Exploring drug utilization patterns, healthcare resource utilization, and epidemiology of rheumatoid arthritis in Colombia: a retrospective claims database study

Daniel G. Fernández-Ávila[1] , Monica Betancur[2] , Amira Kronfly[2] and Edwin Jáuregui[3*]

Abstract

Background In Colombia, there is a lack of recent real- word studies that provide information on the epidemiology and healthcare resource utilization (HCRU) of rheumatoid arthritis (RA) at national level.

Methods To describe the burden of RA in Colombia, focusing on trends in drug utilization patterns, healthcare resource utilization (HCRU), and the epidemiology of adult patients diagnosed with RA between January 2017 and December 2022. This retrospective descriptive study used real-world data obtainedfrom a national claim database, SISPRO (*Sistema de Información para la Protección Social*). We included registries of adult patients diagnosed with RA between 2017 and 2022. We estimated the age-standardized incidence and prevalence of RA each year, drug utilization patterns for disease-modifying antirheumatic drugs (DMARDs) and glucocorticoids, rates of medical consultations, emergency room visits, and hospitalizations, and associated comorbidities and healthcare-related and pharmacy-related costs.

Results Overall, 327,430 unique patients with RA between 2017 and 2022 were included in the analysis, comprising 94,093 incident cases and 722,569 prevalent cases. The age-standardized incidence of RA ranged between 34.7 and 51.4 per 100,000 inhabitants, and the age-standardized prevalence ranged between 0.282 and 0.382 per 100 inhabitants between 2017 and 2022. The proportion of patients prescribed conventional synthetic DMARDs and biologic DMARDs decreased over the study period, from 39.23% in 2017 to 28.61% in 2021 and from 6.07% in 2017 to 3.72% in 2021, respectively. The proportion of patients prescribed targeted synthetic DMARDs increased from 0.9% in 2017 to 1.8% in 2021. The rate of medical consultations increased over the study period (from 2,406.6 in 2017 to 3,354.2 per 1,000 patients with RA in 2022). Consultation costs were the largest among all-cause annual healthcare-related costs.

Conclusion This study described the heavy burden of RA in Colombia with an increasing incidence of RA, and significant healthcare resource utilization and associated costs. Patients with RA in the country are increasingly able to access consultations with specialists and receive advanced therapies. However, there remains a need for efforts to

*Correspondence:
Edwin Jáuregui
edwinjaureguic69@gmail.com

Full list of author information is available at the end of the article

facilitate treatment among this population. These findings emphasize the importance of tailoring RA management strategies to the local context.

Keywords Healthcare resource utilization, Drug utilization patterns, Epidemiology, Rheumatoid arthritis

Background

Rheumatoid arthritis (RA) is a systemic, chronic, autoimmune inflammatory disease characterized by dysregulation of the immune system that provokes destruction of the underlying cartilage and bone structures [1]. RA is the most frequent inflammatory rheumatic disease in Colombia, with a prevalence ranging between 0.24 and 1.49 per 100 inhabitants between 2005 and 2019 [2–5]. The prevalence increases with age and is more frequent in women than in men [1, 4].

Irreversible joint damage and deformity caused by RA affects patient's functionality and quality of life [6]. Additionally, RA is related to several comorbidities, which are often linked to poor health outcomes [7]. In Colombia, up to 82.3% of the prevalent cases in 2019 had any comorbidity, with hypertension being the most frequent [5, 8]. Moreover, RA patients have higher mortality rates than the general population [9]. In 2021, the crude all-cause mortality rate in patients with RA in Colombia was 7.45 per 100,000 inhabitants, being more frequent in older adults [8].

Regarding the pharmacological treatment of RA, the treat-to-target strategy (T2T) guides the clinical decision-making process by setting and assessing the achievement of therapeutic goals, to prevent and stop inflammation and consequently reduce structural damage [10, 11]. Pharmacological therapy is the basis of treatment, with a therapeutic repertoire including analgesic, anti-inflammatory, and glucocorticoid drugs as adjuvants to disease-modifying antirheumatic drugs (DMARDs). DMARDs are subdivided into synthetic (csDMARDs), biological (bDMARDs), and targeted synthetic (tsDMARDs) [10]. The pillar of pharmacological treatment are csDMARDs, with methotrexate as first-line therapy, both as monotherapy and in combination therapy [10, 12]. bDMARDs were introduced as alternatives for patients without a satisfactory response to combined strategies of csDMARDs. However, biologic drugs have been associated with a greater frequency of serious adverse events and higher costs [13, 14]. In 2019, 77.46% and 16.70% of the prevalent patients in Colombia used csDMARDs and bDMARDs, respectively [8].

High economic costs are associated with the treatment of RA and its complications [15]. A meta-analysis of studies conducted in the United States and published between 2000 and 2016 estimated that the annual total cost of direct medical care for a patient with RA was 12,509 USD, for patients using any treatment regimen with DMARDs. However, when considering only bDMARD users, the annual cost increases to 36,053 USD [16]. The cost of treatment is related to the disease activity. In Colombia, drugs represent 53.6% of the total cost for low disease activity and 88.5% for severe disease activity, excluding costs for biologic treatment. For patients with severe disease and who are receiving biologic treatment, drugs represent 97% of the total cost [17].

In Colombia, there are no updated real-world studies that describe the epidemiology and healthcare resource utilization (HCRU) of RA at the national level [2–4, 18, 19]. Thus, this study aimed to describe the burden of RA in Colombia as the trends in drug utilization patterns, HCRU, and epidemiology of adult patients with RA diagnosis between January 2017 and December 2022, using a comprehensive publicly available national claims database (*Sistema de Información para la Protección Social*, SISPRO).

Methods

Study design and participants

We conducted a retrospective descriptive study using real-world data obtained from a national claims database SISPRO to describe trends in HCRU, drug utilization patterns, and epidemiological measures linked to RA diagnosis in Colombia between 2017 and 2022. We included adults (≥18 years) with a diagnosis of RA according to specific International Classification of Diseases-10th Revision (ICD-10) codes (Supplementary Table 1), with a defined place of residence, and available data from SISPRO for the specified study period.

