

Trends and demographic patterns in biologic and corticosteroid prescriptions for inflammatory bowel disease: findings from electronic medical records, 2011–2020

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► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/jim-2022-002486>).

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Accepted 10 August 2022
Published Online First
5 September 2022

ABSTRACT

Prescriptions for biologic therapy for treatment of Crohn's disease (CD) and ulcerative colitis (UC) have increased during the past two decades; however, trends are less clear regarding corticosteroid prescriptions in this context. We designed a cross-sectional study using the IQVIA Ambulatory Electronic Medical Records databases. Weighted linear regressions by age group were used to estimate annual percentage change from 2011 to 2020 in prescriptions for biologics and for corticosteroids among patients with or without biologic prescriptions within the same calendar year. Using 2019 data, we compared patient demographic and lifestyle risk factors using χ^2 test for biologic prescriptions and corticosteroids with or without biologics prescriptions. There was an 11% (CD) and 16% (UC) annual increase in the percentage of patients prescribed biologics during the study period. The percentage of patients with biologics prescriptions prescribed corticosteroids decreased by 2% (CD) and 3% (UC) annually after 2015, while the percentage remained unchanged for corticosteroid prescriptions among patients without biologics. In 2019, differences in medication prescriptions existed by patient's demographic and lifestyle factors for patients with CD (n=52,892) and UC (n=52,280), including a higher percentage prescribed biologics among younger patients, men, those with fewer comorbidities, and current alcohol drinkers, and a higher percentage prescribed corticosteroids without biologics among women, those with more comorbidities, and a history of smoking. While medications continue to evolve during the biologic era, it is important to continue to monitor trends and differences in prescription patterns to assess progress toward optimizing treatment for patients with CD or UC.

INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC), collectively known as inflammatory bowel disease (IBD), are characterized by chronic inflammation of the gastrointestinal tract. In 2015, 3 million US adults self-reported having CD or UC.¹

The goal for IBD treatment is to reduce inflammation, maintain remission, and improve quality of life.² The introduction of biologic agents have changed the conventional way of treating IBD and demonstrated better clinical outcomes, such as improved mucosal healing and declining surgery rates.² As a traditional medication, systemic corticosteroids have been used to treat acute flare-ups quickly,^{3–5} but are not effective to maintain remission.⁶ Some patients may become corticosteroid-dependent after 1 year of treatment,⁷ and long-term use of corticosteroids is associated with numerous complications and increased mortality.^{7,8} Corticosteroid-free clinical remission for 12 months is one of the quality outcome indicators for IBD management.⁹

While the use of biologics has increased during the past two decades,¹⁰ trends for corticosteroids are less clear and may be impacted by different measures, study periods, and data sources.^{11–13} It would be expected that corticosteroid prescriptions would decrease as biologics increase. Both medication types could be prescribed within a year as patients transition from corticosteroids to biologics.^{11–13} Therefore, it is important to monitor trends in corticosteroid prescription among patients with and without biologic prescriptions. Understanding which subgroups are more likely to be prescribed corticosteroids or biologics may provide insights in potential medication accessibility, variations in prescription practice, and disease severity by patient demographics. For example, the prescription pattern may vary by age group because of age-related frailty, comorbidities, and different clinical presentations of IBD symptoms.¹⁴ Finally, some lifestyle risk factors such as smoking and alcohol drinking may impact clinical outcomes in IBD and influence medication effectiveness.¹⁵ Assessing the prescription patterns associated with these risk factors may inform clinical practice. We therefore designed a cross-sectional study to assess trends in prescriptions for biologics and corticosteroids with and without biologics from 2011 to 2020 by age group as well as differences in prescriptions by patient demographics.



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To cite: Xu F, Liu Y, Greenlund K, et al. *J Invest Med* 2022;**70**:1771–1776.

MATERIALS AND METHODS

Database

Data were from IQVIA's Ambulatory Electronic Medical Records (AEMR) database, which contains deidentified information recorded during outpatient encounters for a geographically diverse US patient population, covering data from over 78 million patients and 100,000 physicians.¹⁶ Clinical information such as medication prescription, patient demographic characteristics, medical history, and *International Classification of Diseases (ICD)*, *Clinical Modification* diagnosis codes and Systematized Nomenclature of Medicine (SNOMED) codes were analyzed.

