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Market Share and Costs of Biologic Therapies for Inflammatory Bowel Disease in the United States

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SUMMARY

Background—Real-world data quantifying the costs of increasing biologics use in inflammatory bowel disease (IBD) are unknown.

Aim—To determine the outpatient IBD drug utilization trends, relative market share, and costs in the United States during a nine-year period.

Methods—The Truven MarketScan Database was analyzed for patients with Crohn's disease and ulcerative colitis during 2007–2015. National drug codes were used to identify prescription drugs; Healthcare Common Procedure Coding System J-codes were used to capture biologic outpatient infusions. Proportion of drug usage, relative market share, and per-member per-year costs were analyzed for biologics, immunomodulators, 5-ASAs, and corticosteroids.

RESULTS—In 415,405 patients (188,842 Crohn's disease; 195,183 ulcerative colitis; 31,380 indeterminate colitis; 54.67% female), utilization trends show a consistent rise in the market share of biologics during the nine-year study period. The proportion of patients using biologics increased from 21.8% to 43.8% for Crohn's disease and 5.1% to 16.2% for ulcerative colitis. This contrasts a small decrease in immunomodulator and 5-ASA use for Crohn's disease and relative constancy of other classes including corticosteroids-only use as primary IBD medication from 2007 to 2015. The average biologic-taking patient accounted for $25,275 per-member per-year in

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2007 and $36,051 per-member per-year in 2015. The average pediatric biologic-taking patient accounted for $23,616 per-member per-year in 2007 and $41,109 per-member per-year in 2015. In all patients, the share of costs for biologics increased from 72.9% in 2007 to 85.7% in 2015 (81.7% in 2007 to 94.9% in 2015 in pediatrics).

CONCLUSION—The vast majority of costs allocated to outpatient IBD medications in the United States is attributed to increasing use of biologic therapies despite the relative minority of biologic-taking patients.

Keywords

Biologics; IBD; Crohn's disease; ulcerative colitis; costs of care; pharmaceutical claims

INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC) are inflammatory bowel diseases (IBD) with typical chronic relapsing and remitting disease course,[1] affecting an increasing proportion of the population in the United States (US).[2,3] While potentially debilitating if improperly treated,[4] recent developments in biologic therapies have significantly improved health outcomes in IBD. Expensive, yet effective, biologics are a mainstay of medical therapy options for disease maintenance in both CD and UC.[5]

As a result of increasing biologics use, overall costs of medical care have shifted from acute care services to outpatient pharmacy utilization,[6] with recent evidence suggesting pharmacy costs account for nearly one-half of all disease-related direct expenditures.[7,8,9] This trend in prescription drug costs outpacing all other segments of healthcare is consistent across other chronic diseases.[10,11] Compared to other medication classes, namely 5-ASAs, immunomodulators (mercaptopurine, azathioprine, and methotrexate), and corticosteroids, biologics use represents an increasing impact to rising health care costs in IBD. Traditional biologics, consisting of anti-tumor necrosis factor alpha (anti-TNF) agents such as adalimumab and infliximab, drive the biologic market, but newer agents such as vedolizumab and ustekinumab are increasingly used in clinical practice.

It is not known how the overall outpatient pharmaceutical drug market has evolved in recent years given increasing use of biologics. Therefore, in today's "Era of Biologics," determining cost-effective strategies for biologics in the US remains a major knowledge gap.

The aims of this study were (1) to determine outpatient drug utilization trends and per-member per-year (PMPY) costs of IBD medications; (2) describe the market share of biologics relative to immunomodulators, 5-ASAs, and oral corticosteroids, and (3) assess differences in outpatient IBD medication use between pediatrics and adult IBD populations in the US.

METHODS

Overview

We performed a longitudinal retrospective cohort analysis of CD and UC patients in the Truven Marketscan Commercial Claims and Encounters database from years 2007–2015. The Truven Marketscan database consists of de-identified outpatient, inpatient, and pharmaceutical claims of approximately 40–50 million privately insured patients each year. These claims originate from over 150 large employer-sponsored health insurance plans with patient coverage in all 50 states.

The database includes patient characteristics (age, sex, geographic region), financial variables (inpatient, outpatient, and pharmaceutical costs), and pharmacy-level data (NDC codes, days-supply, strength, administration method). Costs were scaled to February 2017 dollars using the US Census Bureau's Consumer Price Index (CPI). PMPY costs were of the sum of health plan's paid amount and patient's copay and deductible amounts per year for outpatient IBD medications.

