Value-Based Health Care in Inflammatory Bowel Diseases

Creating the Value Quotient

Welmoed K. van Deen

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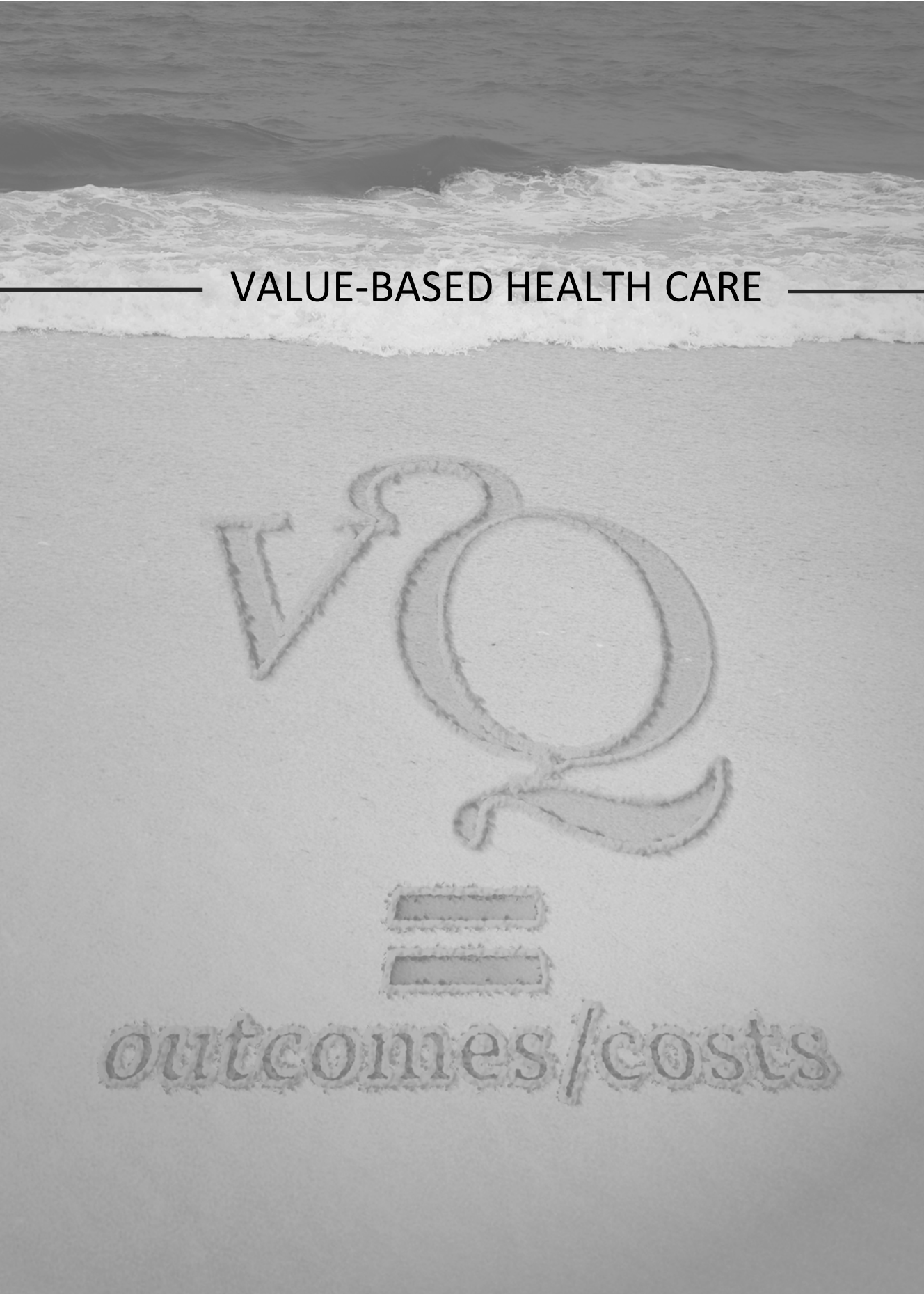
VALUE-BASED HEALTH CARE



Chapter 1.

Introduction

Adapted from
Value-Based Health Care for Inflammatory Bowel Diseases

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Abstract
Increasing health care costs worldwide put the current health care systems under pressure. While many efforts have aimed to contain costs in medicine, only few have achieved substantial changes. Inflammatory bowel diseases (IBD) rank among the most costly of chronic diseases and physicians nowadays are increasingly engaged in health economic discussions. Value-Based Health Care (VBHC) has gained a lot of attention recently, and is thought to be the way forward to contain costs while maintaining quality. The key concept behind VBHC is to improve achieved outcomes per the encountered costs, and evaluate performance accordingly. Four main components need to be in place for the system to be effective: 1) accurate measurement of health outcomes and costs; 2) reporting of these outcomes and benchmarking against other providers; 3) identification of areas in need of improvement based on these data and adjusting the care delivery processes accordingly; and 4) rewarding well-performing participants. In this article we will explore the key components of VBHC, we will review available evidence focusing on inflammatory bowel diseases and we will present our own experience as a guide for other providers.