Data sources and variables

The SISPRO is a government-owned comprehensive structured database containing reports from all healthcare providers in the public healthcare system (*Sistema General de Seguridad Social en Salud*, SGSSS), that covers approximately 98.54% of the Colombian population [20, 21]. The SISPRO is structured in independent modules for outpatient, inpatient, and pharmacy data that contain information reported by different stakeholders of the Colombian healthcare system [22]. For this study, we included information from three independent modules in SISPRO: RIPS (*Registro Individual de Prestación de Servicios de Salud*), SUF (*Cubo de Gestión de la Demanda*), and MIPRES (*Mi Prescripción*) (Supplementary Fig. 1). The data within SISPRO are deidentified and verified for quality using standardized procedures. Data within each module are linked to a patient ID number, which is unavailable to external users. Data could only be accessed at an aggregated level, meaning that individual

patient data could not be retrieved. Consequently, information could not be linked across modules. We extracted the epidemiologic data from SISPRO in September 2023 and the HCRU data in October 2023.

We used the RIPS module to retrieve data for epidemiological measures (incidence and prevalence) and HCRU, defined in this study as the set of medical procedures, drugs, and inpatient and outpatient visits registered for patients with a RA diagnosis. The RIPS module includes data on consultations, procedures, emergency services, hospitalizations, and information about the confirmed or presumptive diagnosis code associated with the provided service (according to the current ICD). Furthermore, it includes the date when the provided health service took place, the health provider institution that offered the service, the type of insurance (contributory or subsidized), and the paying insurance company, as well as information about the age, gender, place of residence, and other demographic characteristics of the patient.

We used the SUF module to retrieve information about the treatments and procedures included in the national health benefits package (*Plan de Beneficios en Salud*, PBS). This module contains information about the number of services and procedures, medications prescribed (coded according to the Anatomical Therapeutic Chemical (ATC) classification, and a national classification system), the amount prescribed, the cost of the drug, and the cost assumed by the user (copayments and fees). For health technologies and services not included in the PBS, we retrieved information from the MIPRES module. This module includes information about the diagnosis for which the health technology or procedure was prescribed, the amount prescribed, the date, type of insurance, age, gender, and ethnicity of the patient.

To estimate drug costs, cost data were retrieved from SISMED (*Sistema de Información de Precios de Medicamentos*), as recommended by the Colombian National Health Technology Assessment (HTA) Agency for Cost Studies [23]. Data from MIPRES were linked to the costs reported in SISMED using the CUM (*Código Único de Medicamentos*, CUM), which is a unique identifier for each drug presentation that is present in both databases. The costs of health services and procedures was retrieved from the SUF module. For abatacept, adalimumab, infliximab, certolizumab pegol, and tocilizumab, information was obtained from SUF, as they have been in the PBS for the whole study period with the indication of treating RA.

The healthcare system in Colombia has a mixed model of public and private financing, with individuals primarily affiliated through two main regimens: the contributory regimen and the subsidized regimen [24]. The contributory regime includes individuals with paying capabilities, such as employees and self-employed workers, whereas the subsidized regime covers unemployed individuals [24].

The following variables were extracted from the databases: gender, age, place of residence, health insurance regime (contributory and subsidized), outpatient medical visits, hospitalizations, procedures performed, laboratory tests, medications, and health benefit costs.

Statistical methods

Data were analyzed descriptively, with categorical variables described as absolute counts and percentages. Missing data were reported, and no data imputation was conducted.

The annual prevalence was determined as the number of patients living with the disease within a year, regardless of when the diagnosis occurred. The annual incidence was estimated as the number of new cases of the disease within a year. 95% confidence intervals (CI) were calculated, where applicable. HCRU was defined as the frequency of medical consultations, drugs prescribed, emergency room visits and hospital admissions. The yearly all-cause healthcare-related cost were estimated in Colombian Pesos (COP) and United States Dollars purchasing power parities (USD PPP) per patient with RA diagnosis, including costs associated to consultations, hospitalization days, imaging procedures (including, articular ultrasound, X-ray, and magnetic resonance image), and laboratories (including, rheumatoid factor and anti-cyclic citrullinated peptide antibodies). Similarly, pharmacy costs were analyzed by the type of medication (csDMARDs, bDMARDs, and tsDMARDs) and the subgroups in each category. The csDMARDs comprised methotrexate, leflunomide, 5-aminosalicylic acid (5-ASA, also known as sulfasalazine), and hydroxychloroquine. bDMARDs included certolizumab pegol, golimumab, infliximab, rituximab, tocilizumab, etanercept, adalimumab, and abatacept. tsDMARDs included were tofacitinib, baricitinib, and upadacitinib. We estimated the proportion of patients prescribed csDMARDs, bDMARDs, and tsDMARDs each year.

Bias

The databases used for this study rely on administrative claims data for clinical details, and they are subject to data coding limitations, data entry errors, and incomplete or inconsistent information. The sources of error included patient reporting inaccuracies, differences in RA diagnostic criteria among physicians, and encoding errors within the SISPRO database. Additionally, some health services might not be captured in the reported claims because the health insurance plan does not cover them; instead, patients may access these services via private healthcare.

Ethics approval and consent to participate

This study adhered to the study protocol and ethical principles rooted in the Declaration of Helsinki. According to local regulations, no Institutional Review Board (IRB)/ Ethics Committee (EC) notification or approval, or patient consent was required, as deidentified data from a claims database were utilized, aligning with local data privacy regulations. The results were presented in accordance with the Strengthening the reporting of observational studies in epidemiology (STROBE) statement [25] and the REporting of Studies Conducted Using Observational Routinely-Collected Health Data (RECORD) Statement [26].

Results

Overall, 327,430 unique patients with RA between 2017 and 2022 were included in the analysis. During that period, 94,093 incident cases and 722,569 prevalent cases. The elevated number of prevalent cases in relation to unique patients arises from the methodology that accounts for each patient visit as a distinct entry.

