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Trends in the epidemiology of inflammatory bowel disease in Colombia by demographics and region using a nationally representative claims database and characterization of inflammatory bowel disease phenotype in a case series of Colombian patients

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Abstract

The incidence of inflammatory bowel disease (IBD) is on the rise in Latin America. The aims of this study were to examine epidemiologic trends of IBD in Colombia by demographics, region, urbanicity, and to describe the IBD phenotype in a large well-characterized Colombian cohort.

We used a national database of 33 million adults encompassing 97.6% of the Colombian population in order to obtain epidemiologic trends of IBD using International Classification of Diseases 10codes for adults with ulcerative colitis (UC) and Crohn disease (CD). We calculated the incidence and prevalence of UC and CD from 2010–2017 and examined epidemiologic trends by urbanicity, demographics, and region. We then examined the IBD phenotype (using Montreal Classification), prevalence of IBD-related surgeries, and types of IBD-medications prescribed to adult patients attending a regional IBD clinic in Medellin, Colombia between 2001 and 2017.

The incidence of UC increased from 5.59/100,000 in 2010 to 6.3/100,000 in 2017 (relative risk [RR] 1.12, confidence interval (CI) (1.09–1.18), $P < .0001$). While CD incidence did not increase, the prevalence increased within this period. The Andes region had the highest incidence of IBD (5.56/100,000 in 2017). IBD was seen less in rural regions in Colombia (RR=.95, CI (0.92–0.97), $p < .01$). An increased risk of IBD was present in women, even after adjusting for age and diagnosis year (RR 1.06 (1.02–1.08), $P = .0003$). The highest IBD risk occurred in patients 40 to 59 years of age. In the clinic cohort, there were 649 IBD patients: 73.7% UC and 24.5% CD. Mean age of diagnosis in CD was 41.0 years and 39.9 years in UC. UC patients developed mostly pancolitis (43%). CD patients

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All study data are presented in the manuscript and supplementary materials. Additional raw data to support the findings of this study are available for SISPRO via request at the following website (a public database): https://web.sispro.gov.co/

The IBD clinic cohort database via correspondence to FJB upon reasonable request.

The authors have no conflicts of interest to disclose.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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developed mostly ileocolonic disease and greater than a third of patients had an inflammatory, non-fistulizing phenotype (37.7%). A total of 16.7% of CD patients had perianal disease. CD patients received more biologics than UC patients (odds ratio: 3.20, 95% CI 2.19–4.69 $P < .001$).

Using both a national representative sample and a regional clinic cohort, we find that UC is more common in Colombia and is on the rise in urban regions; especially occurring in an older age cohort when compared to Western countries. Future studies are warranted to understand evolving environmental factors explaining this rise.

Abbreviations: APC = annual percent change, CD = Crohn disease, CI = confidence interval, IBD = inflammatory bowel disease, ICD = International Classification of Diseases, OR = odds ratio, RR = relative risk, SD = standard deviation, SISPRO = Sistema Integral de Información de Protección Social, UC = ulcerative colitis.

Keywords: Colombians, Crohn's disease, Epidemiology, Hispanics, Latinos, Ulcerative colitis

1. Introduction

Inflammatory bowel disease (IBD) affects ~5 million people worldwide, comprising 0.3% of the population in North America and European countries.[1–4] Since 1990, there has been a steady increase of IBD in newly industrialized countries.[2] A possible explanation for this rise is increased urbanization and exposure to a Western lifestyle in developing countries.[4–6] Despite this global rise, the epidemiology of IBD remains poorly described across Latin America, including in Colombia. There are also no studies exploring IBD trends across various regions within a country, which could highlight disparities in the prevalence of IBD in those areas most rapidly exposed to a Western environment.

Studies in Latin America show a rise in IBD over time, particularly of ulcerative colitis (UC).[7–13] For instance, the incidence of IBD, especially UC, increased over a 17-year period in Mexico, from 0.05 to 0.21/100,000 of IBD cases, in a recently published study.[14] Similarly, four population-based studies demonstrate a remarkable growth in UC and Crohn disease (CD) incidence in Brazil.[15–19] Colombia is a stable democracy with strong US links and has rapidly incorporated US cultural practices in the last 2 decades.[20,21] These changes include a rise in urbanization, an increase in obesity, and an increase in the presence of US fast food chains, all of which can increase IBD risk within regions exposed to these rapid changes.[20,21] Therefore, it is imperative to understand the epidemiologic trends in the incidence of IBD in Colombia in different regions in the hopes of developing public health strategies to prevent and manage it.

In this study, our aims were:

(1) to use national claims data to estimate the national incidence and prevalence of IBD (UC and CD) in Colombia between 2010 and 2017 and to examine incidence trends across specific populations: by gender, age groups, urbanicity, and different regions in Colombia; and
(2) within a sample of patients attending a regional IBD center in Medellin, Colombia, describe the clinical course of IBD in a well-phenotyped large cohort.

We, therefore, used 2 different methodological approaches to accomplish our aims. We determine incidence and prevalence using a national claims database that insures 97.6% of the adult Colombian population.[22] We used the database from the Pablo Tobón Uribe Hospital in Medellín, which has the largest IBD center in Colombia, to describe the phenotype of patients with IBD. Our study provides important epidemiologic information that details disease burden by region in a previously understudied area.

2. Methods

2.1. National claims data to determine the epidemiology of IBD in Colombia

2.1.1. Study population. We used national claims data to capture IBD cases (Fig. 1). This registry called Sistema Integral de Información de Protección Social (SISPRO) stores data of 48 million individuals (33 million adults) and has a coverage of 97.6% of the Colombian population. It was developed by the Ministry of Health and Social Protection in 2010 and captures claims data from health insurance companies (https://www.sispro.gov.co). The registry collects data provided by all hospitals and clinics across Colombia; providers are required to report health information in the form of International Classification of Diseases (ICD)-10 codes. Information provided to this registry undergoes strict quality control checks, cross-referenced with census data and other reputable national registries to ensure accuracy.[23] Each patient has a unique national identification number to track the patient through the database and prevent replication of patients. Prior validation studies of the SISPRO registry indicate that ICD-10 codes in the registry are 83% concordant with the medical records.[24] In IBD studies, prior epidemiologic data using ICD codes have demonstrated acceptable accuracy using ICD codes, especially when cross-referenced with confirmation from patient charts.[25–27] We also confirmed the accuracy of the ICD-codes across our hospital dataset.