Introduction
Worldwide health care costs continue to increase at an alarming pace. Despite differences in care delivery and financial infrastructure, most countries cope with similar trends of increasing health expenditures. It seems to be a universal 'unsolvable' problem (*Figure 1.1a*). Even more disturbingly, the expenditure increase is not consistently accompanied by an increase in quality and improved health outcomes (*Figure 1.1b*).[1] Various factors have been implicated to contribute to the problem: ineffective care delivery, excessive administration costs, non-adherence to guidelines, uncoordinated care, practice of defensive medicine, lack of preventative care, and introduction of new technologies.[2] One overarching notion that has emerged is that necessary preventative care is underdelivered, while unnecessary care is overdelivered. In **Chapter 5** we show that guideline adherence in IBD care is poor as well: many unnecessary services are overdelivered, while preventative services are often lacking. Indeed, due to current fee-for-service payment structure, physicians are incentivized to often deliver more care than is necessary. Patients are usually unaware since there is little reporting on quality and health outcomes by individual physicians or hospitals.

Though reforms have addressed one or more of the abovementioned items, none have managed to achieve substantial savings that bend the overall cost curve. Solutions to reduce health care spending have frequently involved shifting costs around among participants: shifting costs from insurers to patients by increasing the annual premiums; shifting costs between insurers; or shifting costs towards providers by introducing capitated payments. But shifting costs around has not resulted in decreased overall spending in any way.[3] Recently it has become accepted that a complete care redesign, involving all stakeholders, is warranted to solve the health care crisis. Moreover, the right incentives should be put in place for all participants in order to ensure sustainability. An area which is rapidly gaining ground is the area of value-based health care (VBHC) which

solely focuses on achieved health outcomes and associated cost-effectiveness. This review introduces the concepts and rationale behind VBHC and provides early results observed in the care for patients with IBD.

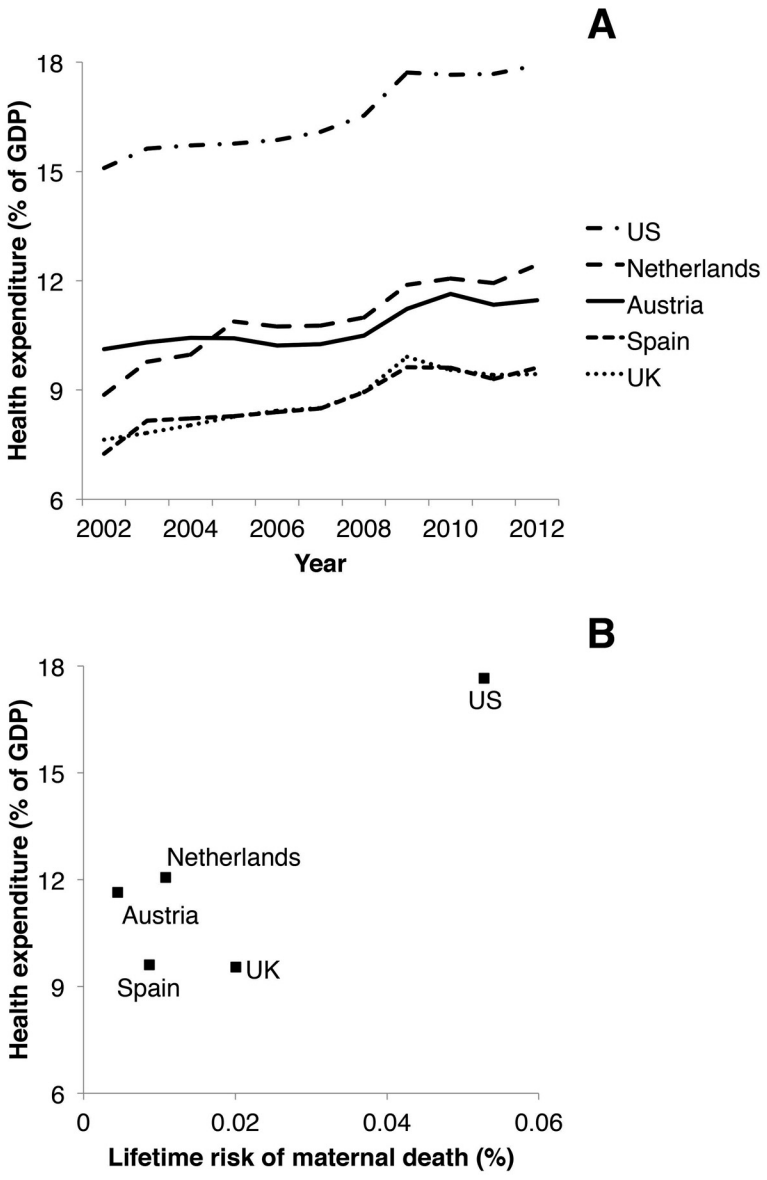

Figure 1.1. Health care data for the U.S. and four European countries. a) Growth in health expenditure as % of GDP between 2002-2012. b) Relation between health expenditure and lifetime risk of maternal death. Source: The World Bank, Health Nutrition and Population Statistics.

Value-based health care

The main concept of VBHC is to evaluate health outcomes and their associated costs at the condition level. Value in health care can be calculated by dividing health outcomes by the costs encountered.[3,4] Four key components need to be addressed to achieve health value improvement. 1) accurate measurement of health outcomes and associated costs; 2) transparent outcome reporting with a classification of performance level (e.g. excellent, good, fair, poor); 3) subsequent improvement of care delivery in a coordinated care setting organized around a single disease; and 4) payment reform to create the proper incentives for health care participants (*Figure 1.2*). We will now discuss the rationale to use those four individual key VBHC components.

