



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

Luis Fernando Valladales-Restrepo^{1,2,3} · Santiago Rubio-Londoño³ · Luisa Fernanda Poveda-Martinez³ · Jorge Enrique Machado-Alba¹

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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.

✉ Jorge Enrique Machado-Alba
machado@utp.edu.co

¹ Grupo de Investigación en Farmacoepidemiología y Farmacovigilancia, Universidad Tecnológica de Pereira-Audifarma S.A., Calle 105 # 14-140, 660003 Pereira, Risaralda, Colombia

² Grupo de Investigación Biomedicina, Facultad de Medicina, Fundación Universitaria Autónoma de las Américas, Pereira, Colombia

³ Semillero de Investigación en Farmacología Geriátrica, Grupo de Investigación Biomedicina, Facultad de Medicina, Fundación Universitaria Autónoma de las Américas, Pereira, Risaralda, Colombia

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 antispasmodics, 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.
- Digestive: Chronic gastritis, gastroesophageal reflux, constipation, cirrhosis, peptic ulcer, hepatitis, irritable colon.
 - Respiratory: Chronic obstructive pulmonary disease, asthma.
 - Urinary: Benign prostatic hyperplasia, urinary incontinence/overactive bladder
 - Skin: Acne, psoriasis.
 - Cancer: Solid and hematological neoplasms.
 - Chronic pain.
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, dipyron, 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, rociverine, trimebutine.
 - 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 Bogota-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	65.7	255,719	66.0	120,865	65.1	< 0.001	< 0.001
Males	196,664	34.3	131,753	34.0	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	54.9	197,117	50.9	117,780	63.4		< 0.001
With chronic comorbidities	258,351	45.1	190,355	49.1	67,996	36.6		< 0.001
Cardiovascular	146,184	25.5	107,973	27.9	38,211	20.6		< 0.001
Endocrine	79,852	13.9	59,844	15.4	20,008	10.8		< 0.001
Neurological	36,935	6.4	27,982	7.2	8953	4.8		< 0.001
Rheumatological	35,487	6.2	27,794	7.2	7693	4.1		< 0.001
Gastrointestinal	19,746	3.4	15,171	3.9	4575	2.5		< 0.001
Psychiatric	18,521	3.2	14,463	3.7	4058	2.2		< 0.001
Urinary	12,685	2.2	9046	2.3	3639	2.0		< 0.001
Renal	12,000	2.1	6573	1.7	5427	2.9		< 0.001
Respiratory	11,103	1.9	8411	2.2	2692	1.4		< 0.001
Indication of analgesic	199,040	34.7	152,505	39.4	46,535	25.0		< 0.001
Infections/fever	82,562	14.4	63,245	16.3	19,317	10.4		< 0.001
Visceral pain	40,151	7.0	30,404	7.8	9747	5.2		< 0.001
Axial musculoskeletal pain	24,338	4.2	18,485	4.8	5853	3.2		< 0.001
Migraine and other headaches	18,670	3.3	14,390	3.7	4280	2.3		< 0.001
Trauma	14,689	2.6	11,417	2.9	3272	1.8		< 0.001
Joint pain	13,467	2.3	10,522	2.7	2945	1.6		< 0.001
Neuropathic pain/radiculopathy	6010	1.0	4757	1.2	1253	0.7		< 0.001
Cancer pain	3752	0.7	3041	0.8	711	0.4		< 0.001
Dental pain	1298	0.2	958	0.2	340	0.2		< 0.001
Non-specific pain	1025	0.2	727	0.2	298	0.2		0.022
Chronic pain	475	0.1	405	0.1	70	0.0		< 0.001
Other types of diagnoses	374,208	65.3	234,967	60.6	139,241	75.0		< 0.001
Type of prescriber								
General medicine	530,257	92.5	353,429	91.2	176,828	95.2	<0.001	< 0.001
Medical specialties	19,119	3.3	15,456	4.0	3663	2.0	<0.001	< 0.001
Surgical specialties	11,123	1.9	9641	2.5	1482	0.8	<0.001	< 0.001
Odontology	7899	1.4	6113	1.6	1786	1.0	<0.001	< 0.001
Unknown	10,694	1.9	7823	2.0	2871	1.5		< 0.001
Number of analgesic medications per patient								
One	406,750	71.0	271,176	70.0	135,574	73.0		<0.001
Two or more	166,498	29.0	116,296	30.0	50,202	27.0		<0.001
Pharmaceutical forms								
Tablet or capsule	509,427	88.9	348,515	89.9	160,912	86.6	<0.001	<0.001
Injectable	64,617	11.3	45,505	11.7	19,112	10.3	<0.001	<0.001
Syrup	40,593	7.1	24,500	6.3	16,093	8.7	<0.001	<0.001
Powder to be reconstituted to oral solution	18,372	3.2	13,540	3.5	4832	2.6	<0.001	<0.001
Suspension	8386	1.5	3885	1.0	4501	2.4	<0.001	<0.001
Transdermal patch	1952	0.3	1832	0.5	120	0.1	<0.001	<0.001
Cream	83	0.0	75	0.0	8	0.0	<0.001	<0.001
Analgesic groups								
Non-opioid pain relievers	516,291	90.1	348,321	89.9	167,970	90.4	<0.001	<0.001
Acetaminophen	347,180	60.6	240,385	62.0	106,795	57.5		<0.001

