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Inflammatory bowel disease : cost-driving factors and the impact of different levels of cost sharing on health resource utilization

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Inflammatory Bowel Disease: Cost-Driving Factors and the Impact of Different Levels of Cost Sharing on Health Resource Utilization

by

Duy Vu Le

Submitted to the Graduate Faculty as partial fulfillment of the requirements for the

Master of Science Degree in

Pharmaceutical Sciences

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An Abstract of

Inflammatory Bowel Disease: Cost-driving Factors and the Impact of Different Levels of Cost Sharing on Outpatient Resource Utilization

by

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Objectives:

Inflammatory bowel disease (IBD) is chronic gastro-intestinal diseases with high annual cost per person. Appropriate outpatient care is crucial in reducing cost and improving patient outcomes in IBD. However, high cost sharing can force patients to forgo necessary outpatient treatments. This research aimed to (1) identify the cost-driving factors of health expenditure in IBD, (2) determine the effect of different cost-sharing levels on outpatient visits, and (3) determine the effect of different cost-sharing levels on medication adherence among patients with IBD.

Method:

This was a retrospective, longitudinal study in which data was collected from 1999 to 2013 using the Medical Expenditure Panel Survey (MEPS). The study sample included all patients who were identified with IBD in MEPS using International Classification of Diseases (ICD) 9 code of 555 and 556, were at least 18 years old, and had some type of insurance (public or private). To identify the cost-driving factors, a logistic regression

was used to determine which multiple baseline factors (age, gender, race, ethnicity, body mass index, education, insurance type, income, smoking, perceived quality of life, region and comorbidity) were significantly associated with higher expenditure in IBD. Appropriate regression models were used to determine whether cost sharing are associated with the number of outpatient visits and medication adherence (measured in term of Medication Possession Ratio). All values were weighted. Results were statistically significant if P-value < 0.05

Result / Discussion:

Significant cost-driving factors included age, body mass index, education, income level, quality of life, Charlson Comorbidity index, and region. The study also found that low outpatient cost-sharing associated significantly with high level of outpatient visits. However, low level of prescription cost-sharing also was not significantly associated with high level of medication adherence. The finding confirmed the existent of financial barriers to care among patients with IBD, which may lead to suboptimal outpatient care. In long term, patients with less outpatient care were at risk of having worsening diseases, higher inpatient use, and increased expenditure.

I dedicated this thesis to my major advisor, professors, family, friends, and colleagues who have been supporting me.

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List of Abbreviations

ACA .....Accountable Care Act

BMI.....Body Mass Index

CAPI .....Computer-Assisted Personal Interview
CCI.....Charlson Comorbidity Index
CD.....Crohn's Disease
CT .....Computed Tomography

ER .....Emergency Room

FPL.....Federal Poverty Line

HDHP.....High – Deductible Health Plan

IBD.....Inflammatory Bowel Disease
IBS .....Irritable Bowel Syndrome
ICD.....International Classification Disease

MEPS .....Medical Expenditure Panel Survey
MEPS-HC .....Medical Expenditure Panel Survey Household Component
MEPS-MC.....Medical Expenditure Panel Survey Medical Component
MPR .....Medication Possession Ratio

NAMCS .....National Ambulatory Medical Care Survey
NHIS .....National Health Interview Survey

PDC.....Proportional Day Covered

SF – 12v2 .....Short form – 12 volume 2
SF-12.....Short form – 12

TNF-a.....Tumor Necrosis Factor - alpha inhibitor

UC.....Ulcerative Colitis

List of Symbols

No symbol was used in this study

Chapter 1

Introduction

1.1 Background

Inflammatory bowel disease (IBD) is a group of chronic diseases characterized by the inflammation of the gastrointestinal lining tissues.[1] IBD is sometimes confused with another gastrointestinal disorder, irritable bowel syndrome (IBS), a condition that produces similar symptoms (i.e., abdominal pain or diarrhea).[2] Unlike IBD, IBS is not involved with any bowel inflammation and, therefore, does not lead to serious complications or interventions. Thus, it is important to distinguish IBD from other dysfunctional gastrointestinal disorders to provide proper management of IBD.

IBD contains two major diseases, ulcerative colitis (UC) and Crohn's Disease (CD), which are also chronic inflammatory conditions of the gastrointestinal lining due to the immune system.[4,5] Their clinical signs, symptoms, presentation, and treatments have many similarities. Both CD and UC typically have a chronic course of alternating periods of flaring and remission.[4,5] Flaring period is when the inflammation and other symptoms occur, while the remission period is marked with the inactivity of the disease.[4,5] Patients with either UC or CD can experience clinical symptoms of diarrhea, abdominal pain, weight loss, fever, and/or bloody stool.[4,5] Even though genetic, environmental, and

intestinal microbial factors have been reported to play a role in causing the auto-immune dysfunction, no definite etiology has been identified in both UC and CD.[4,5]

Despite many overlapping features, CD and UC still have many differences. Diagnosis and differentiation of IBD type (e.g. UC or CD) can still be done based on clinical signs, symptoms, erythrocyte sedimentation rate, blood test, X-rays, colonoscopy, endoscopy, computed tomography (CT), biopsy, and sometimes genetic testing.[4,5]UC is characterized by continuous inflammation limited to the colon with the hallmark of the bloody diarrhea.[5] Patient with UC are more likely to experience toxic megacolon, hemorrhage, or perforation as complications.[5] CD is characterized by interrupted inflammation that can occur on any part of the gastrointestinal tract.[4] Patients with CD can present with severe complications including extra-intestinal inflammation, abdominal obstruction, fistula, stricture, fissure, and malnutrition.[4] The clinical progression of IBD takes decades. In the preclinical phase, a person may experience "microscopic subclinical inflammation", but without clinical signs or symptoms.[6] In early clinical phase, the patient experiences clinical manifestations (intestinal and possible extra-intestinal).[6] Once the patient reaches the clinical phase, marked alterations of bowel structure and functions can lead to complications, disability, surgery, hospitalization, and rarely death.[6]

The therapeutic goal for IBD is to induce and maintain remission, and to improve the quality of life of patients.[4,5] Due to recent advances in IBD, mucosal healing (for UC) and intestinal healing (for CD) have been advocated as another goal.[6] Clinical guidelines have recommended treatment based on severity of UC or CD.[4,5] Anti-inflammatory drugs (amino-salicylates or corticosteroids) are often the first step to induce remission for mild-moderate or moderate-severe UC and CD.[4,5] Amino-salicylates or Immuno-suppressants

(azathioprine and mercaptopurine, methotrexate, cyclosporine) are used to maintain remission.[4,5] Injectable Tumor Necrosis Factor – alpha antagonist (TNF-a) can be employed to induce and/or maintain remission once other medications fail to do so.[4,5] Surgery is the last option, and it usually has its own risks.[4,5] Treatments are individualized based on types of IBD (i.e., UC or CD), tolerability, clinical symptoms, prior treatment, and inflamed location.[4,5]

Prior to TNF-a, the probability of patients with UC requiring surgery after 25 years varied from 20 – 30 %, while that of patient with CD requiring surgery after 20 years reached 70 – 80%.[7] Fortunately, the introduction of TNF-a and other immunosuppressive agents has led to reduction of hospitalization and surgery. Infliximab (a TNF-a) has shown to significantly decrease surgery and hospitalization for CD.[7] Patients on adalimumab (another TNF-a) also reduced hospitalization and surgery after the 1st year and in 2 years follow-up in CD.[7] Besides suppressing the inflammatory activities, the success key of these agents could be due to observed mucosal or intestinal healing. Both immune-suppressants and TNF-a have shown significant tissue healing in IBD.[7] This is significant because tissue healing has benefits such as fewer complications and relapses after surgery.[6] Therefore, the main point in treating IBD is to have appropriate diagnosis, monitoring, and treatments in outpatient setting.

1.2 Healthcare Cost of Inflammatory Bowel Disease and Its Cost-Driving Factors

The prevalence for IBD has been increasing in recent years, about 1.2 – 1.6 million affected patient (about 565,000 CD and 593,000 UC).[8,9] The annual cost per patient is about $10,000 for CD and $7,500 for UC. [10-12,14] Even though IBD has a

relatively small patient size when compared with other chronic diseases, such as diabetes, its high cost per person translates to a significant burden on the healthcare system. IBD's annual direct cost of burden is estimated to be about $ 6.7 billion. Additionally, the indirect-IBD cost (employee absenteeism) were estimated to be about $249 million in United States, using 2006's dollar value.[13]

Previous studies have identified several factors that associated with higher expenditure in IBD.[10,11,12] These factors include age, insurance status, income, BMI, gender, race, smoking status, and education.[10-12,14,15] For instances, oder age ($\geq$ 65), having public health insurance, low income, high BMI ($\geq$ 25), female, being Caucasian, currently smoking, or having a college degree have a higher risk of high health expenditure.[9-12,14,15] Identification of these factors is important because it provides payers necessary information to establish high-risk groups. That would lead to collaboration between payers and health providers to provide appropriate and timely managements in regard to patients' IBD. This collaboration, in turn, may decrease emergency room (ER) visit and hospitalization and, therefore, may decrease IBD-related expenditure.

1.3 Health Utilization in Inflammatory Bowel Disease and Cost Sharing

Due to the flaring and chronic nature of the diseases, patients with IBD are encouraged to make frequent visits to gastroenterologists, get endoscopic monitoring and lab works, and be adherent to complex medical regimen.[16] Thus, the utilization of outpatient care is essential. Due to IBD's expensiveness, access to necessary care and medications is also vital.[16] Unfortunately, prior research has shown the existence of disparities in healthcare access among patients with IBD.[16] Without appropriate

outpatient care, gastro-intestinal lining tissues will be irreversibly damaged leading to worse symptoms, complications, morbidity, and even mortality.[7] Lack of outpatient care may lead to higher rate of emergency visits and hospitalization.[16] Burden on emergency services and hospital also increases inpatient costs leading to higher health expenditure.[15]

Health coverage serves to increase access to necessary care for those who need care.[17] However, as health costs increase annually, different methods have been utilized to curb increasing health expenditure. High out-of-pocket payment, or cost sharing, has been introduced by policy makers, payers, and employers to reduce inappropriate use of medical services and engage patients into making cost-effective decisions.[17] However, high cost sharing can become a barrier to individuals who need adequate outpatient care.[17] In fact, a study showed Consumer-directed Health Plan (a tax-deductible, employer's contribution to employee's health benefit along with high-deductible health plan) resulted significantly higher hospital admission and no cost-saving compared to Point-Of-Service plan in a 3-year follow-up.[18] There are other studies that also looked at the impact of high cost-sharing plans and showed a reduction in use and expenditure of emergency services and hospitals, but they also found a decrease of outpatient use.[19,20] Additionally, the follow-up period of these studies was only 1 year while long-term effect was unknown.[19,20] Therefore, it is debatable that implementing cost sharing can result in cost-saving in the long term, especially in chronic, expensive diseases such as IBD.

