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Title

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Permalink

Journal

ISSN

Authors

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Publication Date

DOI

Peer reviewed

Original Research

An evaluation of health care expenditures in Crohn's disease using the United States Medical Expenditure Panel Survey from 2003 to 2013

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Abstract

Background: Previous estimates of the economic burden of Crohn's disease (CD) varied widely from $2.0 to $18.2 billion per year (adjusted to 2015 $US). However, these estimates do not reflect recent changes in pharmaceutical treatment options and guidelines.

Objective: The goal of this study was to update cost estimates of Crohn's disease based on a representative sample of the US population from the most recent 11 years (2003–2013) of the Medical Expenditure Panel Survey (MEPS). A secondary aim described expenditure trends in respondents with and without Crohn's disease pre-post FDA approvals of new biologics and the American College of Gastroenterology Crohn's disease treatment guidelines.

Methods: Average annual expenditures (total, prescription, inpatient, and outpatient) were evaluated using a pooled cross-sectional design. Respondent data from the most recent 11 years (2003–2013) of MEPS were analyzed. Two-part generalized linear models with power-link were used to estimate the average annual expenditures per patient adjusted to multiple covariates. Confidence intervals (CI) were estimated using bootstrap methods. Difference-in-differences estimations were performed to compare the changes in health care expenditures pre-post FDA approvals of new biologics and the American College of Gastroenterology Crohn's disease treatment guidelines.

Results: The annual aggregate economic burden of CD was $6.3 billion in the US. Respondents with CD had higher total (+$6442; 95% CI: 4864 to 8297), prescription (+$3283; 95% CI: 2289 to 4445), inpatient (+$1764; 95% CI: 748 to 3551), and outpatient (+$1191; 95% CI: 592 to 2160) expenditures compared to respondents without CD. In the difference-in-differences estimation, respondents with CD had significantly higher total ($P = 0.001$) and prescription ($P < 0.001$) expenditures compared with respondents without CD. Although inpatient and outpatient expenditures were higher in respondents with CD, they were not statistically significant.

Conclusions: Respondents with CD diagnosis had higher expenditures compared to respondents without CD diagnosis from 2003 to 2013. This study captured the most recent availability of new treatment options and changes to treatment guidelines, while providing updated estimates of the economic burden of CD in

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the US. However, this research was unable to study the causes of these increased health care expenditures in respondents with CD. Future investigations will need to determine the causal factors for increased expenditures in CD.

Introduction

Crohn's disease is an inflammatory bowel disease of the gastrointestinal tract characterized by abdominal pain, bleeding, diarrhea, fever, flares, weight loss, and fistulas.[1] Prevalence of Crohn's disease in the United States (US) ranges from 26 to 201 cases per 100,000 population[2,3]; with an incidence rate ranging between 3.1 and 14.6 cases per 100,000 person-years.[2] Medical intervention, which has been effective at inducing and maintaining remission, is the primary treatment option for most patients with Crohn's disease.[1] Despite this, severe forms of the disease may require invasive surgery where resection of the colon (e.g., ileocolectomy and right colectomy) is common.

The economic burden of Crohn's disease has been estimated anywhere between $2.0 to $18.2 billion per year or $11,898 to $23,014 per patient with Crohn's disease (adjusted to 2015 $US).[4–7] However, these estimates were based on claims data and not representative of the US population. Gunnarsson and colleagues remedied this problem by evaluating the pooled Medical Expenditure Panel Survey data from 1996 to 2009, a nationally representative population derived from the National Health Information Survey.[8] They reported that the average annual cost was $10,354 per patient with Crohn's disease, with a US national aggregate annual expenditure of $2.5 billion per year (adjusted to 2015 $US).

Recent advances in pharmaceutical treatments have improved disease management and quality of life in patients with Crohn's disease.[9,10] In 2008, the Food and Drug Administration (FDA) approved two self-injectable biologics (adalimumab and certolizumab pegol) for treatment of moderate to severe Crohn's disease. Recently, in 2012, the FDA approved vedolizumab for a similar indication. Previous estimations of the economic burden of Crohn's disease have not captured the recent FDA approval, which likely impacted health care expenditures for patients with Crohn's disease. Additionally, the American College of Gastroenterology released guidelines in 2009 endorsing the use of self-injectable biologics for the treatment of moderate to severe Crohn's disease.[1] This combination of FDA approvals and prescribing practice changes have contributed to a different landscape of Crohn's disease expenditure in the last few years.[1]

The purpose of this study was to quantify the current economic burden of Crohn's disease using a nationally representative sample from 2003 to 2013 of the US that incorporates the recent FDA approvals and changes in practice endorsed by the American College of Gastroenterology. A secondary objective was to measure the trends in health care expenditure patterns to demonstrate the impact of FDA approvals and practice changes from 2003 to 2013.