Table 1 (continued)

Variables	Total		Cities		Municipalities		<i>p</i> value	<i>p</i> value
	[<i>n</i> = 573,248]	%	[<i>n</i> = 387,472]	%	[<i>n</i> = 185,776]	%		
NSAIDs	221,799	38.7	145,753	37.6	76,046	40.9		<0.001
Traditional	221,159	38.6	145,225	37.5	75,934	40.9		<0.001
Selective	690	0.1	575	0.1	115	0.1		<0.001
Dipyrone	4236	0.7	3343	0.9	893	0.5		<0.001
Antispasmodics	78,985	13.8	54,222	14.0	24,763	13.3	<0.001	<0.001
Opioid pain relievers	68,709	12.0	56,417	14.6	12,292	6.6	<0.001	<<0.001
Partial agonists	58,999	10.3	47,878	12.4	11,121	6.0		<0.001
Full agonists	10,527	1.8	9278	2.4	1249	0.7		<0.001
Muscle relaxants	75,327	13.1	50,584	13.1	24,743	13.3	0.006	0.006
Lidocaine	1174	0.2	1078	0.3	96	0.1		<0.001
Others	1656	0.3	1298	0.3	358	0.2	<0.001	<0.001
Morphine equivalents (<i>n</i> = 68,709)	11.3 ± 41.1		12.2 ± 43.8		7.1 ± 24.4			<0.001
Low < 20 mg	62,850	91.5	51,081	90.5	11,769	95.7		<0.001
Intermediate 20–49 mg	3881	5.6	3500	6.2	381	3.1		
High ≥ 50 mg	1978	2.9	1836	3.3	142	1.2		

SD standard deviation, *NSAIDs* non-steroidal anti-inflammatory drugs

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

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

Analgesic	Total		Cities		Municipalities		p Value
	[n = 573,248]	%	[n = 387,472]	%	[n = 185,776]	%	
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
Dipyron	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
Oxycodone	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 + hydrocodone	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
Dipyron + 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

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 3 Comparison of sociodemographic, clinical, and pharmacological variables with geographic regions in a group of patients with analgesic prescriptions, Colombia, 2020

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	66.4	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	27,707	33.8	7885	50.8	1705	85.1
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	967	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	0.0
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	4583	5.6	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		Bogotá-Cundinamarca region		Central region		Pacific region		Oriental region		Amazon-Orinoco region	
	<i>n</i> = 205,694	%	<i>n</i> = 173,312	%	<i>n</i> = 94,820	%	<i>n</i> = 81,977	%	<i>n</i> = 15,524	%	<i>n</i> = 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	0	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 (<i>n</i> = 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		≥80 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		55.3 ± 5.6		71.8 ± 4.3		85.9 ± 4.5	
City	45,272	58.4	129,450	69.6	114,055	68.6	69,260	68.3	29,435	69.9
No chronic comorbidities	70,292	90.6	143,092	76.9	75,888	45.7	20,394	20.1	5231	12.4
With chronic comorbidities	7273	9.4	42,950	23.1	90,303	54.3	80,954	79.9	36,871	87.6
Cardiovascular	1700	2.2	11,695	6.3	48,889	29.4	56,919	56.2	26,981	64.1
Endocrine	906	1.2	10,123	5.4	31,786	19.1	27,295	26.9	9742	23.1
Gastrointestinal	1073	1.4	5240	2.8	6986	4.2	4471	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	4459	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										
General medicine	71,224	91.8	172,444	92.7	153,448	92.3	93,945	92.7	39,196	93.1
Medical specialties	3162	4.1	4659	2.5	5728	3.4	3947	3.9	1623	3.9
Surgical specialties	820	1.1	3122	1.7	3799	2.3	2404	2.4	978	2.3
Odontology	840	1.1	3391	1.8	2451	1.5	968	1.0	249	0.6
Unknown	1921	2.5	4272	2.3	2691	1.6	1313	1.3	497	1.2