We obtained access to the data from the Ministry of Health and Social Protection Agency (FJ, JK and OJC). We extracted data using ICD-10 codes from 2010 to 2017. We queried IBD cases among 16 to 99 years of age and ensured using the unique identifiers that there were no replications of patients. The following ICD codes were ascertained: K50.0 CD of small intestine, K50.1 CD of large intestine, K50.8 other Crohn disease, K50.9 Crohn disease, unspecified, K51.0 UC pancolitis, K51.2 UC chronic proctitis, K51.3 UC proctosigmoiditis, K51.4 inflammatory polyps, K51.5 left sided colitis, K51.8 other UC, and K51.9 UC, unspecified and used to derive epidemiologic data on IBD if at least 2 of these codes were present.

2.1.2. Regions in colombia. Colombia has 6 geographical regions: The Amazon, Andean, Caribbean, Insular, Orinoco, and Pacific regions. The largest is the Andean region with a population of 27,322,252 in 2017; followed by the Caribbean region (10,647,346) and the Pacific region (8,410,059) in 2017. We examined incidence and prevalence trends across the 6 regions and also by urban vs rural regions. Urban is defined by SISPRO as the city (capital) of each state (department) and rural is considered any region outside of the city capital.

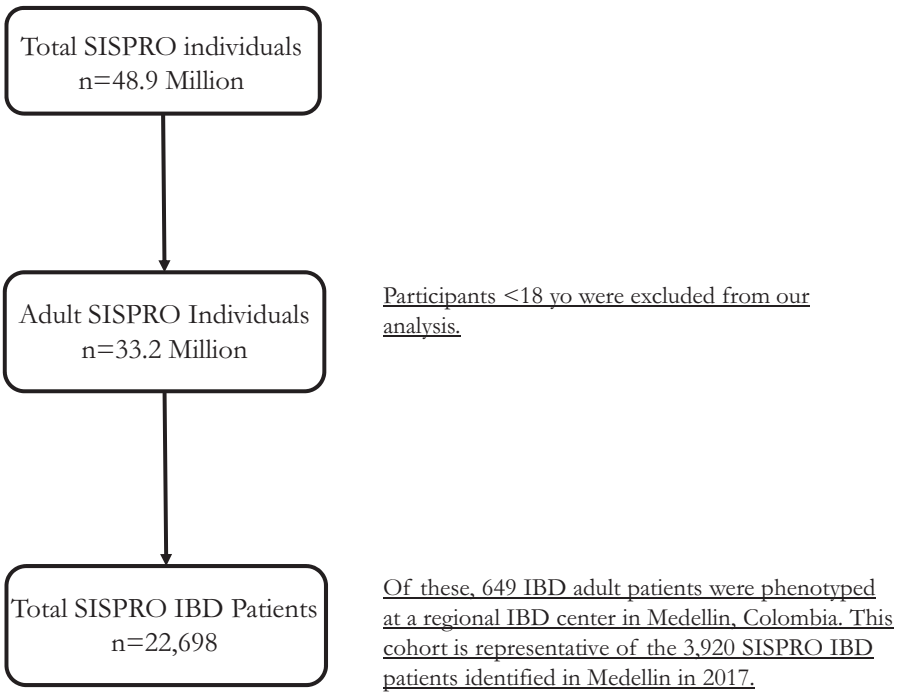

Figure 1. Flow chart of SISPRO individuals examined and IBD patients included in the analysis from 2017.

2.1.3. Statistical analysis. We calculated crude incidence rates for CD, and UC. Annual incidence rates between 2010–2017 were performed and standardized per 100,000 inhabitants. The annual prevalence of IBD, UC and CD was calculated for each year (2010–2017) and adjusted to per 100,000 inhabitants. We stratified incidence and prevalence rates by gender, region, urban vs rural, and age groups (by decade from >18 to < 70 years old). National crude incidence rates were adjusted for year of collection, gender, and age groups.

A Poisson regression model was performed to examine the relative risk (RR) for UC and CD between 2011 to 2017 compared to the baseline of 2010. We used a Davies' test to examine the extent to which the rate of change in incidence was consistent across the study period. Trend analysis was performed using joinpoint regression model to examine the overall incidence trend between 2010 to 2017, adjusting for age, sex and geographical regions. We calculated annual percentage changes (APC) and RR for each year for UC/CD incidence. All tests were considered significant at a *P*-value <.05. These analyses were conducted using R v. 3.3.2 (Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/).

2.1.4. IBD phenotyping cohort. We examined IBD phenotype in a cohort of patients treated at a regional IBD center in Medellin, Colombia (The Pablo Tobón Uribe Hospital). This center provides care to patients with IBD who are referred from across the region. The Ethics Committee of the Pablo Tobón Uribe Hospital approved the study. This cohort included patients with confirmed diagnoses of IBD and receiving care in the hospital's inpatient services, or hospital-affiliated clinics between August 2001-June 2017. ICD-10 codes were used to initially screen patients, and data were verified by residents and attending physicians examining the electronic medical records (FJ, MA, JC, LC, JH, AC).

2.1.5. Diagnosis of IBD and phenotype classification. IBD diagnoses were confirmed by treating physicians after review of clinical, imaging, endoscopic and surgical/pathology reports. We assessed disease severity in terms of patients' clinical course: age of presentation, UC disease severity index (using Truelove & Witt's), need for biologics, time from diagnosis to first biologic, surgeries, and IBD-related hospitalizations. Disease phenotype was characterized using the Montreal Classification.[28,29] Patients with IBD who did not meet criteria consistent with CD or UC were classified as IBD-unclassified.[29,30] We collected clinical history, including diagnosis age, smoking history, and presence of extra-intestinal manifestations. Medication history: 5-ASAs, steroids, immunomodulators, and biologics was recorded.