IBD and medication definition

Patients with IBD were identified using ICD codes (CD: ICD-9-CM: 555, ICD-10-CM: K50; UC: ICD-9-CM: 556, ICD-10-CM: K51) in combination with the SNOMED codes (CD: 34000006, UC: 64766004) from AEMR. We identified outpatient encounters with prescriptions for corticosteroids including prednisone, prednisolone, methylprednisolone, hydrocortisone, and budesonide, and for biologics including adalimumab, infliximab, certolizumab, golimumab, vedolizumab, natalizumab, and ustekinumab.¹⁷ These medications were identified using National Drug Code and SNOMED from AEMR.

Demographic variables

Demographic variables included age group (<18, 18–59, and ≥60 years), sex, race (non-Hispanic white, non-Hispanic black, and other), number of comorbidity categories (0, 1, 2, ≥3 based on counts of acute myocardial infarction, heart failure, stroke, diabetes, depression, chronic obstructive pulmonary disease, obesity, chronic kidney disease, and alcohol use disorder),¹⁸ US region (Northeast, South, Midwest, and West), a history of smoking status, and current alcohol use status.

Statistical analysis

All analyses were performed separately for CD and UC. For trend analysis, proportions of patients with IBD prescribed each medication, overall and by age group (aged <60 and ≥60 years), were calculated from 2011 to 2020. For trends in corticosteroid prescriptions, the analysis was stratified by the appearance of prescription encounters for biologics within the same calendar year—the proportion prescribed corticosteroids among patients with a biologic prescription or without a biologic prescription (corticosteroids with or without biologics). The percentage of patients prescribed each medication was natural log transformed to achieve normality. We first used a restricted cubic spline to assess the linearity of the model. If non-linearity existed, we fit a piecewise linear regression to estimate the slopes. Otherwise, a weighted linear regression on inversed SEs was used to estimate the slope. Annual percentage change (APC) with 1 year increase was derived from the exponential of the year regression coefficient. An interaction term between age group and year was included in the model. Because patterns in healthcare utilization in 2020 may have been affected by the ongoing pandemic, we used 2019 AEMR to assess differences in medication prescriptions by select demographic characteristics. We calculated the proportions of

patients with IBD prescribed biologics and corticosteroids with and without biologics in 2019 with 95% CIs and used χ^2 for group comparisons. We used SAS V.9.4 (SAS Institute, Cary, North Carolina, USA) and R V.3.6.1 for analyses.

RESULTS

From 2011 to 2020, the percentage of patients with IBD prescribed biologics increased from 13.3% to 32.1% for CD (APC: 11%) and from 4.1% to 14.8% for UC (APC: 16%). The APC was higher among patients aged ≥60 years with CD than their younger counterparts (14% vs 11%, p (age×year)=0.04). There was no change in the percentage prescribed corticosteroids among patients with CD or UC with biologic prescriptions from 2011 to 2015, although this was followed by a decrease from 2015 to 2020 for both CD (APC: −2%) and UC (APC: −3%). Corticosteroid prescriptions among patients without biologic prescriptions remained unchanged (figure 1, online supplemental table 1).

In 2019, among 52,892 patients with CD and 52,280 with UC, more patients with CD than patients with UC were prescribed biologics (30.3% vs 13.6%) and corticosteroids with biologics (11.0% vs 5.9%). Among patients with CD or UC prescribed biologics, about half were prescribed adalimumab. Among those prescribed corticosteroids, less than a quarter of patients were prescribed budesonide, a second-generation medication that is better tolerated¹⁹ (results not shown). Compared with younger age groups, the percentage of patients with CD or UC aged ≥60 years prescribed biologics was lower and the percentage of patients with CD aged ≥60 years prescribed corticosteroids with no biologics was higher. A higher percentage of men with CD or UC were prescribed biologics and a lower percentage was prescribed corticosteroids without biologics compared with women. A higher percentage of non-Hispanic black patients with CD were prescribed biologics than were non-Hispanic white patients. Among patients with CD or UC, biologic prescriptions were lower and corticosteroid prescriptions without biologics were higher among those with more comorbidities (table 1). Regionally, biologic prescriptions for both CD and UC were lower in the West compared with the South, and corticosteroid prescriptions without biologics were lower in the Northeast and higher in the West compared with the South. Finally, corticosteroid prescriptions (with or without biologics) were higher among patients with CD and UC with a history of smoking than those without. For both diseases, biologic prescriptions were higher and corticosteroid prescriptions were lower among current alcohol users than non-current alcohol users (online supplemental table 2).