Patients with IBD need adequate outpatient care to avoid preventive emergency visits, and non-elective hospitalization and surgery. High sharing costs, however, can discourage scheduled monitoring and specialist visits among IBD patients. Therefore, it

is essential to determine how different levels of cost sharing would affect health service utilization in IBD.

1.4 Need for Study

Cost sharing, in the form of co-pay and/or deductible, is an important factor that affects the decision of patients to whether seek necessary care.[17] While high cost sharing would discourage patients to seek unnecessary care to reduce health expenditure, high cost sharing can be a barrier of access to care for those who have chronic conditions and also struggle financially when seeking needed health services.[17] Multiple studies have looked at the effect of high cost sharing from High-deductible health plans on utilization and expenditure of outpatient and inpatient care, the results were mixed.[18,19,20] Additionally, most of these studies had a macroscopic examination by including all conditions.[18,19,20] There has been a gap in studying the impact of high cost sharing for a certain chronic condition or a group of closely related diseases, such as IBD.

IBD is a group of chronic conditions that require routine outpatient visits, multiple lab tests, and complex medication regimen to control the flaring symptoms and prevent complications.[4-7] Generally, outpatient care and outpatient medications accounted for 68.8% of CD's total expenditure and 62.4 % of UC's, or about $5.2 billion and $3.7 billion, respectively.[11] A study found annual out-of-pockets per person for CD and UC of a population with predominantly private insurance were about $800 and $400 in 2009, respectively.[11] High cost sharing can add more burden on IBD patients leading to less use of outpatient care and higher use of ER visits and hospitals. This would translate to higher expenditure and more burdens to inpatient facilities. There had not been a study

that looks at cost sharing and health resource utilization in IBD. Thus, it was essential to conduct a study that examines the effect of different cost sharing levels on outpatient utilization among patients with IBD.

Previous studies have shown that certain demographic characteristics of patients with IBD are associated with higher expenditure.[9-12,14,15] However, these studies used different databases and looked at different population groups. Also, previous studies examining health expenditure in IBD did not include all demographic factors. For instance, a German study which determined the cost-driving factors found some factors that were not included in other studies, such as body-mass index or smoking.[15] The purpose of identifying high-spending patients in IBD is to help payers to implement appropriate policies and adequate incentives in order to contain costs. Thus, there was a need of a study that determines a more comprehensive set of factors associating with higher expenditure in IBD.

IBD has shown to be costly.[9-12,14,15] As the prevalence of IBD increases,[9] research has shown that the rate of emergency visits and hospitalization with IBD as the primary cause also increases.[21,22] As a result, the soaring cost of IBD has become a bigger burden on our healthcare system, which has been increasing above the national economic growth.[23] There was a need in research to identify possible methods to contain IBD's costs. One possible solution is to have better access to appropriate outpatient care.[24] This study attempted to examine the effect of cost sharing on IBD patients' outpatient utilization, which had not been done previously. The study also looked at the effect of cost sharing on medication adherence in IBD because outpatient care is comprised of both outpatient visits and medication adherence. Additionally, this study looked at a more

comprehensive list of factors that were associated with high level of expenditure. This comprehensive list included patients' BMI, quality of life and co-morbidity, which was not done in the majority studies related to expenditure in IBD in United States.

1.5 Goal of The Study

To investigate the cost – driving factors of inflammatory bowel disease and the impact of different levels of cost sharing on the health resource among patients with inflammatory bowel disease.

1.6 Specific Aims

1. To identify the cost-associating factors of health expenditure in inflammatory bowel disease.
    - Alternate hypothesis: Factors (age, gender, race, ethnicity, body mass index (BMI), education, insurance type, income, smoking, region, health-related quality of life, and comorbidity) were significant predictors of higher expenditure in IBD.
    - Null hypothesis: Factors (age, gender, race, ethnicity, body mass index (BMI), education, insurance type, income, region, smoking, health-related quality of life, and comorbidity) were not significant predictors of higher expenditure in IBD.

2. To determine the effect of different cost-sharing levels on outpatient utilization in IBD. (*Outpatient visits include doctor-office and outpatient hospital visits*)
    - Alternate hypothesis: low cost sharing could lead to a high number of outpatient visits.
    - Null hypothesis: low cost sharing either decreases or did not affect the number of outpatient visits.
3. To determine the effect of different cost-sharing levels on medication adherence
    - Alternate hypothesis: low cost sharing associated with higher medication adherence.
    - Null hypothesis: low cost sharing associated with low medication adherence.

Chapter 2

Literature Review

This chapter will provide an overview of relevant topics related to the study. The chapter will also cover the literature review. The literature review section will include the following subtopics:

(1) Inflammatory Bowel Diseases

(2) Outpatient and inpatient utilization of Inflammatory Bowel Diseases

(3) Health Expenditure of Inflammatory Bowel Diseases

(4) Factors affecting expenditure of Inflammatory Bowel Diseases

(5) Cost Sharing

(6) Pattern of outpatient utilization with high cost sharing

(7) Summary

2.1 Inflammatory Bowel Disease

Inflammatory Bowel Disease (IBD) refers to a group of diseases caused by the inflammation of the gastro-intestinal tract (GI).[25] The two most common diseases of IBD are Ulcerative Colitis (UC) and Crohn's Disease (CD).[25] Both diseases are characterized by the alternating periods of flaring (active) or remission (inactive).[4,5] UC affects only the

colon and the mucosal lining.[5] Its most common symptom is bloody stool.[5] Patients with severe UC can experience perforation and hemorrhage.[5] CD affects any part of the gastro-intestinal tract and deeper layers of the lining tissue (i.e. muscular lining).[4] Even though patients with CD experience loose stool like UC, they are more likely to experience more severe symptoms and complications such as extra-intestinal inflammation, fissure (cut/tear), fistula (tunnel), malnutrition, and intestinal stricture.[4] Due to different clinical profiles, it is essential to differentiate and appropriately treat UC and CD.[7]

IBD is chronic disorders that manifest mostly in the second or third decades of life.[6] It has been widely known that IBD occurs due to the defection of one's auto-immune system.[6] The cause of this, however, is unknown. It is hypothesized that genetic, environmental, and microbial factors might play a role in the development of the defective immune system.[6] Whatever the cause might be, the consequence of IBD is irreversible and damaging.[6] After the immune system responds abnormally, patients with IBD start to experience symptoms.[6] When the tract's function and structure are altered, it will lead to surgery, complication, and disability.[6]

IBD is treated based on the severity of symptoms.[4,5,7] The goal is to induce and maintain remission.[4,5] For mild to moderate severity, anti-inflammatory agents (aminosalicylates and glucocorticoids) are the first line to induce remission; amino-salicylates and immune-suppressants (azathioprine, mercaptopurine, methotrexate, cyclosporine) are used to retain remission. For more severe cases, intravenous glucocorticoids or tumor necrosis alpha antagonists (TNF-a) are used to induce remission; and TNF-a can also retain remission.[4,5,7] The last option is surgery due to its

risks.[4,5,7] Unlike other chronic diseases, IBD has not had any big development for more than a decade.[7] TNF-a has been the last major development in IBD management, even though the first drug of TNF-a was approved for CD in 1998 and for UC in 2005.[7]

All patients with IBD need to have appropriately individualized regimens to control their diseases in the outpatient setting.[4-7] The majority of patients with IBD will have surgery.[7] Some patients with IBD will have to utilize emergency rooms (ER) and hospitals due to the flaring nature of their diseases.[7,26] However, some hospitalizations and ER visits can be prevented.[21,22] The unnecessary use of inpatient services does not only put more burden on these facilities, it also results in additional constraints on our health resources (i.e., expenditure). Therefore, it is important to examine the health resource utilization of patients with IBD and consider different methods to decrease their inpatient utilization.

2.2 Outpatient and Inpatient utilization of Inflammatory Bowel Disease

IBD is a chronic, inflammatory disease that can severely affects patients' quality of life, productivity, and physical health during the flaring period. Patients with IBD are required to make scheduled specialist visits, be adherent to their medications, and get constant monitoring.[6] *Nightingale et al* evaluated the changes in disease activity, hospitalization, quality of life, and patient satisfaction with a new specialist IBD nursing program in 2-year follow-up at a hospital.[27] The role of IBD nurse specialists was to improve education and provide support, continuous monitoring, and easier access to IBD patients.[27] After two years, the percentage of patient in remission increased from 63% to 69%, the total hospital bed-day decreased, and some of patient satisfaction scores

improved significantly.[27] However, the quality-of-life scores remained unchanged.[27] Even though hospitalization did not decrease in *Nightingale et al,* outpatient care still plays an important role in preventive readmission of recent admission in another study. *Allegretti et al* looked at factors associated with readmission within 90 days of a recent hospitalization in IBD for a period of 2 years.[28] It found that patients with either depression or pain were twice more likely to be readmitted to hospitals, and these factors can be modified by adequate outpatient care.[28] The disadvantages of these studies include short follow-up period and the lack of disease severity. However, these studies demonstrated that better outpatient care can prevent inpatient utilization.

Prescribed medications are an important part in IBD's treatment. Recent research has suggested another goal in treating IBD; that is mucosal or tissue healing, and this can be achieved by adequate outpatient medication regimen.[6,7] Tissue healing can result in fewer complication and fewer post-surgery relapses.[6] In *Loomes et al*, infliximab, a TNF-a, was evaluated in term of health utilization and expenditure of patients with CD (a major category of IBD).[29] The study followed 66 patients 2 years pre- and 2 years post introduction of infliximab; it found that there was a significant reduction in total hospital days, inpatient and outpatient colonoscopies, and major surgeries.[29] By inducing and maintaining remission, medications also improve patients' quality of life and productivity.[30] *Louis et al* studied the effectiveness of adalimumab (TNF-a) on quality of life and productivity in patient either naïve to TNF-a or non-responding to infliximab.[30] After 20 weeks, both types of patients achieved important clinical improvement using the Short Inflammatory Bowel Disease Questionnaire, and the productivity cost-savings were 3070 Euros for TNF-a naïve patients and 2059 Euros for infliximab-responding

patients.[30] Even though the time horizon were short, these studies are still prime examples of the importance of medications in treating IBD. Appropriate regimen and monitoring in outpatient setting may not only prevent unnecessary hospitalization or ER visits, they may improve patients' quality of life and productivity.

