA et al., 2008; MEGA et al., 2015; PAIVA et al., 2023; SANTOS et al., 2019) and catastrophizing (PAIVA et al., 2023). In addition, patients with chronic pain and depression have significantly elevated rates of suicidal ideation (BOHNERT et al., 2019; WHOQOL et al., 1995).

TREATMENT

The treatment of pain presupposes considering the possibilities of a multimodal therapy, which involves non-drug measures, use of drugs and invasive interventions (GUREJE et al., 2018; SIMÕES et al., 2021). Pharmacological treatment includes the use of analgesics, opioids and adjuvants. To assist in the choice of drugs, the WHO proposed a gradual scale of drug potency for each pain intensity. It proposes analgesics alone or in

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drug combinations, which aim at interaction, synergism, and efficacy with fewer side effects (SUBRAMANIAN et al., 2019). In the first step, for mild pain, conventional analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) are suggested. On the second step, for moderate pain, weak opioids are suggested, and on the third step, for severe pain, potent opioids. The use of opioids should start with the weakest, at the recommended dose, followed by progressive titration to effective analgesia with a lower rate of adverse effects (SUBRAMANIAN et al., 2019; GUREJE et al., 2018; SIMÕES et al., 2021; KRAYCHETE et al., 2013; WIERMANN et al., 2014).

Opioids

The term opioid refers to all morphine-analogous compounds widely used worldwide in the treatment of acute and chronic pain (DUARTE et al., 2005). Semisynthetic opioids are obtained from the modification of the acetyl group of morphine, as is the case with heroin (diacetylmorphine). Synthetic opioids, on the other hand, are produced with a phenanthrene nucleus similar to morphine, but produced synthetically. This is the case of methadone derivatives (PEREIRA et al., 2016) and fentanyl.

These compounds exert therapeutic effects by simulating the action of endogenous peptides on opioid stereo-specific receptors, providing a sequence of reactions that determine the activation of modulatory systems and the reduction of acute and chronic pain. Endogenous opioids have been studied more deeply since the 1970s, when studies began to clarify this system, allowing for a greater understanding of them.

Opioids act by binding to pre- or postsynaptic receptors located in the central, peripheral, and neurovegetative nervous systems (HENRIKSEN et al., 2008). In addition to analgesia, they can induce euphoria, relaxation and hypnosis, stimulating the brain's reward systems, which favors recreational use and dependence (HENRIKSEN et al., 2008; MARTINS et al., 2008). There are three main types of opioid receptors — mu, kappa, and delta — with subtypes involved in various functions, such as analgesia, euphoria, respiratory depression, hormonal and gastrointestinal changes, and physical dependence (HENRIKSEN et al., 2008). Opioid drugs are classified as agonists, antagonists, partial agonists, and agonist-antagonists, as shown in Table 1, and supply the national and international markets.

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Table 1: Classification of opioids

Classification	Opioids
Agonist	Morphine, Meperidine, Alfaprodin, Fentanyl, Alfentanyl, Phenoperidine, Codeine, Hydromorphone, Oxymorphone, Methadone, Heroin
Antagonist	Naloxone and Naltrexone
Partial agonist	Buprenorphine and Tramadol
Agonist/antagonist (K agonist/Mu antagonist)	Nalbuphine, Nalorphine, Levalorphane, Pentazocine, Butorphanol and Dezokine

Source: Bridging Old and New in Pain Medicine: An Historical Review

In Brazil, the Unified Health System provides the Brazilian population with three types of opioids: codeine, morphine and methadone. These medicines are listed in the National List of Essential Medicines of the National Medicines Policy (Rename), which establishes guidelines for financing, acquisition, storage, distribution, control, monitoring and dispensation (BRASIL, 1988). The standard recommends the use of opioids mainly in mixed pain, following the WHO schedule and associated with other analgesics.

The effects of chronic and abusive opioid use are widely known, with overdose intoxication being characterized by bradycardia, respiratory depression, hypotension, urinary retention, hypothermia, and central nervous system depression (PALADINI et al., 2023; HENRIKSEN et al., 2008; MARTINS et al., 2012). Toxicity can occur both from acute overuse and prolonged exposure, leading to tolerance and dependence (CASTRO et al., 2022; HENRIKSEN et al., 2008; CHOW et al., 2015). In Brazil, the most common associations are with alcohol, followed by benzodiazepines.