2.1.6. Statistical analysis. We employed Student *t*-tests or Mann Whitney *U* tests to calculate differences in continuous variables with normal and non-normal distributions, respectively. To compare categorical values, chi-square tests were used, and odds ratios (OR) with its 95% confidence interval (CI) were calculated. All tests were considered significant at a *P*-value <.05. Statistical analysis was conducted using Epidat version 3.1 (statistical package for IBM. Durham, NC: Duke University Press).

3. Results

3.1. Incidence of IBD in Colombia

We evaluated over 33 million adult patients (>18 years) in the SISPRO database of which 51.4% were female (Fig. 1, Suppl Table 1, http://links.lww.com/MD/F723) (https://www.sispro.gov.co). We calculated annual crude incidence rates for IBD, UC, and CD between 2010 to 2017. The IBD incidence in the year

Table 1

Incidence and prevalence data of IBD, UC, and CD in Colombia stratified by age, gender, urbanicity and region in Colombia (SISPRO) in 2017 and change from 2010 to 2017.

Total adult population at risk population in 2017 n = 33,884,324	IBD incidence	Change from 2010 to 2017	UC incidence	Change from 2010 to 2017	CD incidence	Change from 2010 to 2017	IBD prevalence	Change from 2010 to 2017	UC prevalence	Change from 2010 to 2017	CD prevalence	Change from 2010 to 2017
National incidence and prevalence in 2017*	7.04	+0.16	6.30	+0.71	0.74	−0.55	67.07	+24.41	58.14	+20.51	8.93	+3.89
Age groups (by years)												
18-29	3.46	+1.90	3.09	+2.09	0.37	−0.19	36.27	+27.9	30.10	+23.72	6.17	+4.18
30-39	6.30	+1.12	5.69	+1.59	0.61	−0.47	58.66	+27.97	50.51	+23.67	8.15	+4.29
40-49	7.03	+0.31	6.33	+0.95	0.70	−0.64	67.59	+25.34	60.06	+22.36	7.53	+2.98
50-59	10.31	−0.51	9.03	+0.04	1.28	−0.55	92.39	+23.92	80.20	+18.36	12.19	+5.56
60-69	11.04	−3.31	9.74	−1.96	1.30	−1.34	109.75	+13.6	97.31	+13.35	12.44	+0.25
>70	11.77	−8.76	10.87	−7.12	0.90	−1.63	106.18	−16.58	91.93	−18.56	14.25	+1.97
Gender												
Male	5.93	+0.26	5.38	+0.6	0.55	−0.34	59.42	+23.53	51.43	+19.57	7.99	+3.96
Female	8.09	+0.07	7.17	+0.81	0.93	−0.73	74.19	+25.28	64.43	+21.46	9.77	+3.82
Geographic region:												
Amazon	1.78	0.42	1.69	0.62	0.09	−0.20	10.06	1.21	9.52	3.69	0.53	-2.48
Andean	5.56	0.53	4.93	0.36	0.63	0.17	57.97	21.57	49.60	16.77	8.37	+4.80
Caribbean	2.00	−2.54	1.78	−0.92	0.22	−1.61	27.82	10.30	25.1	11.07	2.31	-0.77
Insular	1.29	−0.08	1.29	−0.08	0.00	0.00	–	–	15.43	8.61	–	–
Orinoco	2.10	−1.61	1.99	−0.13	0.12	−1.47	11.17	-2.30	10.23	-1.04	0.94	-1.25
Pacific	5.15	2.26	4.68	2.52	0.46	−0.27	33.44	17.49	29.32	15.76	4.11	+1.72

CD = Crohn disease, IBD = inflammatory bowel disease, UC = ulcerative colitis, SISPRO = Sistema Integral de Información de Protección Social.
* Incidence and prevalence data adjusted to per 100,000 habitants.
– data not available for this year.

2010 was 6.88/100,000 and increased to 7.04/100,000 by 2017, driven by a rise in UC. UC incidence rates rose between 2010 and 2017 from 5.59 to 6.30/100,000 by 2017 (Table 1). Within this period, CD incidence did not increase and appeared to slightly drop (from 1.29 to 0.74). Using a Poisson model, we determined the annual change of UC and CD incidence from 2010 to 2017 using 2010 as the reference year. The annual relative risk for UC increased in 2012, 2013, 2014 and 2017 (Fig. 2, Suppl Table 2, http://links.lww.com/MD/F725). Then, using joinpoint regression models, we found an APC in new UC cases of (APC:

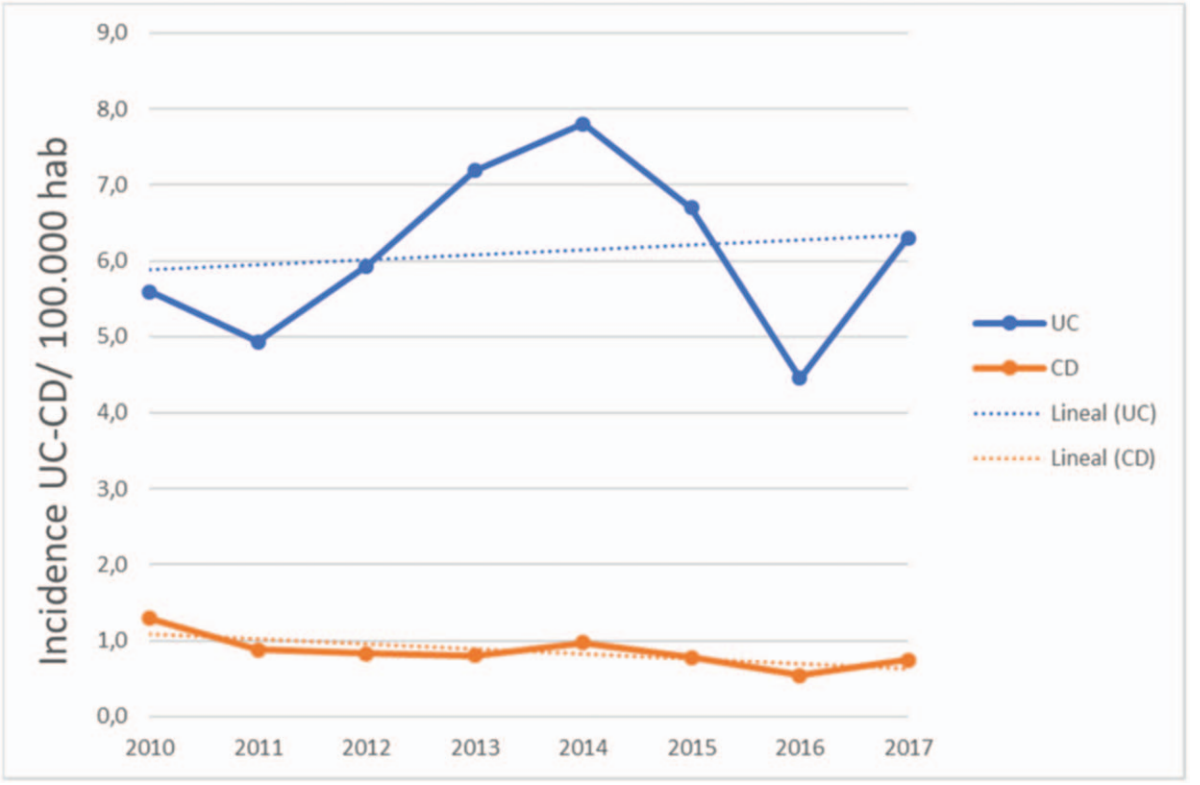

Figure 2. Incidence rates of ulcerative colitis and Crohn disease per 100,000 habitants from 2010 to 2017 in Colombia.

+1.12%, 95% CI (+1.09 to + 1.18), $P < .0001$). In contrast, the APC for CD appeared to decrease in this time-period (APC: -0.66, 95% CI (-0.60% to - 0.87%) $P < .001$). Analyses were adjusted for age, gender and region. These analyses indicate an increasing annual risk of UC, not of CD, in Colombia between 2010 to 2017 (Table 1).

3.2. Urbanicity, regions in Colombia and their relationship to IBD incidence

We found a lower incidence rate of IBD in patients from rural vs. urban settings in Colombia (RR = .75, 95% CI (0.72–0.77), $P < .01$). After adjusting for current age, gender, and year of diagnosis, the relative risk reduction of IBD (UC and CD) in rural versus urban settings was 5% (RR = .95, 95% CI (0.92–0.97), $P < .01$). UC was more common than CD in the sample as a whole and was higher in urban than rural areas (9,781 UC cases in the city vs 5,812 UC cases in the rural areas). Table 1. We examined incidence within Colombia's 6 geographic regions. We found that the most densely populated region, the Andes, also had the highest incidence of IBD (both UC and CD) in all years examined (5.50 in 2017; Tables 1 and 2). The lowest incidence of IBD was observed in the insular region (1.29 in 2017); Table 2. We observed similar incidence trends by region when we examined UC and CD separately; see Figure 4.

Table 2

Trend analysis by year of IBD incidence stratified by age groups and regions in Colombia.

IBD incidence	Point Estimate (RR)	95% CI	*P*-value
Year of diagnosis Reference year 2010			
2011	0.88	0.83–0.94	<.01
2012	0.95	0.8–1.01	.085
2013	1.07	1.01–1.13	.02
2014	1.17	1.10–1.24	<.01
2015	1.06	1.00–1.13	.03
2016	0.85	0.80–0.91	<.01
2017	1.04	0.98–1.11	.16
Age Group Reference age 18–29			
30–39	1.05	0.99–1.10	.1
40–49	1.06	1.00–1.12	.03
50–59	1.10	1.04–1.16	<.01
60–69	1.04	0.98–1.10	.14
>70	1.00	0.98–1.10	.93
Geographical region: Reference region: Andean region			
Amazon	0.89	0.77–1.01	.94
Caribbean	0.92	0.88–0.96	<.01
Insular	0.86	0.26–2.01	.77
Orinoquia	0.89	0.79–0.98	.03
Pacific	0.91	0.87–0.95	<.01

IBD = inflammatory bowel disease, RR = relative risk, CI = confidence interval.