Methods

Design

Health care expenditures (total, prescription, inpatient, and outpatient) for Crohn's disease were evaluated using a pooled cross-sectional design based on a representative sample of the noninstitutionalized US population from 2003 to 2013. The pooled dataset provides longitudinal assessment of a nationally representative sample.

Sample

Respondent data based on the most recent 11 years (2003–2013) from the Medical Expenditure Panel Survey (MEPS) were pooled to answer the research objectives.[11] The pooled survey set comes from the subsample of the National Health Interview Survey households and provides a nationally representative sample of the noninstitutionalized US population. The consolidated MEPS Household Component files contain information on health care expenditures, demographics, socioeconomic characteristics, insurance information, employment information, health status, and

satisfaction with health care. Yo identify patients with Crohn's disease, the MEPS Medical Condition files were merged using a unique patient identifier to the MEPS Household Component.

Patient demographics for each year were collected and included age, race, body mass index category (underweight, normal, overweight, and obese), physical activity (defined as spending an half hour or more in moderate to vigorous physical activity at least five times a week), perceived health status (poor, fair, good, very good, and excellent), insurance status (uninsured, public only, and any private), diabetes (yes/no), current smoking status (yes/no), poverty status (poor/negative, near poor, low income, middle income, and high income), region (Northeast, Midwest, South, and West). Poverty status was categorized based on the federal poverty level: negative or poor (less than 100%), near poor (100% to less than 125%), low income (125% to less than 200%), middle income (200% to less than 400%), and high income (greater than or equal to 400%). Baseline Charlson comorbidity index (CCI) was calculated based on the modifications developed by Quan and colleagues.[12]

Dependent variables

The outcomes of interest were total expenditures, prescription drug expenditures, inpatient expenditures and outpatient expenditures. Total expenditures captured all payments related to health care services (direct payments, out-of-pocket payments, and insurance payments). Total prescription drug expenditures included all amounts paid by patients (out-of-pocket) and insurance payers for prescription drugs. Expenditures for over-the-counter medications were not recorded by MEPS. Inpatient expenditures included all expenses for direct hospital care (room, board, diagnostic and laboratory work, and imaging); provider services were not included in hospital bills (e.g., anesthesiologists, radiologists, and other specialists). Outpatient expenditures included all provider visits (physician and non-physician) in the ambulatory setting. All expenditures were adjusted for inflation using the Consumer Price Index to reflects costs in 2015 $US.

Statistical analysis

Baseline characteristics were compared across respondents diagnosed with Crohn's disease and respondents not diagnosed with Crohn's disease using *t*-test for continuous variables and chi-square test for categorical variables. Means and standard errors (SE) were presented for continuous data and frequency and proportions were presented for discrete data.

To generate estimates of health care expenditures that would be generalizable to the US population, designated MEPS survey weights were applied.[13] Further, potential confounding covariates were controlled for by constructing multiple regression models that produced valid estimates for the association between health care expenditures (dependent variable) and a diagnosis of Crohn's disease (main predictor of interest). Covariates were selected based on the Anderson–Newman conceptual model of social determinants of health care utilization.[14] Selected covariates included age, race, body mass index category, physical activity, perceived health status, insurance status, CCI, current smoking status, poverty status, and region. Only subjects with complete data were incorporated into the regression models.

The analysis employed a two-part generalized linear model (GLM) to address the large proportion of patients incurring zero health care expenditures.[15,16] The first part estimated the likelihood of having nonzero health care expenditures using a logit model. The second part used a GLM, with power-link and gamma distribution to estimate the association between Crohn's disease and the various health care expenditures, conditioned on whether the respondent had nonzero health care expenditures.[17] The analysis included calculation of 95% confidence intervals from 1000 bootstrapped samples using the method of recycled predictions.[18] Model specification was assessed with Pearson correlations between residuals and predicted expenditures and Hosmer–Lemeshow goodness-of-fit tests.

