Prescribing Pattern of Analgesics in Colombia. Are there Differences between Capital Cities and Municipalities? A Cross-Sectional Study

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Abstract

Background Analgesics provide multiple clinical benefits but they are not without risks.

Objective The aim of this study was to compare the outpatient prescribing pattern of analgesics between cities and municipalities in Colombia and to identify the variables associated with prescribing opioid analgesics.

Methods This was a cross-sectional study that identified the prescription of analgesics for outpatient use from a population database of 8.5 million Colombians. A descriptive, bivariate, and multivariate analysis was performed.

Results A total of 573,248 patients were identified who had received prescriptions for an analgesic. Mean age was 46.5 ± 23.6 years and 65.7% were females. The most commonly prescribed analgesics were non-opioid analgesics, antispasmodics, and opioid analgesics. The average milligram equivalent of morphine was higher in capital cities than in municipalities. Age ≥ 65 years (odds ratio [OR] 2.60, 95% confidence interval [CI] 2.54–2.67), male sex (OR 1.09, 95% CI 1.07–1.11), dispensing in cities (OR 2.25, 95% CI 2.20–2.30) and experiencing chronic pain (OR 13.25, 95% CI 10.89–16.14) were associated with an increased risk of receiving an opioid analgesic.

Conclusions Differences were found in the prescription of analgesics between capital cities and municipalities. The use of opioids does not appear to be in line with the recommendations for clinical practice, and they were mainly prescribed for elderly males with chronic non-oncological pain and for residents of capital cities.

Key Points

The prescription pattern of analgesics in Colombia is heterogeneous, with differences between cities and municipalities.

The greatest dispensing of opioids and the highest doses occurred in the capital cities.

Males, adults over 40 years of age, from capital cities, and with chronic pain were factors associated with a higher probability of receiving opioids.
1 Introduction

The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” [1]. Pain can be classified according to its neurophysiological mechanism, etiology, affected region, intensity, and duration [2]. Thus, pain can be classified as nociceptive and non-nociceptive (neuropathic pain), acute or chronic (3 or more months) [2, 3], and, according to the visual analog scale (VAS), as mild (score 1–3), moderate (score 4–7), or severe (score 8–10) [2, 4].

Analgesics are commonly prescribed for pain relief or modulation in a wide variety of clinical contexts [2]. In recent years, the use of analgesics has increased steadily in both developed and developing countries [5]. According to the World Health Organization (WHO) analgesic pain scale, acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are effective for treating all pain intensities and should be used alone for patients with mild pain or in combination with opioids for other steps on the WHO analgesic ladder, while partial opioid agonists (codeine and tramadol) should be used for moderate pain. If these fail to achieve adequate pain control or if the pain is severe, full opioid agonists, such as morphine, oxycodone and fentanyl, among others, should be used [4, 6].

Although analgesics provide a number of benefits, they are not without risks since they are related to various adverse reactions. NSAIDs are associated with gastrointestinal bleeding and unfavorable cardiovascular events [7], while opioids are related to dependence, addiction and abuse, particularly when used for chronic non-oncological pain [8, 9]. Previous opioid use is an important risk factor for future opioid misuse, even when opioids are prescribed for a medical indication [10]. The misuse of analgesics contributes to increased morbidity and mortality rates, deterioration of quality of life, greater demand for health resources, and increased health care costs [5]. Consequently, on 26 October 2017, the Department of Health and Human Services declared the opioid crisis a public health emergency in the United States [11].

However, there are few published studies that address the general prescription analgesic use patterns according to the geographical regions of a country, and no studies have been found that compare patterns between capital cities and municipalities. Previously, a study performed in Colombia found that the prescription of outpatient antibiotics varied according to geographical areas of the country, age groups, cities, and municipalities [12]. In 2020, Colombia had 50,372,424 inhabitants. It has a health system that offers universal coverage to the entire population, through two affiliation schemes, one contributory or paid by employers and workers and another subsidized by the state for those who do not have the ability to pay, and includes a benefit plan with different painkillers, including opioids. Medications are delivered to patients at no cost, except for a small co-pay. A deeper understanding of analgesic prescribing patterns can help guide educational interventions focusing on their appropriate use. We therefore sought to compare the patterns of outpatient analgesic prescriptions between capital cities and municipalities in Colombia and to identify the variables associated with the prescription of opioid analgesics.

2 Materials and Methods

An observational cross-sectional study was conducted to examine the prescription patterns for the different medications used as outpatient analgesics. The study was based on a population medication dispensing database that collects information from approximately 8.4 million people affiliated with the Colombian Health System through six health insurance companies, corresponding to approximately 30.0% of the active population affiliated with the contributory or paid regime and 6.0% of those affiliated with the state-subsidized regime, which represents 16.6% of the Colombian population as a whole.

Patients who were treated with analgesic drugs, including opioids, NSAIDs, acetaminophen, dipyrone, lidocaine (transdermal patches), muscle relaxants and intestinal anti-spasmodics, among others, were identified from 1 to 29 February 2020. Patients of any sex and age who were treated at an outpatient medical consultation were selected. A database was designed based on medication use in the affiliated population; data were systematically obtained by the dispensing company (Audifarma SA), which collected the following groups of patient variables:

1. Sociodemographic: Sex, age, dispensing city/municipality (the word ‘city’ was used for all capital cities of departments [regions], and the word ‘municipality’ was used for all other populations with fewer inhabitants).

- Capital cities and municipalities identified in the study: See Annex 1
• Geographic areas: The place of residence was categorized by department according to the regions of Colombia and taking into account the classification of the National Administrative Department of Statistics (DANE) of Colombia, as follows:
  - Caribbean Region: Atlántico, Bolívar, Cesar, Córdoba, La Guajira, Magdalena, Sucre, San Andrés, Providencia and Santa Catalina.
  - Central Region: Antioquia, Caldas, Quindío, Risaralda, Caquetá, Huila and Tolima.
  - Bogotá-Cundinamarca Region.
  - Eastern Region: Boyacá, Meta, Norte de Santander, Santander, Arauca and Casanare.
  - Pacific Region: Cauca, Chocó, Nariño, Valle del Cauca.
  - Amazon-Orinoco Region: Amazonas, Guaviare, Guainía, Vaupés, Vichada, and Putumayo.

2. Diagnoses related to the prescription of analgesics were identified from the main and secondary diagnoses indicated by the patient’s International Classification of Diseases, Tenth Revision (ICD-10) codes obtained from the medical formula and were categorized as follows: infectious diseases and fever, visceral pain, headaches, trauma, joint pain, neuropathic pain and radiculopathies, cancer pain, dental pain, chronic pain and unspecified pain.

3. Chronic comorbidities were identified from the main and secondary diagnoses indicated by the ICD-10 codes of the selected patients between 1 November 2019 and 29 February 2020. Comorbidities were grouped into four categories: no comorbidities and one, two and three or more pathologies, for which the following groups of diseases were taken into account:
  - Cardiovascular: High blood pressure, ischemic heart disease, tachyarrhythmias, heart failure, peripheral arterial disease.
  - Endocrine: Diabetes, hypothyroidism, dyslipidemia, obesity, hyperthyroidism.
  - Rheumatological: Osteoarthritis, rheumatoid arthritis, osteoporosis, fibromyalgia, systemic lupus erythematosus, systemic sclerosis, ankylosing spondylitis.
  - Renal: Chronic kidney disease.
  - Psychiatric: Depression, anxiety, bipolar affective disorder, sleep disorders, psychosis.
  - Neurological: Peripheral neuropathies, chronic pain, dementia, migraine, epilepsy, Parkinson's disease, stroke, mental retardation.