Patient identification

Patients were included in our sample if they met the following inclusion criteria: (1) at least two distinct IBD diagnoses (defined under the International Classification of Diseases, Ninth Revision (ICD-9) as 555.xx for Crohn's disease and 556.xx for ulcerative colitis; the ICD-10 codes are K50.xx and K51.xx, respectively); and (2) at least one pharmaceutical claim between 2007–2015. To classify a patient as CD or UC, the total number of distinct CD and UC were summed, and if 80% or more of these diagnoses were 555.xx/K50.xx or 556.xx/K51.xx, the patient was classified as CD or UC, respectively. If neither condition was satisfied, the patient was classified as having indeterminate colitis (IC).

Prescription drug identification

To capture drug utilization of outpatient medications for IBD, we examined patients who had at least one pharmaceutical claim or outpatient infusion/injection for a biologic medication (adalimumab, certolizumab pegol, golimumab, infliximab, natalizumab, vedolizumab, ustekinumab), immunomodulator (azathioprine, mercaptopurine, methotrexate sodium), 5-ASA (mesalazine, sulfasalazine), or oral corticosteroid (prednisone or prednisolone).

Assignment of maintenance medication

To examine the market share of patients' primary IBD medication, we followed a hierarchical system to classify patients receiving more than one medication (e.g., combination therapy using biologics and immunomodulators). Patients receiving a biologic medication were assigned to the maintenance biologic category, regardless of concomitant use of immunomodulators, 5-ASAs, or corticosteroids. Patients receiving an immunomodulator (not on biologics) were assigned to the maintenance immunomodulator category, regardless of concomitant use of 5-ASAs or corticosteroids. Patients receiving a 5-ASA (not on biologics or immunomodulators) were assigned to the maintenance 5-ASA category regardless of concomitant use of corticosteroids. Patients who were only receiving

corticosteroids were assigned to the corticosteroid category, and we assumed that these patients were not on an appropriate IBD maintenance medication.

Statistical analysis

All descriptive statistical analyses were performed using Stata 14.2 (College Station, TX). Means, median, and standard deviations for PMPY costs in 2017 dollars were calculated.

RESULTS

Summary of patients

Table 1 shows the summary of included patients. The study cohort consisted of 415,405 patients (188,842 CD; 195,183 UC; 31,380 IC). CD, UC, and IC patients were comparable in age, gender, geographical region, and insurance type. Pediatric patients (0–18 years) represented 9.2% (17,296), 4.8% (9,368), and 6.8% (2,133) of all CD, UC, and IC patients, respectively. Among the entire study cohort, 75.0% (311,368) had at least one pharmaceutical claim for either a biologic, immunomodulator, 5-ASA or corticosteroid from 2007–2015.

Outpatient Drug Utilization and Market Share

During the nine-year time span, the proportion of all patients using biologics increased nearly three-fold from 7.1% in 2007 to 20.5% in 2015. In CD, the proportion of patients using biologics increased from 21.8% to 43.8%, with a decrease in immunomodulators (27.2% to 18.0%) and 5-ASAs (34.1% to 21.6%). In UC, the proportion of patients using biologics increased from 5.1% to 16.2%, with a relative constancy in immunomodulators (17.1% to 13.7%) and 5-ASAs (59.0% to 53.7%). The proportion of patients using corticosteroid-only as primary IBD medication remained stable for CD (16.9% to 16.6%) and UC (18.8% to 16.2%) (Figure 1).

Among patients who had at least one pharmaceutical claim or a biologic infusion in any given year (n=311,368), utilization trends over the nine-year time span show a consistent rise in the market share of biologics (Figure 2). From 2007 to 2015, biologics use increased from 13.7% (22.6% CD, 5.3% UC) to 30.1% (44.8% CD, 16.7% UC); immunomodulator use decreased from 22.7% (28.2% CD, 17.9% UC) to 16.0% (18.5% CD, 14.1% UC); 5-ASA use decreased from 48.6% (35.3% CD, 61.5% UC) to 39.2% (22.1% CD, 55.1% UC); and corticosteroid-only use remained relatively stable at 14.9% (13.9% CD, 15.4% UC) to 14.7% (14.7% UC, 14.2 % UC).