Morphine

Morphine, derived from phenanthrene, is the prototype of opioids, classified as a strong opioid and pure agonist of mu, delta and kappa receptors. In addition to analgesia, it promotes sedation, anxiolysis and effects such as euphoria, dysphoria, hallucinations, respiratory depression, bradycardia, hypotension, nausea, vomiting, constipation, urinary retention, pruritus and bronchospasm (KRAYCHETE et al., 2013). The release of histamine can cause rash and bronchospasm, and its use can lead to tolerance and dependence. Its bioavailability varies by route: oral (35–75%), parenteral (~100%), with onset of action in 15–30 minutes and half-life of 3–4 hours. It crosses the blood-brain barrier slowly, and may cause adverse effects outside the plasma peak. It is metabolized mainly by conjugation with glucuronic acid, generating metabolites such as M6G, which is more potent and excreted by the kidneys, and M3G, associated with neurotoxicity (SUBRAMANIAM et al., 2019). The

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initial dose ranges from 0.05 to 0.2 mg/kg, with no defined maximum dose. In the ATC/DDD system, it has a N02AA01 code, with a DDD of 0.1 g orally and 30 mg parenterally and rectally (WHO, 2024).

Methadone

Methadone is a synthetic opioid agonist of mu, kappa, and delta receptors, and non-competitive antagonist of NMDA receptors. It can be administered by several routes, with oral bioavailability between 67% and 95%. Due to the high lipophilia, it has a rapid onset and plasma peak in 2.5 hours, lasting about 10 hours (BARBOSA et al., 2015; CASTRO et al., 2022). It has a long half-life (8 to 59 hours) and great interindividual variability, requiring caution in management. It can cause accumulation and respiratory depression, especially during sleep and in the elderly, as well as cardiotoxicity, including QT prolongation and arrhythmias such as Torsade de Pointes (BARBOSA et al., 2015). Side effects include sedation, changes in weight, sweating, constipation, sexual dysfunction, pruritus, and arrhythmia. Conversion to morphine requires clinical experience, with variable equianalgesic relationships. Its differential is in its action on NMDA receptors, useful in the control of neuropathic pain, hyperalgesia, and tolerance (BARBOSA et al., 2015). It is metabolized in the liver and intestine, with urinary (20–50%) and fecal (10–45%) excretion, without formation of active metabolites (BARBOSA et al., 2015). Doses vary widely (2.5 to 930 mg/day), with caution for chronic non-cancer pain, and it is recommended not to exceed 40 mg/day; above 200 mg/day, cardiac monitoring is required (KRAYCHETE et al., 2013). In the ATC/DDD system, it has a code N07BC02, with a DDD of 25 mg for the oral and parenteral routes (WHO, 2024).

Opioids in Brazil

In Brazil, opioid prescription grew by about 485% between 2015 and 2019, according to ANVISA (PASTRANA et al., 2014). Despite this, the country faces difficulties in the availability of these drugs due to strict legal control, historically influenced by anti-trafficking policies that also impact access to essential raw materials (PASTRANA et al., 2012). Since the beginning of the twentieth century, Brazil has implemented legislation and strategies on narcotics, culminating in Decree No. 9,761/2019, which, although it represents the most recent adjustment of the National Drug Policy, does not explicitly mention opioids. Studies indicate that the illicit use of these substances, such as heroin and unregulated fentanyl, is

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rare and irregular in the country, with no significant differences between ethnic-racial groups, educational levels, or religions (MAIA et al., 2021). In medical use, Brazil follows WHO guidelines, adopting strategies such as RENAME, the creation of ANVISA, and the Sentinel network for pharmacovigilance (GUIRRO et al., 2023). Free access to medicines in the SUS is guaranteed by the National Medicines Policy and reinforced by the CEAF and by the Clinical Protocols and Therapeutic Guidelines (OLIVEIRA et al., 2019; GUIRRO et al., 2023). The dispensation of opioids is regulated by SVS/MS Ordinance No. 344/1988, which requires a Special Control Prescription in two copies, except for codeine, morphine, and methadone, when used by patients registered in the National Program for Pain Care and Palliative Care (CASTRO et al., 2022).