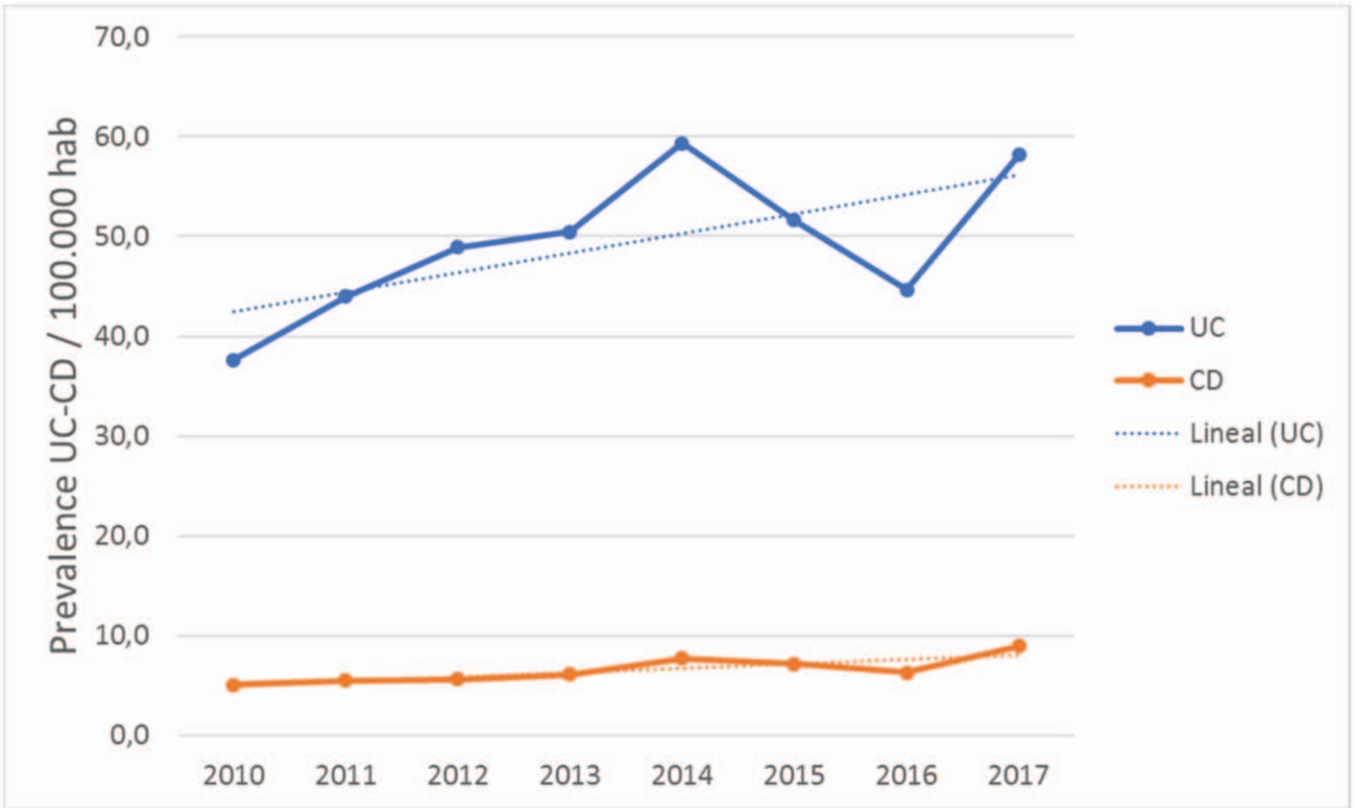

Figure 3. Point prevalence of ulcerative colitis and Crohn disease per 100,000 habitants from 2010 to 2017 in Colombia.

3.3. IBD incidence and trends observed across age groups and gender

In an unadjusted analysis of IBD incidence and gender in 2010 to 2017, we found that females had higher IBD rates compared to men (RR 1.26, 95% CI 1.18–1.26, $P < .001$). This gender difference emerged even after adjusting for current age and year of diagnosis (RR 1.06 [1.02–1.08], $P = .0003$). Women were at increased risk for both UC and CD compared to men (Table 1); the increased risk for CD was RR 1.04 95% CI 1.02 to 1.05, $P < .001$ and for UC was RR 1.34 (1.24–1.46) $P < .001$. We stratified IBD incidence by age groups from >18 to >70 years old, adjusting for year of diagnosis and gender. Using Poisson models, the highest IBD risk occurred in patients 40–49 (RR 1.06 95% CI (1.00–1.12), $P = .03$), and 50 to 59 years of age (RR 1.10 95% CI (1.04–1.16), $p < .01$); when compared to ages 18 to 29 yrs. There was no significant association between age group and type of IBD (Table 2 and Supp Table 2, http://links.lww.com/MD/F725).

3.4. Prevalence of IBD in Colombia

The prevalence of IBD (UC and CD) in Colombia increased from 2010 to 2017 (Table 1, Fig. 3). In 2010, the IBD prevalence was 42.66, and in 2017 the prevalence increased to 67.07/100,000. Similar to incidence, the prevalence of UC was higher than the prevalence of CD in all years examined (Table 1, Suppl Table 3, http://links.lww.com/MD/F727). In 2010, the prevalence of UC was 37.63/100,000, and the prevalence increased to 58.14/100,000 in 2017. The prevalence of CD in 2010 was 5.04/100,000 versus 8.93/100,000 in 2017 (Table 1, Suppl Table 3, http://links.lww.com/MD/F727). We examined prevalence trends across the 6 regions in Colombia. We found the highest prevalence in the Andean region, followed by the Pacific and the Caribbean regions (Fig. 5). Prevalence rates increased steadily over time in all 6 regions (Table 1). Prevalence rate patterns by gender and age group are similar to those for incidence rates (Suppl Table 3, http://links.lww.com/MD/F727).

3.5. IBD phenotype in a Colombian IBD clinic

3.5.1. Patient demographics and IBD phenotype. A total of 649 IBD patients were identified. Of these, 52.1% were women. The majority (73.7%; n = 478) had UC. Gender differences were observed: there were more women with UC (56.3%) (95% CI: 6.3–18.8, $P < .001$) and more men with CD (95% CI: 11.3% - 32.7%, $P < .001$). Mean age of diagnosis was similar for CD (41.7; standard deviation (SD) 16.8) and for UC (40.2; SD 15.8), $P = .341$. Fifty-one percent of CD patients developed CD after age 40, whereas only 5% developed CD before age 16 (Table 3). Similarly, only 2.3% of patients with UC were diagnosed before age 16, whereas 46.8% were diagnosed after age 40. Mean time from symptom onset to diagnosis was 13.5 months for CD and