Due to the flaring activity and severity, a high portion of patients with IBD resort to the use of ER visits and hospitals.[6] As IBD's prevalence increases, the use of these services also increases.[7] *Ananthakrishman et al* looked at the trend in ambulatory and emergency visits in IBD from 1994 to 2005 using the National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey.[21] The study showed a significant increase of 165% in ER visits even though the rate of IBD's prevalent increase was not as proportionally high.[21] *A Nationwide Analysis In Severity And Outcomes of IBD Hospitalization* study also found that there was an un-proportional increase in low – and moderate – severity hospitalizations compared to the high-severity hospitalizations in 1998, 2004, and 2007.[22] While high-severity hospitalizations increased proportionally with the rise in IBD prevalence, the rate of increase of less severe, non-elective IBD was significantly higher than that of IBD prevalence.[22] The finding of this study is significant because it tried to classified the severity of IBD when admitted to hospitals, and only a few studies attempted to include severity. Even though these two studies only provide a cross-sectional information of hospitalizations due to IBD of each year, they still allow us to see an unfavorable trend of the unnecessary, possibly preventable utilization of inpatient care. Inpatient services are overloaded, additional burden can decrease the quality of care and increase expenditure.[27] Patients should be

encouraged to have adequate outpatient care to treat their IBD, promote healing and quality of life, and avoid inpatient services.

2.3 Health Expenditure of Inflammatory Bowel Diseases

As the prevalence and health utilization of IBD population increase,[8,9] the health expenditure of IBD would also increase. There were multiple studies examining the IBD expenditure. Even though they provide somewhat unequal sample sizes, these findings pointed out the expensiveness of IBD. Using PharmMetrics Database, *Kappelman et al* examined the direct expenditure of IBD in 2004.[10] The study determined the annual costs per capita were $8,265 for CD and $5,066 for UC.[10] The study also determined that 31 %, 33%, and 35% were attributable to hospitalization, outpatient care, and prescription in CD, respectively; and the corresponding distribution was 38%, 35% and 27% for UC.[10] This translated to the annual IBD-related expenditures of $3.6 billion for CD and $2.7 billion UC.[10] The advantage of this study was to gather a robust number of IBD patients using a commercial database. However, it fails to capture the costs of IBD in those with public insurances (only 1% of the population had Medicaid, and patients with Medicare was excluded).[10]

Another study, *Gunnarsson et al*, examined IBD-related expenditure using the Medical Expenditure Panel Survey (MEPS), a nationally public database from 1996 - 2009.[11] The study found that the insurers were likely to pay $2.04 billion for CD and $0.53 billion for UC annually. The annual costs were about $3.2 billion for CD and $0.92 billion for UC.[11] *Gunnarsson et al* also employed sensitivity analysis to reduce uncertainty and increase robustness of the results.[11] *Park et al* also studied IBD's

expenditure from 1996 to 2011 using MEPS.[12] Even though this study did not provide an annually cumulative cost, it confirmed the high annual IBD cost per capita, $10,364 for CD and $7,827 for UC. Additionally, it showed a significantly higher expenditure in patients using public insurance due to a significantly higher inpatient expenditure.[12] An advantage of this study over other expenditure studies was the employment of the Health-related quality of life comorbidity index as a measure of severity.[12] However, these two studies still had some weaknesses. The number of IBD subjects from MEPS was not as robust as that of the commercial databases; and these studies looked at the expenditure over 14 and 17 years without the consideration of TNF-a approval since 1999 and the implementation of Medicare part D in 2005.

Besides American studies, there are other international studies that examined IBD's expenditure. *Prenzler et al* found the annual cost per capita was EUR 3,767.26 for CD and EUR 2,477.72 for UC in 2007 (or about $5,200 and $3,400 using 2007 exchange rate, respectively).[15] The distribution of CD expenditure was 68.5 % for medication, 20.5% for inpatient, and 11% for outpatient; the corresponding distribution for UC was 74%, 10%, and 16%, respectively. Compared to the figures of *Kappelman et al*, Germany spent more on medications and outpatient care, and less inpatient care.[10,15] And the German annual costs for CD and UC per capita seemed to be lower than those in the United States.

A systematic review study, Rocchi et al, compiled IBD-related expenditure studies in Canada to provide a comprehensive view of the cost of burden of IBD.[31] the study determined an annual cost of $1.2 billion, with about 33%, 43%, and 24% attributed to inpatient care, prescriptions, and outpatient care, respectively.[31] This

distribution was similar to that in the United States.[10,31] While Canadian cost of burden may be less than American costs ($1.2 billion vs $6.3 billion),[10,31] Canadian estimated prevalence was less than that of the United States (233,000 vs 1,200,000).[10,31]

In summary, IBD is expensive. Even though it affects a small number of people, but its cost of burden is large.[10-12,15,31] Cost-containing methods are needed to decrease burden on the soaring cost of our healthcare system. One cost-containing method is to lower the inpatient expenditure by helping patients to avoid unnecessary emergency services.[21,22] This can be done by improving access and quality of outpatient care, which will also assist patients to have better control on the diseases and have better quality of life.[16]

2.4 Factors affecting expenditure of Inflammatory Bowel Diseases

While studying annual expenditure and annual per capita of IBD, several studies found that only a small number of IBD patients account for a large proportion of the total cost.[12,15] Thus, it is important to identify certain characteristics that associate with higher expenditure.

Kappelman et al identified age and region as significant factors of expenditure.[10] Using MEPS, *Gunnarsson et al* was able to incorporate more demographic factors into its study.[11] *Gunnarsson et al* identified age, gender, education, income, type of health insurance, and comorbidity as significant factors.[11] Also using MEPS, *Park et al* found income and type of health insurance as significant factors of IBD-related expenditure.[12] Whereas *Kappelman et al* was able to gather a big studied population, it lacked of many

demographic characteristics that help to identify risks for higher expenditure. Studies that used MEPS had more comprehensive demographic factors, but they lacked of a robust sample size and did not take into accounts of events affecting IBD's expenditure such as Medicare part D.

Prenzler et al also attempted to identify factors associated with higher IBD cost.[15] More severe diseases, age, gender, and body-mass index (BMI) were found to be cost-driving factors.[15] However, this study only examined German patients.[15] Its generalizability to American patients could be questionable.

The cost of IBD remains expensive as the prevalence of IBD increases.[6,8,21,22] It is important to identify high-cost-associating factors to form a high-risk group. The insurers can provide incentives and additional assistance to these high-risk patients in treating their IBD.

2.5 Cost Sharing

As the healthcare expenditure has been soaring at a faster rate than the national economic growth, this healthcare system becomes more unsustainable.[17] There have been many methods of cost containment. Switching to generic drugs, higher premium, or different care models (i.e., Preferred Provider Organization, Health Maintenance Organization) have not been successful at reigning in the healthcare costs.[17] Recently, high cost sharing has become a more popular strategy and promoted by health insurers.[17] Medical cost sharing is defined by the Healthcare Insurance Exchange as the amount that "you pay out of your own pocket"; it includes deductibles, copayments, and/or similar

charges without the premium.[32] Whereas high premiums can decrease patients' accessibility to health coverage, high cost sharing allows patients to buy health coverage with low premium.[33] However, high cost sharing can still discourage people to utilize health services like high-premium strategy.[23] The purpose of high cost sharing is to reduce cost of health care by allowing patients to play a bigger role in the decision-making process.[23] With high cost sharing, patients must make more cost-conscious choices.[23] While high cost sharing may have some cost-reducing effectiveness, the burden may fall on patients with low incomes, chronic diseases, or both.[33] About 20 % of private insurance have the deductible of $2,500 or higher, excluding copay at each visit.[23] Low-income patients may be forced to forgo necessary medical are to save money.[17] In short term, it may result in cost-saving; but the cost may exceed the saving amount in long term. This is due to uses of ER and hospital services for preventive causes.[17, 23] In a survey, 23% reported to possibly skip some needed medical care because of high out-of-pocket.[23] Thus, the implementation of high cost sharing should consider the possible implication of the policy.

The effect of high cost sharing is still questionable. While some can argue that it provides more choices to patients and can be cost-saving, others point out that high cost sharing can decrease patients' access to proper care.[17,23,33,34] Additionally, high cost sharing depends on patients to make good choices when using health care, but it fails to recognize patients' health knowledge to make correct decision.[17,35] Thus, it is important to conduct more research on high cost sharing to determine its effect.

2.6 Pattern of outpatient utilization with high cost sharing

2.6.1 Health utilization and high cost sharing

Multiple studies have looked at the impact of high cost sharing on outpatient and inpatient utilization, and outpatient and inpatient expenditures. However, the results have been mixed and remained inconclusive. One study, *Chandra et al,* examined the impact of copayment increases to Medicaid patients in Massachusetts, using the Common Wealth Health database.[36] The study did not find significant changes in medical (outpatient, ER, hospital, prescription) spending and utilization.[36] However, the study's follow-up was only one year after the change in copayment, so it was not possible to determine the long-term effects. Also examining the effect of high cost sharing, *Waters et al* looked at the enrollees of high-deductible health plan (HDHP) one year before and one year after the enrollment.[19] There was a significant decrease in the level of use in primary-care physicians, outpatient care, and ER; but there was a significantly increased use of prescriptions.[19] While it might seem beneficial that there was a decrease in expenditure, but the change was not significant.[19] The significantly decreased outpatient utilization could be interpreted as patients either making more cost-conscious choices or skipping their outpatient care.[19] Unfortunately, *Waters et al* could not report the effect of HDHP on inpatient care.[19]

Focusing only on inpatient utilization, *Wharam et al* compared a HDHP group to another matched traditional-insurance group for 1 year.[20] The study found that there was a significantly smaller number of ER visits among HDHP members, which was due to less subsequent ER visits after the first visit from HDHP members (a decrease of 24%,

p=0.002). Additionally, the ER-related hospital admissions were less in the HDHP group.[20] While the results showed a positive impact of high cost sharing, the study did not include outpatient utilization, and the follow-up period was only one year. Once again, the long-term effect was undetermined. The same authors decided to perform a 2-year, longitudinal study about the impact of HDHP on ER and hospitalization.[36] Even though the rate of non-emergent visits to the ER decreased significantly (-19.6% and -18.1% in year 1 and 2), the emergency visits to the ER did not change significantly.[36] *Wharam et al* also found that while hospitalization rates decreased in first year (-22.8%), hospitalization in second year remained unchanged (+1.9%).[36] Even though the study did not examine outpatient utilization, it showed the initial positive impact of high cost sharing on inpatient uses. However, as the study progressed, the positive impact of high cost sharing faded. If patients chose to skip outpatient care to save money, the trend of ER visits and hospitalization might have gone up in a longer follow-up period.