4. Type of prescriber: General practice, medical specialties (internal medicine, pediatrics, geriatrics, physiatrist, family doctor, rheumatology, oncology, psychiatry, neurology, cardiology, dermatology, nephrology, allergology, pulmonology, endocrinology or anesthesiology), surgical specialties (general surgery, orthopedics, traumatology, maxillofacial surgery, cardiovascular surgery, gastroenterology, neurosurgery, obstetrics), and dentistry.

5. Analgesics [13]:
  - Opioid analgesics: partial agonists (tramadol, codeine) and full agonists (morphine, buprenorphine, fentanyl, hydromorphone, meperidine, tapentadol, oxycodone, hydrocodone)
  - Morphine milligram equivalent (MME) conversion factor [8]: Hydrocodone (1.00), tramadol (0.10), codeine (0.15), hydromorphone (4.00), oxycodone (1.50), meperidine (0.10), transdermal fentanyl (2.40), transdermal buprenorphine (1.70), and tapentadol (2.50). Data were obtained from the recorded doses and the amount of medications dispensed. The total monthly dose was classified as follows:
    - Low dose: < 20 mg morphine equivalent
    - Intermediate dose: 20–49 mg morphine equivalent
    - High dose: ≥50 mg morphine equivalent
  - Non-opioid analgesics: Acetaminophen, dipyrone, non-selective NSAIDs (ibuprofen, diclofenac, acetylsalicylic acid, naproxen, meloxicam, piroxicam, nimesulide, ketorolac, tenoxicam, pizotifen, lornoxicam, ketoprofen, indomethacin, fenoprofen, dexketoprofen, dexibuprofen) and cyclooxygenase (COX)-2 selective NSAIDs (celecoxib, valdecoxib, parecoxib, lumiracoxib, etoricoxib).
• Intestinal antispasmodics: Hyoscine N-butyl bromide, fenoverine, mebeverine, otilonium, papaverine, rocerverine, triimebutine.
• Muscle relaxants: Methocarbamol, tizanidine, cyclobenzaprine, thiocolchicoside.
• Lidocaine patches.
• Others: Diacerein, glucosamine, capsaicin.
• Combinations: Any pharmaceutical form that includes two or more analgesics.

6. Pharmaceutical forms: Tablet or capsule, powder for reconstituted oral solution, syrup, suspension, solution for injection, and transdermal patches.
7. Number of analgesic medications per patient: Grouped into two categories (one analgesic and two or more analgesics) based on prescriptions received during the month of February.

The protocol was approved by the Bioethics Committee of the Universidad Tecnológica de Pereira under the category ‘research without risk’ (approval number 01-110520). The principles established by the Declaration of Helsinki were respected and no personal data were collected from the patients.

Data were analyzed using the statistical package SPSS Statistics, version 26.0 for Windows (IBM Corporation, Armonk, NY, USA). A descriptive analysis was performed with frequencies and proportions for the qualitative variables and measures of central tendency and dispersion for the quantitative variables. Quantitative variables were compared using Student’s t test or analysis of variance (ANOVA), while categorical variables were compared using the Chi-square test. Binary logistic regression models were performed using the prescription of opioid analgesics as a dependent variable; the covariates were those that were significantly associated with opioid prescriptions in the bivariate analyses. A level of statistical significance was determined at \( p < 0.05 \).

### 3 Results

During the month of February 2020, 1,700,095 affiliates were given some medication, of which 573,248 (33.7%) affiliates were dispensed some analgesics; these were distributed throughout 25 capital cities and 161 different municipalities (Appendix 1). A total of 65.7\% (\( n = 376,584 \)) were females. The mean age was 46.5 ± 23.6 years (range 0.3–103.8 years), divided into the following age groups: <18 years (\( n = 77,565; 13.5\% \)), 18–44 years (\( n = 186,042; 32.5\% \)), 45–64 years (\( n = 166,191; 29.0\% \)), 65–79 years (\( n = 101,348; 17.7\% \)) and ≥ 80 years (\( n = 42,102; 7.3\% \)).

#### 3.1 Outcomes

A total of 67.6\% (\( n = 387,472 \)) of patients were prescribed analgesics in capital cities; the majority were in the Caribbean region (\( n = 205,694; 35.9\% \)), followed by the Bogotá-Cundinamarca region (\( n = 173,312; 30.2\% \)), the Central region (\( n = 94,820; 16.5\% \)), the Pacific region (\( n = 81,977; 14.3\% \)), the Eastern region (\( n = 15,524; 2.7\% \)) and the Amazon-Orinoquía region (\( n = 2003; 0.3\% \)).

A total of 77 different medications were prescribed: 71.0\% (\( n = 406,750 \)) of patients received only one prescription, while 29.0\% (\( n = 166,498 \)) received two or more prescriptions. A total of 97.6\% (\( n = 559,702 \)) of patients received a prescription for oral analgesics, with tablets or capsules being the most prescribed pharmaceutical form (\( n = 509,427; 88.9\% \)) (Table 1). The most commonly used analgesic groups were non-opioid analgesics, followed by antispasmodics and opioid analgesics (Table 1). The most prescribed analgesic was acetaminophen, followed by naproxen and hyoscine N-butyl bromide (Table 2). The most frequent indications for the use of analgesics were diagnoses related to infectious diseases and fever (Tables 1, 3, 4).

A total of 45.1\% (\( n = 258,351 \)) of all patients had some chronic pathology (Table 1). Of these, 61.4\% (\( n = 158,683 \)) had one comorbidity, 25.7\% (\( n = 66,489 \)) had two comorbidities, and 12.8\% (\( n = 33,179 \)) had three or more comorbidities. These comorbidities predominated in those who were 65 years of age or older (\( n = 117,299/142,728; 82.2\% \)). The top 10 comorbidities were arterial hypertension (\( n = 142,832; 24.9\% \)), diabetes mellitus (\( n = 42,761; 7.5\% \)), hypothyroidism (\( n = 22,473; 3.9\% \)), chronic osteoarthritis (\( n = 18,678; 3.3\% \)), other headaches (\( n = 13,678; 2.4\% \)), dyslipidemia (\( n = 13,649; 2.4\% \)), chronic kidney disease (\( n = 12,000; 2.1\% \)), chronic gastritis (\( n = 11,804; 2.1\% \)), chronic pain (\( n = 11,413; 2.0\% \)), migraine (\( n = 10,954; 1.9\% \)) and depressive disorders (\( n = 8356; 1.5\% \)).

#### 3.2 Comparison Between Capital Cities and Municipalities

Statistically significant differences were found between capital cities and municipalities. Prescriptions for two or more analgesics, in tablet or capsule form, were more common among patients in cities, as were prescriptions for antispasmodics, opioid analgesics and lidocaine. However, in municipalities it was most common to prescribe analgesics...
Table 1: Comparison between capital cities and municipalities with some sociodemographic, clinical and pharmacological variables, in a group of patients with analgesic prescriptions, Colombia, 2020