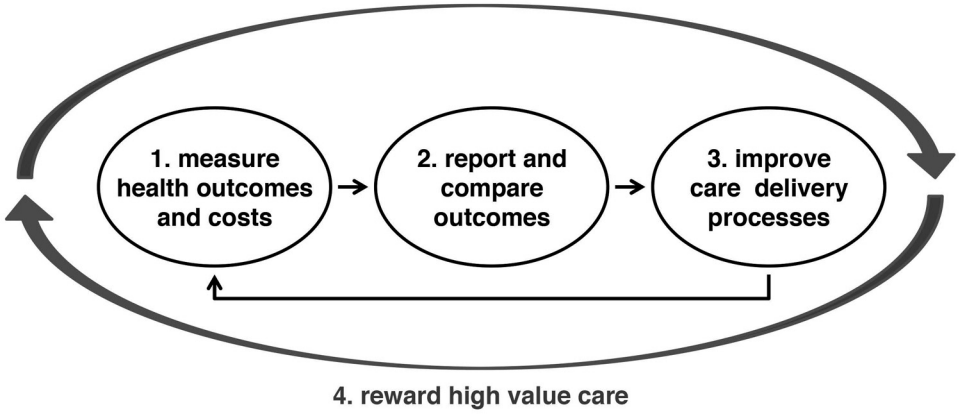

Figure 1.2. The four components of value-based health care represented in a positive feedback loop on the provider level, which can be accelerated by rewarding high value care on a regulatory level: 1) measure value (i.e. outcomes and costs); 2) report and benchmark outcomes against other providers; 3) improve the care delivery process based on observed outcomes; and 4) reward high value care.

I) Measurement of value

To measure value in health care both health outcomes (i.e. quality) as well as costs will need to be measured accurately. We will start by discussing the general theory on different ways to measure quality of care and outcomes in health care, and we will also discuss specific measurements used in IBD. Thereafter we will discuss costs measurement and discuss one particularly useful method: time-driven activity-based costing (TDABC).

Quality

Quality of care can be assessed using structure, process, or outcome measures.[5] A structural measure is related to the structure of the care delivery, for example the number of gastroenterologists that work in a hospital. Process measures are related to the process of care delivery, for example the percentage of patients that were tested for tuberculosis prior to starting an anti-TNFα agent. Outcome measures are related to the outcomes of the delivered care, for example the quality of life of a patient after a certain procedure. Structure measures are usually easy to measure but are generally poorly correlated with

outcomes. Outcome measures on the other hand are what matters most to the patient. However, it can take a long time to assess outcomes, especially in chronic disease management, which generates delays in quality reporting. Process measures are easier to measure and represent the medical practice well. However, process measures should be closely correlated with outcomes in order to be meaningful.[5,6]
To measure health value, Porter[7] proposes to always measure value around what is important to the patient. Outcomes, or results, are what counts to patients and therefore he proposes to measure value based on achieved results, instead of using surrogate markers such as structure and process measures. However, while health outcomes should be used to assess value, process measures can be very useful to improve internal processes. Porter proposes to measure outcomes in 3 tiers: 1) health status achieved or retained, 2) the quality and time of the recovery process, and 3) the sustainability of the achieved health status.[7]

Additionally, the use of patient reported outcomes (PROs) is an upcoming field. The U.S. Food and Drug Administration (FDA) requires the use of validated PROs in clinical trials for drugs and medical device labeling.[8] In 2004, the National Institutes of Health (NIH) launched the Patient Reported Outcomes Measurement Information System (PROMIS) initiative (www.nihpromis.gov). This initiative aims to support progress in clinical research by building and validating common item banks of PROs that measure symptoms and outcomes applicable to a wide variety of diseases. This will facilitate straightforward interpretation of clinical trial data and make comparisons between different studies easier.[9]

IBD Quality measures have been developed by the American Gastroenterology Association (AGA) in conjunction with the Crohn's and Colitis Foundation America (CCFA) in 2011.[10] These are 10 process quality indicators (Qis) related to adherence to IBD practice guidelines, consisting of 8 outpatient Qis and 2 inpatient Qis. Additionally the CCFA developed a separate set of 10 process indicators, of which 5 overlap with the AGA Qi set. A set of 10 outcome measures was developed by the CCFA as well and include corticosteroid use, hospitalizations and emergency department (ED) visits, productivity, quality of life, malnutrition, anemia, nighttime bowel movements or leakage, incontinence, and narcotics use.[6] Within the PROMIS framework a gastrointestinal (GI) symptom bank was developed as well. The GI symptom bank consists of scales applicable to both patients with a GI disease and to the general population. GI symptoms are measured in seven domains: gas/bloating flatulence, nausea/vomiting, diarrhea, constipation, bowel incontinence/soilage, heartburn/reflux, and disrupted swallowing.[11]

At UCLA we are currently measuring all outcomes relevant to patients: disease control, quality of life (QoL) and (work) productivity.[12] All three are used to 1) monitor achieved outcomes (tier 1); 2) estimate the time to recovery and the level of discomfort during flares (tier 2); and 3) measure relapse rate (tier 3). All outcomes are assessed on a regular basis to establish the performance of the implemented care program as well as to allow for early intervention in case of disease progression. Specific care scenarios with different frequencies of outcome monitoring are allocated based upon individual risk profiles. In

addition, the AGA process Qis are tracked internally in order to identify areas for process improvement. *(Ho, A.D. et al, unpublished data)*

Chapter 2 discusses the development and validation of a simple score for remote monitoring of disease activity. The score consists of solely PROs and is specifically designed for implementation on a mobile application for patients. In **Chapter 3** the impact of IBD on work productivity is assessed. **Chapter 4** describes the development of a single quantifiable health outcome metric based on individual patients' preferences.