2.6.2 Prescriptions and high cost sharing

Besides affecting outpatient and inpatient care, high cost sharing can also impact the utilization of prescribed medications. *Colombi et al* examined three different levels of copayments (low, medium, and high) with medication adherence on oral diabetes medications.[37] The study found that low-copayment groups had higher medication adherence than high-copayment groups in both patients less than 65 years old and patients greater or equal to 65 years old.[37] Additionally, the total health expenditure for patients less than 65 years old was significantly less in the low-payment group.[37] Even

though the scope of this study was small – only investigating oral diabetes medications, it yielded significant findings.

Goldman et al is a systematic review that also examined the effect of cost sharing on prescription medications.[38] *Goldman et al* selected 132 studies and found that an increase of 10% in out-of-pocket could lead to a 2% decrease in medication utilization or expenditure.[38] The study also found some correlation between high copayment and increased use of inpatient care (i.e., hospital, ER visits).[38] *Kaisaeng et al* is another study that found a higher risk of delaying or discontinuing expensive oral cancer medications in beneficiaries over 65 years old with high out-of-pocket.[39] These study show that high cost sharing can be detrimental to sicker populations.

High cost sharing has been found to negatively impact medication adherence. *Kazerooni et al* found lower adherence of statins (measured as Medication Possession Ratio) in low-income groups with copayment (a MPR decrease of 0.05, $p < 0.05$) .[40] The risk of non-adherence was not found in patients with higher socioeconomic status.[40] In another study, lower cost sharing was found to be a predicting factors of adherence to oral diabetes medications.[41] In fact, major health insurers (Humana, WellPoint, and Aetna) reduced the cost sharing for preventive medications in hypertension, asthma, diabetes, asthma, stroke, osteoporosis, and other chronic diseases in order to improve medication adherence among chronically ill patients in 2013.[42] A patient whose prescriptions' cost sharing was waived saved about $500 annually compared to those with copayment.[39] It shows that cost sharing plays an important role in outpatient pharmacy care.

2.6.3 Conclusion on the role of cost sharing on health resource utilization

Overall, the conclusion for the impact of high cost sharing has not been reached. In some cases, high cost sharing can be productive, especially in a younger, healthier populations; but it can lead to worse health outcomes in other cases, such as older, chronically ill populations. However, some studies have shown the negative impacts of high cost sharing on patients who required adequate health care.[38-41] Unfortunately, there has been a gap in studying the impact of cost-sharing in one certain disease, especially a disease or a group of diseases with high cost per capita like IBD.

2.7 Summary

IBD is a chronic, inflammatory diseases that can lead to devastating symptoms during the flaring periods. Adequate outpatient care and appropriate medication regimen are required to maintain IBD patients' general being, functionality, and productivity. Without sufficient outpatient care, patients with IBD would rely on inpatient care. IBD already has a high per-capita cost, an increase of ER visits and hospitalization due to preventable causes will result in additional constraints on available health resources. Recently, high cost-sharing policy has been implemented to contain healthcare costs by making patients to be more cost-conscious in seeking care. However, it can make patients with IBD to forgo their outpatient care due to high out-of-pocket payments leading to an increase in inpatient utilization. Thus, it is important to examine the impact of high cost sharing on outpatient utilization and expenditure in IBD. Currently, no study has measured the extent of different levels of cost sharing on the characteristics of health utilization of patients with IBD. Additionally, prior studies provided different lists of

factors that associate with higher costs in patients with IBD. A more complete list of cost-driving factors will assist policy makers and payers to implement additional incentives and assistance to high-risk patients in order to help these patient avoiding ER visits and hospital admission. This study will study the cost-driving factors and the impact of different levels of cost sharing on patients with IBD.

Chapter 3

Methodology

This chapter will describe the methodology used in this study. The methodology is designed to achieve the objective and, therefore, the goal of the study. This chapter will cover the following topics:

(1) Study design

(2) Data source

(3) Patient inclusion/exclusion criteria

(4) Study definition

(5) Study variables

(6) Theoretical Model

(7) Data analysis

3.1 Study design

This was a retrospective, longitudinal study using a secondary database. Patient inclusion criteria were used to identify adults with IBD (either CD or UC) with a type of

insurance. Data collected from 1999 to 2013 in Medical Expenditure Panel Survey (MEPS), a secondary database, was used to identify patients with IBD for this study.

3.2 Data Source

The Medical Expenditure Panel Survey (MEPS) is a nationally representative survey which draws the civilian, non-institutionalized respondents from National Health Interview Survey (NHIS).[43] MEPS, created in 1996, collects information of individuals and families, their medical providers, and their employers.[43] The collected data includes respondents' demographics, health service uses, well-being, costs, and insurance.[43] MEPS is a publicly accessible by any one. MEPS has 3 major components – the Household component, the Medical Component, and the Insurance component.[43]

Since MEPS draws households from the samples of NHIS, it is important to understand the sample design of NHIS.[44] NHIS uses a "stratified, multistage probability cluster sampling design".[44] NHIS divided 50 states and District of Columbia into approximately 1,900 primary sample units, and each unit contains a county, a group of county, or a metropolitan area.[44] The first stage of sampling is to draw about 400 PSU.[44] In the second stage, area segments and permit segments are used to identify samples within a PSU.[44] In an area segment, an expected eight, twelve, or sixteen addresses are geographically chosen. In permit segments, an expected four addresses are chosen using the updated lists of building permits issued. Additionally, Asian, African American, Hispanic, and low-income populations are oversampled to have a better representation in the database.

The Household component of MEPS (MEPS-HC) collects information from each person in a household including demographics, health conditions, health status, health service uses, costs, sources of payment, employment, income, and access and satisfaction of care.[43] Information about each household member is collected using either paper or computer-assisted personal interview (CAPI). The data-collection process of MEPS-HC has the rotating panel sample design.[43] A panel of sample households is selected each year, and its data is collected over the next two and a-half years for the 2-year-worth of information.[43] The two-year data is broken down to 5 rounds of surveys (*see Figure 1*).[43] At the beginning of the second year of a panel, a new panel of sample households is started. This ensures the "continuous and current estimates of health care expenditures" in any calendar year.[43]

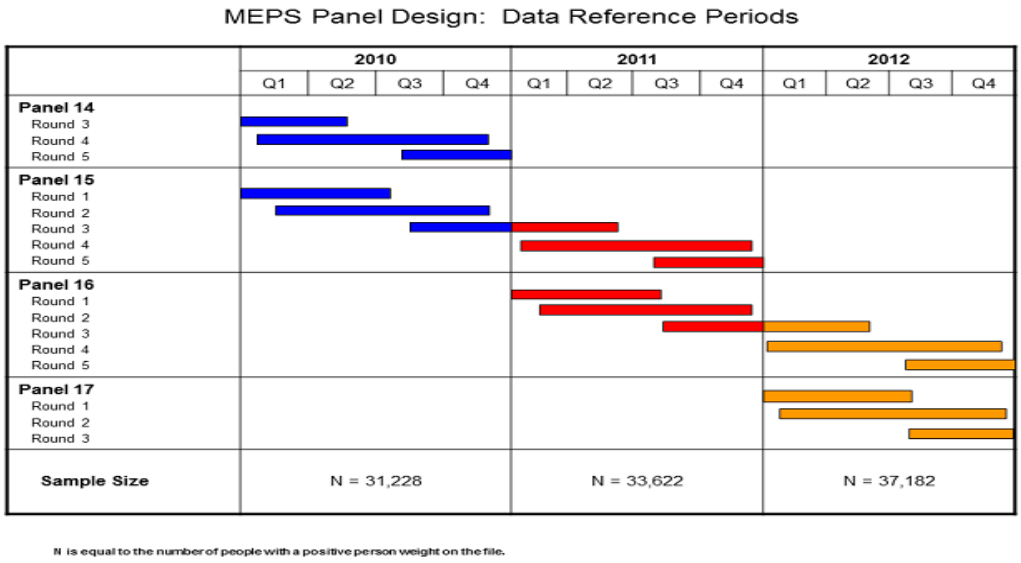


Figure 3.1: Rotating panel sample design of MEPS-HC (provided by MEPS website)

For example, Panel 15 starts to collect data of individuals and households at the beginning of January 2011 in Figure 1. It continues to collect data for round 2 in 2011 and collect data for round 3 past 2011. Panel 15 completes its subsequent data collection

process for round 3, 4 and 5 at the end of 2012. At the beginning of 2012, panel 16 starts its data collection for round 1 at the beginning of January 2012. Panel 16's data collection will last for 2 years and end at the end of 2013. The same strategy is followed each year.

Due to the wide, comprehensive range of questions, questionnaire modules are grouped into sections and administered in a skipped pattern.[43] That means not all of the questions are administered in one round; some questions are rotated. For example, the quality of life survey, SF-12, is administered in round 2 and 4. MEPS also included the medical component (MEPS-MC), which requests data from health institutions, medical providers, and pharmacies to supplement or replace the data received in MEPS-HC. MEPS-MC includes questionnaires in regard to medical and financial data for a medical events (i.e, doctor visits).

Approximately 13,000 households and more than 30,000 respondents are interviewed each year. The responding rate is about 50 – 78 % each year.[43]

3.3 Patient Inclusion/Exclusion criteria

3.3.1 Patient inclusion criteria

All respondents who had been diagnosed with IBD from the 1999 – 2013 MEPS data files with the age of 18 or above will be included in this study. Using International Classification of Diseases 9 (ICD-9) of 555 and 556,[10-12,45] patients with IBD were identified.