Epidemiology

The age-standardized incidence of RA in Colombia ranged between 34.7 and 51.4 per 100,000 inhabitants between 2017 and 2022, with the highest incidence occurring in 2019 (Supplementary Table 2). Between 2017 and 2019, the incidence rate was higher among patients aged 60 to 64 years (ranged between 82.4 and 121.9 per 100,000 inhabitants), between 2020 and 2022,

the group with the highest incidence was 65 to 69 years (ranged between 96.9 and 118.6 per 100,000 inhabitants) (Fig. 1A) (Supplementary Table 2). The incidence was higher in women (ranged between 55.1 and 82.7 per 100,000 inhabitants) than in men (ranged between 13.2 and 17.2 per 100,000 inhabitants) (Fig. 1B). The incidence rate was higher in the subsidized regimen between 2017 and 2021 (ranged between 40.18 and 69.69 per 100 inhabitants) compared to the contributory regimen (ranged between 32.64 and 44.56 per 100 inhabitants).

The age-standardized prevalence of RA ranged between 0.282 and 0.382 per 100 inhabitants between 2017 and 2022. The highest prevalence of RA was among cases between 65 and 69 years, throughout the study period, ranging between 0.694 and 0.959 per 100 inhabitants (Fig. 1C) (Supplementary Table 3). The prevalence was higher among women (ranging between 0.435 and 0.589 per 100 inhabitants), than among men (ranging between 0.096 and 0.1332 per 100 inhabitants) (Fig. 1D). The prevalence was higher in the contributory regimen throughout the study period (ranged between 0.342 and 0.531 per 100 inhabitants) compared to the subsidized regimen (ranged between 0.159 and 0.335 per 100 inhabitants).

Drug utilization patterns

The proportion of patients prescribed csDMARDs decreased from 39.23% in 2017 to 26.98% in 2021, with leflunomide being the most frequently prescribed (ranging between 17.83% in 2017 and 12.41% in 2021)
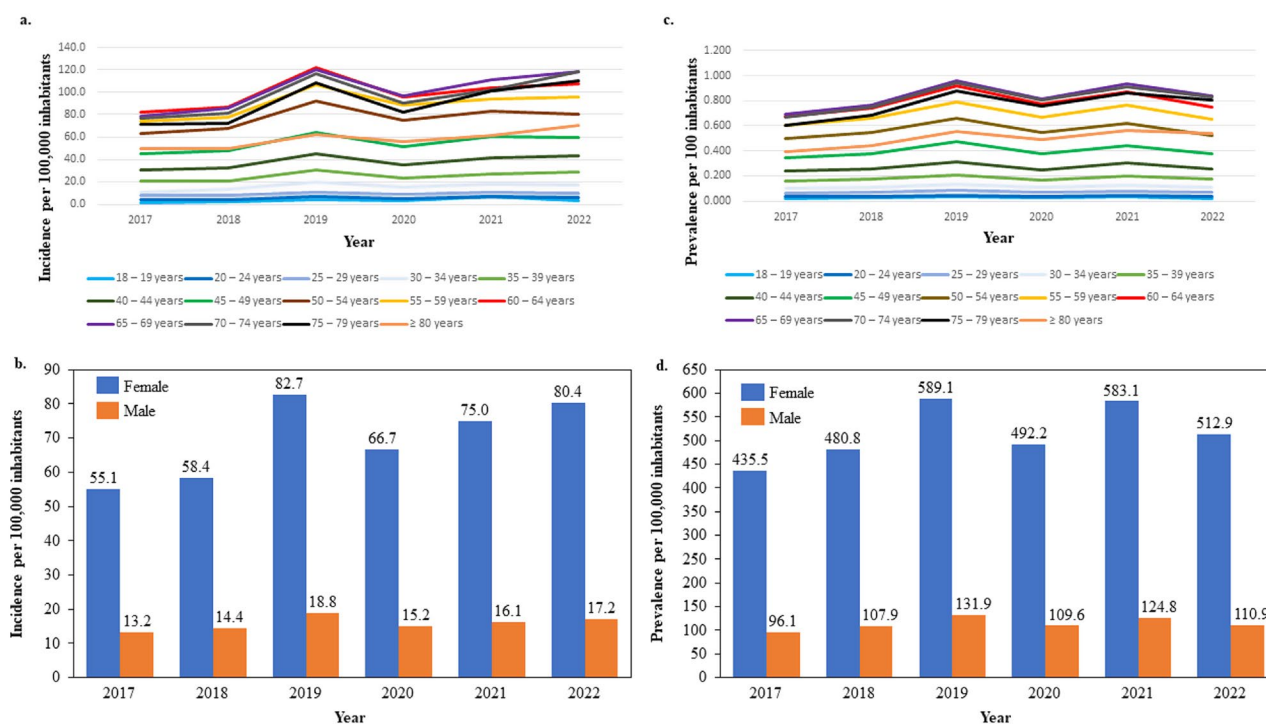
Fig. 1 Incidence rate and prevalence of rheumatoid arthritis according to age and sex

(Table 1). This was followed by chloroquine and methotrexate, with the proportion of patients with prescriptions ranging between 7.02% and 13.02%, and 2.49% and 4.72%, respectively.

The proportion of patients prescribed bDMARDs decreased from 6.07% in 2017 to 3.72% in 2021. The bDMARD most prescribed was etanercept, with the proportion of patients prescribed ranging between 1.14% and 2.27%. This was followed by adalimumab, with a proportion of patients prescribed ranging from 0.44 to 1.16%, tocilizumab from 0.67 to 1.09%, and rituximab from 0.90 to 1.05%.

The proportion of patients prescribed tsDMARDs ranged from 0.91% in 2017 to 1.79% in 2021, with tofacitinib accounting for most patients prescribed (ranging between 0.91% and 1.41%). Baricitinib began to be prescribed in 2019, accounting for 0.01% of the patients prescribed that year, and increased to 0.38% in 2021. Upadacitinib started to be prescribed in 2021, with only one patient prescribed that year, subsequently in 2022 prescriptions increased to 255 patients prescribed. The proportion of patients prescribed glucocorticoids ranged between 23.57% and 57.66%, with prednisolone being the most frequently prescribed (ranging between 16.92% and 50.72%). Due to the periodicity of the database updates, the prescription data for 2022 were incomplete and therefore not reported.