Costs

For accurate value calculations, costs need to be measured in great detail. In most hospitals, accounting systems are designed for reimbursement purposes. Hence, costs are calculated using the charges on individual line items, and not always directly correlate with actual costs[13]. To truly understand what the costs of a treatment process are, the time-driven activity-based costing (TDABC) method can be used. This method calculates costs of a care process based on the amount of time spent for every step in the care process. This time is then multiplied with the costs per time-unit of the resources (e.g. personnel, space, equipment) involved.[14] The use of TDABC offers the benefit of accurate cost measurement, and is simultaneously a way to get insight in how to make care delivery more cost effective. TDABC will help hospitals identify areas in the care process that can be delivered more efficiently, estimate the financial benefits of task differentiation between different providers, and calculate return on investment of quality improvement.[14]

TDABC pilots have been run in a variety of centers in Belgium[15,16], at the Cleveland clinic (U.S.A)[17], the University of California Los Angeles (U.S.A.)[18], the Boston Children's Hospital (U.S.A.)[19], and the University of Calgary (Canada)[20]. The Belgian study estimated costs using TDABC in 5 outpatient clinics and reported improvements in operations based on TDABC results. Through internal benchmarking times for procedure steps between different departments more effective methods were identified.[16] The Cleveland Clinic used TDABC to map and cost two heart valve procedures. They were able to estimate accurate costs for each of the processes and found that calculated costs were approximately 10% lower than the costs calculated using the administrative data. Additionally the TDABC method helped them to identify redundancy in their processes, to reassign tasks in order to have everyone perform tasks at the top of their license, and to get a closer insight on non-billable activities.[17] Using TDABC the Boston Children's hospital was able to decrease total visit time for plagiocephalic care with 19.9% (7:29 minutes) due to workflow improvements. Costs increased by 7.7% ($8.22) per visit, but this was offset by the additional time available to see two extra patients per day.[19] The UCLA department of Neurosurgery reports similar advantages using a continuous cycle of identification of variation, identifying the most cost-effective solution, and process improvement.[18]

At UCLA we started to use the TDABC model to assess the costs associated with Qi implementation in clinic. We identified seven types of personnel involved in the Qi process in the GI clinic. For the IBD clinic total costs for general IBD measures including

vaccinations, documentation of disease activity and tobacco use were $80.33, addition of bone loss assessment increased the costs to $91.41, and addition of process costs for checking hepatitis B and tuberculosis prior to anti-TNFα therapy initiation was $108.76. *(Ho, A.D. et al, unpublished data)* In future efforts, radiology costs and lab costs will be estimated using TDABC as well for a more comprehensive value calculation.
U.S. wide health care utilization and the costs associated with IBD care are evaluated in **Chapter 5**. When no reliable costs are available health care utilization can be a meaningful proxy for costs of care. Therefore, **Chapter 6** evaluates health care utilization in IBD patients treated at the UCLA Center for IBD and compares it to a matched control group of IBD patients. IBD related indirect costs due to losses in work productivity are assessed in **Chapter 3.**

II) Outcome reporting

Outcome registries are thought to increase value by driving patient and physician improvements. If outcome registries are publicly available, patients can choose the best medical practice for their care and avoid physicians with bad outcomes. On the other hand, registries offer the potential for providers to benchmark themselves against other practitioners and identify areas where they are lagging behind and subsequently improve. The effect of health registries in Sweden was recently analyzed in depth by the Boston Consultancy Group (BCG). Sweden has had an interest in tracking outcomes since the 1800s and implemented official registries covering a broad array of diseases in the 1970s. Sweden's health outcomes are among the best in Europe, while costs are around average. BCG found that while reporting on acute lymphoblastic leukemia (ALL) survival rates, ALL treatments dramatically improved with an increase in survival rates from 12% in the early 1970s to 89% in 2005. Similarly, side effects from cataract surgery decreased dramatically. Though no comparative studies were done, some indications of the impact of disease registries were found. Two hospitals with low outcomes in survival rates after a myocardial infarction changed their practice after public reporting and achieved a 50% reduction in 30-day mortality within two years of the report.[21]

Disease specific examples are identified as well. A steady rise in in vitro fertilization (IVF) success rates was observed in the U.S., after the Centers for Disease Control and Prevention started publicly reporting in-vitro fertilization (IVF) outcomes. This can be illustrated by a decrease in the number of IVF cycles entailing the transfer of three or more embryos from 83% to 35%.[22] Similarly, in the cardiac surgery field, a decrease was observed in mortality rates after coronary artery bypass graft (CABG) surgery from 3.2% in 1996 to 2.2% in 2005 in the presence of a public reporting system.[23] In a blog post for the Harvard Business Review, Toby Cosgrove, Chief Executive Officer of the Cleveland Clinic, reported a decrease in infections after surgery by 40% and a decrease of urinary tract infections by 50% after reporting of provider performance data.[24] In Europe, several countries have implemented registries as well, measuring quality indicators, outcomes and/or patient satisfaction data.[25]