3.3.2 Patient exclusion criteria

Patients who were younger than 18 years old will be excluded. Those who reported as uninsured (i.e., having no public or private or any type of health insurance) were also be excluded.

3.4 Study Definition[46]

- Outpatient care: office-base medical visits, outpatient visits, and outpatient pharmacy
- Office-based clinics: non-institutional clinics in which physicians provide care.
- Outpatient clinics: institutional clinics in which patients receive care but stays in less than 24 hours.
- Inpatient care: emergency room visits and hospitalization.
- Emergency room (ER): the medical department in which patients can receive urgent care with no appointment needed.
- Hospital: an inpatient care facility in which medical staff (i.e., physicians, nurses, etc…) provide needed care for ill and injured patients, and where patients stay overnight.

3.5 Study Measures

3.5.1 Dependent Variables

a) <u>Expenditure and utilization</u>

Expenditure and number of visits were the dependent variables in objective 1 (expenditure only) and objective 2 (number of outpatient visits only). For objective 1, expenditure included the inpatient, outpatient, and prescription

charges. For both objective 2, the number of outpatient visits was comprised of both hospital outpatient visits and office-based visits.

b) Medication Adherence

For objective 3, medication adherence was the dependent variable. Medications play an important role in IBD as they facilitate remission and tissue healing. Medications are the main outpatient tool to control symptoms; being adherent, therefore, is important in preventing ER visits and hospitalization.[6,7] Medication adherence was the better way to measure how high cost sharing affects outpatient care in term of medications.

Two frequently used methods to measure medication adherence are Medication Possession Ratio (MPR) and Proportion of Days Covered (PDC). The majority of adherence formulas yielded the similar adherent rate.[47] However, since PDC is used to calculate adherence of smaller periods, and it tends to underestimate adherence, this study chose MPR.[47] MPR is the adherence measurement between the number of supply days the medication and the number of days within that period.[47] MPR was calculated by dividing the total supplied days by the sum of the number of days from first dispense to the date of last dispense and the number of supplied days at the last dispense.[47]

$$\text{MPR} = \frac{Total\ Rx\ days\ of\ supply}{\#\ of\ days\ in\ this\ period} = \frac{Total\ Rx\ days\ of\ supply}{last\ Rx\ date - first\ Rx\ date + last\ Rx\ days\ of\ supply}$$

Prior to 2010, MEPS did not provide the medication supply days. In order to estimate the supply days, a study used 2010 data to form a scheme that approximated the distribution of supply days for the data files of previous years.[48] This study broke down the number of dispensed quantity into different levels of approximated days of supply (i.e., dispensed quantity $\leq$ 60 meant 30 days of supply, or dispensed quantity of $\geq$ 60 and < 90 meant 60 supplied days, etc…).[48]

This study also used the similar approach to approximate the number of days supplied for data files prior to 2010. However, since same classes of medications used in IBD could have different administration frequency and routes, the approximate days of supplied were class-specific (i.e., supplied days of amino-salicylates $\leq$ 120 means 30 days of supply, while supplied days of azathioprine $\leq$ 60 means 30 days of supply). [48]

3.5.2 Independent Variables

a) Demographic variables

For all objectives, a more comprehensive list of factors based on prior studies were used to determine the cost-driving factors in IBD.[10-12,14,15] These factors included age, gender, race, ethnicity, body mass index (BMI), education, region, insurance type, income, smoking, health-related quality of life, and comorbidity.

- Age was taken as a continuous value.
- Gender was categorized into either male (1) or female (0).
- Race was categorized into either Black (0), White (1), and other (2).

- Ethnicity was divided into non-hispanic and Hispanics.
- BMI was classified into underweight (<18.5), normal (18.5-24.99), and overweight (> 25) according to the World Health Organization.[49]
- Education was classified as less than high school (0), high school degree (1), and more than high school (2).
- Insurance was either private or public. Public insurance contains Medicaid, Medicare, TriCare, or other public coverages offered by city or county governments. Private insurance is comprised of commercial plans.
- Income was classified based on federal poverty line (FPL) - low income (< 200 % FPL), middle income (200% - 500% FPL), and upper income (> 500% FPL) of 2013 after inflation adjustment.
- Smoking was classified as currently smoking or not.
- Region was divided into South, Northeast, West, and Midwest.
- Health-related quality of life was taken from the Survey Form 12 (or SF-12) given to each respondent in round 2 and round 4. The SF-12 has 2 components – the Mental Component and Physical Component.[43] The SF-12 is a shorter form of the SF-36 version, but it also has a high correlation with SF-36, which is a validated survey for quality of life.[50] Like SF-36, SF-12 measures 8 domains including physical functioning, physical limitations, bodily pain, general health perceptions, energy and vitality, social functioning, emotional problems and limitations, and mental health.[50] Both components have shown internal reliability and validity on Europe Quality-5 Dimension (EQ-5Q), a

validated quality of life survey.[51] The standard deviation of SF-12 was 10.[52] The average of SF-12 was calculated for the scores of both round 2 and 4. SF-12 was another continuous variable of this study.

- Comorbidity was calculated using the Charlson Comorbidity Index (CCI). CCI is a weighted method used to assess the mortality outcomes using the International Classification Diseases category.[53] CCI was the third continuous variable.

b) Cost sharing

For objective 2, cost sharing was an independent variable while all of the demographic variables (covariates) were controlled. Cost sharing was not a direct measure in MEPS, so it was calculated by dividing the out-of-pocket cost by the total expenditure (out-of-pocket and insurance payment) of outpatient visits (office-based and hospital outpatient visits) for each person.[54] The median of all cost-sharing values was calculated. The median was used as a cutoff point, patients who have cost sharing below the median are categorized as having low cost-sharing level, and those with cost sharing equal to or greater than the median are categorized as having high cost-sharing level.

For objective 3, cost sharing was calculated by dividing out-of-pocket by total cost of prescriptions of each patient. Using median as the cutoff, the cost-sharing values were then categorized as having either high or low prescription cost-sharing level.

The names of independent and dependent variables provided readily by MEPS are illustrated in appendix A. The questions included in SF-12v2 are shown in appendix B.

3.6 Theoretical Model

There are many Health Utilization and Behavior Models that help to explain the care-seeking behavior of a patient. These models act as a guide in a process of selecting significant factors that influence patients to seek care.[55] One of these widely known models is Andersen Health Service Utilization Model.[56] This model was developed by Andersen in 1968.[56] Its purpose is to combine the "individual and contextual determinants" of an individual leading to that person's care-seeking decision.[56] The model is comprised of three main constructs – predisposing factors, enabling factors, and need factors. Predisposing factors contain demographic, social/cultural, and health-related attitudinal characteristics that influence people's care-seeking behavior even before they are sick.[55,56] Demographic characteristics can include age, gender, married status, ethnicity, or culture. For instance, an older white male may be more likely to seek health services than a young, black male. Enabling factors are those that allow or facilitate people to utilize health services whether they are inclined to seek care or not. Enabling factors can include insurance, income, or even availability of health services.[55,56] For example, a person with low-income is probably less likely to seek care than a person with higher income. Need factors is the individual perception of whether getting care is necessary.[55,56] Need factors are often the most immediate ones that influence patients to utilize health services. Examples of need factors include well-being, newly diagnosed diseases, or when disease becomes more severe.[55] Together, these

factors help to indicate a patient's behavior in utilizing health services, as illustrated in picture 3-1.

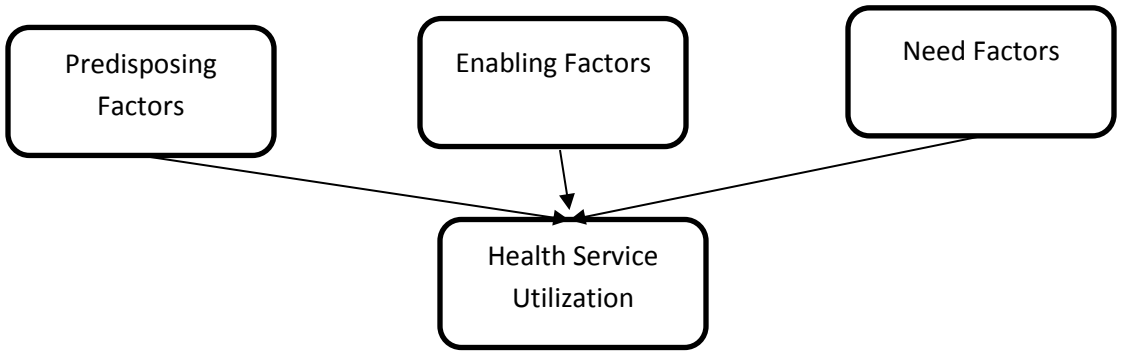
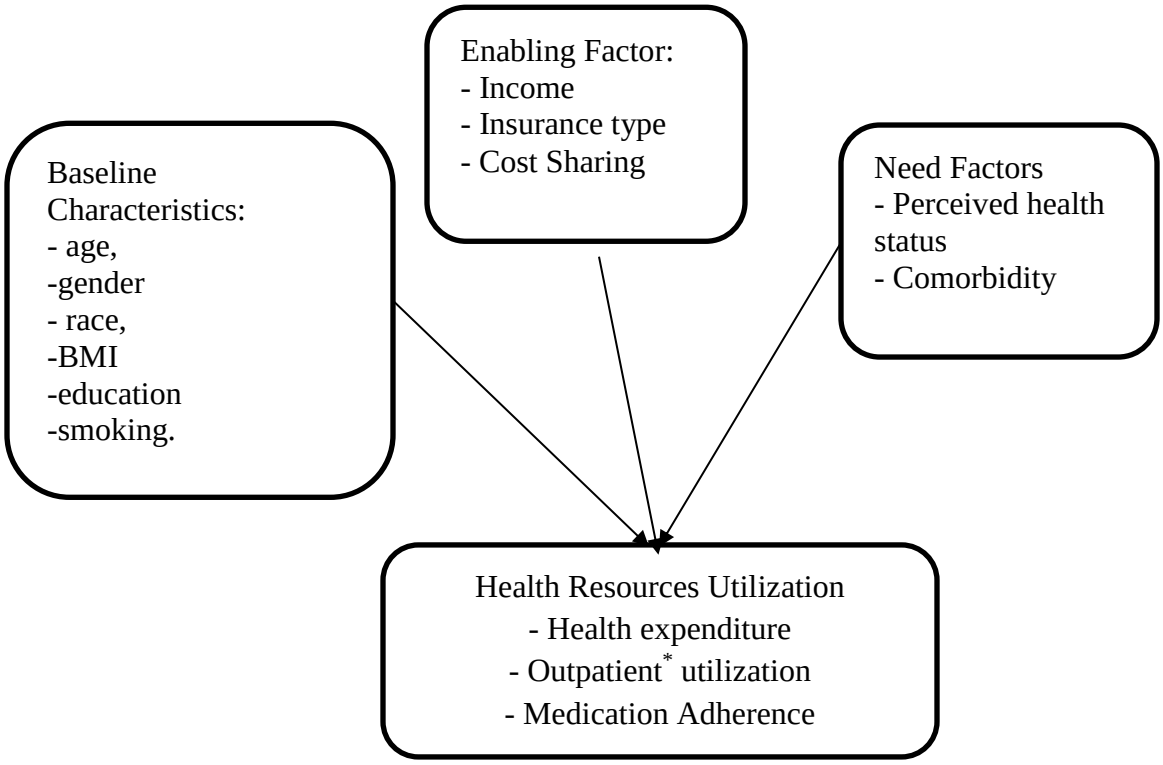


Figure 3.2: Andersen Health Services Utilization Model

In this study, health service utilization was expressed as total annual expenditure, number of outpatient visits, and medication adherence. The interest was to investigate the tendency of utilizing care of patients with IBD.