Table 4 (continued)

Variables	<18 years		18–44 years		45–64 years		65–79 years		≥80 years	
	[n = 77,565]	%	[n = 186,042]	%	[n = 166,191]	%	[101,348]	%	[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	3486	8.3
Traditional	21,837	28.2	105,753	56.8	70,530	42.4	19,594	19.3	3445	8.2
Selective	1	0.0	138	0.1	352	0.2	155	0.2	44	0.1
Dipyron	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	
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

Table 5 Multivariate analysis of the variables associated with having dispensations of opioid analgesics, in a group of outpatients, Colombia, 2020

Variables	Sig ^a	OR ^b	95%CI ^b	
			Lower	Upper
Age < 40 years	< 0.001	Reference	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

^aStatistical significance. ^bOdds Ratio. ^c95% Confidence interval

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 that 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].

Opioids are widely used in the treatment of acute pain, cancer pain, and chronic non-cancer pain [4, 6, 9]. The use of these analgesics has been increasing [37], especially in patients without cancer compared with those with neoplasias (75% vs. 29%) [38]. However, there is a growing controversy regarding their use to treat non-oncological pain because this recommendation is based on limited

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 analgesics, 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 analgesics 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, therefore they would potentially have a higher risk of experiencing adverse drug reactions.

Some study limitations are based on the interpretation of the results of observational studies from drug databases since medical records were not accessed to clearly identify

the indications for prescription of analgesics, the intensity and anatomical distribution of pain, and the etiology of chronic pain. Likewise, it was not possible to access all the ICD-10 codes related to pain, and the use of medications prescribed outside the health system, over-the-counter medications, or medications delivered by a means other than the dispensing company is unknown.

5 Conclusion

We can conclude that differences were found in the prescription of different analgesic groups between capital cities and municipalities and that opioid analgesic use was higher in cities, mainly among elderly males with non-cancer-related chronic pain. Recognizing the variables associated with the use of all analgesics 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.

Table 6 Capital cities and municipalities included in the study

Capital cities (<i>n</i> = 25)	Armenia, Barranquilla, Bogota, Bucaramanga, Cali, Cartagena, Cucuta, Ibague, Leticia, Manizales, Medellin, Mocoa, Monteria, Neiva, Pasto, Pereira, Popayan, Quibdo, Riohacha, San Jose del Guaviare, Santa Marta, Sincelejo, Tunja, Valledupar, Villavicencio
Municipalities (<i>n</i> = 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, Cicuco, Cienaga, Cienaga de Oro, Circasia, Coloso, Corinto, Corozal, Cotorra, Dos Quebradas, Duitama, El Banco, El Carmen de Bolivar, El Cerrito, El Guamo, El Paso, El Penon, El Reten, Envigado, Espinal, Facativita, Filandia, Florida, Floridablanca, Fonseca, Fundacion, Funza, Fusagasuga, Galapa, Galeras, Ginebra, Girardot, Giron, Guacari, Guamal, Hatillo de Loba, Ipiales, Itagui, Jamundi, Juan de Acosta, La Dorada, La Jagua de Ibirico, La Mesa, La Tebaida, La Union (Sucre), La Union (Valle), La Virginia, Loriga, Los Palmitos, Magangué, Mahates, Malambo, Maria la Baja, Miranda, Momil, Mompos, Monitos, Montecristo, Montenegro, Morroa, Neira, Norosi, Nueva Granada, Ovejas, Palestina, Palmira, Patia, Pinillos, Planeta Rica, Plato, Pradera, Pueblo Nuevo, Puerto Escondido, Puerto Tejada, Purisima, Quimbaya, Regidor, Repelon, 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, Simiti, Since, Soacha, Sogamoso, Soledad, Soplaviento, Supia, Talaigua, Nuevo Tierralta, Tiquisio, Tolu, Tolviejo, Toro, Tuchin, Tulua, Tumaco, Turbaco, Turbana, Villamaria, Villanueva (Bolívar), Viterbo, Yotoco, Yumbo, Zambrano, Zarzal, Zipaquirá, Zona Bananera

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Declarations

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Consent to participate Not applicable, is a retrospective observational study.

Consent for publication All authors agree with the publication.

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