Annual mean health care expenditures prepost FDA approvals of new biologics and the American College of Gastroenterology Crohn's disease treatment guidelines were compared using difference-in-differences estimation based on linear regression.[19] The analysis also described trends in annual health care expenditures for respondents with Crohn's disease and respondents without Crohn's disease from 2003 to 2013 using fractional polynomial fits.

Statistical significance was set at an α of < 0.05. All analyses were performed using STATA SE 13 (College Station, Texas).

Table 1
Baseline characteristics of respondents with and without Crohn's disease in the US population, 2003–2013

Variables	CD group ($N = 522{,}064$)	Non-CD group ($N = 277{,}716{,}457$)	*P*-value
Age (years), mean (SE)	47.27 (1.41)	38.42 (0.16)	<0.0001
Male, *n* (%)	211,671 (40.55%)	130,592,850 (47.03%)	0.0886
Race, *n* (%)			
White	481,678 (92.26%)	226,474,653 (81.55%)	<0.0001
Black	35,121 (6.73%)	31,595,583 (11.38%)	
Other	5265 (1.01%)	19,646,221 (7.07%)	
Weight category, *n* (%)			
Underweight	25,301 (4.85%)	3,941,455 (1.42%)	<0.0001
Normal	212,602 (40.72%)	70,877,302 (25.52%)	
Overweight	145,355 (27.84%)	70,951,810 (25.55%)	
Obesity	118,642 (22.73%)	60,994,045 (21.96%)	
Missing	20,164 (3.86%)	70,951,845 (25.55%)	
Physical activity, *n* (%)			
Yes	243,659 (46.67%)	114,757,005 (34.22%)	<0.0001
No	256,943 (49.22%)	95,036,410 (41.32%)	
Missing	21,461 (4.11%)	67,923,042 (24.46%)	
Health status, *n* (%)			
Poor	74,671 (14.30%)	8,272,989 (2.98%)	<0.0001
Fair	115,833 (22.19%)	24,647,137 (8.87%)	
Good	195,123 (37.38%)	72,592,339 (26.14%)	
Very good	109,712 (20.02%)	89,895,907 (32.37%)	
Excellent	25,176 (4.82%)	79,202,998 (28.52%)	
Missing	1550 (0.003%)	3,105,086 (1.12%)	
Insurance, *n* (%)			
Uninsured	39,270 (7.52%)	28,213,176 (10.16%)	0.0267
Public	77,814 (14.91%)	57,975,737 (20.88%)	
Private	404,980 (77.57%)	191,527,544 (68.97%)	
Smoker, *n* (%)			
Yes	88,691 (16.99%)	37,653,405 (13.56%)	<0.0001
No	388,405 (74.40%)	158,069,816 (56.92%)	
Missing	44,968 (8.61%)	81,993,236 (29.52%)	
Poverty status, *n* (%)			
Poor/negative	66,409 (12.72%)	36,328,317 (13.08%)	0.3236
Near poor	8280 (1.59%)	12,504,983 (4.50%)	
Low income	72,077 (13.81%)	37,597,400 (13.54%)	
Middle income	162,556 (31.11%)	84,483,189 (30.42%)	
High income	212,742 (40.75%)	106,802,568 (38.46%)	
Charlson comorbidity index, mean (SE)	0.53 (0.08)	0.36 (0.004)	0.0393
Region, *n* (%)			
Northeast	114,594 (21.95%)	50,029,850 (18.01%)	0.0312
Midwest	159,799 (30.61%)	62,512,778 (22.51%)	
South	140,729 (26.96%)	99,830,752 (35.95%)	
West	105,393 (20.19%)	63,086,583 (22.72%)	
Missing	1550 (0.30%)	2,256,494 (0.81%)	

CD, Crohn's disease.
SE, standard error.

Results

The survey-weighted set contained an annual average population of 277,716,457 in the US. Of these, there was an annual average of 552,064 (0.2%) respondents with a diagnosis of Crohn's disease (Table 1). The Crohn's disease population was on average older (47 versus 38 years old), more likely to be white (92% versus 82%), had poor health (14% versus 3%), more likely to be normal and underweight (46% versus 27%), more likely to be physically active (47% versus 34%), be privately insured (78% versus 69%), and experienced more comorbidities (CCI of

Table 2
Adjusted average annual health care expenditures per patient with and without Crohn's disease in the US population, 2003–2013