| Variables                              | Total   | Cities   | Municipalities | p value | p value |
|----------------------------------------|---------|----------|----------------|---------|---------|
|                                        | [n = 573,248] | [n = 387,472] | [n = 185,776] |         |         |
| Females                                | 376,584 | 255,719  | 120,865        | < 0.001 | < 0.001 |
| Males                                  | 196,664 | 131,753  | 64,911         | 34.9    |         |
| Age, years (mean ± SD)                 | 46.5 ± 23.6 | 47.3 ± 23.1 | 44.9 ± 24.4    | < 0.001 | < 0.001 |
| No chronic comorbidities               | 314,897 | 197,117  | 117,780        | 63.4    |         |
| With chronic comorbidities             | 258,351 | 190,355  | 67,996         | 36.6    | < 0.001 |
| Cardiovascular                         | 146,184 | 107,973  | 38,211         | 20.6    | < 0.001 |
| Endocrine                              | 79,852  | 59,844   | 20,008         | 10.8    | < 0.001 |
| Neurological                           | 36,935  | 27,982   | 8,953          | 4.8     | < 0.001 |
| Rheumatological                        | 35,487  | 27,794   | 7,693          | 4.1     | < 0.001 |
| Gastrointestinal                       | 19,746  | 15,171   | 4,575          | 2.5     | < 0.001 |
| Psychiatric                            | 18,521  | 14,463   | 4,058          | 2.2     | < 0.001 |
| Urinary                                | 12,685  | 9,046    | 3,639          | 2.0     | < 0.001 |
| Renal                                  | 12,000  | 6,573    | 5,427          | 2.9     | < 0.001 |
| Respiratory                            | 11,103  | 8,411    | 2,692          | 1.4     | < 0.001 |
| Indication of analgesic                | 199,040 | 152,505  | 46,535         | 25.0    | < 0.001 |
| Infections/fever                       | 82,562  | 63,245   | 19,317         | 10.4    | < 0.001 |
| Visceral pain                          | 40,151  | 30,404   | 9,747          | 5.2     | < 0.001 |
| Axial musculoskeletal pain             | 24,338  | 18,485   | 5,853          | 3.2     | < 0.001 |
| Migraine and other headaches           | 18,670  | 14,390   | 4,280          | 2.3     | < 0.001 |
| Trauma                                 | 14,689  | 11,417   | 3,272          | 1.8     | < 0.001 |
| Joint pain                             | 13,467  | 10,522   | 2,945          | 1.6     | < 0.001 |
| Neuropathic pain/radiculopathy         | 6010    | 4757     | 1,253          | 0.7     | < 0.001 |
| Cancer pain                            | 3752    | 3041     | 711            | 0.4     | < 0.001 |
| Dental pain                            | 1298    | 958      | 340            | 0.2     | < 0.001 |
| Non-specific pain                      | 1025    | 727      | 298            | 0.2     | 0.022   |
| Chronic pain                           | 475     | 405      | 70             | 0.0     | < 0.001 |
| Other types of diagnoses               | 374,208 | 234,967  | 139,241        | 75.0    | < 0.001 |
| Type of prescriber                     |         |         |                |         |         |
| General medicine                       | 530,257 | 353,429  | 176,828        | 95.2    | < 0.001 |
| Medical specialties                    | 19,119  | 15,456   | 3,663          | 2.0     | < 0.001 |
| Surgical specialties                   | 11,123  | 9,641    | 1,482          | 0.8     | < 0.001 |
| Odontology                             | 7899    | 6113     | 1,786          | 1.0     | < 0.001 |
| Unknown                                | 10,694  | 7823     | 2,871          | 1.5     | < 0.001 |
| Number of analgesic medications per patient |         |         |                |         |         |
| One                                    | 406,750 | 271,176  | 135,574        | 73.0    | < 0.001 |
| Two or more                            | 166,498 | 116,296  | 50,202         | 27.0    | < 0.001 |
| Pharmaceutical forms                   |         |         |                |         |         |
| Tablet or capsule                      | 509,427 | 348,515  | 160,912        | 86.6    | < 0.001 |
| Injectable                              | 64,617  | 45,505   | 19,112         | 10.3    | < 0.001 |
| Syrup                                  | 40,593  | 24,500   | 16,093         | 8.7     | < 0.001 |
| Powder to be reconstituted to oral solution | 18,372 | 13,540   | 4,832          | 2.6     | < 0.001 |
| Suspension                             | 8386    | 3885     | 4501           | 2.4     | < 0.001 |
| Transdermal patch                      | 1952    | 1832     | 120            | 0.1     | < 0.001 |
| Cream                                  | 83      | 75       | 8              | 0.0     | < 0.001 |
| Analgesic groups                       |         |         |                |         |         |
| Non-opioid pain relievers              | 516,291 | 348,321  | 167,970        | 90.4    | < 0.001 |
| Acetaminophen                          | 347,180 | 240,385  | 106,795        | 57.5    | < 0.001 |
as monotherapy, as a syrup or suspension, and in the form of non-opioid analgesics and muscle relaxants (Table 1). Acetaminophen was the most widely used analgesic in cities, while NSAIDs were the most widely used in municipalities (Table 1). Drug combinations containing two or three active ingredients predominated in capital cities, especially acetaminophen with codeine (Table 2). The average MME was higher in capital cities than in municipalities (Table 1).

### 3.3 Comparison Among Geographic Regions

The use of two or more analgesics was more frequent in the Pacific Region. Acetaminophen was the most commonly administered analgesic in all regions of the country, followed by NSAIDs. Dispensation of opioid analgesics predominated widely in the Central region, but the average MME was highest in the Bogota-Cundinamarca region (Table 3).

### 3.4 Comparison Among Age Groups

For each of the age groups, females and residents of capital cities represented the majority. In those under 18 years of age, the rate of prescriptions for two or more analgesics was lower than in the other age groups. The pharmaceutical forms of tablets or capsules predominated strongly among those older than 18 years of age, while syrup and oral suspension were more frequently prescribed for those younger than 18 years of age. The lowest proportion of acetaminophen prescriptions occurred between 18 and 44 years; NSAIDs predominated for those groups. Opioid analgesics were used more frequently after 45 years of age, and the average MME increased with increasing age (Table 4).

### 3.5 Multivariate Analysis

Multivariate analysis found that in all groups, being older than 40 years of age, being male, being treated in a capital city, receiving the prescription from a medical or surgical specialty, and having a diagnosis related to visceral pain, trauma, headache, musculoskeletal pain, neoplastic pain, joint pain, neuropathic pain or chronic pain increased the likelihood of receiving opioid analgesics, while having diagnoses related to dental pain and infectious diseases or fever reduced this risk (Table 5).

### 4 Discussion

The prescription patterns of analgesics for outpatients of any age and sex in the Colombian population were identified and differences or similarities in the dispensation of these medications according to geographic regions, capital city versus municipality, and age group, as well as the variables associated with the use of opioid analgesics, were described. In general, analgesics were more commonly used for females, as evidenced in Asian countries [14], Europe [15–18], and North America [19]. However, males had a higher risk of

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**Table 1** (continued)

| Variables          | Total     | Cities | Municipalities | $p$ value | $p$ value |
|--------------------|-----------|--------|----------------|-----------|-----------|
|                    | $[n = 573,248]$ | $[n = 387,472]$ | $[n = 185,776]$ |           |           |
| NSAIDs             | 221,799  | 145,753 | 76,046         | 0.001     | 0.001     |
| Traditional        | 221,159  | 145,225 | 75,934         | 0.001     | 0.001     |
| Selective          | 690      | 575     | 115            | 0.001     | 0.001     |
| Dipyrones          | 4236     | 3343    | 893            | 0.001     | 0.001     |
| Antispasmodics     | 78,985   | 54,222  | 24,763         | 0.001     | 0.001     |
| Opioid pain relievers | 68,709   | 56,417  | 12,292         | 0.001     | 0.001     |
| Partial agonists   | 58,999   | 47,878  | 11,121         | 0.001     | 0.001     |
| Full agonists      | 10,527   | 9,278   | 1,249          | 0.001     | 0.001     |
| Muscle relaxants   | 75,327   | 50,584  | 24,743         | 0.001     | 0.001     |
| Lidocaine          | 1174     | 1,078   | 96             | 0.001     | 0.001     |
| Others             | 1656     | 1,298   | 358            | 0.001     | 0.001     |
| Morphine equivalents $[n = 68,709]$ | 11.3 ± 41.1 | 12.2 ± 43.8 | 7.1 ± 24.4 | 0.001     | 0.001     |
| Low < 20 mg        | 62,850   | 51,081  | 11,769         | 0.001     | 0.001     |
| Intermediate 20–49 mg | 3881   | 3,500   | 381            | 3.1       |           |
| High ≥ 50 mg       | 1978     | 1,836   | 142            | 1.2       |           |

SD standard deviation, NSAIDs non-steroidal anti-inflammatory drugs
being prescribed opioids, as evidenced by Cragg et al. in a meta-analysis and systematic review [20], and in those older than 65 years of age, as documented in a cohort of patients in The Netherlands [21].