Medical consultations

The rate of medical consultations increased from 2406.6 in 2017 to 3354.2 per 1,000 patients with RA in 2022. Between 2017 and 2019, the highest rate of consultations was with general practitioners, ranging between 772.4 and 804.0 per 1,000 patients with RA (Table 2). From 2020 to 2022, the highest rate of consultation was with rheumatologists, increasing from 769.5 per 1,000 patients with RA in 2020 to 851.8 per 1,000 patients with RA in 2022. The third most common consultation was with internal medicine, with the rate of consultation ranging between 94.7 and 252.9 per 1,000 patients with RA. The rate of consultations with orthopedists increased over the years, starting in 2017 at a rate of 20.7 per 1,000 patients

Table 1 Prescriptions of disease-modifying anti-rheumatic drugs and steroids among patients with rheumatoid arthritis diagnosis by year

Medication	2017		2018		2019		2020		2021	
	n*	%**	n*	%**	n*	%**	n*	%**	n*	%**
csDMARDs	**37,059**	**39.23**	**38,979**	**36.18**	**50,834**	**36.98**	**31,951**	**26.98**	**39,711**	**28.61**
Chloroquine	12,298	13.02	12,425	11.53	14,122	10.27	8,309	7.02	11,451	8.25
Hydroxychloroquine	1,897	2.01	2,153	2.00	2,929	2.13	3,879	3.28	4,401	3.17
Leflunomide	16,846	17.83	18,710	17.37	23,629	17.19	15,450	13.05	17,224	12.41
Methotrexate	3,491	3.70	3,374	3.13	6,492	4.72	2,949	2.49	5,256	3.79
Sulfasalazine	2,527	2.67	2,317	2.15	3,662	2.66	1,364	1.15	1,379	0.99
bDMARDs	**5,733**	**6.07**	**5,829**	**5.41**	**7,055**	**5.13**	**4,612**	**3.89**	**5,170**	**3.72**
Abatacept	186	0.20	120	0.11	129	0.09	135	0.11	0	0.00
Adalimumab	1,031	1.09	929	0.86	1,593	1.16	517	0.44	1,080	0.78
Certolizumab pegol	217	0.23	86	0.08	162	0.12	181	0.15	126	0.09
Etanercept	2,147	2.27	2,332	2.16	2,381	1.73	1,651	1.39	1,582	1.14
Golimumab	59	0.06	38	0.04	48	0.03	70	0.06	46	0.03
Infliximab	138	0.15	127	0.12	163	0.12	132	0.11	163	0.12
Rituximab	923	0.98	1,127	1.05	1,450	1.05	1,117	0.94	1,243	0.90
Tocilizumab	1,032	1.09	1,070	0.99	1,129	0.82	809	0.68	930	0.67
tsDMARDs	**859**	**0.91**	**1,163**	**1.08**	**1,579**	**1.15**	**1,925**	**1.63**	**2,488**	**1.79**
Baricitinib	0	0.00	0	0.00	19	0.01	204	0.17	530	0.38
Tofacitinib	859	0.91	1,163	1.08	1,560	1.13	1,721	1.45	1,957	1.41
Upadacitinib	0	0.00	0	0.00	0	0.00	0	0.00	1	0.00
Glucocorticoids	**54,474**	**57.66**	**25,394**	**23.57**	**63,201**	**45.97**	**33,898**	**28.62**	**67,774**	**48.83**
Deflazacort	2,864	3.03	3,083	2.86	3,214	2.34	3,292	2.78	3,345	2.41
Dexamethasone	2,286	2.42	2,443	2.27	2,268	1.65	1,178	0.99	6,934	5.00
Hydrocortisone	450	0.48	534	0.50	565	0.41	297	0.25	190	0.14
Methylprednisolone	956	1.01	1,108	1.03	1,286	0.94	1,656	1.40	3,121	2.25
Prednisolone	47,918	50.72	18,226	16.92	55,868	40.64	27,475	23.20	54,184	39.04
Prednisone	2,846	3.01	961	0.89	714	0.52	395	0.33	343	0.25

csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biologic disease-modifying antirheumatic drugs; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs

*Number of patients with prescriptions of each medication, **Proportion of patients with a prescription of each medicatio

Table 2 Number of overall medical consultations related to rheumatoid arthritis by each year of study

Consultation type	2017		2018		2019		2020		2021		2022	
	Number of consultations	Rate*	Number of consultations	Rate*	Number of consultations	Rate*	Number of consultations	Rate*	Number of consultations	Rate*	Number of consultations	Rate*
General practice	75,958	804.0	85,460	793.3	106,401	773.9	91,471	772.4	104,327	751.6	103,006	819.7
Rheumatologist	26,948	285.2	50,194	465.9	85,360	620.9	91,127	769.5	132,470	954.4	107,043	851.8
Orthopedist	1,954	20.7	3,846	35.7	5,414	39.4	4,219	35.6	5,424	39.1	6,492	51.7
Physiatrist	957	10.1	2,360	21.9	2,981	21.7	2,402	20.3	4,398	31.7	5,418	43.1
Internal Medicine	8,950	94.7	18,399	170.8	29,321	213.3	29,953	252.9	31,692	228.3	28,357	225.7
Physiotherapy	3,581	37.9	5,886	54.6	10,836	78.8	11,609	98.0	24,491	176.4	20,483	163.0
Family Medicine	1,140	12.1	2,936	27.3	4,203	30.6	5,215	44.0	9,444	68.0	12,346	98.2
Nutritionist	657	7.0	655	6.1	1,069	7.8	8,314	70.2	17,596	126.8	14,249	113.4
Nursing	2,258	23.9	4,778	44.4	6,315	45.9	14,528	122.7	21,352	153.8	18,497	147.2
Psychology	894	9.5	2,212	20.5	1,546	11.2	6,199	52.3	10,192	73.4	12,520	99.6
Occupational therapy	1,682	17.8	2,756	25.6	6,156	44.8	9,174	77.5	16,593	119.5	8,837	70.3
Ophthalmology	611	6.5	1,096	10.2	1,222	8.9	955	8.1	860	6.2	473	3.8
Social work	197	2.1	126	1.2	382	2.8	420	3.5	1,195	8.6	3,227	25.7
Pain and palliative care specialist	559	5.9	1,093	10.1	1,198	8.7	1,041	8.8	1,299	9.4	1,702	13.5
Other medical specialties	101,027	1,069.3	82,479	765.6	121,718	885.4	157,109	1,326.7	142,456	1,026.3	78,836	627.4
Total	227,373	2,406.6	264,276	2,453.2	384,122	2,794.1	433,736	3,662.6	523,789	3,773.7	421,486	3,354.2