Expenditures[a]	CD group (N = 522,064)	Non-CD group (N = 277,716,457)	Difference
Total, mean (95% CI)	$12,084 ($10,460, $13,933)	$5641 ($5551, $5729)	$6442 ($4864, $8297)
Prescription, mean (95% CI)	$4624 ($3637, $5795)	$1342 ($1305, $1396)	$3283 ($2289, $4445)
Inpatient, mean (95% CI)	$3314 ($2301, $5150)	$1549 ($1500, $1598)	$1764 ($748, $3551)
Outpatient, mean (95% CI)	$1647 ($1049, $2617)	$456 ($441, $472)	$1191 ($592, $2160)

CD, Crohn's disease.
CI, confidence interval.
[a] Results from two-part generalized linear models controlling for baseline factors with 95% CI from 1000 bootstrapped samples.

0.53 versus 0.36) compared to respondents who did not have Crohn's disease. Distribution across the US regions was different between respondents (P = 0.03). Respondents with Crohn's disease were mostly in the Midwest (31%), followed by the South (27%), Northeast (22%), and West (20%). Respondents without Crohn's disease were mostly in the South (36%), followed by the West (23%), Midwest (23%), and Northeast (18%). Both respondents with and without Crohn's disease reported having equivalent distribution across poverty status (P = 0.32).

Health care expenditures

The US national annual aggregate total cost estimates in individuals with Crohn's disease was approximately $6.3 billion dollars per year. Of this, prescription expenditures represented $2.4 billion, inpatient expenditures represented $1.7 billion, and outpatient expenditures represented $0.9 billion per year.

Overall, Crohn's disease respondents had higher expenditures compared to non-Crohn's disease respondents (Table 2). Adjusted annual total health care expenditures for Crohn's disease respondents were higher compared to the rest of the US population ($12,084 versus $5641) after adjusting for baseline factors. Crohn's disease respondents had higher adjusted annual prescription ($4624 versus $1342), inpatient ($3314 versus $1549), and outpatient ($1647 versus $456) expenditures compared to the rest of the US population. Confidence limits for all expenditures did not overlap.

Difference-in-differences estimation for health care expenditures

Respondents with a diagnosis of Crohn's disease had a higher increase in total expenditures from baseline (+$4778) compared to respondents without a diagnosis of Crohn's disease (Table 3, P = 0.001). Similarly, prescription expenditures increase from baseline was greater for respondents with Crohn's disease (+$4371) compared to respondents without Crohn's disease (P < 0.001). Although outpatient expenditure had a greater increase from baseline for respondents with Crohn's disease compared to respondents without Crohn's disease (+$122), this was not statistically significant (P = 0.657). In contrast, respondents with Crohn's disease had a higher reduction in inpatient expenditures compared to non-respondents (-$423), but this result was non-significant (P = 0.669).

From 2003 to 2013, total, prescription, and outpatient expenditures increased for respondents with Crohn's disease pre-post the FDA approvals of new biologics and the American College of Gastroenterology guideline updates (Fig. 1). In contrast, inpatient expenditures increased only to drop steeply over time. Unlike respondents with Crohn's disease, health care expenditures for respondents without Crohn's disease remained relatively stable from 2003 to 2013.

Discussion

There is a wide variation in the economic burden of Crohn's disease on the US population. The present study reports that the US aggregate total economic burden for Crohn's disease was $6.3 billion annually, which is higher compared to a previous report of $2.0–3.6 billion (adjusted to 2015 $US)[4]; and lower compared to a different report that estimated the total direct costs of Crohn's disease as $12.8 to $18.2 billion (adjusted to 2015 $US)[7] It also reports total expenditures per patient per year as $12,542 which was lower compared to previous estimates of $17,500[4] to $24,500[5]; and higher compared to a previous

Table 3
Difference-in-differences estimation before and after the index date

Outcome variable	Baseline			Follow-up			Difference-in-differences"	P-value[a]
	Non-CD group	CD group	Difference	Non-CD group	CD group	Difference		
Total expenditures, mean (SE)	$5137 (247)	$8708 (1058)	$3571 (1033)	$4985 (250)	$13,333 (975)	$8349 (949)	$4778 (1402)	0.001
Prescription expenditures, mean (SE)	$867 (109)	$1783 (465)	$916 (454)	$829 (110)	$6115 (428)	$5287 (417)	$4371 (616)	<0.001
Outpatient expenditures, mean (SE)	$331 (49)	$946 (207)	$616 (202)	$297 (49)	$1035 (191)	$738 (186)	$122 (275)	0.657
Inpatient expenditures, mean (SE)	$3124 (174)	$4414 (746)	$1291 (729)	$3002 (176)	$3869 (688)	$868 (669)	−$423 (989)	0.669

CD, Crohn's disease.
SE, standard error.
[a] Difference-in-differences test based on linear regression.

estimate of $10,364.[20] Further, in the difference-in-differences estimations, total and prescription expenditures in respondents with Crohn's disease had a higher increase compared to respondents without Crohn's disease pre-post FDA approvals of new biologics and the American College of Gastroenterology Crohn's disease treatment guidelines.