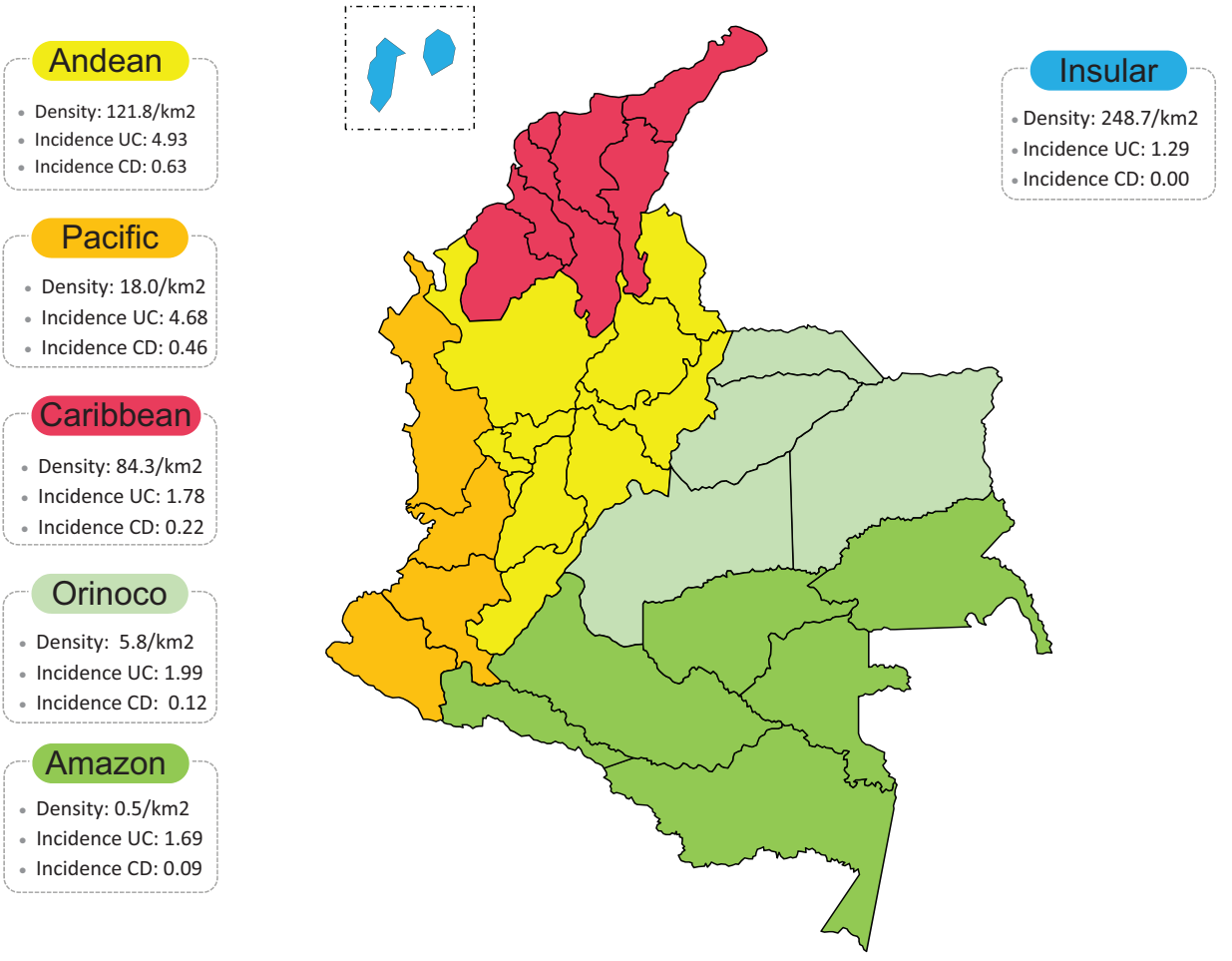

Figure 4. Map of Colombia showing the density and incidence of ulcerative colitis (UC) and Crohn's disease (CD) by regions in 2017.

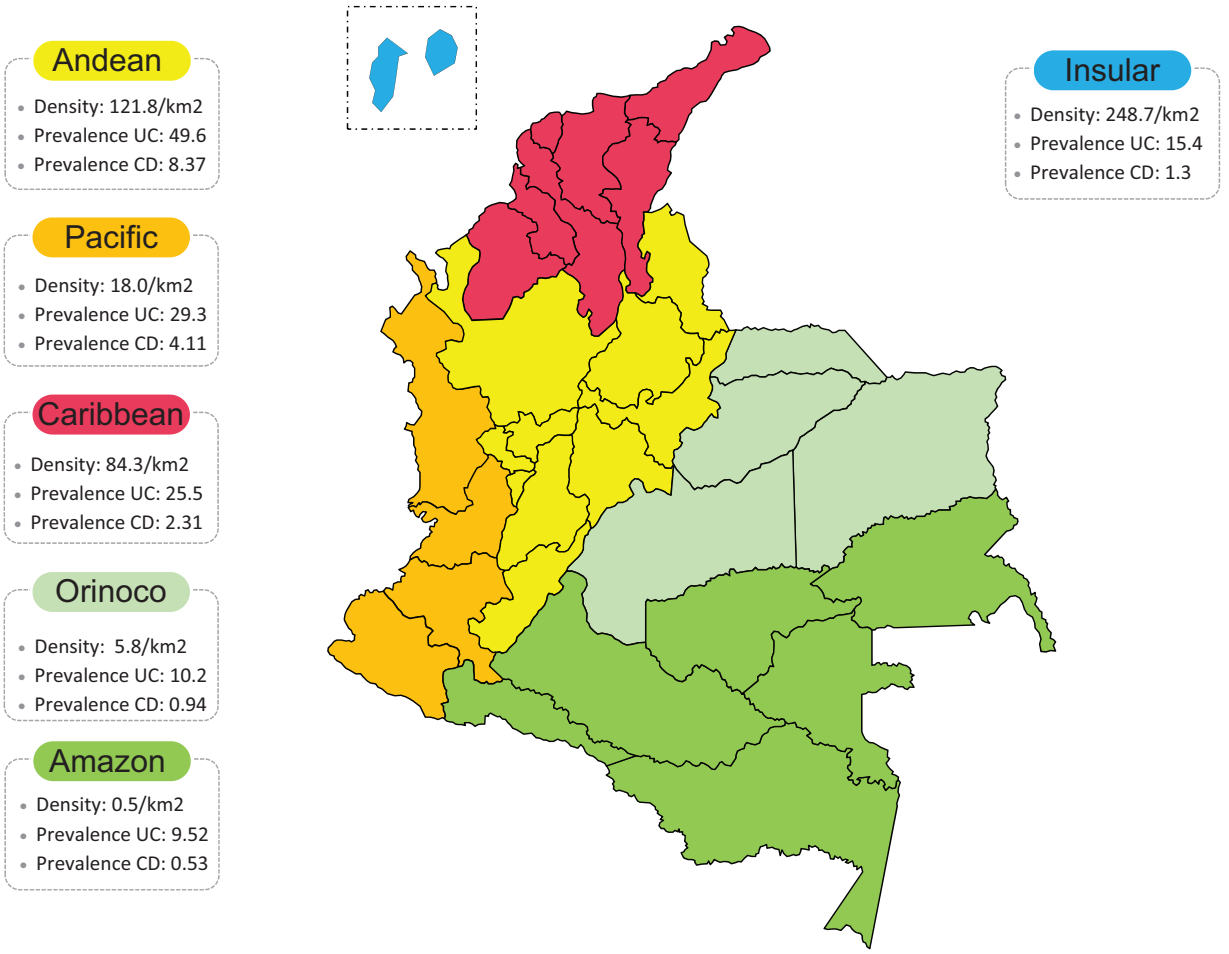

Figure 5. Map of Colombia showing the density and prevalence of ulcerative colitis (UC) and Crohn's disease (CD) by regions in 2017.