DISCUSSION

This study confirmed that prescriptions for biologics among patients with IBD increased during the recent decade,²⁰ and the rate of increase was similar for both CD and UC. Changes in corticosteroid prescriptions from 2011 to 2020 differed by presence of biologic prescriptions, with no change in corticosteroid prescriptions among patients without biologic prescriptions, and a decrease in corticosteroid prescriptions among patients with biologic prescriptions from 2015 to 2020. A Canadian study similarly

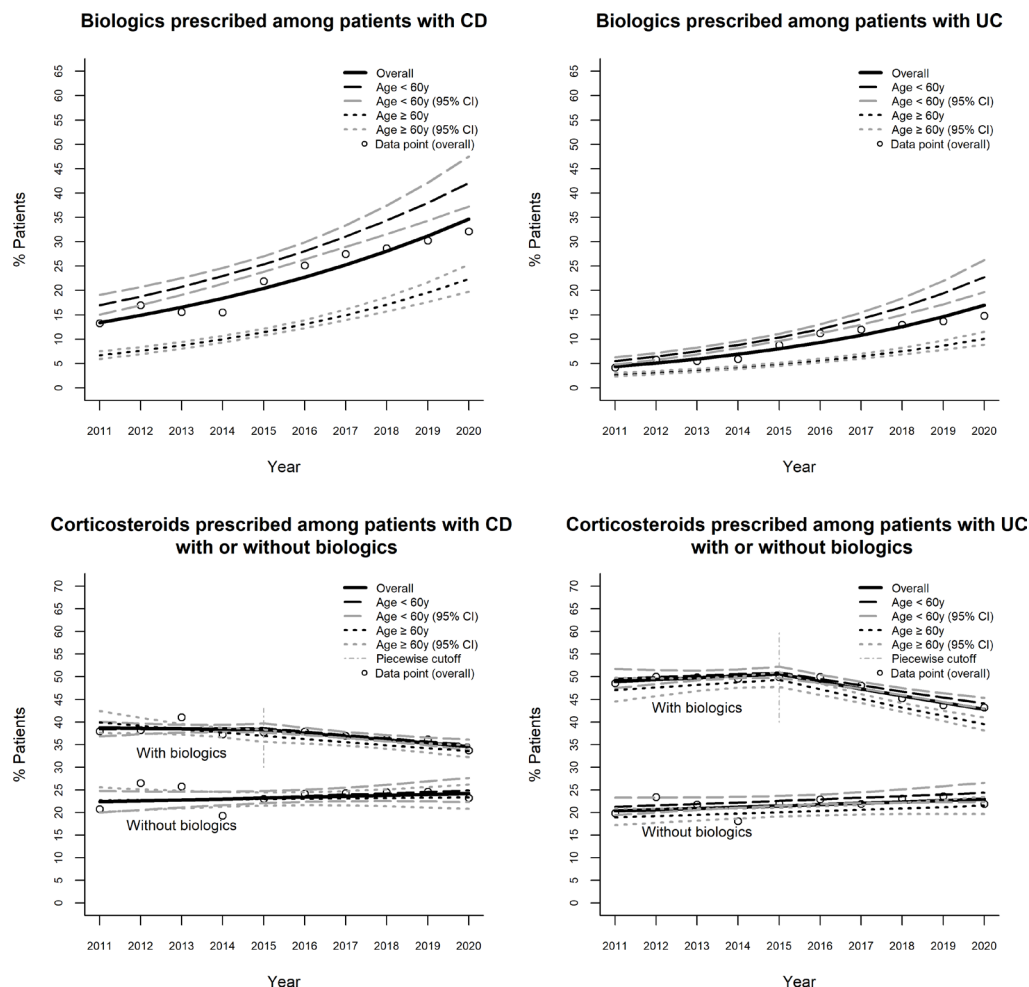


Figure 1 Percentage of patients with Crohn's disease (CD) or ulcerative colitis (UC) who were prescribed biologics or corticosteroids (with or without a biologic prescription within the same calendar year), overall and by age and year, 2011–2020 IQVIA. y, years.

attributed decreases in mean annual corticosteroid doses prescribed for patients with IBD to recent antitumor necrosis factor (anti-TNF) use and clinicians' awareness of serious side effects of long term use of corticosteroids.¹¹

In 2019, fewer than one-fifth of patients with IBD were prescribed corticosteroids without biologics. The reasons corticosteroids are prescribed for patients with IBD are multifaceted, possibly due to immediate effectiveness of corticosteroids to reduce acute inflammation, lack of response to other medications, difficulty tapering off corticosteroids, inaccessibility to other treatment options due to inadequate insurance, or inappropriate steroid prescription practice.¹¹ Monitoring patterns of biologics and corticosteroids can help to assess progress toward management goals and to identify potential areas for improvement in care. Strategies are needed to better understand and address the possibility of patients' unnecessary or excessive exposure to corticosteroids.