The current study estimates differed from previous reports due to several reasons. Previous reports were limited to a claims database from a single payer[4] or integrated database based on a single year.[5] Restriction to a single payer may not be representative of the US population such as the uninsured and elderly. Moreover, limiting analysis to a single year failed to capture expenditure changes across time. Previously low estimates of disease burden were based on data from 1994 to 1995, which did not incorporate recent changes in pharmaceutical treatments and clinical guidelines.[5] By averaging the most recent 11 years using a representative sample of the US population, we improved the external validity of our findings and captured recent changes in pharmaceutical treatments and clinical guidelines. Additionally, the higher estimated aggregate economic burden reported by Yu and colleagues[7] included indirect costs, which accounted for 28% of total costs associated with Crohns's disease. Indirect costs, such as work productivity and externalities, are difficult to estimate due to methodological differences that yield inconsistent results.[21,22] We opted to not include indirect costs in order to focus on direct expenditures.

In previous literature, a large proportion of health care expenditures for Crohn's disease were historically due to inpatient expenses (e.g., surgical resection of colon). In a report by Gibson and colleagues, gastrointestinal surgery was associated with a large proportion of the costs compared to patients without surgery ($60,147 versus $15,698, $P < 0.01$) despite only occurring in 7.4% of the Crohn's disease population.[6] The introduction of infliximab in 1999 as the first tumor necrosis factor-alpha inhibitor for Crohn's disease, provided rapid and long term remission delaying or preventing surgical interventions. However, infliximab is delivered by infusion, which may have limited uptake of infliximab treatment as a standard of practice. In 2008, adalimumab and certolizumab pegol were approved by the FDA as the first self-injectable tumor necrosis factor-alpha inhibitors for Crohn's disease, thereby opening access to a convenient form of
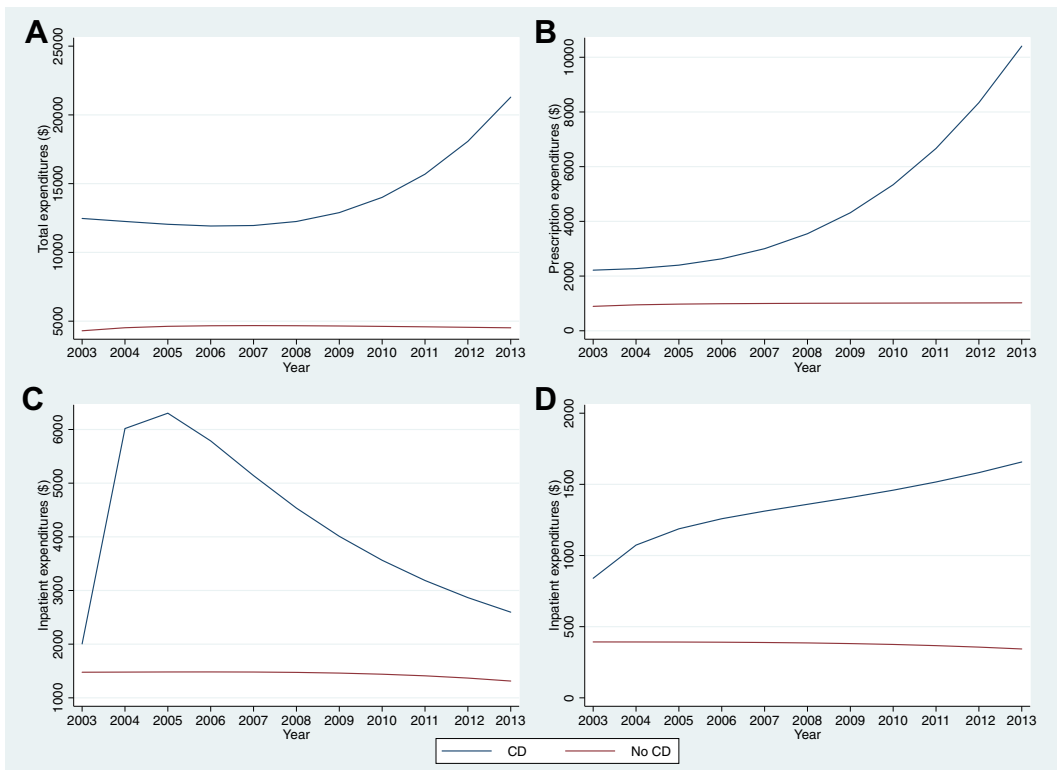
Fig. 1. Expenditure trends for respondents with and without Crohn's disease, 2003–2013. Total health care expenditures increased over time for respondents with Crohn's disease (A). Similar increases were reported for prescription expenditures (B). Inpatient expenditures increased but dropped steeply for respondents with Crohn's disease (C). Outpatient expenditures increased at a slower rate for respondents with Crohn's disease compared to total and prescription expenditures (D). Respondents without Crohn's disease had relatively stable expenditures from 2003 to 2013.