A subgroup analysis of pediatric patients 0–18 year olds (n=28,797) showed a marked difference in outpatient IBD medication use compared to the entire cohort. The pediatric patients showed a significantly higher use of biologics and lower use of immunomodulators, 5-ASAs, and corticosteroid-only. In pediatric patients, the market share of biologics increased from 19.1% in 2007 to 45.9% in 2015. The rate of market share growth per-year was significantly higher in pediatric patients compared to the general cohort.

Per-Member Per-Year IBD Medication Costs

Figure 3 shows the PMPY costs allocated to outpatient IBD medications for patients using biologics, immunomodulators, 5-ASAs, or corticosteroid-only as their primary maintenance medication. Among patients on biologic therapies, the PMPY costs attributed to outpatient IBD medications increased from 2007 to 2015, with a high rate of increase from 2011 to 2015. For outpatient IBD medications, the average biologic-taking patient accounted for $25,275 PMPY in 2007 and $36,051 PMPY in 2015. The average pediatric biologic-taking patient accounted for $23,616 PMPY in 2007 and $41,109 PMPY in 2015. These PMPY cost trends for biologics greatly exceed cost trends for immunomodulators, 5-ASAs, or corticosteroids. Although 5-ASA-taking patients had a steady rise of PMPY costs, their less-than $5,000 PMPY in 2015 sharply contrasts the average PMPY costs attributable to biologic-taking patients. Compared to biologic- or 5-ASA-taking patients, immunomodulator-taking or corticosteroid-alone patients accounted for a small proportion of the total costs attributed to outpatient IBD medications. An all-medication comparison shows that the share of PMPY costs for biologics increased from 72.9% to 85.7% in 2015. In pediatric patients, PMPY costs attributed to biologics increased from 81.7% to 94.9% in 2015.

DISCUSSION

We present the most comprehensive analysis to date of real-world outpatient pharmaceutical utilization and costs in IBD in the US. Our research specifically aimed to address an undescribed health services impact of prescription IBD medication use with a focus on biologics. In our study, we determined the PMPY costs of outpatient IBD medications, quantifying the cost impact of increasing biologics use in the US. We found that outpatient IBD medication use is driven by increasing biologics use as mainstay therapy for disease control. A key finding in our study highlights that the PMPY costs of an average patient in 2015 receiving biologic therapy ($36,051/year) is nearly eight times costlier (<$5,000/year) and approximately thirty-six times costlier (~$1,000) than an average patient receiving 5-ASAs and immunomodulators, respectively.

The aggregate data we outline here also indicate that increasing market share trends for both biologics and 5-ASAs will likely continue if the current utilization trajectory occurs. From a clinician perspective, corticosteroid-sparing therapy plans are evidence-based and necessary to optimize long-term health outcomes, maximize quality of life, and minimize opportunity loss.[12,13,14,15] Considering biologics' effectiveness in achieving mucosal healing,[16,17,18,19] and drug industry's active development pipelines and research investment in newer therapies, extrapolation of market share and cost trends for biologics is reasonable and possibly underestimated for the foreseeable future.

Another interesting finding in our analysis is that biologics' market share in pediatric patients outpaces the market share in all patients. Pediatric patients also had less corticosteroid-only maintenance therapy. This may reflect the known phenotypic difference between adult- versus pediatric-onset IBD.[20] Children with IBD often present with worse disease severity requiring early biologics use as first-line maintenance therapy.[21] Although outside the scope of this study, proactive outpatient IBD care with the treatment goal of

corticosteroid-free remission may be more nationally standardized and implemented in pediatric IBD care models.[22]

Our findings corroborate other notable studies using claims data. Rubin et al[23] also used the Truven Markescan data showing increasing use of IBD pharmacotherapies over a 5-year time period (2006–2010) in the US. Kirchgesner et al[24] used the French national health insurance data showing increasing anti-TNF with corresponding decline in IBD-related surgery until the end of 2014. Rocchi et al[25] used private and public Canadian claims data and showed that cost of IBD medications now outpace hospitalization costs. These studies and our analysis support the conclusion that the management of IBD has evolved in the last decade to increasingly rely on escalating pharamcotherapies, particularly biologics. With this trend, pharmacy-related health care utilization represents the major cost driver in IBD across developed countries.