Based on previous studies, factors that influence expenditure in IBD include age, gender, race, ethnicity, body mass index (BMI), education, region, and smoking. These are baseline variables, and they also fitted the definition of predisposing factors of the Andersen Health Service Utilization Model. The need factors of the model would include the severity of symptoms and diseases. Because it was impossible to collect clinical data to determine the severity of the diseases from MEPS, the need factors in the study included only perceived health status and comorbidity. Since greater comorbidity and lower perceived quality of life could affect patients' welling being and tendency to use health service, this study decided to use perceived health status and comorbidity under the need factors.

Both income and insurance has been already defined by the Andersen model classified as enabling factors. Like income and insurance, cost sharing was a factor that also allowed patients to obtain services. For example, a person might decide to skip a treatment if the person could not afford the treatment due to high out-of-pocket payment. Thus, cost sharing fitted the definition of enabling factors. So, income, insurance, and cost sharing was included in the enabling construct. The applied Andersen Health Services Utilization Model is illustrated in figure 3-2:



* **outpatient include office-based and hospital outpatient visits**

Figure 3.3: Applied Andersen Health Services Utilization Model

3.7 Data Analysis

This study examined different types of health expenditures retrospectively from 1999 to 2013 in IBD, these expenditure figures were adjusted with inflation. Since the growth of health expenditure has been faster than the national economic growth, health-related expenditure, MEPS has recommended to use Personal Healthcare Index constructed by Centers of Medicare and Medicaid Services to adjust for health-related expenditures.[57] For instance, to express $1,000,000 of the 2000 health expenditure in 2012, $1000,000 is multiplied by a factor of 1.41 (106.8/75.7 – both are personal health indices from 2012 and 2000, respectively). Similar to health expenditure, prescription expenditures over the year were adjusted in the same manner, but the inflation factor was calculated using the Component Price Index for Prescription drugs.[57] The Personal Healthcare Index is shown in Appendix C.

Descriptive statistics were used to describe the studied population. For objective 1, a regression model will be used to determine factors associating with higher total annual expenditure; the dependent variable of total annual expenditure per capita was categorized as either “high” or “low” using the median as the cutoff. For objective 2, the regression model was used to determine the impact of different levels of cost sharing on outpatient visits, the dependent variable of outpatient visits was categorized as either “high” or “low” using the median as the cutoff. For objective 3, A regression model was used to determine whether high cost sharing associated with low adherence (expressed as MPR) using the median as the cutoff point.

Sub-group analysis was also conducted. The sub-group analysis examined the effect of cost sharing on the elderly in 2005 and after. The purpose was to examine the effect of the introduction of Medicare part D.

The complex survey design of MEPS was incorporated by using person-level weights for stratum, cluster, and individual persons to obtain unbiased national estimates. All statistic values were considered as significant as p-value $\leq$ 0.05. All statistical analyses were conducted using the SAS software (Version 9.3 SAS Institute Inc., Cary, NC, USA).

Chapter 4

Results

This chapter contains a description of the studied population and the results carried out by the statistical analysis.

(1) Patient population

(2) Baseline Characteristics

(3) Factors affecting health expenditure

(4) Factors affecting health expenditure

(5) Effect of Medical Cost Sharing on Outpatient Utilization

4.1 Patient Population

A total of 391 patients met the study criteria and were included in the data analysis. The selection of the patient population for the study is described in the Figure 3. There were 223,530 respondents in 14 longitudinal panels (years 1999 – 2012). Among these, only 447 respondents were identified to have diagnosis of IBD. Among these, about 56 patients were uninsured and were excluded from the study sample. The final study population included 391 patients with IBD and having either public or private health insurance.

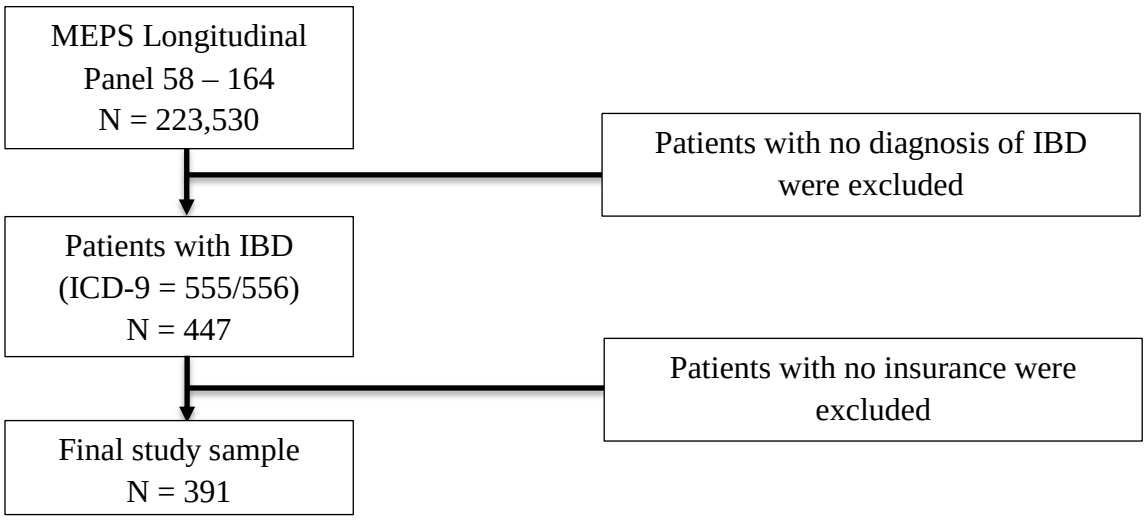


Figure 4.1: Selection process for the final study sample

4.2 Baseline characteristics:

The socio-demographic characteristics of the study population are summarized in Table 1. As shown in Table 1, assigning weights gave a number of 9,499,909 which represented a national cohort of patients with IBD who had some type of health insurance. The majority of the study population were females (N = 225, 57.8%), Caucasians (N=227, 75.3%), non-Hispanics (N=355, 96%), with a high school degree or higher (N=334, 88.6%), and with annual income of $23,000 or more, or greater than 200% of 2013 Federal Poverty Level, (N = 241, 70.3%). Additionally, those with private insurance (N=306, 84.7%), having normal or higher-than-normal weights (N=333, 86.6%), and non-smoking (N=289, 76.1%) also represented the majority of the sample. Patient with IBD tended to stay in the South (N=137, 32.7%) and the Mid-west (N=110, 28.2%). The average age of this sample was 47.6 years old. The average of SF-12 score

reported for quality of life was 42. Based on the diagnoses, the average CCI score was 0.85.

The mean cost sharing percentages were 16% for outpatient visits and 31% for prescription. When using ICD-9 code of 555 and 556 to select medications for IBD, MEPS not only provided medications used to treat IBD (i.e., mesalamine), but also included medications for conditions related to IBD, such as malnourishment or pain. The resulting mean of Medication Possession Ratio was 0.88 for this sample group. And the average of inflation-adjusted annual health expenditure was $14,357.

Baseline Characteristics	N = 391	Weighted, % (N = 9,949,909)
Age, mean (standard deviation – S.E.)	----	47.6 (0.74)
Gender		
Males	166	42.4
Race		
Caucasian	277	75.3
African American	28	3.9
Others	86	20.8
Ethnicity		
Hispanics	36	4.4
Education		
Less than high school	53	10.6
High school	109	21.6
More than high school	225	67.0
Health Insurance Type		
Private only	306	84.7
Annual Income level		
Less than $ 23.000	150	29.8
$ 23,000 – $ 57,500	153	40.3
More than $57,500	88	30.0
Body Mass Index		
Underweight (<19.5)	58	13.3
Normal (19.5 – 25)	142	38.2
Overweight (>25)	191	48.4
Smoking		
Yes	66	16.0
No	289	76.0
Don't know/Not sure	36	16.0
SF-12 score, mean (S.E.)	---	42 (14)
CCI, mean (S.D.)	---	0.85 (0.06)
Region		
Northeast	60	19.3
Midwest	110	28.2
South	137	32.7
West	74	18.4
Outpatient Cost Sharing %, mean (S.E.)	---	16 (1.3)
Number of outpatient visits (SE)	---	2.8 (0.05)
Prescription Cost Sharing %, mean (S.E.)	---	31 (1)
Medication Possession Ratio, mean (S.E.)	---	0.88 (0.05)
Total expenditure in dollars, mean (S.E.)	---	14,357 (3091)

Table 4.1: Demographic characteristics of the study population

4.3 Factors affecting health expenditure

The medium of annual expenditure was $6660, which was used as the cut-off point to categorize expenditure as either high or low. Using the high level of expenditure as the reference group, binary logistic regression was employed to determine which baseline factors significantly associate with the high expenditure among patients with IBD. Table 2 shows the results of the regression.