*Rate of consultations per 1,000 patients with rheumatoid arthritis

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with RA, which increased to 51.7 per 1,000 patients with RA in 2022. Similarly, the number of family medicine consultations increased throughout the period, with a rate of 12.1 per 1,000 patients with RA in 2017, which increased to 98.2 per 1,000 patients with RA in 2022.

Hospital admissions and emergency room visits

Over the study years, the rate of hospital admissions fluctuated, increasing from 2017 to 2018 (from 53.4 to 85.4 per 1,000 patients with RA), followed by a subsequent decrease over the following years and a further increase between 2021 and 2022, reaching a rate of 95.8 per 1,000 patients with RA in 2022 (Table 3). The rate of admissions was higher in males than in females over the years, ranging between 60.5 and 114.3 per 1,000 patients with RA in males versus 55.7 and 100.3 per 1,000 patients with RA in females. According to age group, patients aged 18 to 19 years had the highest rate of hospital admission, ranging from 90.1 per 1,000 patients with RA in 2017 to 146.9 per 1,000 patients with RA in 2022, with a peak in 2021 with a rate of 282.4 per 1,000 patients with RA. Hospitalization rates were also higher in patients aged above 60 years. In this group, in 2017, the highest rate was in patients aged 65 to 69 years, with a rate of 74.9 per 1,000 patients with RA, while in 2022, it was in patients aged 70 to 74 years, with a rate of 121.5 per 1,000 patients with RA.

The number of emergency room visits related to RA diagnosis decreased throughout the study period. In 2017, the rate of emergency room visits peaked, with 88.8 emergency room visits per 1,000 patients diagnosed with RA, decreasing to a rate of 20.6 per 1,000 patients diagnosed with RA in 2022 (Table 3). In 2017, the groups with the highest rate of emergency room visits were patients aged 40–44 years (120.0), followed by those aged 50 to 54 years (101.2). In 2022, the highest rate was in patients 18 to 19 years (73.4), followed by those aged 20 to 24 years (52.9). When analyzing the distribution of emergency visits by sex, the rate per 1,000 patients with an RA diagnosis was regularly higher in males throughout the study period. Females had a rate of 95.1 visits in 2017, dropping to 21.4 in 2022, whereas males had a rate of 88.0 in 2017, decreasing to 25.4 in 2022.

Healthcare-related and pharmacy costs

Consultation costs were the largest among all healthcare-related costs. Consultation costs dropped from 25,142,401 USD PPP in 2017 to 16,732,917 USD PPP in 2018 (Table 4). Subsequently, consultation cost increased between 2019 and 2021, reaching 36,391,280 USD PPP in 2021. Subsequently, in 2022, the costs of consultations declined to 23,031,841 USD PPP. Regarding pharmacy-related costs, the cost per patient was $6,777 USD PPP in 2017, reaching a peak in 2018 at 9,179 USD PPP per patient (Table 4). Costs started to decline in the

subsequent years until 2021, with 3,805 USD PPP per patient. When analyzing costs by type of drug, tsDMARDs were the most expensive, with a peak in 2018 at 909,584,806 USD PPP. Afterward, the costs for all patients continually declined until 456,959,438 USD PPP in 2021. bDMARDs expenditures started at 62,966,462 USD in 2017 and peaked at 78,743,927 USD PPP in 2019. In 2020 and 2021, costs fell from 56,044,637 USD PPP in 2020 to 52,710,269 USD PPP in 2021.

Comorbidities

Within the MIPRES module, the largest proportion of associated diagnoses included diseases of the musculoskeletal system (ranged between 36.2% and 68.2%), neuroendocrine, nutritional, and metabolic diseases (ranged between 7.6% and 15.7%), diseases of the nervous system (ranged between 1.9% and 4.0%), signs, symptoms, and abnormal clinical and laboratory findings (ranged between 10.5% and 31.7%) (Supplementary Table 4). Similarly, within the SUF module, the biggest proportion of associate diagnoses included diseases of the musculoskeletal system (ranged between 70.9% and 100.0%), endocrine, nutritional, and metabolic diseases (ranged between 1.4% and 3.8%), diseases of the circulatory system (ranged between 3.3% and 13.1%), signs, symptoms, and abnormal clinical and laboratory findings (ranged between 0.7% and 4.1%), and factors that influence the health state and contact with health services (ranged between 1.8% and 3.8%) (Supplementary Table 5). The most frequently reported among diseases of the musculoskeletal system were arthritis, osteoporosis, arthrosis, Sjogren's syndrome and join pain. The more frequent endocrine, nutritional and metabolic diseases included diabetes, hypothyroidism, dyslipidemia, obesity and vitamin D deficiency.

Discussion

This study described the drug utilization patterns, HCRU, and epidemiology of adult patients with RA over a six-year period through a retrospective analysis of a national administrative claims database in Colombia. Our findings provide updated insights and valuable information for customizing RA management strategies to the local context.