Several differences in prescription patterns related to age and comorbidities were identified. While prescriptions for biologics increased for both age groups across the study period, biologic prescriptions were lower among older patients compared with younger patients. Older age was also positively associated with corticosteroid prescriptions

without biologics for CD. This finding is consistent with previous studies that older patients with IBD are more likely to be treated with maintenance corticosteroids and less likely to initiate steroid-sparing agents than younger patients despite the established evidence of toxicity of long-term use of corticosteroids.²¹ Similarly, we observed that more age-related comorbidities were negatively associated with biologic prescriptions but positively associated with corticosteroid prescriptions without biologics because of the safety concerns of biologic use among older patients.¹⁴ With a growing number of older patients with IBD in the USA,²² strategies tailored to older patients with IBD are needed to ensure they are receiving safe yet effective treatment for their condition.

Several differences in prescription patterns by sex, race/ethnicity, and region were also identified. Women were more likely to be prescribed corticosteroids but less likely to be prescribed biologics than were men. Previous studies indicated women with IBD were more likely than men to use steroids and terminate or switch biologics due to intolerance.^{23 24} Another explanation could be due to sex-related disparities in access to care.²³ Findings regarding racial/ethnic disparities of biologics use have been inconsistent.^{25 26} Our study showed a moderately higher proportion

Table 1 Percentage of patients with Crohn's disease or ulcerative colitis with prescriptions of biologics or corticosteroids* (with and without biologics), overall and by age, sex, race and ethnicity, and number of comorbidities, 2019 IQVIA

Patient characteristic	Crohn's disease						Ulcerative colitis					
	Biologics†			Corticosteroid‡ with biologics			Biologics†			Corticosteroid‡ with biologics		
	%	(95% CI)	P value	%	(95% CI)	P value	%	(95% CI)	P value	%	(95% CI)	P value
Overall	N=52, 892	30.3 (29.9 to 30.7)	—	11.0 (10.7 to 11.3)	—	—	N=52 280	13.6 (13.4 to 13.9)	—	5.9 (5.7 to 6.1)	—	—
Age (years)												
<18	2.8	41.3 (38.7 to 43.8)	0.001	16.8 (14.9 to 18.7)	<0.001	0.004	1.4	22.3 (19.3 to 25.3)	0.003	12.5 (10.1 to 14.9)	<0.001	0.89
18–59 (ref)	59.6	37.1 (36.6 to 37.6)	—	13.6 (13.2 to 13.9)	—	—	53.4	18.0 (17.5 to 18.4)	—	7.9 (7.6 to 8.3)	—	—
≥60	37.6	18.8 (18.3 to 19.3)	<0.001	6.6 (6.2 to 6.9)	<0.001	<0.001	45.2	8.3 (7.9 to 8.6)	<0.001	3.3 (3.1 to 3.6)	<0.001	0.89
Sex												
Female (ref)	58.1	29.3 (28.7 to 29.8)	—	11.0 (10.7 to 11.4)	—	—	55.9	12.6 (12.2 to 13.0)	—	5.5 (5.2 to 5.8)	—	—
Male	41.9	31.8 (31.2 to 32.4)	<0.001	11.0 (10.6 to 11.4)	0.88	<0.001	44.1	15.0 (14.5 to 15.5)	<0.001	6.5 (6.1 to 6.8)	<0.001	0.04
Race and ethnicity												
Non-Hispanic white (ref)	77.7	30.8 (30.3 to 31.2)	—	11.3 (11.0 to 11.6)	—	—	77.1	13.8 (13.5 to 14.1)	—	6.0 (5.8 to 6.2)	—	—
Non-Hispanic black	5.8	32.9 (31.2 to 34.6)	0.01	11.9 (10.8 to 13.1)	0.30	0.94	4.7	14.5 (13.1 to 15.9)	0.34	6.3 (5.3 to 7.2)	0.57	0.41
Other§	2.0	29.4 (26.7 to 32.2)	0.36	12.4 (10.4 to 14.4)	0.30	0.29	2.6	15.1 (13.2 to 17.0)	0.16	7.3 (5.9 to 8.7)	0.05	0.43
Unknown	14.6	27.1 (26.1 to 28.1)	<0.001	8.8 (8.1 to 9.4)	<0.001	<0.001	15.7	12.4 (11.7 to 13.1)	<0.001	5.3 (4.8 to 5.7)	0.01	0.001
Number of comorbidities¶												
0 (ref)	69.3	33.2 (32.7 to 33.7)	—	11.7 (11.4 to 12.1)	—	—	69.9	15.0 (14.6 to 15.3)	—	6.5 (6.2 to 6.7)	—	—
1	22.6	25.8 (25.0 to 26.6)	<0.001	10.1 (9.5 to 10.6)	<0.001	<0.001	22.2	11.4 (10.9 to 12.0)	<0.001	5.0 (4.6 to 5.4)	<0.001	<0.001
2	6.1	19.5 (18.1 to 20.9)	<0.001	7.4 (6.5 to 8.3)	<0.001	<0.001	5.9	8.9 (7.9 to 9.8)	<0.001	4.0 (3.3 to 4.7)	<0.001	<0.001
≥3	2.0	13.8 (11.7 to 15.9)	<0.001	7.3 (5.7 to 8.8)	<0.001	<0.001	2.0	6.5 (5.0 to 8.0)	<0.001	3.3 (2.2 to 4.4)	<0.001	<0.001