The analysis of the literature reveals inequalities and gaps in universal access to medicines by the public sector in Brazil. Although the constitutional principle of social justice proposes equality of access, this right is influenced by factors such as geographic distribution, availability and quality of human and technological resources, care models and financing mechanisms (KULKAMP et al., 2008; BARROS et al., 2020). Despite the increase in federal participation in drug spending — from 11% in 2010 to 16% in 2016 — the scenario of shortages in the public sector, added to the high cost of medicines in the private sector, still hinders access for the population (BARROS et al., 2020). Part of Brazilians resort to direct payment to obtain medicines, compromising family income, or to judicialization to guarantee access (OLIVEIRA, 2019; BARRETO et al., 2016). According to a national survey, 77.9% of people with pain said they had paid to obtain the medications (CELLA et al., 2016). With regard to palliative care, Brazil has limited availability of morphine and a reduced number of services in view of population demand. There is also a widespread lack of knowledge among the population, professionals, and managers on the subject, in addition to a cultural denial of the dying process, which contributes to avoidable suffering (RODRIGUES et al., 2022).

The inappropriate use of medications is another challenge, with 50% of drugs being prescribed, dispensed, or used irrationally, according to ANVISA (LEAL et al., 2020). The National Drug Policy, of 2001, seeks to promote rational use and scientific development in the area (BRASIL, 2001). In the specific case of opioids, there are barriers related to the health system — such as the low priority of cancer treatment and bureaucracy —, to professionals — who are often afraid of inspection, do not follow guidelines, or lack

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adequate training — and to the patients themselves, who show fear of dependence, adverse effects, or associate use with the proximity of death (CELLA et al., 2016).

OBJECTIVES

To quantitatively analyze the evolution of the dispensation of opioid analgesics — specifically codeine, morphine and methadone — by the Pharmacy of the Health Department of Minas Gerais and Brazil, in the period from 2018 to 2023, quantifying their consumption and identifying variations and trends over time.

METHODOLOGY

This is a quantitative study, whose data collection regarding the populations of Minas Gerais and Brazil was carried out from the database made available by the Department of Informatics of the Unified Health System (DATASUS) / Ministry of Health – Tabnet. The data covered the period from 2018 to 2023.

The variables were collected between January 1, 2023 and February 2024, through retrospective consultation of the dispensing records stored in the DATASUS platform database. Data collection followed the following sequence for data verification: choice of the "Health Information" option, with search restriction in the following tab: 1) Health care - outpatient production (SAI/SUS); 2) Option for place of service - from 2008 onwards; 3) Selection by geographic coverage for the states of the federation; 4) with outpatient production for group 06 drugs.

From the list of drugs, the following were selected: 1) codeine in liquid presentations, 30 mg and 60 mg; 2) oral morphine released in 10mg, 30mg, 60mg, 100mg presentations; and 3) oral methadone in 5 mg and 10 mg presentations.

The morphine doses were added up and converted into grams, and stored in an Excel spreadsheet. The conversion of each opioid into morphine equivalents was performed according to the data in table 2 below, obtained through the recommendations of SBED and the Brazilian Society of Oncology. The data obtained were analyzed by descriptive statistics.

Table 2: Table of conversion of opioids into morphine equivalents

Opioid		Approximate Oral Equianalgesic Dose of Morphine
Methadone	4mg	30mg
Codeine	200mg	30mg

Source: http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf

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To consult the estimate of the total number of inhabitants in Minas Gerais and Brazil, per year, data from the same database: Tabnet were searched. In this situation, we chose the Demographic and Socioeconomic tab.

The present study adopted the ATC/DDD methodology recommended by the WHO Drug Utilization Research Group. The DDD is a technical unit of measurement, developed for use in epidemiological studies of drug use and consumption. It is part of the ATC/DDD system that was recommended by the WHO Collaborating Centre for Drug Statistics methodology from 1982 (UN, 2023), (WHO, 2024).

This is not a recommended dose for medical prescription, nor do they intend to analyze the effectiveness of the drugs. Consumption data expressed in DDD provide an approximate estimate of the therapeutic intensity of drug use. It is a single unit of measurement, independent of price and pharmaceutical form, which makes it possible to assess trends in drug consumption and make comparisons between different populations (UN, 2023; CASTRO et al., 2000; ALVIM et al, 2015).