Earlier investigations in Colombia have used data from the RIPS module within SISPRO to determine the prevalence of RA in the country, and substantial efforts have been made to improve the quality and quantity of data reported in the RIPS module [27]. A study based on RIPS reported a prevalence of 0.9% in 2005 [3]. S study conducted in Colombia between 2012 and 2016 using data from RIPS reported a prevalence of 0.52% [4]. In our study, the age-standardized prevalence of RA ranged between 0.28% and 0.38% between 2017 and 2022. This finding is similar to that of a previous study in the country using the using national data collected by the

Table 3 Hospital admissions and emergency room visits related to rheumatoid arthritis diagnosis by age and sex

Characteristic	2017 n	2017 Rate*	2018 n	2018 Rate*	2019 n	2019 Rate*	2020 n	2020 Rate*	2021 n	2021 Rate*	2022 n	2022 Rate*
Emergency room visits												
Age group												
18–19 years	8	dat	30	70.1	74	124.8	16	32.5	3	5.7	26	73.4
20–24 years	115	83.8	105	69.2	102	52.7	69	43.7	87	46.5	81	52.9
25–29 years	173	77.4	521	205.4	292	93.1	178	66.1	111	36.3	68	25.2
30–34 years	236	70.0	218	57.2	309	65.4	91	23.2	69	14.7	45	10.8
35–39 years	488	94.6	578	97.3	279	38.5	95	16.0	207	29.5	111	17.7
40–44 years	805	120.0	532	71.1	322	34.4	839	106.0	225	23.1	409	46.6
45–49 years	821	84.9	663	62.7	402	30.4	305	28.8	201	16.3	341	30.9
50–54 years	1,353	101.2	985	66.3	629	34.3	333	21.8	172	9.9	372	24.9
55–59 years	1,362	97.5	1,120	69.8	593	29.4	573	32.6	223	11.0	274	15.4
60–64 years	1,107	88.0	1,186	82.2	608	32.2	516	31.2	189	9.7	211	12.0
65–69 years	909	90.5	1,082	92.7	465	30.2	427	31.1	233	14.3	261	17.0
70–74 years	495	71.4	535	64.8	452	41.0	178	17.8	161	13.6	124	11.0
75–79 years	276	57.5	550	99.1	178	24.2	93	14.4	70	9.3	115	15.6
>80 years	241	61.6	404	87.2	190	31.2	210	37.0	250	36.8	146	22.2
Total	8,389	88.8	8,509	79.0	4,895	35.6	3,923	33.1	2,201	15.9	2,584	20.6
Sex												
Female	7,076	95.1	6,841	81.3	3,960	37.5	3,096	34.4	1,723	16.0	2,087	21.4
Male	1,313	88.0	1,668	97.7	935	43.4	827	44.9	478	22.6	497	25.4
Hospital admissions												
Age group												
18–19 years	32	90.1	25	58.4	47	79.3	15	30.5	148	282.4	52	146.9
20–24 years	57	41.5	88	58.0	102	52.7	185	117.1	155	82.8	186	121.6
25–29 years	60	26.9	172	67.8	70	22.3	107	39.7	256	83.8	315	116.8
30–34 years	106	31.4	400	104.9	388	82.1	279	71.1	258	54.9	306	73.3
35–39 years	355	68.8	432	72.7	305	42.1	542	91.0	368	52.5	561	89.4
40–44 years	238	35.5	510	68.1	498	53.3	476	60.2	542	55.6	727	82.9
45–49 years	475	49.1	896	84.7	646	48.8	432	40.8	755	61.1	1127	102.0
50–54 years	692	51.7	1455	98.0	1006	54.9	615	40.2	1105	63.5	900	60.2
55–59 years	631	45.1	1249	77.9	1642	81.3	964	54.9	1910	94.0	1859	104.3
60–64 years	772	61.4	1370	95.0	1135	60.1	907	54.8	1220	62.9	1470	83.9
65–69 years	752	74.9	1084	92.9	1252	81.4	799	58.2	684	41.9	1710	111.4
70–74 years	355	51.2	563	68.2	573	52.0	905	90.3	889	75.2	1367	121.5
75–79 years	286	59.6	498	89.7	423	57.6	272	42.2	383	51.0	784	106.4
>80 years	234	59.8	459	99.1	616	101.1	477	84.1	522	76.9	678	103.2
Total	5045	53.4	9201	85.4	8703	63.3	6975	58.9	9195	66.2	12,042	95.8
Sex												

Table 3 (continued)

Characteristic	2017		2018		2019		2020		2021		2022	
	n	Rate*	n	Rate*	n	Rate*	n	Rate*	n	Rate*	n	Rate*
Female	4143	55.7	7498	89.1	6843	64.7	5599	62.2	7243	67.2	9803	100.3
Male	902	60.5	1703	99.8	1860	86.3	1376	74.7	1952	92.3	2239	114.3

*Rate of emergency room visits or hospital admissions per 1,000 patients with rheumatoid arthrit

High-Cost Disease Fund (*Cuenta de Alto Costo*, CAC), which reported a prevalence of 0.24% in 2019 [5].

In our study, we observed a consistent increase in the incidence of RA over time, except for a decrease in 2020. From 2021 to 2022, the incidence continued to increase. These findings align with the global burden of disease report, which documented an increasing trend in the age-standardized incidence rate of RA [28]. The temporary decrease in 2020 may be attributed to a reduced diagnostics during the COVID-19 pandemic, which led to a proven decline in new diagnoses of many diseases [29, 30]. There is controversy regarding the further increase in the incidence of RA following COVID-19. A Colombian cohort study suggested an increase in the incidence rate of inflammatory arthritis after COVID-19, with the greatest increase occurring before the first year post-covid [31]. Moreover, a systematic review and meta-analysis indicated a higher risk of developing at least 11 immune-mediated diseases after SARS-CoV-2 infection [32]. Nevertheless, other studies found no evidence of this association [33, 34]. In Latin America, COVID-19 has significantly impacted rheumatology care, with patients experiencing increased disease activity, reduced medication adherence, and challenges in accessing follow-up care [35]. Additionally, consultation fees and adherence to medication adherence both declined [36].