Gender, race, ethnicity, insurance type and smoking status did not show a significant association with high level of expenditure. Meanwhile, age, BMI, education, income level, quality of life (SF-12 score), CCI, and region were identified as significantly cost-driving factors. As age increased, it was less likely to belong in the high-expenditure group (OR 0.978; 95% CI, 0.961 - 0.995). Compared to overweight patients, underweight people did not significantly associate with high expenditure, but normal-weight people were 1.6 times more likely to have higher expenditure (95% CI, 1.065-2.43). There was no significant difference in the odd of having high expenditure between patients with associate/college degrees and with only high-school degrees. However, patients who did not graduate from high school were 2.67 times more likely to have high expenditure (95% CI, 1.33-5.36). Also, patients who had low income (< $23,000 per year) were 48% less likely to have high expenditure compared to people earning more than $23,000 annually (OR 0.516; 95% CI, 0.268-0.994). Even though higher SF-12 scores (indicating better quality of life) associated significantly with the high level of expenditure (OR 1.025; 95% CI, 1.003-1.047), the effect of the correlation was small (only 2.5%). Interestingly, having higher CCI score were 25% less likely to have high expenditure (OR 0.745; 95% CI: 0.617-0.899). Patients residing in Northeast

region were 67% less likely to have high cost than those staying the South (OR 0.33; 95% CI, 0.192-0.556). While other region were also less likely to have a high level of expenditure than the South, those results were not significant.

Category	Reference Group	Odd Ratio Estimate	95 % Confidence Interval	
			Lower	Upper
Age*	----	0.978	0.961	0.995
Gender				
Female	Male	0.687	0.471	1.002
Race				
Black	Caucasian	0.884	0.537	1.455
Other		1.156	0.710	1.882
Ethnicity				
Hispanics	Non-hispanics	1.459	0.897	2.374
Body mass Index				
Underweight	Overweight	0.978	0.466	2.09
Normal weight*		1.608	1.065	2.43
Education				
< high school*	High school	2.673	1.333	5.358
> high school		0.996	0.619	1.604
Insurance Type				
Public	Private	1.068	0.554	2.057
Income level				
<$23,000*	$23,000-$57000	0.516	0.268	0.994
>$57,000		0.708	0.416	1.206
Smoking Status				
No	Yes	0.735	0.446	1.211
SF-12 Score (Q.O.L)*	----	1.025	1.003	1.047
CCI*	----	0.745	0.617	0.899
Region				
Northeast*	South	0.33	0.192	0.566
Midwest		0.794	0.488	1.293
West		0.993	0.565	1.745

** Statistically Significant*

Table 4.2: Logistic Regression results to determine expenditure-driving factors

4.4 Effect of Medical Cost Sharing on Outpatient Utilization

The median of IBD-related outpatient visits was 1 visit per year, which was used as the cut-off to categorize either low or high level of outpatient visits. Meanwhile, the median cost sharing proportion for outpatient visits was 0.087, which was also used as the cut-off point for either low or high level of cost sharing. Using the high level of outpatient visits as the reference group, the logistic regression was utilized to determine whether different levels of cost sharing significantly associated with the levels of outpatient utilization. Table 3 shows the results of the regression.

Gender, education, insurance type, income level, smoking status, SF-12 scores, CCI, and region did not significantly associate with different levels of outpatient utilization for IBD. However, race, ethnicity, BMI, and cost sharing were significantly associated with outpatient resource uses. Both black and other races were 2.5 and 2 times, respectively, more likely to seek outpatient care for IBD than Caucasian (95% CI, 1.44 - 4.43 and 1.43 – 3.23, respectively). Interestingly, Hispanics were also more likely to seek outpatient care for IBD than non-Hispanics by 4.5 times (95% CI, 2.35-8.66). There was no difference between normal and overweight patients, but under-weight patients were 56% less likely to use outpatient care compared to overweight patients (0.434; 95% CI, 0.23-0.809). Compared to high outpatient cost sharing, patients with low cost sharing were three times more likely to make outpatient visits than patients with high cost sharing (OR 3.26; 95% CI, 1.87 – 5.7).

Category	Reference Group	Odd Ratio Estimate	95 % Confidence Interval	
			Lower	Upper
Age	----	1.011	0.998	1.024
Gender				
Female	Male	1.33	0.911	1.94
Race				
Black*	Caucasian	2.53	1.44	4.43
Other*		2.15	1.43	3.23
Ethnicity				
Hispanics*	Non-hispanics	4.52	2.35	8.66
Body mass Index				
Underweight*	Overweight	0.434	0.23	0.809
Normal weight		0.71	0.5	1.02
Education				
< high school	High school	0.786	0.367	1.68
> high school		0.904	0.6	1.37
Insurance Type				
Public	Private	1.4	0.787	2.5
Income level				
<$23,000	$23,000 - $57000	0.685	0.427	1.097
>$57,000		0.781	0.475	1.285
Smoking Status				
No	Yes	0.9	0.582	1.392
SF-12 Score (Q.O.L)	----	1.012	0.989	1.035
CCI	----	0.96	0.84	1.097
Region				
Northeast	South	0.718	0.448	1.153
Midwest		1.305	0.781	2.18
West		0.718	0.483	1.069
Outpatient Cost sharing				
Low*	High	3.26	1.87	5.7

** Statistically Significant*

Table 4.3: Logistic Regression results to determine factors affecting the level of outpatient utilization

4.5 Effect of Prescription Cost Sharing on Medication Adherence Among IBD Patients

The median of MPR of medications prescribed for IBD was 0.52, which was used as the cut-off point to categorize the level of medication adherence as either high or low. The median of medication cost sharing was 0.25; so 0.25 was used as a cut-off point as either high or low prescription cost sharing. Binary logistic regression was utilized to determine whether different levels of cost sharing significantly associated with the levels of medication adherence. High level of medication adherence was used as the reference group. Table 4 shows the results of the analysis.

The majority of the baseline characteristics were identified as non-significant factors. Only ethnicity and smoking status significantly associated with the level of medication adherence. Hispanics were 3.6 times more likely than non-Hispanics to be more adherent to IBD-related medications (95% CI, 1.8 – 7.34). Surprisingly, non-smokers were 0.48 times or 52% less likely to have high level of medication adherence for IBD-related prescriptions (95% CI, 0.29 – 0.79). In this analysis, even though patients with low prescription cost sharing level were 32 % less likely to be in the more adherent group than people with high cost sharing level, the finding was not significant (95% CI, 0.43-1.1).

Category	Reference Group	Odd Ratio Estimate	95 % Confidence Interval	
			Lower	Upper
Age	----	0.984	0.968	1.0
Gender				
Female	Male	1.019	0.734	1.416
Race				
Black	Caucasian	1.031	0.681	1.73
Other		1.144	0.683	1.913
Ethnicity				
Hispanics*	Non-hispanics	3.670	1.832	7.35
Body mass Index				
Underweight	Overweight	1.226	0.822	3.119
Normal weight		1.208	0.494	1.776
Education				
< high school	High school	1.161	0.493	2.746
> high school		0.748	0.480	1.176
Insurance Type				
Public	Private	1.13	0.622	2.06
Income level				
<$23,000	$23,000 - $57000	1.332	0.788	2.26
>$57,000		1.17	0.723	1.89
Smoking Status				
No*	Yes	0.479	0.29	0.79
SF-12 Score (Q.O.L)	----	1.006	0.978	1.035
CCI	----	1.087	0.931	1.268
Region				
Northeast	South	0.62	0.373	1.061
Midwest		0.847	0.499	1.431
West		1.170	0.658	2.07
Prescription Cost sharing				
Low	High	0.68	0.43	1.1

** Statistically Significant*

Table 4.4: Binary Logistic Regression results to determine factors affecting the level of medication adherence

Due to the time horizon of 14 years, this study also looked at the effect of cost sharing among patients with IBD who were older than 65 years old after Medicare Part D was implemented in 2005. Using 2005 as a cut-off point, there were 45 subjects who were identified as elderly ($\geq$ 65 years old) and had IBD. Compared to high level of cost sharing, older patients with low levels of cost sharing were 3 times more likely to be adherent to those with high cost sharing (OR 3.143; 95% CI, 2.5 – 3.9). The sample size of patients who were 65 years or older before 2005 was not sufficient for an analysis.

Chapter 5

Discussion

This chapter will discuss the results of the study, its implication, limitation, and future research in the following order:

(1) First objective: cost-driving factors among patients with IBD

(2) Second objective: the effect of outpatient cost sharing on number of IBD-related outpatient visits

(3) Third objective: the effect of prescription cost sharing on medication adherence

(4) Limitation

(5) Future research

5.1 First objective: cost-driving factors among patients with IBD

The majority of the sample were non-Hispanic Caucasians who had at least a high school degree, middle or upper income level, private insurance, normal or over weight, fairly distribution of gender, and non-smoking status. Most patients were from South and Midwest regions. The average SF-12 was 45, which was below the score of a normal person's SF-12 score of 50.[58] This population also had a low CCI (0.85) probably due to relatively young sample population (~47 years old). The prescription cost sharing was 31,

which was relatively high, but it might be because our data also included medications for IBD and for other conditions. The average expenditure, $14,357, was in line with the findings of previous studies.[10-12]

Age, BMI, education, income level, quality of life, CCI, and region were identified as significantly cost-driving factors among patients with IBD. As age decreased with IBD, the expenditure for these conditions was more likely to increase. One possible explanation was due to the natural course of IBD. The majority of diagnoses of Crohn's Disease and the peak of Ulcerative Colitis occur before the age of 40.[6,8] While IBD is expensive in general, stabilizing the diseases' flaring can be even more costly than remission maintenance leading to higher expenditure in patients less than 65 years old. Additionally, the finding of effect of age on the health expenditure is in line with *Prezler et al*, while *Kappelman et al* and *Gunnarson et al* reported different results.[10,11,15] This might have been because this study included BMI and disease severity, while *Kappelman et al* and *Gunnarson et al* did not.

In term of weight, normal weight was more likely to have higher expenditure than overweight. This finding contradicts with the results of *Prezler et al* in which higher BMI had higher spending.[15] However, BMI can be misleading because some people can still have high BMI if they have high muscle composition. Numerous sources have found that BMI might not be the best assessment of overweight or obesity.[59,60] Some have recommended waist circumference measurement.[59] In term of education, patients who did not graduate from high school also were 2.7 times more likely to have higher costs compared to those who graduated from high school or had higher degrees. Patients without high school degree were less educated and less able to take care of themselves.