Inherent to large database analyses, we acknowledge that our findings rely on the accuracy of insurance coding data to provide a snapshot of real-word drug utilization and direct costs. A primary advantage of our analysis is the leveraging of data over nine consecutive years. Our surveillance of the literature indicates that most published studies using the Truven Marketscan database have not attempted to include such large data over a contiguous time horizon. Of note, the data we show originate before the incorporation of biosimilars in the US for the treatment of IBD. Analysis of subsequent years after market stabilization of biologics and biosimilars in the U.S. may reveal similar cost reductions for originator biologics previously reported in European countries with increasing biosimilar use.[26]

In summary, our analysis uniquely explores the cost impact of increasing biologics use from outpatient IBD care in the US. The findings from our study further reiterate the ongoing need to develop patient-centered, cost-effective pharmacotherapy strategies by judiciously incorporating biologics in individualized therapy plans.

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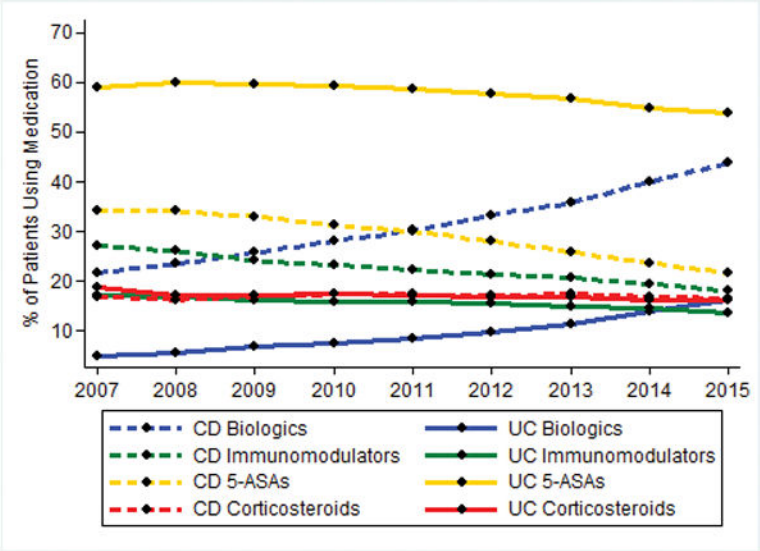

Figure 1. Outpatient IBD Medication Utilization Trends

The proportion of patients using biologics increased for CD and UC, with a decrease in immunomodulator and 5-ASA use in CD and stable IBD medication use including corticosteroid-only from 2007 to 2015.

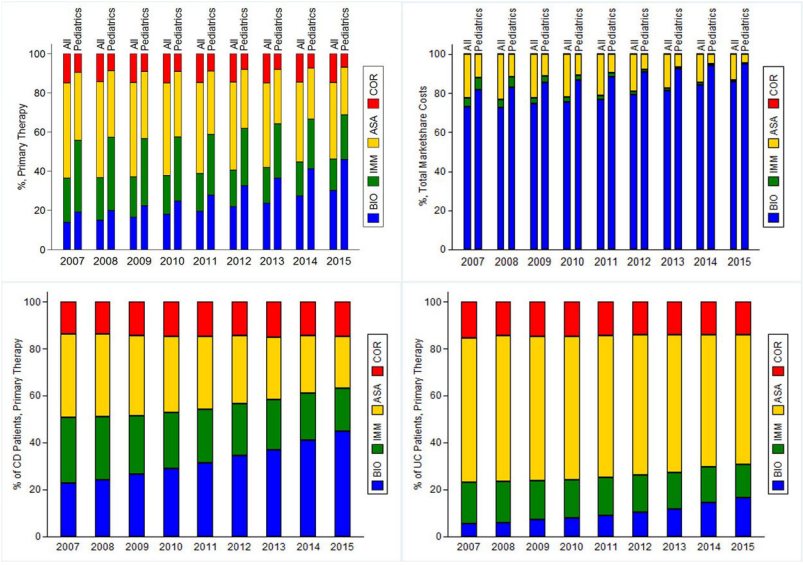

Figure 2. Increasing Market Share of Biologic Therapies

The proportion of patients using biologics and costs allocated to biologics compared to other IBD medications have increased every year from 2007 to 2015.