During our study period, a substantial proportion of patients diagnosed with RA (60.77% and 73.02%) were not prescribed csDMARDs, We also observed a decrease in the proportion of patients prescribed csDMARDs over time. This suggests an underuse of csDMARDs in the country. This occurs despite the recommendations from both local [12] and international clinical practice guidelines (CPGs) [10, 37] advising their prompt initiation in patients with RA, especially those treatment naïve. Similar trends have been described outside Latin America (LATAM). A study using administrative databases in Italy reported that only 43.2% of patients were prescribed csDMARDs [38]. Similarly, in Germany, 43.1% of newly diagnosed RA patients had received a csDMARD prescription within the first year of diagnosis [39] and in the United States, it was 52.8% [40]. Early DMARDs initiation during the course of the disease not only reduces disease progression but also helps avoid complications, ultimately mitigating the impact of the disease on patients' quality of life [40]. Concerns regarding the initiation of DMARDs, including the perceived aggressive and harmful nature of the drugs, potential side effects, combination with other drugs, and the time to benefits [41]. Thoughtful consideration of these aspects combined with physician education about CPGs may lead to improvements in the proportion of patients initiated with adequate treatment.

In our study, the most commonly prescribed csDMARD was leflunomide, followed by chloroquine and

Table 4 All-cause annual healthcare-related cost and pharmacy-related cost in patients with rheumatoid arthritis diagnosis by year

	2017	2018	2019	2020	2021	2022
Average all-cause annual healthcare-related cost						
Cost for all patients in USD PPP						
Consultation's cost	$ 25,142,401	$ 16,732,917	$ 22,467,111	$ 36,744,756	$ 36,391,280	$ 23,031,841
Hospital admission cost *	$ 468,975	$ 603,419	$ 561,457	$ 527,825	$ 403,622	$ 354,403
Procedures cost **	$ 2,860,200	$ 6,750,821	$ 5,562,834	$ 11,490,856	$ 5,266,869	$ 6,356,080
Imaging procedures ***	$ 268,268	$ 696,295	$ 333,560	$ 306,268	$ 360,065	$ 315,420
Laboratories ****	$ 68,896	$ 694,942	$ 205,336	$ 183,396	$ 211,448	$ 213,861
Cost per patient in USD PPP						
Consultation cost	$ 266	$ 155	$ 163	$ 310	$ 262	$ 183
Hospital admission cost *	$ 566	$ 549	$ 440	$ 629	$ 364	$ 282
Procedures cost**	$30	$63	$40	$97	$38	$ 51
Imaging procedures ***	$3	$6	$2	$3	$3	$3
Laboratories ****	$1	$6	$1	$2	$2	$2
Cost USD PPP all patients	$ 28,471,575	$ 24,087,158	$ 28,591,402	$ 48,763,437	$ 42,061,770	$ 29,742,324
Cost USD PPP per patient	$ 301	$ 224	$ 208	$ 412	$ 303	$ 237
Pharmacy-related cost						
Cost in USD PPP						
csDMARDs	$ 14,922,141	$ 19,642,704	$ 10,067,161	$ 13,259,536	$ 18,031,917	-
bDMARDs	$ 62,966,462	$ 59,518,949	$ 78,743,927	$ 56,044,637	$ 52,710,269	-
tsDMARDs	$ 562,121,936	$ 909,584,806	$ 783,945,643	$ 586,423,485	$ 456,959,438	-
Steroids	$ 299,627	$ 145,992	$ 281,198	$ 228,523	$ 435,472	-
Costs in USD PPP all patients	$ 640,310,165	$ 988,892,450	$ 873,037,929	$ 655,956,180	$ 528,137,096	-
Costs in USD PPP per patient	$6,777	$9,179	$6,350	$5,539	$3,805	-

csDMARDs: conventional synthetic disease-modifying antirheumatic drugs; bDMARDs: biologic disease-modifying antirheumatic drugs; tsDMARDs: targeted synthetic disease-modifying antirheumatic drugs; USD PPP: United States Dollars purchasing power parities

*Total cost divided by the total number of patients who were hospitalized each year, **All procedures with ICD-10 codes M053, M058, M059, M060, M068, M069, ***imaging procedures including, articular ultrasound, X-ray and magnetic resonance image), ****Laboratories including, rheumatoid Factor and anti-cyclic citrullinated peptide antibod

methotrexate. A previous study conducted in Colombia between 2012 and 2014, had reported that the most frequently used drugs were methotrexate, chloroquine, and leflunomide [42]. Subsequently, a study conducted between 2015 and 2018 in patients with RA in a specialized institution in the Caribbean region of Colombia reported a transition to leflunomide as the drug of choice, aligning with our results [43]. In their cohort, methotrexate was the medication with the highest proportion of use within 2015 and 2017, whereas in 2018, leflunomide became the most commonly used medication [43].

Our results align with previous work conducted in the country, which identified etanercept and adalimumab as the most frequently prescribed bDMARDs [44]. This trend may be influenced by etanercept being included in the PBS. In our study, bDMARDs prescriptions decreased, while the proportion of patients prescribed tsDMARDs increased, specifically, tofacitinib was the most frequently prescribed tsDMARD throughout the study period. Additionally, after the introduction of baricitinib, its prescriptions increased over time. A Brazilian study also reported a rising use of tsDMARDs, which aligns with our results [45]. Furthermore, they identified factors associated with the initiation of tsDMARDs in patients with RA, including the age (≥50 years),

proximity to healthcare facilities (patients residing over 160 km from the health center were less likely to initiate tsDMARD treatment), and previous use of csDMARDs [45]. Factors such as the costs of medications may contribute to different prescription patterns across affiliation regimens. For instance, a cohort of patients with RA using national data collected by the CAC reported that most individuals were affiliated with the contributory regimen [5]. Further research should consider analyzing HCRU according to aspects such as the type of regimen affiliation and differences between rural and urban areas.