To obtain the DDD values for each drug, the ATC/DDD index was consulted through an electronic page with the following address: http://www.whocc.no/atcddd (WHO, 2023). The DDD values for each substance are presented in Table 3.

Table 3: DDD Values for Each Opioid Substance By Oral Route

ATC Group	Opioid	DDD
N07BC02	Methadone	25 mg
N02AA01	Morphine	0.1g
N02AA08	Codeine	0.15g

Source: http://www.whocc.no/atcddd(55)

The methodology of the Statistically defined daily dosis S-DDDs, translated as statistically defined daily dose, classified by the Anatomical Therapeutic Chemical (ATC), was chosen with the objective of maintaining an already consolidated and reliable standard of international scientific studies on the consumption of medicines (UN, 2023).

The S-DDD is the statistical measure of the DDD calculated for the chosen population, which in this study were the populations of Brazil and Minas Gerais. The report of the INCB board on the consumption of analgesic opioids was considered as a reference and for comparison. The amount between 100 and 200 S-DDDs per million inhabitants per day is pointed out as inadequate. A value less than 100 S-DDDs is considered very inadequate as shown in table 4 (UNITED NATIONS, 2017).

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Table 4: DDD Values for Each Opioid Substance By Oral Route

	Value of S-DDD per million inhabitants
Adequate	Greater than 200
Inadequate	between 100 and 200 S-DDD
Very inappropriate	less than 100 S-DDD

Source: UNITED NATIONS. International Narcotics Control Board for 2016.

Based on the data collected on opioid consumption and the DDD corresponding to each drug, the data were tabulated in an Excel spreadsheet for the application of the formula of daily dose per million inhabitants/day and, subsequently, the daily dose defined per million inhabitants was adjusted for the population. This unit offers a rough idea of the volume of population treated with a usual dose of a given drug per day.

The release of the drugs and the annual average withdrawn were calculated in grams/day. The utilization metrics used in the present study were:

Daily dose defined per million inhabitants/day (DDD/1,000,000 DP).

The following formula was used:

$$\frac{S-DDD}{1.000.000PD} = 6X10\left(\frac{annual\ quantity\ of\ opioid\ expressed\ in\ the\ unit\ of\ measurement\ of\ DDD}{DDD\ in\ gramsX\ 365\ X\ annual\ population)}\right)$$

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DDD= defined daily dose established by the WHO

S-DDD/1,000,000P D = annual grams of opioid / (DDDX 365 X annual population) X 1,000,000

S-DDD= statistically defined daily dose

DP= person day

In which: annual gram is equal to grams dispensed of the opioid in the year;

Daily dose defined per million inhabitants/day corrected for the size of the population using the SUS, i.e., 72% (DDD72%/1000PD). To this end, the following calculation was performed:

$$\frac{S-DDD}{1.000.000PD} = 6X10\left(\frac{annual\ quantity\ of\ opioid\ expressed\ in\ the\ unit\ of\ measurement\ of\ DDD}{DDD\ in\ grams\ X\ 365\ X\ annual\ population\ X0.72)}\right)$$

Regarding the ethical aspects of the research, this study did not require submission to an ethics committee, and there was no possibility of physical or moral damage from the perspective of the individual and the collectivities, and therefore the principles of Resolution No. 466, of December 12, 2012 and Resolution 510 of April 7, 2016, were respected.

RESULTS

The amounts of each drug in milligrams, in their form of presentation, are shown in Table 5. The calculated annual doses of morphine equivalents in grams and the S-DDD per million inhabitants of each opioid selected in the study were calculated and presented in Table 6.

Table 5: Quantities of each drug in its form of presentation per unit (tablets or vials).