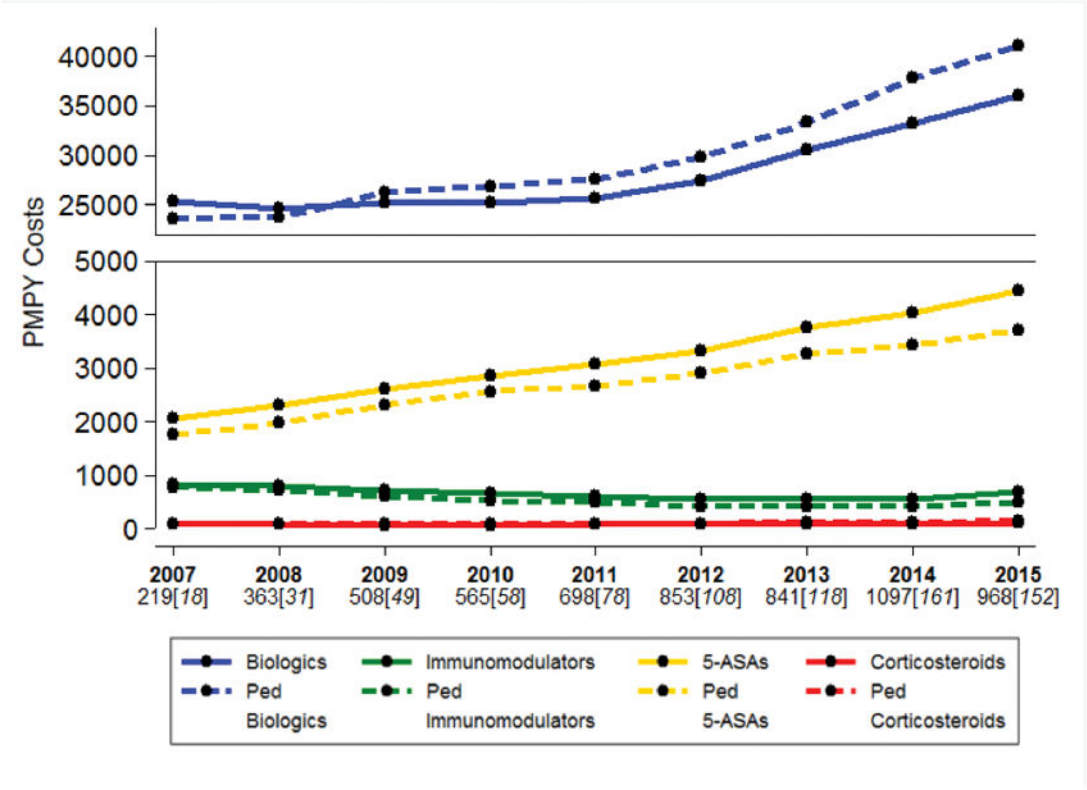

Figure 3. IBD Medication Per-Member Per Year (PMPY) Costs

Biologics outpace other medications in rate-of-increase and total PMPY costs.

Table 1

Patient Characteristics

	Crohn's Disease	Ulcerative Colitis	Indeterminate Colitis
Total (n=415,405)	188,842	195,183	31,380
Female, n (%)	105,538 (55.9)	104,374 (53.5)	17,183 (54.8)
Pediatric *, n (%)	17,296 (9.2)	9,368 (4.8)	2,133 (6.8)
Insurance **			
EPO/PPO	121,417 (69.2)	124,277 (68.4)	20,159 (69.4)
HMO/Cap POS ***	26,664 (14.1)	26,829 (14.8)	4,150 (14.3)
POS	13,217 (7.5)	13,496 (7.4)	2,222 (7.6)
HDHP/CDHP	12,799 (7.3)	13,486 (7.4)	1,927 (6.6)
Comp	3,464 (2.0)	3,700 (2.0)	611 (2.1)
Region			
Northeast	40,860 (21.6)	42,904 (22.0)	8,154 (26.0)
North Central	47,978 (25.4)	44,506 (22.8)	6,782 (21.6)
South	70,828 (37.5)	71,464 (36.6)	11,429 (36.4)
West	25,300 (13.4)	32,820 (16.8)	4,423 (14.1)
Unknown	3,876 (2.1)	3,489 (1.8)	592 (1.9)
Using IBD medications			
Any	139,015 (73.6)	148,665 (76.2)	23,688 (75.5)
Biologics	58,701 (31.1)	22,704 (11.6)	6,655 (21.2)
Immunomodulators	63,289 (33.5)	39,957 (20.5)	8,093 (25.8)
5-ASAs	89,987 (47.7)	135,800 (69.6)	20,190 (64.3)
Corticosteroids	111,010 (58.8)	120,913 (62.0)	20,397 (65.0)

* Pediatric is defined as patients between 0–18 years old.

** Patients were classified under the insurance plan of their first UC or CD diagnosis.

*** HMO/Cap Place of Service are capitated plans. All other plans are non-capitated.