11.8 months for UC. Very few patients had a first-degree relative with IBD (less than 2% of IBD patients), Table 3.

Pancolitis was more common than left-sided colitis or proctitis in UC (43% vs 32.7% vs 24.2%, respectively). CD patients mostly developed ileocolonic disease (37.7%) and isolated terminal ileum disease (37.1%). Only a few patients had involvement of the upper GI tract (4.0%). The most common CD behavior, using the Montreal classification, was inflammatory (non-penetrating/non-stenosing) (37.0%), followed closely by penetrating (36.4%). A total of 16.7% of CD patients had perianal disease (Table 3). Extra-intestinal manifestations, particularly arthralgias, were more common in CD than in UC (Table 3). Patients with CD had more IBD-surgeries and hospitalizations than patients with UC (Table 3).

3.5.2. Disease severity. As noted above, UC and CD patients developed IBD mostly after age 40. UC and CD patients diagnosed before age 40 had greater UC disease severity index scores at diagnosis compared to patients diagnosed after age 40 (OR: 1.53, 95% CI 1.05–2.23, $P=.04$). Younger UC patients were almost twice as likely to receive biologics compared to patients diagnosed after age 40 (OR: 1.7, 95% CI 1.8–2.67, $P=.02$). Similarly, CD patients diagnosed before age 40 were twice as likely to require biologics (OR 2.2 95% CI 1.16–4.15, $P=.01$) and surgical intervention (OR 2.12, 95% CI 1.11–4.06, $P=.02$) than CD patients diagnosed after age 40, despite adjusting for duration of disease to prevent lead time bias. There was no difference in hospitalization frequency in those diagnosed before or after age 40 (data not shown). However, once a patient required a biologic, time from diagnosis to first biologic was similar for patients diagnosed before and after age 40 (mean time 5.27 years [SD 6.35] vs 4.19 years [SD 5.77], respectively, F [1,152] = 1.143, $P=.287$). Therefore, IBD patients diagnosed after age 40, which represents the mean age of presentation, tend to have fewer IBD-related complications than those presenting at younger ages including surgeries and need for biologics.

4. Discussion

We report estimates of IBD incidence and prevalence by demographic region in Colombia. This report characterizes Colombia overall as a nation with intermediate IBD prevalence, particularly with respect to UC, and similar in prevalence to countries such as India and Japan.[2] We also found that most patients with IBD were located in the Andean region, a mostly urban region characterized by high elevation. IBD afflicts more women, and IBD onset is older (in the fourth and fifth decades of life) compared to Western IBD populations. In the IBD clinic cohort, we also find that age of presentation is also older than Western descriptions and we find that IBD phenotype is largely

Table 3

Demographic and clinical characteristics of IBD patients seen in a regional IBD Clinic.

Characteristics	Ulcerative colitis n: 478	Crohn's disease n: 159	*P-value*
Age (mean yr, SD)	40.2 (15.8)	41.7 (16.0)	.34
Sex (F: M)	1.3:1	1:1.5	< .001
Duration of disease (mean years, SD)	9.8 (7.8)	7.1 (6.6)	<.01
Clinical Manifestations			
Diarrhea	89.5%	72.3%	<.01
Bleeding	84.1%	56.6%	<.01
Abdominal pain	62.8%	72.7%	.02
Weight loss	22.8%	35.2%	<.01
Truelove Disease Severity Index			
S0: Remission	8.1%		
S1: Mild	20.0%		
S2: Moderate	26.5%		
S3: Severe	46.4%		
Montreal Classification UC			
E1: Proctitis	24.2%		
E2: Left-sided	32.7%		
E3: Pancolitis	43.1%		
Montreal Classification CD			
A1: 16 yr or younger		5.0%	
A2: 17–40 yr		44.1%	
A3: > 40 yr		50.9%	
L1: Terminal ileal disease		37.1%	
L2: Colonic		21.2%	
L3: Ileocolonic		37.7%	
L4: Upper gastrointestinal disease		4.0%	
P: Perianal disease		16.7%	
B1: Nonstricturing, nonpenetrating		37.0%	
B2: Stricturing		26.6%	
B3: Penetrating		36.4%	
Smoking at time of diagnosis	16.5%	18.9%	NS
Appendectomy	4.6%	10.1%	NS
Family history of IBD	1.1%	0.6%	NS
Extraintestinal manifestations:	31.1%	35.2%	.04
Joints	11.3%	14.5%	
Erythema nodosum	2.7%	2.5%	
Oral ulcers	1.5%	1.9%	
Primary sclerosing cholangitis	2.7%	1.3%	
Uveitis	1.1%	0.6%	
Pyoderma gangrenosum	1.1%	0.6%	
Medications			
5-ASAs	94.6%	37.4%	<.01
Steroids (oral and IV)	55.0%	66.0%	.83
Immunomodulators (6-MP and Azathioprine)	41.4%	57.9%	<.01
Biologic Therapies (anti-TNFs only)	21.3%	46.5%	<.01
Time from diagnosis to first biologic, mean in yrs. (SD)	5.11 (5.82)	4.15 (6.23)	.028
IBD-related abdominal surgeries	12.1%	39.6%	<.01
IBD-related hospitalisations	55.4%	69.5%	<.01

IBD = inflammatory bowel disease, NS = no significant, SD = standard deviation.

similar to that reported in the literature. This study illustrates for the first time an emerging IBD burden in Colombia that distinguishes by demographics, region and urbanicity.