Due to the nature of the available data, it remains hard to assess whether observed effects are directly caused by the registries or by progress in the medical sciences. A

literature review from the U.S. Agency for Healthcare Research and Quality analyzing 97 qualitative and 101 quantitative studies, found overall substantial evidence that reporting leads to improvements in the quality measures and moderate evidence that reporting might lead to a reduction in mortality. They also showed that reporting requirements mainly drive changes in physician behavior rather than in patient behavior (e.g. choosing a different doctor based on reports).[26] Furthermore, there is emerging evidence that introduction of public reporting systems leads to a reduction in costs. A recent retrospective controlled study found a decrease of 13.7% in CABG prices and 11.4% in percutaneous transluminal intervention (PTI) prices after introduction of a public reporting system.[27]

IBD outcome registries are being built as well. As mentioned above the AGA developed a set of 10 Qi measures for IBD specifically.[10] Reporting of 8 of the 10 AGA quality measures to the Centers for Medicare and Medicaid Services (CMS) is required in specific conditions in the U.S., and reporting of those measures to CMS is directly linked to reimbursements.[18] In 2013, the British Society of Gastroenterology launched a national IBD specific registry as well, which includes information on number of patients, admissions, surgeries, and medication use for national benchmarking.[28]

III) Care coordination

In order to deliver high value care, the most accurate treatment should be chosen for the right patient at the right location at the right time. Practice guidelines have been installed by many physician associations. However, guidelines are not followed consistently. In a 2010-2012 U.S. nationwide analysis we showed that 42% of Crohn's disease patients was prescribed 5-ASA even though not supported by current guidelines, and steroid sparing medication was prescribed infrequently while 9% of all IBD patients used long term (>3 months) steroids.[29] Reasons for guideline non-adherence could be a lack of incentives for guideline adherence, lack of access to guidelines, or a lack of trust towards guidelines.[30]

Care coordination has been proposed to be a key need in order to improve care quality. Care coordination includes the use of evidence based care pathways by a multidisciplinary care team ensuring continuity of care and engaging the patient in the care process.[31] A study in an insurance claims database analyzing continuity of care, defined as the percentage of visits with the same provider, showed that moderate improvements in care continuity in patients with chronic diseases were associated with substantial improvements in outcomes and decreases in complications and costs.[32] A review assessing the effect of care coordination systems in chronic disease management found positive effects on quality of life, functional status and health outcomes, satisfaction scores, guideline adherence, and compliance.[31] Additionally, routine collection of PROs was shown to be beneficial for patient-provider communication and for monitoring of treatment response and detecting unrecognized problems in cancer patients.[33] Furthermore, it is shown that health care systems organized around primary care are associated with lower health care expenditures and that systems with a weak primary care infrastructure are associated with worse health outcomes.[34] The U.S. patient-centered medical home (PCMH) is a model that explores this further. PCMH can be

described as a model for care that includes primary care access, comprehensiveness, care coordination, and continuity of care. Hundreds of pilots have been initiated over the U.S. and the first controlled results suggest improved outcomes, reduced health care utilization, and cost savings due to initiation of a PCMH.[35]

For IBD specifically, the Royal Adelaide hospital in Australia found a significant decrease in costs and fewer hospitalizations after introduction of a coordinated care infrastructure in a controlled study.[36] Hospitals in the UK, Italy, The Netherlands, Canada, and Austria have been working with integrated care models as well, though no outcomes are presented.[37] The UCLA Center for IBD, launched in 2012, uses an approach that combines all components of coordinated care and outcome measurements. Multidisciplinary care pathways for IBD were developed and implemented, which include evidence-based practice management, task differentiation and coordination between providers, and collection of outcomes. PROs are collected routinely using a patient facing mobile application, which is used for patient monitoring and outcome reporting. This is all supported by a solid IT infrastructure, with a provider portal and a patient facing mobile application (UCLA eIBD, available for iOS and Android). This infrastructure also facilitates patient-provider communication and education, and offers wellness programs. Health care providers can evaluate their patients' outcomes, health care utilization and associated costs.[12,38] A controlled analysis using a payer database of 49 UCLA IBD Center patients versus 245 IBD controls showed a significant decrease in corticosteroid use from 31% to 12%, and 1.3-3.4 times more frequent biomarker testing. Non-significant decreases in emergency department (ED) visits (75% decrease), hospitalizations (89% decrease), and office visits (25% decrease) was observed as well[39]. **Chapter 6** describes this evaluation in more detail.

IV) Payment reform to reward value

Value based insurance design (VBID) is an approach to use insurance models that reward high value care. Initial efforts were mainly focused on cost sharing strategies, while the value component has only been added in pilots more recently. In the famous RAND health insurance experiment (1974-1982) it was shown already that health care is affected by a certain price elasticity, which is shown by a higher demand for medical care if co-payments for patients are lower.[40] However, nonspecific cost sharing strategies target necessary care as well as unnecessary care, which is why the introduction of value in insurance designs is important. The first area in which VBID was implemented is in the prescription drug arena. Incentives can be targeted to patients, health care professionals, or both. Throughout the Organisation for Economic Co-operation and Development (OECD) member countries, different approaches are already being utilized by governments to stimulate cost-effective drug use using cost sharing strategies. Strategies used to incentivize patients include lowering co-payments or waiving the maximum allowed payment cap for essential medications or generic variants of drugs. Strategies aimed at physicians include compulsory guideline-based prescribing and benchmarking against other physicians, coupled with either financial penalties or rewards.[41]