*With or without a biologic prescription within the same calendar year. The denominators are all patients with CD or UC.

†Including adalimumab, infliximab, certolizumab, golimumab, vedolizumab, natalizumab, and ustekinumab.

‡Including prednisone, prednisolone, methylprednisolone, hydrocortisone, and budesonide.

§Others include Hispanics, non-Hispanic Asians, and other racial/ethnic groups.

¶Comorbidities include cardiovascular disease (acute myocardial infarction, heart failure, and stroke), diabetes, depression, chronic obstructive pulmonary disease, obesity, chronic kidney disease. ref, referent group.

of biologic prescriptions among non-Hispanic black patients with CD than their non-Hispanic white counterparts. Blacks have been reported to have worse disease activity symptoms than whites.²⁷ As blacks are often under-represented in the clinical trials,²⁸ further investigation is needed to disentangle this association. Our study also indicated regional prescription variations with the West associated with a lower proportion of patients with IBD having prescriptions for biologics but a higher proportion having prescriptions for corticosteroids without biologics compared with the South. Differences in prescription pattern may indicate regional quality of care for IBD.

Furthermore, certain lifestyle risk behaviors may impact IBD treatment regimens.¹⁵ Our study found that biologic prescriptions were less common, but corticosteroid prescriptions with or without biologics were more common among patients with IBD with a history of smoking than never smokers. This finding is consistent with previous studies that reported smoking as a risk factor for non-adherence of anti-TNF agents²⁴ and a positive association between smoking and corticosteroid use and dependency. Although our study could not differentiate ex-smokers from current smokers, ex-smokers were less likely to be corticosteroid-dependent than current smokers among patients with CD.¹⁵ While current alcohol use was associated with biologic prescriptions, it has a negative impact on the gut microbiome and may alter effectiveness of biologic agents indirectly.²⁹ Clinicians may need to closely monitor treatment outcomes of smokers and alcohol drinkers during therapeutic treatment and advise them to quit smoking and drinking alcohol to maximize treatment effectiveness as well as improve overall health.

There are a few limitations in the study. First, outpatients in AEMR are a nationwide convenience sample and are not nationally representative. Second, information on insurance status was unavailable and this may influence prescription patterns. Third, we did not assess dose, timing, and duration of corticosteroid prescriptions due to the incomplete information from AEMR. Fourth, Hispanic ethnicity was not included as a separate racial/ethnic category because AEMR does not have complete information about ethnicity. Fifth, AEMR does not have reasons for prescriptions. Although uncommon, it is possible some medications might be prescribed for conditions other than IBD. Finally, the observed associations might represent an overestimation or underestimation due to unstandardized SNOMED codes and self-reported records.

In conclusion, this study provided insights on recent trends in prescriptions for biologics and corticosteroids from outpatient clinical practices in the USA based on the electronic medical records data. As IBD medications continue to evolve, it is important to continue to monitor prescription patterns to examine progress toward optimizing IBD therapeutic treatment.

Contributors FX: concept and design of the study, data acquisition, analyses, data interpretation, drafting manuscript, critical revision for important intellectual content, manuscript approval for journal submission. YL: concept or design of the study, data acquisition, analyses, data interpretation, critical revision for important intellectual content, manuscript approval for journal submission. KG: data interpretation, critical revision for important intellectual content, manuscript approval for journal submission. SC: concept or design of the study, data interpretation, critical

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Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval An institutional review board approval was not required for studies using the IQVIA data.

Provenance and peer review Not commissioned; externally peer reviewed.

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