Presentation	Brazil/ MG	2018	2019	2020	2021	2022	2023	Difference (2023-2018) (%)
Codeine								
3 mg/ml oral solution (per 120 ml vial)	**Brazil**	1.829	1.831	2.368	3.155	5.765	8.554	+5.937 (+325)
	MG	224	168	317	315	279	240	0 (0)
30 mg (per tablet)	**Brazil**	4.899.687	5.882.678	6.848.339	7.458.775	7.860.010	8.382.332	+2.727.203 (+56)
	MG	395.708	127.610	448.720	467.902	460.476	417.542	-20.366 (-5)

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60 mg (per tablet)	Brazil	210.571	235.970	344.790	376.152	383.799	521.351	+264.337 (+126)
	MG	4.080	576	12.330	23.608	19.896	24.106	+17.640 (+432)
Morphine								
10 mg/ml (per 1 ml ampoule)	Brazil	47.235	44.038	55.729	61.581	72.631	103.300	+47.474 (+101)
	MG	6.853	873	1.809	2.055	2.557	2.703	-4.381 (-64)
10 mg/ml oral solution (60 ml vial)	Brazil	8.875	6.488	8.095	7.241	8.265	9.775	-74 (-1)
	MG	25	18	4	25	48	88	+51 (+204)
10 mg (per tablet)	Brazil	3.728.465	3.943.407	4.384.025	4.627.035	4.905.820	5.570.075	+1.364.998 (+37)
	MG	169.140	53.750	205.520	287.260	295.200	337.900	+135.040 (+80)
30 mg (per tablet)	Brazil	2.278.151	2.076.173	2.523.564	2.414.229	2.327.303	2.223.169	-256.699 (-11)
	MG	234.210	57.170	232.410	271.840	266.000	81.410	-165.860 (-71)
Controlled-release 30 mg (per capsule)	Brazil	114.368	113.855	114.835	120.640	106.885	121.158	-3.310 (-3)
	MG	7.680	3.240	5.600	5.300	5.240	6.360	-2.070 (-27)
Controlled-release 60 mg (per capsule)	Brazil	62.718	63.104	61.463	37.483	44.736	48.615	-18.381 (-29)
	MG	4.116	2.266	4.750	3.370	4.644	4.888	+378 (+9)
Controlled Release 100 mg (capsule)	Brazil	23.441	24.528	17.941	14.767	12.922	15.539	-9.482 (-40)
	MG	1.185	130	360	90	0	300	-935 (-79)
Methadone								
5 mg (per tablet)	Brazil	546.733	694.825	824.192	986.480	1.102.306	1.340.510	+670.942 (+123)
	MG	50.220	13.100	60.030	65.180	71.856	82.482	+24.590 (+49)
10 mg (per tablet)	Brazil	895.451	1.015.864	1.389.476	1.500.217	1.623.713	1.835.774	+782.224 (+87)
	MG	90.638	49.372	152.266	178.620	195.862	195.374	+87.698 (+97)
10 mg/ml for injection (per 1 ml ampoule)	Brazil	418	235	1.079	390	1.302	1.560	+1.017 (+243)
	MG	0	0	0	0	0	0	0 (0)

Source: DATASUS Tabnet

Table 6: Annual consumption in S-DDD per million inhabitants of opioids released by the health departments in Minas Gerais and Brazil

Years	2018	2019	2020	2021	2022	2023	Difference % (2023 – 2018) and Standard deviation
Codeine							

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Total annual dose in grams	**Brazil**	159.734.610	190.748.400	226.279.650	246.521.670	259.174.140	283.264.260	(+61%)
	MG	12.196.680	3.923.340	14.315.520	15.566.940	15.108.480	12.644.100	(+4%)
S-DDD	**Brazil**	19,4	23,0	27,1	29,3	30,6	30,2	(+56%) SD= 6.95
	MG	22,1	7,1	25,6	27,7	26,7	22,2	(+1%) SD= 4.13
Morphine								
Total annual dose in grams	**Brazil**	120.634.105	115.398.864 (-4,34%)	133.498.287	130.571.443	131.237.093	136676260	(+3%)
	MG	9.349.119	2.512.179	9.524.327	11.419.165	11.404.311	5.608.256	(-40%)
S-DDD	**Brazil**	22,0	20,9	24,0	23,3	23,2	22,1	(-1%) SD= 1.05
	MG	16,9	4,5	17,0	20,3	20,2	9,9	(-41%) SD= 5.75
Methadone								
Total annual dose in grams	**Brazil**	11.689.011	13.633.235	18.017878	19.935.350	21.751.264	25.063.410	(+96%)
	MG	1.157.480	559.220	1.822.810	2.112.100	2.317.900	2.157.410	(+86%)
S-DDD	**Brazil**	8,5	9,9	13,0	14,2	15,4	16,1	(+89%) SD= 2.79
	MG	2,1	1,0	3,3	3,8	4,1	3,8	(+81%) SD= 1.11
Morphine Equivalent								
Total annual dose in grams	**Brazil**	183.363.610	189.006.644	228.197.764	234.965.010	244.159.563	265.256.326	(+32%)
	MG	15.808.541	3.240.485 (-79,5%)	12.127.358	14.282.231	14.250.058	8.044.224	(-49%)
S-DDD	**Brazil**	33,5	34,2	41,0	41,9	43,2	42,5	(+27%) SD= 3.95
	MG	28,6	5,8	21,7	25,3	25,2	14,2	(+50%) SD= 7.82