The most frequently prescribed pharmacological group was non-opioid analgesics, which is in line with the recommendations of clinical practice guidelines [4, 6, 9] previously reported in other works [5, 18, 22]. The most commonly used analgesic was acetaminophen, similar to what has been published in other studies [16, 23], followed by NSAIDs. The most commonly used NSAID in this report was naproxen, and its rate of use was very high compared with the rates reported in other studies (25.4% vs. 1.6–8.0%) [5, 24, 25]; however, in other countries, other active principles predominate, such as diclofenac (Iran: 49.2%, and India: 22.8%) [24, 26], acetylsalicylic acid (Nigeria: 62.2%) [25], nimesulide (Italy: 20.0%) [15], and ketoprofen (Malaysia: 17.5%) [5]. The proportion of prescription of COX-2 selective NSAIDs has been demonstrated to be low in different studies [17, 25, 26], similar to the findings of this report, probably due to its cardiovascular safety problems and its association with various adverse reactions [7].

If non-opioid analgesics fail to modulate pain, or when pain is moderate or severe, the use of opioid analgesics is

### Table 2  Comparison between capital cities and municipalities with the most widely dispensed analgesic drugs, Colombia, 2020

| Analgesic                                | Total [n = 573,248] | Cities [n = 387,472] | Municipalities [n = 185,776] | p Value |
|------------------------------------------|---------------------|----------------------|-----------------------------|---------|
| An active principle (n = 38 drugs)       | 537,941             | 93.8                 | 357,890                     | 92.4    | 180,051   | 96.9   | < 0.001 |
| Acetaminophen                            | 304,361             | 53.1                 | 204,205                     | 52.7    | 100,156   | 53.9   | < 0.001 |
| Naproxen                                 | 145,383             | 25.4                 | 92,416                      | 23.9    | 52,967    | 28.5   | < 0.001 |
| Hyoscine                                 | 75,587              | 13.2                 | 51,365                      | 13.3    | 24,222    | 13.0   | 0.022  |
| Diclofenac                               | 72,098              | 12.6                 | 49,088                      | 12.7    | 23,010    | 12.4   | 0.003  |
| Methocarbamol                            | 68,557              | 12.0                 | 44,855                      | 11.6    | 23,702    | 12.8   | < 0.001 |
| Ibuprofen                                | 27,249              | 4.8                  | 19,409                      | 5.0     | 7840      | 4.2    | < 0.001 |
| Tramadol                                 | 22,328              | 3.9                  | 16,832                      | 4.3     | 5496      | 3.0    | < 0.001 |
| Dipyrone                                 | 3004                | 0.5                  | 2341                        | 0.6     | 663.0     | 0.4    | < 0.001 |
| Lidocaine                                | 1174                | 0.2                  | 1078                        | 0.3     | 96        | 0.1    | < 0.001 |
| Diacerein                                | 1158                | 0.2                  | 984.0                       | 0.3     | 174.0     | 0.1    | < 0.001 |
| Oxycodeone                               | 961                 | 0.2                  | 836                         | 0.2     | 125       | 0.1    | < 0.001 |
| Morphine                                 | 824                 | 0.1                  | 735                         | 0.2     | 89        | 0.0    | < 0.001 |
| Buprenorphine                            | 755                 | 0.1                  | 730                         | 0.2     | 25        | 0.0    | < 0.001 |
| Hydromorphone                            | 709                 | 0.1                  | 678                         | 0.2     | 31        | 0.0    | < 0.001 |
| Tapentadol                               | 707                 | 0.1                  | 676                         | 0.2     | 31        | 0.0    | < 0.001 |
| Two or more active ingredients (n = 39 drugs) | 55,625             | 9.7                  | 47,033                      | 12.1    | 8592      | 4.6    | < 0.001 |
| Acetaminophen + codeine                  | 37,823              | 6.6                  | 32,036                      | 8.3     | 5787      | 3.1    | < 0.001 |
| Acetaminophen + hydrococode              | 6681                | 1.2                  | 5737                        | 1.5     | 944       | 0.5    | < 0.001 |
| Ibuprofen + methocarbamol                | 3162                | 0.6                  | 2627                        | 0.7     | 535       | 0.3    | < 0.001 |
| Acetaminophen + methocarbamol            | 2105                | 0.4                  | 1736                        | 0.4     | 369       | 0.2    | < 0.001 |
| Ibuprofen + hyoscine                     | 1304                | 0.2                  | 1099                        | 0.3     | 205       | 0.1    | < 0.001 |
| Dipyrone + hyoscine                      | 1291                | 0.2                  | 1040                        | 0.3     | 251       | 0.1    | < 0.001 |
| Tramadol + acetaminophen                 | 791                 | 0.1                  | 708                         | 0.2     | 83        | 0.0    | < 0.001 |
| Trimebutine + simethicone                | 688                 | 0.1                  | 603                         | 0.2     | 85        | 0.0    | < 0.001 |
| Cyclobenzaprine + lysine clonixinate     | 668                 | 0.1                  | 607                         | 0.2     | 61        | 0.0    | < 0.001 |
| Naproxen + sumatriptan                   | 629                 | 0.1                  | 579                         | 0.1     | 50        | 0.0    | < 0.001 |
| Glucosamine + chondroitin                | 581                 | 0.1                  | 390                         | 0.1     | 191       | 0.1    | 0.809  |
| Acetaminophen + caffeine + acetylsalicylic acid | 491            | 0.1                  | 398                         | 0.1     | 93        | 0.1    | < 0.001 |
| Pinaverium + simethicone                 | 330                 | 0.1                  | 302                         | 0.1     | 28        | 0.0    | < 0.001 |
| Acetaminophen + caffeine                 | 205                 | 0.0                  | 193                         | 0.0     | 12        | 0.0    | < 0.001 |
| Tizanidine + acetaminophen               | 128                 | 0.0                  | 115                         | 0.0     | 13        | 0.0    | < 0.001 |
| Variables                                      | Caribbean region | Bogotá-Cundinamarca region | Central region | Pacific region | Oriental region | Amazon-Orinoco region |
|------------------------------------------------|------------------|---------------------------|---------------|---------------|-----------------|-----------------------|
| | [n = 205,694] % | [n = 173,312] % | [n = 94,820] % | [n = 81,977] % | [n = 15,524] % | [n = 2003] %   |
| Females                                      | 133,116  64.7   | 115,101  64.4   | 62,274  65.7   | 54,912  67.0   | 10,010  64.5   | 1226  61.2         |
| Males                                        | 72,578  35.3    | 58,211  33.6    | 32,546  34.3   | 27,065  33.0   | 5514    35.5    | 777  38.8         |
| Age, years (mean ± SD)                       | 40.1 ± 22.9     | 46.1 ± 22.7     | 50.6 ± 22.9   | 59.1 ± 21.9   | 45.2 ± 22.2   | 38.5 ± 23.6       |
| City                                         | 104,221  50.7   | 152,044  87.7   | 71,020  74.9   | 46,701  57.0   | 11,558  74.5   | 2003  100.0       |
| No chronic comorbidities                     | 152,530  74.2   | 87,621  50.6    | 37,484  39.5   | 33,207  40.5   | 3660    23.6    | 148    7.4         |
| With chronic comorbidities                   | 53,164  25.8    | 85,691  49.4    | 57,336  60.5   | 54,270  66.2   | 7639    49.2    | 298    14.9        |
| Cardiovascular                                | 25,869  12.6    | 48,373  27.9    | 34,953  36.9   | 33,207  40.5   | 3660    23.6    | 148    7.4         |
| Endocrine                                     | 12,481  6.1     | 27,746  16.0    | 18,705  19.7   | 16,977  20.7   | 3847    24.8    | 106    5.3         |
| Gastrointestinal                              | 4612   2.2      | 6712   3.9      | 4646   4.9     | 3225   3.9     | 539     3.5      | 17     0.8         |
| Neurological                                  | 10,068  4.9     | 13,419  7.7     | 7186   7.6     | 5258   6.4     | 697     6.2      | 49     2.4         |
| Urinary                                      | 2649   1.3      | 3366   1.9      | 2581   2.7     | 3803   4.6     | 262     1.7      | 24     1.2         |
| Psychiatric                                   | 3771   1.8      | 4823   2.8      | 6146   6.5     | 3136   3.8     | 642     4.1      | 10     0.5         |
| Rheumatological                               | 8237   4.0      | 9634   5.6      | 10,119 10.7   | 5990   7.3     | 1459    9.4      | 57     2.8         |
| Respiratory                                   | 2129   1.0      | 3691   2.1      | 3068   3.2     | 1955   2.4     | 253     1.6      | 7      0.3         |
| Renal                                         | 817    0.4      | 1670   1.0      | 3169   3.3     | 6039   7.4     | 305     2.0      | 1      0.1         |
| Chronic pain                                  | 1003   0.5      | 4487   2.6      | 4501   4.7     | 1330   1.6     | 96      0.6      | 3      0.1         |
| Indication of analgesic                       | 58,267  28.3    | 73,761  42.6    | 37,534 39.6   | 23,470 28.6   | 5795    37.3     | 273    13.6        |
| Infections/fever                              | 23,763 11.6     | 32,956 19.0     | 14,102 14.9   | 9444   11.5    | 2217    14.3     | 105    5.2         |
| Visceral pain                                 | 11,837 5.8      | 14,258 8.2      | 8219   8.7     | 5476   6.6     | 1211    7.8      | 64     3.2         |
| Axial musculoskeletal pain                    | 8617   4.2      | 7518   4.3      | 4173   4.4     | 3419   4.2     | 588     3.8      | 28     1.4         |
| Migraine and other headaches                  | 5786   2.8      | 7589   4.4      | 3186   3.4     | 1570   1.9     | 531     3.4      | 15     0.7         |
| Trauma                                        | 4334   2.1      | 5959   3.4      | 2481   2.6     | 1553   1.9     | 345     2.2      | 24     1.2         |
| Joint pain                                    | 3399   1.7      | 3283   1.9      | 3889   4.1     | 2266   2.8     | 602     3.9      | 31     1.5         |
| Neuropathic pain/radiculopathy                | 1812   0.9      | 2066   1.2      | 1266   1.3     | 530    0.6      | 334     2.2      | 3      0.1         |
| Cancer pain                                   | 784    0.4      | 1550   0.9      | 776    0.8     | 522    0.6      | 122     0.8      | 5      0.2         |
| Dental pain                                   | 382    0.2      | 515    0.3      | 172    0.2     | 213    0.3      | 15      0.1      | 2      0.1         |
| Non-specific pain                             | 258    0.1      | 216    0.1      | 423    0.4     | 119    0.1      | 9       0.1      | 0      0.0         |
| Chronic pain                                  | 94     0.0      | 172    0.1      | 173    0.2     | 14     0.0      | 24      0.2      | 0      0.0         |
| Other types of diagnoses                      | 147427 71.7    | 99,551 57.4    | 57,286 60.4   | 58,507 71.4   | 9729    62.7     | 1730   86.4        |
| Type of prescriber                            |                  |                    |                  |                  |                  |                     |
| General medicine                              | 198,791 96.6    | 156,094 90.1    | 86,510 91.2    | 77,283 94.3    | 10,489  67.6    | 1171   58.5        |
| Medical specialties                           | 2399   1.2      | 10,092 5.8      | 2723   2.9     | 2567   3.1      | 1344    8.7      | 4      0.2         |
| Surgical specialties                          | 1882   0.9      | 5400   3.1      | 1876   2.0     | 1452   1.8      | 514     3.3      | 0      0.0         |
| Odontology                                    | 1132   0.6      | 2284   1.3      | 581    0.6     | 393    0.5      | 3511    22.6     | 0      0.0         |
| Unknown                                       | 2511   1.2      | 2100   1.2      | 3944   4.2     | 1000   1.2      | 310     2.0      | 829    41.4        |
Table 3 (continued)