Patient-targeted approaches include policies that for example lower co-payments for high-value drugs specifically, to improve patient adherence. In a 2013 paper reviewing 13 studies assessing the effect of reduced co-payments found an increase in quality but no reduction in health expenditure.[42] The majority of studies assessed the effect of reducing co-payments on diabetes and hypertension medication. Reductions of 25%-100% in copayments were found to increase adherence by on average 3% after one year. As expected, an increase in prescription drug expenditure was observed for insurers, but overall health expenditure was generally not affected. Two studies evaluated health care utilization and found reduction in office visits, ED visits and hospitalizations. Furthermore, two studies that included disease management with the VBID did observe decreased overall expenditures.[42] Another 2014 review, incorporating 10 studies (of which seven overlap with the previous review), had comparable conclusions and observed an improvement in medication adherence from 2-5 percentage points and found lack of evidence for changes in expenditure, outcomes, or health care utilization.[43] A more in depth analysis of 76 VBID plans introduced by a large pharmacy benefit manager found increased adherence in VBID plans that offered more generous benefits, targeted high-risk patients, had wellness programs, and made benefits available only for mail orders. Plans including disease management programs had higher adherence rates, but interestingly enough, disease management programs had a consistently negative effect on adherence improvements after introduction of VBID. The authors conclude this effect might be explained by the fact that VBID and disease management both aim for the same goal, or because baseline adherence was relatively high in those programs and the effect we observe is a ceiling effect.[44] A third review assessing the effect of drug insurance cost-sharing strategies for patients with cardiovascular related chronic diseases confirmed positive effects on adherence rates, though effects on outcomes remained unclear.[45]

Non-pharmacy patient-targeted VBID approaches, mostly targeted at preventative services, are thought to be of high value to the health care system. The 2010 U.S. Patient Protection and Affordable Care Act (ACA) or 'Obamacare' requires coverage without cost-sharing of certain preventive health services. Among these services are women's preventive health services. This includes vaccinations, screening, and preventive treatments for certain risk groups.[46,47] Inclusion of secondary preventive services is theoretical of high value as well. An analysis from the University of Michigan's Center for Value Based Insurance Design estimated that addition of certain secondary preventative services in high deductible health plans would lead to a 5.1-5.6% increase in premiums. Nevertheless, over the long term, including those services is thought to increase health value.[48]

Programs targeting treating physicians are implemented as well. Initial efforts to incentivize performance and accountability for providers are pay for performance programs (P4P), where physicians are rewarded or penalized when reaching certain quality targets, which are usually process measures. Additionally, the ACA allows health care providers to form Accountable Care Organizations (ACOs). ACOs are provider organizations organized around primary care, in which all participants are accountable for the quality and outcomes of care. The provider group is eligible to share in health care

savings with the insurers when they reach certain quality targets. These quality targets are focused around four domains: patient/caregiver experience, care coordination and patient safety, preventive health, and care for at-risk populations.[49] Similarly, in different European countries payment reforms are being pursued, including rewards for the introduction of disease management programs in Germany, and bundled payments for episodes of care in The Netherlands.[50] The effect of P4P programs on costs and outcomes is unclear, because only few good quality studies are available.[51] Studies mostly show either a null effect or a marginal positive effect. The experience with ACOs and bundled payments incorporating quality incentives is still limited. Reported results on quality, outcomes and costs are mixed, and nine out of 32 CMS ACO contracts were discontinued.[51] Best results are thought to result from bundled payments for episodes of care coupled to quality targets.[4]

In the field of gastroenterology there is interest for implementation of VBID as well. Saini et al. suggest as an example to introduce higher co-payment for upper endoscopies when the indication is gastroesophageal reflux disease (GERD) than when the indication is dysphagia.[52] We propose to introduce VBID in a comprehensive structure that incentivizes all stakeholders involved in IBD care to utilize high value care, which includes incentives for insurers, physicians, and patients. Physicians should be rewarded for good performance on a disease specific level. Using a cost-sharing insurance design, physicians with better outcomes should be at low financial risk, while having large financial benefits, while physicians with worse outcomes would have high risks with low benefits. This would result in a model in which savings with excellent outcomes are rewarded with a large percentage of shared savings for the provider, while savings with suboptimal outcomes are only rewarded with a small percentage of the savings, and savings with bad outcomes are not rewarded at all. On the other side of the spectrum, physicians with high costs and bad outcomes would be penalized by a high percentage of sharing in financial losses, while high cost with better outcomes should only be penalized with a smaller percentage in shared losses, and in cases where the provider achieves excellent outcomes financial penalties should be forgiven (*Figure 1.3*). Expected outcomes should be risk-adjusted based on the population mix. This structure is similar to the structure used by the second arm of the Medicare Shared Savings Program.[49] Furthermore, patients should be incentivized to participate in their care. At UCLA, we calculate individual participation scores based on whether patients participate in patient education, partake in home monitoring, and comply with scheduled visits, procedures, and tests. We propose that patients should be financially rewarded based on their participation score, which will stimulate better outcomes. In **Chapter 4** we also discuss a method to incorporate patient preferences in VBID.