Source: DATASUS Tabnet

Regarding the presentations of the medications, it was observed that the most common and frequently dispensed form was codeine of 30 mg per tablet and methadone of 10 mg per tablet, in a similar way, both in Brazil and in Minas Gerais. Morphine dispensation was higher in the form of 10 mg tablets, followed by 30 mg tablets, both rapid-release, in Brazil. In Minas Gerais, the most commonly used morphine was 30 mg per rapid-release tablet.

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In the period from 2018 to 2023, the data indicate a progressive growth in the release of opioids, with codeine being higher, followed by morphine and methadone. It is noted that the presentation of 30 mg of codeine had an increase of 71% in Brazil and 5% in Minas Gerais. In the case of morphine, the presentation of 10 mg per tablet, the most consumed, had an increase of 49% in Brazil and 99.8% in Minas Gerais. The most used methadone in this period, 10 mg per tablet, had an increase of 105% in Brazil and 115% in Minas Gerais. The analysis of the S-DDDs of the opioids released in the Health Secretariats of Minas Gerais and Brazil in these years reveals that the most consumed opioid both in Brazil and in Minas Gerais was codeine. Exceptions occurred in 2018, when more morphine was consumed in Brazil than codeine, and in Minas Gerais, where the amount released continuously decreased in milligrams and S-DDD in the years 2021 to 2023. When comparing the total dispensation of methadone and codeine, an annual progressive increase in the S-DDD per million inhabitants was verified. This fluctuating profile, with increases and troughs in consumption, followed the global consumption of codeine, for example, when in 2000 world consumption was 170 tons, in 2016 there was a maximum increase of 293.7 tons and in 2019 a reduction to approximately 220 tons, according to the 2020 report by the International Narcotics Control Board.

In the observed period, the data point to frequent fluctuations both in Brazil and in Minas Gerais, in relation to the types of presentation, rapid or controlled release, and concentrations of opioids. The decline in the release of opioids in 2019 stands out, especially in Minas Gerais. In Brazil, an oscillation was observed with a reduction in some morphine presentations. Methadone was reduced only in the injectable presentation. Despite the variations, the consumption of codeine increased by 25% and oral methadone by 16%. Considering the amount of morphine equivalents released, that year, there was an increase of 3.07%. In Minas Gerais, the reduction was more relevant, with repercussions on the total of morphine equivalents and a reduction corresponding to approximately 79.5%. Methadone was the opioid that showed the greatest decrease, around 48%, followed by morphine 26% and codeine 25%.

In 2020, a return to growth in the release of all opioids can be observed, with the exception of morphine in the 60mg and 100mg controlled-release presentations in the data for Brazil and oral morphine solution in Minas Gerais. That year, MG had a return to the same level of release as in 2018, with a growth in release of 374% compared to 2019 and a reduction of 23.28% compared to 2018.

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In 2021, the amount of morphine released fell again by 2.2%, but did not affect the release of the total amount of morphine equivalent, which increased by 20.7%.

In the following years (2022 and 2023), the dispensation of these drugs followed a progressive growth trend in Brazil. Only morphine in the 30mg presentation had an 11% reduction in release. It can be observed that morphine consumption increased in relation to the total milligrams of this drug, however, when we observed the relationship with the population, i.e., the S-DDD, we noticed a progressive reduction in those years from 43.2 to 42 (Table 5).

The DDD follows the oscillations of the doses released in the period studied, confirms the reductions that occurred in the years 2019 and 2022 both in Brazil and in Minas Gerais. Regarding methadone, in Brazil there is a consumption with constant growth. In Minas Gerais, with the exception of 2019, this same trend of increased consumption was maintained.