| Variables                                      | Caribbean region [n = 205,694] | %     | Bogotá-Cundinamarca region [n = 173,312] | %     | Central region [n = 94,820] | %     | Pacific region [n = 81,977] | %     | Oriental region [n = 15,524] | %     | Amazon-Orinoco region [n = 2003] | %     |
|------------------------------------------------|-------------------------------|-------|------------------------------------------|-------|-----------------------------|-------|-----------------------------|-------|-------------------------------|-------|---------------------------------|-------|
| **Number of analgesic medications per patient** |                               |       |                                          |       |                              |       |                             |       |                               |       |                                 |       |
| One                                            | 148,928                       | 72.4  | 119,385                                  | 68.9  | 65,453                       | 69.0  | 60,962                      | 74.4  | 10,610                        | 68.3  | 1420                            | 70.9  |
| Two or more                                    | 56,766                        | 27.6  | 53,927                                   | 31.1  | 29,367                       | 31.0  | 21,015                      | 25.6  | 4914                          | 31.7  | 583                             | 29.1  |
| **Pharmaceutical forms**                       |                               |       |                                          |       |                              |       |                             |       |                               |       |                                 |       |
| Tablet or capsule                               | 173,412                       | 84.3  | 155,338                                  | 89.6  | 87,110                       | 91.9  | 77,904                      | 95.0  | 14,125                        | 91.0  | 1615                            | 80.6  |
| Injectable                                      | 18,786                        | 9.1   | 24,372                                   | 14.1  | 12,089                       | 12.7  | 7453                        | 9.1   | 1719                          | 11.1  | 236                             | 11.8  |
| Syrup                                          | 21,711                        | 10.6  | 11,409                                   | 6.6   | 3960                         | 4.2   | 2257                        | 2.8   | 985                           | 6.3   | 278                             | 13.9  |
| Powder to be reconstituted to oral solution     | 5037                          | 2.4   | 5781                                     | 3.3   | 3747                         | 4.0   | 3256                        | 4.0   | 483                           | 3.1   | 77                              | 3.8   |
| Suspension                                     | 5975                          | 2.9   | 1222                                     | 0.7   | 881                          | 0.9   | 196                         | 0.2   | 82                            | 0.5   | 31                              | 1.5   |
| Transdermal patch                              | 229                           | 0.1   | 766                                      | 0.4   | 710                          | 0.7   | 231                         | 0.3   | 15                            | 0.1   | 3                               | 0.1   |
| Cream                                          | 0                             | 0.0   | 9                                        | 0.0   | 25                           | 0.0   | 49                          | 0.1   | 15                            | 0.0   | 0                               | 0.0   |
| **Analgesic groups**                           |                               |       |                                          |       |                              |       |                             |       |                               |       |                                 |       |
| Non-opioid pain relievers                      | 184,059                       | 89.5  | 155,117                                  | 89.5  | 86,056                       | 90.8  | 75,453                      | 92.0  | 13,892                        | 89.5  | 1792                            | 89.5  |
| Acetaminophen                                   | 111,909                       | 54.4  | 103,883                                  | 59.9  | 62,994                       | 66.4  | 58,860                      | 71.8  | 8450                          | 54.4  | 1152                            | 57.5  |
| NSAIDs                                         | 87,836                        | 42.7  | 70,892                                   | 40.9  | 32,514                       | 34.3  | 22,936                      | 28.0  | 6855                          | 44.2  | 815                             | 40.7  |
| Traditional                                     | 87,749                        | 42.7  | 70,764                                   | 40.8  | 32,272                       | 34.0  | 22,760                      | 27.8  | 6849                          | 44.1  | 814                             | 40.6  |
| Selective                                      | 100                           | 0.0   | 140                                      | 0.1   | 258                          | 0.3   | 185                         | 0.2   | 6                             | 0.0   | 1                               | 0.0   |
| Dipyrone                                       | 630                           | 0.3   | 1376                                     | 0.8   | 1638                         | 1.7   | 590                         | 0.7   | 5                             | 0.0   | 8                               | 0.4   |
| Antispasmodics                                  | 29,327                        | 14.3  | 24,916                                   | 14.4  | 13,491                       | 14.2  | 8709                        | 10.6  | 2257                          | 14.5  | 311                             | 15.5  |
| Opioid pain relievers                          | 19,470                        | 9.5   | 20,241                                   | 11.7  | 20,355                       | 21.5  | 6401                        | 7.8   | 2177                          | 14.0  | 90                              | 4.5   |
| Partial agonists                                | 18,297                        | 8.9   | 17,156                                   | 9.9   | 16,487                       | 17.4  | 4989                        | 6.1   | 2026                          | 13.1  | 61                              | 3.0   |
| Full agonists                                   | 1350                          | 0.7   | 3322                                     | 1.9   | 4170                         | 4.4   | 1494                        | 1.8   | 172                           | 1.1   | 30                              | 1.5   |
| Muscle relaxants                                | 30,926                        | 15.0  | 20,476                                   | 11.8  | 11,456                       | 12.1  | 9781                        | 11.9  | 2481                          | 16.0  | 222                             | 11.1  |
| Lidocaine                                      | 148                           | 0.1   | 452                                      | 0.3   | 431                          | 0.5   | 134                         | 0.2   | 9                             | 0.1   | 0                               | 0.0   |
| Others                                         | 321                           | 0.2   | 146                                      | 0.1   | 873                          | 0.9   | 265                         | 0.3   | 24                            | 0.2   | 27                             | 1.3   |
| Morphine equivalents (n = 68,709)              | 9.4 ± 44.1                    |       | 12.5 ± 39.4                              |       | 11.9 ± 42.4                  |       | 11.3 ± 41.1                 |       | 12.0 ± 34.9                   |       | 8.5 ± 31.9                     |       |
| Low < 20 mg                                     | 18,687                        | 96.0  | 17,550                                   | 86.7  | 18,763                       | 92.2  | 5729                        | 89.5  | 2056                          | 94.4  | 85                              | 94.4  |
| Intermediate 20–49 mg                           | 345                           | 1.8   | 1914                                     | 9.5   | 1122                         | 5.5   | 430                         | 6.7   | 67                            | 3.1   | 4                               | 4.4   |
| High ≥50 mg                                     | 428                           | 2.2   | 777                                      | 3.8   | 470                          | 2.3   | 242                         | 3.8   | 54                            | 2.5   | 1                               | 1.1   |