Conclusion

The introduction of VBHC is inevitable, but approaches on how to achieve value in health care differ. The key concepts include 1) measurement of outcomes and costs; 2) benchmarking of outcomes and costs 3) implementation of a value-based clinical system; and 4) the introduction of incentives for delivery of high-value care. Although the

introduction of incentives is mainly in the hands of regulators and insurers, the first three concepts can be driven from within the medical community. Payment reforms are emerging worldwide, and the medical community should be closely involved in the development of these contracts. By implementing the first three components in their care practice, providers can improve their care delivery processes and ensure high-value care delivery. These efforts will be rewarded financially as well after the formal introduction of VBID programs. Results on the effects of value-based approaches are still very limited, but many pilot programs are running and initial results are encouraging. We described the approach at UCLA as guidance for implementation of VBHC for care delivery.

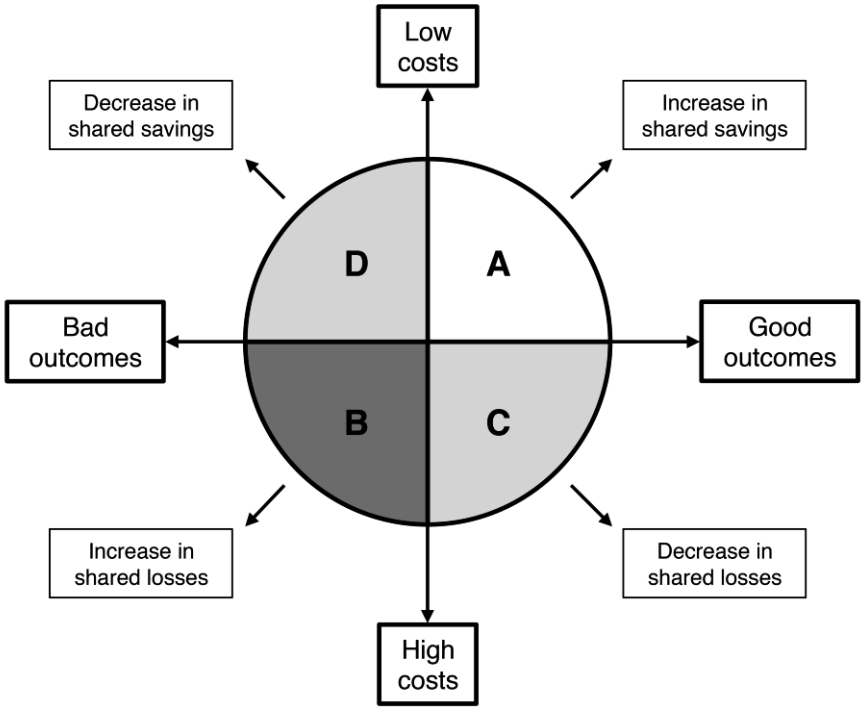

Figure 1.3. Proposed VBID mechanism. Providers are incentivized to deliver high value care by increases is shared savings when delivering better outcomes at lower than expected costs (segment A). Conversely, providers are disincentivized to deliver low value care by increases in shared losses when delivering worse outcomes at higher than expected costs (segment B). When delivering better outcomes at higher than expected costs, shared losses will decrease (segment C), while shared savings will decrease when delivering worse outcomes at lower than expected costs (segment D). Benchmark outcomes and costs are risk-adjusted based on the population mix.

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Conflict of interest statement.
WKD declares no conflict of interest. EE and DWH have a patent Value-Based Health Care Management Systems and Methods issued to UCLA.

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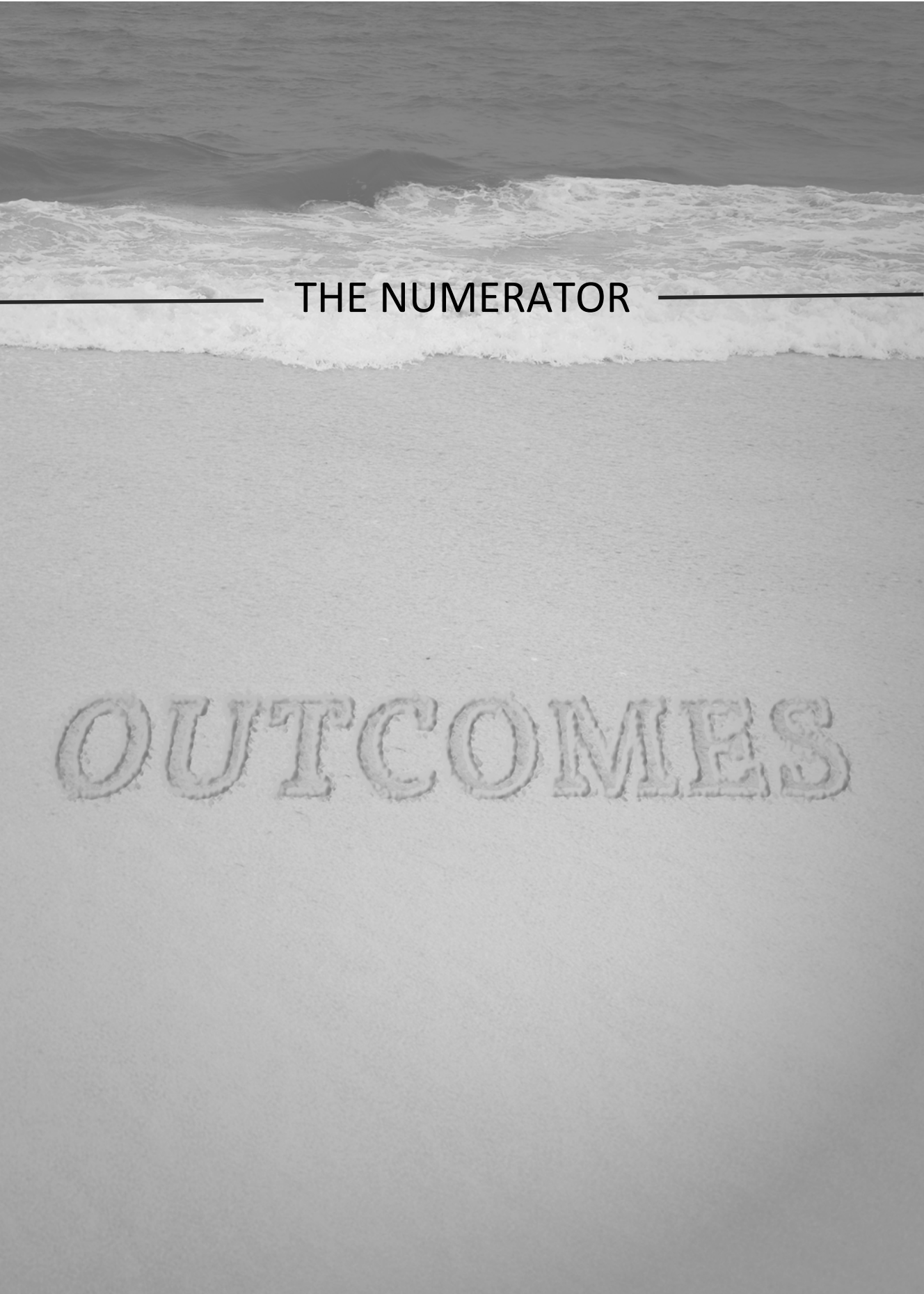
THE NUMERATOR
OUTCOMES