When comparing the total dispensation of methadone and codeine, there was a progressive annual increase in the DDD per million inhabitants. This profile followed what is observed in the rest of the world. However, in relation to morphine alone, moments of consumption fluctuations can be observed, such as in 2019 and 2022 with drops in consumption values in milligrams and in the corresponding DDD. Considering the total morphine equivalent, the mean DDD release value was 40, lower than the DDD considered by the WHO as very inadequate (Table 6).

DISCUSSION

In recent years, opioid consumption has been the subject of increasing international attention, especially due to its impacts on public health and inequalities in access. This study analyzed the outpatient dispensation of opioids by the SUS in Brazil and Minas Gerais between 2018 and 2023, revealing consumption patterns classified as "very inadequate" (PIOVEZAN et al., 2022). Justifications for this underutilization include cultural and social attitudes, lack of knowledge among health professionals, low priority of chronic pain as a public policy, and overly restrictive regulations (PIOVEZAN et al., 2022; BARROS et al., 2019).

Despite the long historical history of pain treatment, the paradigm shift remains slow, and myths about pain still persist, such as the idea that it is necessary for diagnosis (BRENNAN et al., 2007). Although the right to access essential medicines is guaranteed by

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WHO and UN guidelines, and the Brazilian constitution, morphine consumption remains low in developing countries, including Brazil (BARROS et al., 2019; BRENNAN et al., 2007). Barriers such as scarcity of resources, bureaucracy in supply, and high regulatory costs also hinder safe and balanced access to opioids.

In relation to health professionals, underuse of opioids is observed, especially outside the oncological and postoperative context, a reflection of opioidophobia and insufficient training (BARROS et al., 2019). Codeine was the most consumed analgesic in the period studied, as also reported by the International Narcotics Control Board (INCB) and by Moreira de Barros et al. (2019), although its use is still low, with only 2.6% of patients with chronic pain using this type of medication, and 25.3% without any analgesic treatment.

Even in a system such as the SUS, based on universality and equity, access to medicines varies according to the health policy in force in each state. According to the Atlas of Palliative Care, 12% of services reported difficulties in accessing opioids (RODRIGUES et al., 2022). The Morphine S-DDD values — 14.5 in Minas Gerais and 40.5 in Brazil in 2023 — reflect a worrying scenario of avoidable suffering at the end of life (RODRIGUES et al., 2022).

The impact of uncontrolled pain also extends to the health care chain, mainly affecting vulnerable populations, who depend on the SUS (COSTA et al., 2011). The significant reduction in consumption in 2019, for example, can be explained by shortages, import failures, demographic characteristics, and possible errors in reporting to DATASUS (COSTA et al., 2011).

This study was limited by the use of secondary data, which made it impossible to analyze non-medical use, self-medication, or the separation between human and veterinary prescriptions. Even so, the need to monitor opioid consumption in Brazil and Minas Gerais is reinforced as part of the effort to ensure adequate pain management, as pointed out by Castro et al. (2022).

CONCLUSION

Between 2018 and 2023, the dispensation of opioids in Brazil and Minas Gerais presented a consumption profile far below the recommended, with S-DDD values below 100, a limit considered "very inadequate" by the WHO's International Narcotics Control Board. Despite a moderate growth trend in the period — an annual average of 5.36% in Brazil and 56% in Minas Gerais — significant fluctuations were observed, such as the 374%

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increase in Minas Gerais in 2019. In 2023, the consumption rate was 42.5 S-DDD/million inhabitants, showing an increase of 32% compared to 2018, but still insufficient in view of population needs. Even with advances in the understanding of pain and the expansion of palliative care, regional inequalities, underuse of opioids, and structural barriers that prevent adequate access persist, especially for SUS patients. Such disparities compromise the right to dignified treatment of pain, generating avoidable suffering for thousands of Brazilians. The findings of this study highlight the urgency of improving public policies, ensuring equity in the distribution of medications, and strengthening professional training on the proper management of opioids, always focusing on the safety and well-being of patients. As a limitation, the difficulty in accessing consistent data stands out, aggravated by the absence of recent demographic censuses, which partially compromises the accuracy of the analyses.

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