SD standard deviation, NSAIDs non-steroidal anti-inflammatory drugs
Table 4  Comparison of sociodemographic, clinical, and pharmacological variables with the age groups in a group of patients with analgesic prescriptions, Colombia, 2020

| Variables                              | < 18 years | 18–44 years | 45–64 years | 65–79 years | 280 years |
|----------------------------------------|------------|-------------|-------------|-------------|-----------|
|                                        | [n = 77,565] % | [n = 186,042] % | [n = 166,191] % | [101,348] % | [n = 42,102] % |
| Females                                | 40,015 51.6 | 12,2647 65.9 | 114,909 69.1 | 69,752 68.8 | 29,261 69.5 |
| Males                                  | 37,550 48.4 | 63,395 34.1 | 51,282 30.9 | 31,596 31.2 | 12,841 30.5 |
| Age, years (mean ± SD)                 | 7.9 ± 5.4 32.0 ± 7.4 | 114,055 68.6 | 71.8 ± 4.3 | 85.9 ± 4.5 |
| City                                   | 45,272 58.4 | 129,450 69.6 | 70,292 90.6 | 129,450 69.6 | 70,292 90.6 |
| No chronic comorbidities               | 7273 9.4 | 42,950 23.1 | 90,303 54.3 | 90,303 54.3 | 90,303 54.3 |
| With chronic comorbidities             | 1700 2.2 | 11,695 6.3 | 48,889 29.4 | 56,919 56.2 | 26,981 64.1 |
| Cardiovascular                         | 906 1.2 | 10,123 5.4 | 31,786 19.1 | 56,919 56.2 | 56,919 56.2 |
| Gastrointestinal                       | 1073 1.4 | 5240 2.8 | 6986 4.2 | 4771 4.4 | 1976 4.7 |
| Neurological                           | 2161 2.8 | 14,924 8.0 | 9965 6.0 | 5591 5.5 | 4294 10.2 |
| Urinary                                | 135 0.2 | 584 0.3 | 2745 1.7 | 4762 4.7 | 4599 10.6 |
| Psychiatric                            | 291 0.4 | 3608 1.9 | 7460 4.5 | 4513 4.5 | 2649 6.3 |
| Rheumatological                        | 133 0.2 | 3026 1.6 | 14,887 9.0 | 13,027 12.9 | 4414 10.5 |
| Respiratory                            | 1454 1.9 | 872 0.5 | 2062 1.2 | 3674 3.6 | 3041 7.2 |
| Renal                                  | 24 0.0 | 156 0.1 | 1185 0.7 | 5166 5.1 | 5469 13.0 |
| Indication of analgesic                | 33,481 43.2 | 83,712 45.0 | 54,223 32.6 | 21,931 21.6 | 5693 13.5 |
| Infections/fever                       | 24,279 31.3 | 34,863 18.7 | 16,802 10.1 | 5390 5.3 | 1228 2.9 |
| Visceral pain                          | 4403 5.7 | 19,448 10.5 | 10,954 6.6 | 4276 4.2 | 1070 2.5 |
| Axial musculoskeletal pain             | 568 0.7 | 9758 5.2 | 9761 5.9 | 3527 3.5 | 724 1.7 |
| Migraine and other headaches           | 1880 2.4 | 11,096 6.0 | 4591 2.8 | 950 0.9 | 153 0.4 |
| Trauma                                 | 2322 3.0 | 6645 3.6 | 3789 2.3 | 1499 1.5 | 434 1.0 |
| Joint pain                             | 43 0.1 | 870 0.5 | 5775 3.5 | 5145 5.1 | 1634 3.9 |
| Neuropathic pain/radiculopathy         | 109 0.1 | 2231 1.2 | 2504 1.5 | 904 0.9 | 262 0.6 |
| Cancer pain                            | 151 0.2 | 1093 0.6 | 1463 0.9 | 776 0.8 | 269 0.6 |
| Dental pain                            | 86 0.1 | 697 0.4 | 410 0.2 | 91 0.1 | 14 0.0 |
| Non-specific pain                      | 186 0.2 | 336 0.2 | 321 0.2 | 142 0.1 | 40 0.1 |
| Chronic pain                           | 21 0.0 | 138 0.1 | 186 0.1 | 100 0.1 | 30 0.1 |
| Other types of diagnoses               | 44,084 56.8 | 102,330 55.0 | 111,968 67.4 | 79,417 78.4 | 36,409 86.5 |
| Type of prescriber                     | 71,224 91.8 | 172,444 92.7 | 153,448 92.3 | 93,945 92.7 | 39,196 93.1 |
| General medicine                       | 3162 4.1 | 4659 2.5 | 5728 3.4 | 3947 3.9 | 1623 3.9 |
| Medical specialties                    | 820 1.1 | 3122 1.7 | 3799 2.3 | 2404 2.4 | 978 2.3 |
| Surgical specialties                   | 840 1.1 | 3391 1.8 | 2451 1.5 | 968 1.0 | 249 0.6 |
| Odontology                             | 1921 2.5 | 4272 2.3 | 2691 1.6 | 1313 1.3 | 497 1.2 |
Table 4 (continued)