Early referral to a rheumatologist for patients with suspected RA is infrequent in most countries within LATAM [46]. It is estimated that the time to the first visit with a rheumatologist is approximately 17 months after symptom onset [47]. In our study, the frequency of medical consultations increased over the study period. Between 2017 and 2019, the highest percentage of consultations were with general practitioners. However, thereafter, the highest rate of consultation was with rheumatologists. This transition indicates an improvement in access to specialist rheumatology consultations in the country, which could potentially lead to better outcomes for patients with RA [48, 49]. Comprehensive RA care includes interdisciplinary care involving periodical

consultations with rheumatologists, psychologists, nutritionists, physical and rehabilitation medicine, occupational therapists, physiotherapists, and nurses [50]. In our study, other frequently consulted specialists included internal medicine, physiotherapy, nursing, and nutrition, which may be translated to a more comprehensive care for patients with RA. Additionally, we identified a trend of decreasing ER visits over the study period, while hospital admissions fluctuated, but generally increased. This highlights the potential need for additional efforts in RA management to enhance patient outcomes. In recent years, as integrated healthcare models have been implemented in Colombia, cohorts have been established to evaluate patient outcomes [43].

Since 2015, Colombian insurers must report RA population to the CAC [51], including those not affiliated to the SGSSS [51]. The inclusion of RA as a mandatory report to the CAC is expected to enhance disease reporting across Colombia, potentially improving epidemiological surveillance and healthcare planning for RA management.

The economic costs associated with RA are substantial and are mainly driven by high pharmacy costs. In our study, annual pharmacy-related costs per patient ranged between 3,805 and 9,179 USD PPP. Among pharmacy costs, tsDMARDs were the most expensive, followed by bDMARDs; however, the costs of both decreased over time, likely due to price regulations and the introduction of biosimilar medications [52, 53]. A Colombian cohort of patients diagnosed with RA who were treated with bDMARDs or tofacitinib after failure of cDMARDs or first bDMARD reported that drug cost accounted for 97.2% of the average annual direct cost of care per patient [54]. In their study, the average annual cost of treatment per patient with bDMARDs was higher than that for treatment with tofacitinib [54]. Similarly, a study in Medellin, Colombia, estimated that 87,9% of the direct costs in patients with RA was related to medications [55]. Furthermore, additional research conducted in the country identified that drug expenses increase with the RA severity. They reported that drugs represent 53.6% of the total cost for low disease activity, 75.2% for moderate disease activity, 88.5% for severe disease activity, and 97% for severe disease activity with biologic treatment [17]. In this study, we estimated healthcare-related and pharmacy-related costs, however there is still need for further research addressing the indirect costs of RA in the country, encompassing aspects such as productivity losses, disability, and decreased quality of life.

This study provided insights into the drug utilization patterns, HCRU, and epidemiology of adult patients with RA over a six-year period using a national administrative claims database, which provides a large and diverse sample size that reflects the real-world clinical practice and healthcare utilization patterns. Our results supplied insights into routine care delivery and patient outcomes in diverse healthcare settings, including consultations, ER visits, and hospitalizations [56]. However, this study had some limitations. This study relied on administrative claims data for clinical details, which may be subject to data coding limitations, data entry errors, and incomplete or inconsistent information, leading to potential measurement errors [56]. Nevertheless, the SIS-PRO database utilized in this study undergoes internal quality checks, including data validation and cleaning to ensure reliability and accuracy [57]. Moreover, the database lacks information on disease severity, which may affect treatment patterns and consequently the healthcare-related and pharmacy-related costs. In addition, access was limited to deidentified data, precluding the linking of individual patient data longitudinally. Consequently, aspects such as treatment persistence, discontinuation, and combinations could not be assessed. Finally, the data obtained from SISPRO represent the population affiliated to the SGSSS (approximately 98.54% [21]), limiting its generalizability to this specific population.

Conclusions

In conclusion, this study described the heavy burden of RA in Colombia and highlighted an increasing incidence of RA, accompanied by significant healthcare resource utilization and associated costs. Patients with RA in the country are increasingly being able to access consultations with specialists and advanced therapies. However, there remains a need for efforts to facilitate treatment because there is an important number of patients each year who are not being prescribed DMARDs despite CPG's recommendations.

The study findings emphasize the importance of tailoring RA management strategies to the local context and addressing healthcare disparities to ensure that all RA patients receive appropriate care. Additionally, continued efforts to educate physicians and promote adherence to clinical practices are essential for optimizing patient outcomes. These results should be evaluated and validated by further research. As new medications continue to emerge, ongoing research and efforts to improve healthcare access will be essential to improve the quality of life for RA patients in Colombia and the region.

Abbreviations

ATC	Anatomical Therapeutic Chemical
bDMARDs	Biological disease-modifying antirheumatic drugs
CI	Confidence intervals
COP	Colombian Pesos
csDMARDs	Synthetic disease-modifying antirheumatic drugs
CUM	Código Único de Medicamentos
DMARDs	Disease-modifying antirheumatic drugs
EC	Ethics Committee
HCRU	Healthcare resource utilization
HTA	Health Technology Assessment
CAC	High-Cost Disease Fund (Cuenta de Alto Costo)
ICD-10	International classification of diseases-10th revision

IRB	Institutional Review Board
LATAM	Latin America
MIPRES	Mi Prescripción
PBS	Plan de Beneficios en Salud
RA"	Rheumatoid Arthritis
RECORD	REporting of Studies Conducted Using Observational Routinely-Collected Health Data
RIPS	Registro Individual de Prestación de Servicios de Salud
SGSSS	Sistema General de Seguridad Social en Salud
SISMED	Sistema de Información de Precios de Medicamentos
SISPRO	Sistema de Información para la Protección Social
STROBE	Strengthening the reporting of observational studies in epidemiology
SUF	Cubo de Gestión de la Demanda
T2T	Treat-to-target strategy
tsDMARDs	Targeted synthetic disease-modifying antirheumatic drugs
USD PPP	United states Dollars purchasing power parities

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Supplementary Material 6

Declarations

Author details

[1]Rheumatology Unit, Hospital Universitario San Ignacio – Pontificia Universidad Javeriana, Bogotá, Colombia
[2]Medical department, Abbvie Cluster North-LATAM, Bogotá, Colombia
[3]Riesgo de Fractura S.A.-CAYRE, Bogotá 110221, Colombia

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