Although not surprising, our study demonstrates that UC incidence is rising within the 7-year time span examined across 20 million adult Colombians. The incidence of IBD in 2010 was 6.88 and increased to 7.04/100,000 by 2017, driven by the increase in UC within this time-period. In our IBD clinic, we also went from having 202 patients in 2009 to 649 in 2017.[8] IBD data from Latin America are scarce, but a few population studies exist. Panama, Uruguay, Argentina, Mexico, Colombia and Brazil have reported increased UC rates in their population studies.[15,17,31–33] The incidence of CD in Brazil has also risen sharply from 0.68 in 1991–1995 to 5.48 in 2015.15,18 Similarly, the incidence of both CD and UC in Puerto Rico has more than doubled between 1996 and 2000 (3.07–7.74).[13] Our UC incidence and prevalence data mirror those reported in these other Latin American studies.

Interestingly, we did not find a rise in CD incidence in Colombia; in fact, CD even appeared to decline within this period. In our country, many centers lack the ability to perform capsule endoscopy or magnetic resonance enterography in patients with suspected CD, which can make diagnosis difficult when ileocolonoscopy is normal. Nevertheless, it is also possible that environmental factors are at play. For instance, the Andes region, where prevalence of IBD is highest, is also characterized by distinctly high prevalence of Helicobacter pylori with cagA

expression, an infection that may offer protection against developing CD.[34] Nonetheless, despite the slight decrease in CD incidence, the prevalence of both UC and CD in Colombia is on the rise. Our study, therefore, mirrors epidemiologic data observed in other developing countries and highlights a worrisome increased global burden of IBD.[2]

Urbanicity and geographical region in Colombia also appear to influence incidence and prevalence of IBD.[6,35,36] The Andes region has the highest incidence of IBD (5.56/100,000 in 2017). The Andean region is densely populated, containing the majority of the country's urban areas: Bogotá (population 7.9 million), Medellin (population 1.9 million), and Cali (population 2.4 million). The native diet in this region varies, but increased Westernization has changed people's diets due to easy access to fast-food restaurants and US-based superstores.[20,21] We observe a difference in IBD incidence of 5% between rural and urban communities after adjusting for gender, age, and year of diagnosis. Differences in rural versus urban may be secondary to differences in lack of healthcare or lack of gastroenterologists per capita in the more rural areas of Colombia. However, the difference between urban and rural areas is just 5%, suggesting that an "IBD-promoting" environment may also be evolving in rural Colombia as well. Importantly, because we used the Colombian government's definition of rural communities (i.e., any municipality that is not the capital of its respective region), future studies should focus more on differences in environmental exposures between cities and more remote areas in Colombia.

We found that IBD presents at a later age in Colombia—based on both the national-level claims data and in the Medellin IBD center. The median ages of diagnosis for UC and CD in the US are 34.9 and 29.5 years of age, respectively.[37] This is a similar age of diagnosis to that reported in other Western countries with high IBD incidence.[38] In turn, IBD in Colombia develops in the fourth and fifth decade of life. In the local clinic, we found that both CD and UC are diagnosed in the early forties. We know that these findings are not due to time since diagnosis; in the clinic, onset of symptoms is meticulously recorded. Interestingly, this finding is also observed in Hispanics born in their native countries who emigrate to, and develop IBD in the US.[39] However, this "protection" is lost for US-born Hispanics, who mirror an age of presentation of white, non-Hispanic Americans.[39] These findings suggest that disease onset may depend on duration of exposure to an IBD-promoting environment. If such is true, we may find younger IBD onset in future generations of Colombians.

Last, we find that frequency of IBD-related complications is more common in those diagnosed before age 40. Patients had a more severe presentation of UC disease at diagnosis and both UC and CD required more biologics when diagnosed prior to age 40. However, IBD luminal disease location and frequency of extra-intestinal manifestations seem to be similar to that reported in other centers.[38,40,41] These findings suggest that perhaps younger age of disease results in more aggressive disease, which is consistent with Western studies.[42]

4.1. Limitations

Our study has several limitations that we have thoughtfully considered and addressed. Our epidemiologic data is based on SISPRO, a national database of all patients who registered at any hospital and/or clinic in Colombia. We did not have access to individuals with IBD who never sought medical attention. With this caveat, the SISPRO sample is representative of the estimated adult population in Colombia. In 2015, approximately 97.6% of the total Colombian adult population was recorded in the SISPRO registry and therefore our findings portray a close estimate of IBD trends in the Colombian adult population.[43] This 97.6% capture rate of the population is similar to that reported in Scandinavian countries and is much higher than what can be achieved in the US or other Latin American countries.

Additionally, although the SISPRO registry is not validated specifically for IBD, it has been validated yearly since 2010 and has 83% concordance (or positive predictive value) with medical records.[24] Prior studies in IBD also find acceptable accuracy of ICD codes for identifying IBD.[25–27] To address this limitation, we used 2 ICD codes for diagnosis and evaluated the SISPRO registry ICD-10 codes with a cohort of our hospital IBD patients to ensure they matched IBD diagnosis and found similar results. Prior studies using ICD-codes to find disease also use 80% positive predictive value as an acceptable cut-off[44,45]. Another limitation of our study is that our IBD phenotype data is from a regional IBD center, where IBD patients across the region seek care which could perhaps be interpreted as a more complicated, severe IBD cohort. However, it is important to recognize that this is a regional center and not a tertiary referral center. This regional IBD center sees patients that are biologic naïve and often times have been recently diagnosed and sent by GI doctors who do not feel comfortable treating IBD. Therefore, we feel that this cohort is representative of IBD patients of all severities seen within this region.

In conclusion, this is the first study to describe detailed estimates of the national epidemiology of Colombia by demographics and regions and to provide a detailed description of a large 600 patient IBD cohort (the largest in Colombia). Our data supplement recent studies in Latin America. We demonstrate increased rates of UC in the most urban parts of Colombia. We believe studies such as ours will lead to an examination of the environmental triggers in the hopes of preventing IBD in the future.

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