| Variables                          | <18 years [n = 77,565] | 18–44 years [n = 186,042] | 45–64 years [n = 166,191] | 65–79 years [n = 101,348] | ≥80 years [n = 42,102] |
|------------------------------------|-------------------------|---------------------------|---------------------------|--------------------------|------------------------|
|                                   | %                       | %                         | %                         | %                        | %                      |
| Number of analgesic medications per patient |                         |                           |                           |                          |                        |
| One                               | 68,513                  | 88.3                      | 113,672                   | 61.1                     | 109,687                | 66.0                   | 79,134                  | 78.1                     | 35,744                  | 84.9                     |
| Two or more                       | 9052                    | 11.7                      | 72,370                    | 38.9                     | 56,504                 | 34.0                   | 22,214                  | 21.9                     | 6358                    | 15.1                     |
| Pharmaceutical forms              |                         |                           |                           |                          |                        |                        |                          |                          |                        |                          |
| Tablet or capsule                 | 30,067                  | 38.8                      | 177,536                   | 95.4                     | 161,139                | 97.0                   | 99,339                  | 98.0                     | 41,346                  | 98.2                     |
| Injectable                         | 3458                    | 4.5                       | 35,595                    | 19.1                     | 19,616                 | 11.8                   | 5099                    | 5.0                      | 849                     | 2.0                      |
| Syrup                             | 40,056                  | 51.6                      | 260                       | 0.1                      | 99                     | 0.1                    | 83                      | 0.1                      | 95                      | 0.2                      |
| Powder to be reconstituted to oral solution | 670                     | 0.9                       | 4910                      | 2.6                      | 6700                   | 4.0                    | 4228                    | 4.2                      | 1864                    | 4.4                      |
| Suspension                        | 8288                    | 10.7                      | 40                        | 0.0                      | 23                     | 0.0                    | 16                      | 0.0                      | 19                      | 0.0                      |
| Transdermal patch                 | 4                       | 0.0                       | 212                       | 0.1                      | 665                    | 0.4                    | 600                     | 0.6                      | 471                     | 1.1                      |
| Cream                             | 0                       | 0.0                       | 12                        | 0.0                      | 31                     | 0.0                    | 28                      | 0.0                      | 83                      | 0.0                      |
| Analgesic groups                  |                         |                           |                           |                          |                        |                        |                          |                          |                        |                          |
| Non-opioid pain relievers         | 73,848                  | 95.2                      | 160,040                   | 86.0                     | 148,331                | 89.3                   | 94,049                  | 92.8                     | 40,023                  | 95.1                     |
| Acetaminophen                     | 56,231                  | 72.5                      | 76,412                    | 41.1                     | 95,502                 | 57.5                   | 81,031                  | 80.0                     | 38,004                  | 90.3                     |
| NSAIDs                            | 21,838                  | 28.2                      | 105,883                   | 56.9                     | 70,853                 | 42.6                   | 19,739                  | 19.5                     | 34,866                  | 8.3                      |
| Traditional                       | 21,837                  | 28.2                      | 105,753                   | 56.8                     | 70,530                 | 42.4                   | 19,594                  | 19.3                     | 34,445                  | 8.2                      |
| Selective                         | 1                       | 0.0                       | 138                       | 0.1                      | 352                    | 0.2                    | 155                     | 0.2                      | 44                      | 0.1                      |
| Dipyrone                          | 576                     | 0.7                       | 2337                      | 1.3                      | 1023                   | 0.6                    | 245                     | 0.2                      | 55                      | 0.1                      |
| Antispasmodics                    | 5891                    | 7.6                       | 42,356                    | 22.8                     | 20,941                 | 12.6                   | 7558                    | 7.5                      | 2239                    | 5.3                      |
| Opioid pain relievers             | 550                     | 0.7                       | 17,911                    | 9.6                      | 27,043                 | 16.3                   | 16,709                  | 16.5                     | 6496                    | 15.4                     |
| Partial agonists                  | 532                     | 0.7                       | 16,947                    | 9.1                      | 23,553                 | 14.2                   | 13,404                  | 13.2                     | 4563                    | 10.8                     |
| Full agonists                     | 19                      | 0.0                       | 1142                      | 0.6                      | 3806                   | 2.3                    | 3501                    | 3.5                      | 2059                    | 4.9                      |
| Muscle relaxants                  | 1886                    | 2.4                       | 29,373                    | 15.8                     | 31,381                 | 18.9                   | 10,777                  | 10.6                     | 1910                    | 4.5                      |
| Lidocaine                         | 2                       | 0.0                       | 142                       | 0.1                      | 453                    | 0.3                    | 357                     | 0.4                      | 220                     | 0.5                      |
| Others                            | 0                       | 0.0                       | 52                        | 0.0                      | 712                    | 0.4                    | 673                     | 0.7                      | 219                     | 0.5                      |
| Morphine equivalents (n = 68,709) | 2.9 ± 6.6               | 8.0 ± 40.3                | 11.9 ± 42.9               | 12.7 ± 38.9              | 14.8 ± 42.3            | 14.8 ± 42.3            |                          |                          |                        |                          |
| Low < 20 mg                       | 534                     | 97.1                      | 17,123                    | 95.6                     | 24,726                 | 91.4                   | 14,884                  | 89.1                     | 5583                    | 85.9                     |
| Intermediate 20–49 mg             | 13                      | 2.4                       | 448                       | 2.5                      | 1520                   | 5.6                    | 1259                    | 7.5                      | 641                     | 9.9                      |
| High ≥ 50 mg                      | 3                       | 0.5                       | 340                       | 1.9                      | 797                    | 2.9                    | 566                     | 3.4                      | 272                     | 4.2                      |

SD standard deviation, NSAIDs non-steroidal anti-inflammatory drugs
recommended [4, 6, 9]. In this analysis, it was found that 12% of patients received medications from this pharmacological group and that the most commonly used opioid analgesic was codeine, consistent with what was previously found in Colombia [27]. In contrast, in the US, McDonald et al. reported that the most frequently prescribed opioid was hydrocodone [28], while in some studies conducted in countries in Europe and Asia, the use of tramadol predominated [14, 17, 26]. The variations in the prescription patterns of various pharmacological groups can be explained by differences in prescribing habits, state policies on pain management, types of preferred medications, analgesic availability in each country, health systems, and specific regional marketing by the pharmaceutical industry.

The use of fixed-dose drug combinations containing analgesics with different mechanisms of action may be necessary to increase efficacy and reduce the frequency of adverse drug reactions [29]. Analgesic combinations are appropriate for pain management and have been recommended by the WHO, especially for the management of pain of moderate to severe intensity [30]. In this study, it was found that fewer than one-tenth of patients had dispensing of these pharmaceutical forms, which is consistent with what was reported in Japan and India (6.7–13.9%) [31, 32]. However, it is important to note that these medications can be used incorrectly and can be dangerous in overdose [29]. They are currently not included in the list of essential medicines [33]. Some studies have shown that the frequency of use and prescription patterns of analgesics vary according to the geographical area of each country [34–36], which was also seen in this report. No published studies comparing the prescription patterns for analgesics between a country’s capital cities and municipalities were found; however, in Germany, Hoffmann et al. found that the lowest proportion of inhabitants receiving dipyrone prescriptions were those who lived in Eastern states; the prevalence of almost all of these districts was below the national average, while the highest prescription rate was found for Northwestern states [34]. In the US, the use of prescription opioids varied geographically in terms of MME, treatment duration, and use of long-acting opioids [35], and in England, Mordecai et al. evaluated the geographical pattern of opioid prescription in primary care for a year and a half using MME and found that opioids were dispensed more frequently in the North than in the South and in areas of greater social deprivation [36]. Similarly, in our study, it was found that the central region had the highest prescription rate of opioids, but the region with the highest average MME was Bogotá-Cundinamarca. The wide variation in the prescription of opioids may reflect the weak consensus on the appropriate use of these medications to treat pain, especially chronic non-oncological pain. In addition, low prescription rates of these medications indicate insufficient treatment, while their frequent use may indicate misuse [28].