home-therapy without infusion. In recent years, health care expenditures have shifted from the inpatient setting to the prescription setting due to the improvements associated with the introduction of biologics into standard of care for Crohn's disease.[23]

This study found that prescription expenditure was a large proportion of the total expenditures for Crohn's disease (36%) followed by inpatient (25%), and outpatient (9%) expenditures. In contrast, Park and colleagues reported that inpatient expenditures represented a large proportion of total expenditures (36%) compared to prescriptions (8%) using MEPS data spanning from 1996 to 2011.[20] Similarly, Gibson and colleagues reported that inpatient expenditures represented 46% of total expenditures while prescription expenditures only represented 12%.[6] This appears reasonable given that costs may have shifted from inpatient to prescription expenditures due

to the introduction of biologics in recent years.[23,24] The current study used MEPS data from the most recent 11 years to capture recent changes in prescribing practices. Hence, our prescription expenditure estimates were larger compared to those reported using older MEPS data.

This study did not evaluate the relationship between health care expenditures and Crohn's disease severity, as the data were limited by the specificity of the ICD-9-CM codes, which were restricted to the first three digits. Therefore, stratification by small, large, and non-specified intestinal Crohn's disease was not possible. Different severities of Crohn's disease require different treatment strategies. For instance, a patient with moderate-to-severe Crohn's disease may be prescribed a costly biologic or immunosuppressant, whereas, a patient with mild-to-moderate disease may receive corticosteroids and

sulfasalazine. As such, determination the health care expenditures for different severity levels of Crohn's disease was not possible.

Additionally, it was not possible to determine the actual number of medications used from 2003 to 2013, which would provide further granularity for prescription drug utilization. The study used patient-reported prescription drug expenditures, which were not mapped to the actual prescription drug files. Future analysis will incorporate the MEPS prescription file to correlate the actual number of biologics, immunomodulators, steroids, and other prescription drugs related to Crohn's disease along with prescription drug expenditures. The introduction of adalimumab and certolizumab pegol in 2008 may have resulted in rising utilization as the demand for convenient administration of biologics increased, resulting in an increase in prescription expenditures over time.

Despite these limitations, the findings provided some important insight on the economic burden of Crohn's disease. Using the most recent 11 years of the MEPS data, this resrach captured recent updates in pharmaceutical availability and treatment guideline. It also estimated the economic burden of Crohn's disease using robust methods to account for the large proportion of patients with zero health care expenditure, which reduced biased estimations. Generalizability was maximized by using a national representative sample of the US population. In addition, the contrast between changes in expenditures from baseline was further captured by difference-in-differences estimations. Future investigations into the economic burden of Crohn's disease will need to focus on the association between drug utilization and expenditures over time including potential decreases in the number of surgical interventions to capture other meaningful dimensions for Crohn's disease treatment.

Conclusion

This study estimated that the US national aggregate economic burden of Crohn's disease was $6.3 billion dollars per year using the most recent 11 years of the MEPS data. Prescription expenditures make up an increasing proportion of total expenditures. By using the most recent 11 years of the MEPS data, this research addressed previous limitations in expenditure estimates by incorporating recent updates in pharmaceutical availability and treatment guideline. Future

investigations should evaluate the factors and benefits associated with prescription expenditure increase.

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