These less educated patients were less likely to have good jobs, and, thus, IBD can be a heavier burden for them than for patients who graduated from high school, which could lead to worse disease states and higher expenditure. This finding is different from *Gunnarson et al*, which also used MEPS and found that older age, college degrees, or female would incur more costs to the insurers.[11] However, *Gunnarson et al* did not examine BMI, CCI, quality of life, and smoking as factors affecting IBD.

In term of income level, people with lower income were less like to spend for the diseases. While it is understandable that patients with low income would be less likely to spend on their conditions' treatments, it is actually alarming because this shows the existence of financial barriers to care among poor patients. Spending less may lead to worse disease states and higher expenditure and inpatient use in the long term.[33,34]

In term of SF-12 score, patients with higher quality of life were more like to have high expenditure. For those with IBD, more spending can result in better control of the diseases leading to better quality of life. However, the odd of having higher expenditure for having better quality of life was small (2.5%). Surprisingly, low CCI was less likely to incur high expenditure. Since younger age was associated with high expenditure, and young patients tended to have lower CCI scores, it might explain why low CCI was associated with low expenditure.

In term of geographic areas, patients residing in the South were significantly more likely to incur more cost than those in the Northeast region. The finding was similar to that of *Gunnarson et al* even though the result in *Gunnarson et al* was not significant.[11] This could be due to variation in pricing and different rate of utilization among the region. In this analysis, patients from the Northeast region were less likely to make

outpatient visits and be adherent to medication than the South. Even though these findings were not significant, but the trends might have reflected in significantly lower health expenditure of the Northeast when compared to the South.

5.2 Second objective: the effect of outpatient cost sharing on number of IBD-related outpatient visits

Race, ethnicity, BMI, and cost sharing were the factors that significantly affected the number of outpatient visits. In this sample population, both black and other races were more likely to make IBD-related outpatient visits. Hispanics with IBD were also more likely to make more outpatient visits than non-Hispanics. These racial and ethnic differences could be due to cultural differences. Only small percentages of patients with IBD were from these minority groups (3.9% black, 20% others, and 4.4% Hispanics). Since IBD is not common among minorities and has debilitating symptoms, these patients might be more likely to seek outpatient care than Caucasian patients. However, this result should not discard the possibility of ethnic and racial disparity in IBD, since this population only included those with some type of insurance.

Underweight patients were less likely to visit outpatient clinic. Without proper care, patients with IBD would have a high risk of being malnourished due to GI problems.[4,5,7] Thus, it was possible that patients who were underweight due to inadequate care (or low outpatient visits).

Patients with lower outpatient cost sharing were more likely make more IBD-related outpatient visits than those with high outpatient cost sharing. This finding shows that out-of-pocket payment played a significant role in patients' tendency in outpatient

utilization. This also means that patients who had higher out-of-pocket costs would have less outpatient care. In this study, out-of-pocket costs represented a financial barrier to care in IBD. This finding is consistent with prior research showing that high out-of-pocket costs would lead to a decrease of outpatient visits.[17,23,33,34] For IBD, this can be more troublesome because worse disease states can lead to increased hospitalization, poor patient outcomes, and increased costs.

5.3 Third objective: the effect of prescription cost sharing on IBD-related medication adherence

The study did not find significant association between demographic factors and medication adherence, except ethnicity and smoking status. In term of ethnicity, Hispanics were more likely to be adherent to non-Hispanics, which again could be due to cultural differences. In term of smoking status, smokers was more likely to be adherent than non-smokers. Previous studies have reported overuse of pain medications among smokers.[61] In this sample, some pain medications were included in the in the final analysis, and about 8% reported "refuse/don't know" for smoking. Additionally, smokers could have tried to be adherent to compensate for their smoking habit, since smoking has been known to negatively affect CD. These factors could have altered the true effect of smoking on medication adherence.

In term of cost sharing, the analysis did not show a significant correlation between different levels of cost sharing and medication adherence. These studies have identified younger age, female, college degrees, costs, and side effects.[62-65] Some of these studies only focused a certain drug class or were conducted on a smaller geographic scales. Our

result might also have been due to the study's relative small sample. Additionally, all medications used to calculate MPR included multivitamins and pain medications, beside medications used for IBD.

In a subgroup analysis, Medicare beneficiaries, who had IBD since 2005, with prescription low cost sharing had higher medication adherence than those with high cost sharing. This showed that high cost sharing might have significant negative impact on medication adherence, especially for patients who are in the donut hole. The finding is consistent with the results of prior research that examined the impact of the Part D coverage gap.[66]

5.4 Limitation

Like many other cost-sharing studies, this study had the longitudinal design. All numeric values were presented as the average over two years. This can be considered as a strength since it was more appropriate to study the effect of the cost sharing over the years. However, since this study's data was from MEPS, the following-up period was limited in only two years due to MEPS' panel design. IBD is chronic, so two years might not be long enough to see true impacts.

Another limitation was that data collected in MEPS were survey-based. So it was difficult to verify the accuracy of the data collection and data entry process. Other limitations of using a retrospective database included missing information, social desirability bias. However, many studies have used MEPS and deemed that the database has an acceptable quality.

The sample population was 391 patients. This small sample size could have affected the results. However, the weighted numbers represented a population of about 10 million patients. Due to the low prevalence of IBD (~1.2 millions), the study also used a 14-year time horizon. Multiple changes have occurred during these 14 years such as policy change and introduction of new medication. To limit the error, the study purposely chose to examine 1999 – 2013 because 1999 was the first year after TNF-alpha, a newest drug class, was approved by FDA for CD. While other medications were introduced during this period, most were just changes in the drug delivery system (i.e., Pentasa). Additionally, this study also tried to examine the effect of Medicare part D since it was a major public prescription-related policy change. It found that high cost sharing have a significant negative impact on medication adherence in those who were eligible for Medicare Part D.

Another limitation of this study was the lack of severity. IBD is treated by on clinical severity. Unfortunately, there has not been a database that provides both expenditure and clinical severity of these conditions in the U.S. This study used quality of life and CCI to measure the general health of patients with IBD, but these measures could not replace clinical severity of IBD.

5.5 Implications of the Findings and Future Studies

This study was one of a few IBD studies that examined a more comprehensive lists of cost-driving factors with a longitudinal design. It also included quality of life, CCI, and BMI. To the authors' knowledge, there has not been a study that included BMI

in the U.S. The study found that age, education, BMI, income level, quality of life, CCI, and region were significantly associated with health expenditure in IBD.

The study found that younger age, normal weight, no high school degree, low income, high quality of life, residing in the South region, and low CCI were significant cost-driving factors. However, high expenditure for both quality of life were justified because better quality of life would have cost-saving effects as patients would be less likely to seek inpatient care. The impact of BMI was not as consistent with the literature, partly because BMI has been found to be not accurate in certain cases. Thus, future expenditure-related studies need to examine the effect of BMI. Also, younger patients tend to have lower CCI scores. Therefore, this study suggests that to identify the high-spending group, policy-makers and insurers may use age, education, income level, and region of residency. Payers should then promote cost-saving strategies (i.e., additional educational programs) with these high-spending patients. Even though there would be extra costs in short term, but it would also promote better self-care, reduce inpatient visits, and decrease overall costs in the long term.

While the study found that cost sharing was a significant factors in patients' tendency to seek outpatient care, it was not the case for medication adherence. The results supported the belief in which high cost sharing can be a barrier to optimal outpatient care and, thus, lead to unnecessary inpatient visits. In order to cut long-term costs and improve access to care, both availability of insurance coverage and low out-of-pocket are required. The Affordable Care Act was implemented in 2014 resulting in millions of Americans obtaining insurance. Even though this would improve insurance coverage, high deductibles from these plans can create barriers to obtain care.[67] In order to cut long-term

costs and improve access to care, both availability of insurance coverage and low out-of-pocket are required. Another prominent example is Medicare part D, in which beneficiaries can fall into the donut hole when reaching a certain amount of spending.[68] While in donut hole, these patients have to a pay much higher out-of-pocket amount for medications, which might lead to medication non-adherence, worsening diseases, and probably more additional costs to the society than saving. Fortunately, donut hole will be closed by 2020.[68]

Future studies should consider to adapt a longer period of follow-up to gain a better understanding of how cost sharing affects outpatient care. Additionally, they should consider to study only drugs used in IBD treatment, instead of including medications for IBD-related conditions. If possible, a bigger sample would more likely to show whether cost sharing is a significant factors of medication adherence. Future studies should also find ways to incorporate clinical severity as an independent variables. Using this study a framework, future studies can also examine other autoimmune diseases.

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Appendix A

Short form – 12 Health Survey Questionnaires, Version 2

1. In general, would you say your health is:
   ☐ Excellent ☐ Very Good ☐ Good ☐ Poor

The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	YES, Limited a lot	YES, limited a lot	No not limited at all
2. Moderate activities such as moving a table, pushing a vacuum cleaner, or playing golf.	☐	☐	☐
3. Climbing several flights of stairs	☐	☐	☐

During the past 4 weeks, have you had any of the following problems with your work or other regular activities as a result of your physical health?

	YES	NO
4. Accomplished less than you would like	☐	☐
5. Were limited in the kind of work or other activities	☐	☐

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	YES	NO
6. Accomplished less than you would like	☐	☐
7. Did work or activities less carefully than usual	☐	☐

8. During the past 4 weeks, how much did pain interfere with your normal work (including work outside the home and housework):

☐ Not at all ☐ A little bit ☐ Moderately ☐ Quite a bit ☐ Extremely

These questions are about how you have been feeling during the past 4 weeks.

For each question, please give one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks

	All of the time	Most of the time	A good bit of the time	A little of the time	None of the time
9. Have you felt calm and peaceful?	☐	☐	☐	☐	☐
10. Did you have a lot of energy?	☐	☐	☐	☐	☐
11. Have you felt down-hearted and blue?	☐	☐	☐	☐	☐

12. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc…)?

☐ All the time ☐ Most of the time ☐ Some of the times ☐ A little of the time ☐ None of the time

Appendix B

Personal Health Care and Component Price Indices by Year

Industry / Commodity or Service Year	1. Personal health care (Overall)	2. Prescription Drugs
1999	73.6	69.9
2000	75.7	73.0
2001	78.5	76.9
2002	80.9	80.9
2003	83.5	83.4
2004	86.5	86.2
2005	89.1	89.2
2006	91.8	93.1
2007	94.8	94.4
2008	97.3	96.7
2009	100.0	100.0
2010	102.7	104.3
2011	104.8	108.7
2012	106.8	112.6
2013	108.4	113.2