| Variables                                      | Sig\(^a\) | OR\(^b\) | 95% CI\(^b\) |
|------------------------------------------------|------------|-----------|---------------|
| Age < 40 years                                 | < 0.001    | Reference | Reference     |
| Age 40-64 years                                | < 0.001    | 2.463     | 2.409 2.517   |
| Age > 65 years                                 | < 0.001    | 2.608     | 2.547 2.671   |
| Man                                            | < 0.001    | 1.092     | 1.072 1.111   |
| Capital cities                                 | < 0.001    | 2.256     | 2.209 2.304   |
| Medical specialties                            | < 0.001    | 1.200     | 1.151 1.251   |
| Surgical specialties                           | < 0.001    | 1.517     | 1.444 1.593   |
| Dental pain                                    | < 0.001    | 0.305     | 0.226 0.414   |
| Fever and infectious diseases                  | < 0.001    | 0.475     | 0.459 0.492   |
| Visceral pain                                  | 0.001      | 1.061     | 1.025 1.097   |
| Trauma                                         | < 0.001    | 2.010     | 1.923 2.102   |
| Migraine and other headaches                   | < 0.001    | 2.008     | 1.927 2.093   |
| Axial musculoskeletal pain                     | < 0.001    | 2.945     | 2.855 3.037   |
| Neoplastic pain                                | < 0.001    | 3.260     | 3.036 3.502   |
| Joint pain                                     | < 0.001    | 4.744     | 4.574 4.921   |
| Neuropathic pain and radiculopathy             | < 0.001    | 5.082     | 4.812 5.367   |
| Chronic pain                                   | < 0.001    | 13.258    | 10.89 16.141  |

\(^a\)Statistical significance. \(^b\)Odds Ratio. \(^b\)95% Confidence interval
evidence and because their long-term effectiveness is poor [37]. However, we found that chronic pain was the main risk factor for being prescribed opioid analogues, which is consistent with that found by Campbell et al. in Australia [39]. Many prescribers use opioids for chronic pain management because they believe that it would be unethical to withhold these medication options, regardless of the pain etiology, without considering their effectiveness, the frequency of adverse reactions, and their association with an increased need for medical care services and the generation of morbidity and mortality [36]. The Centers for Disease Control and Prevention (CDC) guidelines recommend the use of non-opioid analogues for the treatment of chronic pain, saving opioids only for when it is expected that the benefits for pain control and improved function exceed those risks [9].

On the other hand, the perception of health authorities in Latin America is that drug abuse is a growing problem, but the quantity and quality of information is limited [40]. In Colombia, Yucumá et al. found a mean rate of 3.9 cases of mental and behavioral disorders due to opioid use per 100,000 inhabitants, with an increase in cases, since it went from 1.6/100,000 inhabitants in 2009 to 5.0/100,000 inhabitants in 2018, with a predominance of males and in the central region of the country [41]. The latter is consistent with the findings of this research in which it was shown that these groups of patients had a greater dispensing of opioids by those experiencing chronic cancer-related pain. Recognizing the variables associated with the use of all analogues should allow clinicians to recognize the risks related to their use in special populations, especially the use of NSAIDs by those with cardiovascular diseases or the use of potentially addictive opioids by those experiencing chronic cancer-related pain. The identification of possible variables associated with the differences in the use of opioids between regions of the country allows new research to be carried out to determine if they are clinically relevant.

### 5 Conclusion

We can conclude that differences were found in the prescription of different analogue groups between capital cities and municipalities and that opioid analogue use was higher in cities, mainly among elderly males with non-cancer-related chronic pain. Recognizing the variables associated with the use of all analogues should allow clinicians to recognize the risks related to their use in special populations, especially the use of NSAIDs by those with cardiovascular diseases or the use of potentially addictive opioids by those experiencing chronic cancer-related pain. The identification of possible variables associated with the differences in the use of opioids between regions of the country allows new research to be carried out to determine if they are clinically relevant.

### Appendix 1

See Table 6.

| Capital cities (n = 25) | Armenia, Barranquilla, Bogota, Bucaramanga, Cali, Cartagena, Cucuta, Ibague, Leticia, Manizales, Medellin, Mocoa, Monteria, Neiva, Pasto, Pereira, Popayan, Qibdo, Riohacha, San Jose del Guaviare, Santa Marta, Sincelejo, Tunja, Valledupar, Villavicencio |
|------------------------|---------------------------------------------------------------------------------------------------------------|
| Municipalities (n = 161) | Acacias, Agustin Codazzi, Albania, Algarrobo, Altos del Rosario, Andalucia, Anserma, Arjona, Arroyohondo, Barrancas, Barranco de Loba, Bello, Bosconia, Buenaventura, Buga, Bugalagrande, Caicedonia, Calamar, Calarca, Campo de La Cruz, Canalete, Candelaria (Atlantico), Candelaria (Valle), Cartago, Cerete, Chalan, Chia, Chinchina, Chinu, Cucuco, Cienaga, Cienaga de Oro, Circasia, Coloso, Corinto, Corozal, Cotorza, Dos Quebradas, Duitama, El Banco, El Carmen de Bolivar, El Cerrito, El Guamo, El Paso, El Penon, El Reten, Envigado, Espinal, Facatativá, Filandia, Florida, Floridablanca, Fonseca, Fundacion, Funza, Fusagasuga, Galapa, Galeras, Ginebra, Girardot, Giron, Guacari, Guamal, Hatillo de Loba, Ipiales, Ibagué, Jamundi, Juan de Acosta, La Dorada, La Jagua de Ibirico, La Mesa, La Tebaida, La Union (Sucre), La Union (Valle), La Virginia, Lorica, Los Palmitos, Magangué, Mahates, Malambo, Maria la Baja, Miranda, Momil, Mompos, Monitos, Montecristo, Montenegro, Morroa, Neira, Norosí, Nueva Granada, Ovejas, Palestina, Palmira, Patia, Pinillos, Planeta Rica, Plato, Pradera, Pueblo Nuevo, Puerto Escondido, Puerto Tejada, Purisima, Quimbaya, Regidor, Repeón, Rio Viejo, Rionegro, Riosucio, Roldanillo, Sabanagrande, Sabanalarga (Atlantico), Sahagun, Salamina (Caldas), Salamina (Magdalena), Sampues, San Andres de Sotavento, San Antero, San Bernardo del Viento, San Cristobal, San Jacinto, San Juan de Betulia, San Juan del Cesar, San Juan Nepomuceno, San Marcos, San Onofre San Pedro (Sucre), San Pedro (Valle), San Pelayo, San Sebastian, Buenavis, Santa Ana, Santa Rosa, Santa Rosa de Cabal, Santander de Quilichao, Simbota, Sinche, Soacha, Sogamoso, Soledad, Sopaviento, Supia, Talaguna, Nuevo Tierralta, Tiquisio, Tolú, Toluviejo, Toro, Tuchin, Tulua, Tumaco, Turbo, Turbana, Villamaria, Villanueva (Bolivar), Viterbo, Yotoco, Yumbo, Zambrano, Zarzal, Zipaquirá, Zona Bananera |
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Declarations

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Conflicts of interest/competing interests Luis Fernando Valladales-Restrepo, Santiago Rubio-Londoño, Luisa Fernanda Poveda-Martínez, and Jorge Enrique Machado-Alba declare no conflicts of interest.

Ethics approval The protocol was approved by the Bioethics Committee of the Universidad Tecnológica de Pereira in the category of risk-free research. The ethical principles established by the Declaration of Helsinki were respected (reference number: 01-110520).

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