Chapter 2.

Development and Validation of an Inflammatory Bowel Diseases Monitoring Index for Use with Mobile Health Technologies

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Abstract

Background & aims
Mobile health technologies are emerging rapidly and an increasing number of people use smartphones. Remote monitoring is thought to be of value for inflammatory bowel disease (IBD) management but no tools are currently available. We tested the ability of an IBD monitoring tool, which might be used with mobile technologies, to assess disease activity in patients with Crohn's disease (CD) or ulcerative colitis (CD).

Methods
This prospective observational study consisted of a score development phase and a validation phase. IBD patients filled out a set of patient reported outcomes which were compared to clinical disease activity indices. Predictors for disease activity were identified and a prediction score was developed, which was subsequently validated in an independent cohort.

Results
In total, 110 Crohn's disease (CD) and 109 ulcerative colitis (UC) patients were included in the development phase. The developed CD score consisted of liquid stool frequency, abdominal pain, well-being, and patient assessed disease control. The UC score included stool frequency, abdominal pain, rectal bleeding, and patient assessed disease control. The score was validated in 301 CD and 265 UC patients. The AUC of the ROC for detecting clinical disease activity was 0.90 for CD and 0.91 for UC; for endoscopic activity the AUC was 0.63 for CD and 0.82 for UC. Both scores were responsive to changes in disease activity (P<0.003); The ICC for test-retest reliability was 0.94 for both CD and UC.

Conclusions
We developed and validated a monitoring score for CD and UC patients for implementation on mobile technology. The score predicts clinical disease activity in both CD and UC reliably. Endoscopic healing is predicted accurately for UC but not CD.

Introduction
The shift from symptom-oriented to prevention-oriented care delivery has accelerated the development of mobile health (mHealth) technologies and is thought to radically transform health care delivery.[1] Smartphone adoption is increasing rapidly, with 64% of Americans using smartphones in 2014 of which 62% used their phones to look up health information.[2] Many health applications (apps) are available, most of which provide health information or support data collection.[3] For IBD patients, apps are available that assist in tracking symptoms, logging meals, and managing medications.[4,5] These apps can create reports for providers but do not allow for real-time interactions between patient and provider.

Self-monitoring and self-management for chronic diseases is widely practiced in diabetes care[6] and anticoagulation therapy[7]. Additionally, e-technologies for symptom reporting

between patients and providers are increasingly used in chronic diseases.[8] One compelling example is the diabetes app WellDoc, a U.S. Food and Drug Administration (FDA) approved app which can only be used after prescription by a health care provider[3,9]. Several systems for online symptom reporting and disease management have been developed for IBD. In the Danish Constant-Care web system, UC patients filled out a clinical symptom score and logged fecal calprotectin levels weekly; based on these scores the system made real-time recommendations for adjusting mesalamine dosing. This approach was shown to empower patients and decrease relapse duration.[10,11] Similarly, individualization of infliximab dosing in CD patients was reported to be practical and feasible.[12] A study evaluating another home tele-management system in UC (UC-HAT) did not show significant differences in disease activity and quality of life (QoL) between users and controls, and more than 1/3 of the patients discontinued participation.[13] An ongoing multicenter randomized controlled trial is testing the use of a mobile tele-management system using text messaging in IBD. This system sends personalized alerts and educational texts, and assesses symptoms and side-effects, based on which treatment can be modified.[14]

Patient Reported Outcomes (PROs) are increasingly used to evaluate health status, and the importance of PROs in outcome measurement, symptom management, and quality improvement efforts is increasingly recognized.[15] Furthermore, the use of PROs as primary outcome measures for evaluating effectiveness of IBD interventions is progressively supported by the FDA.[16] Therefore, PROs are promising for use in mHealth apps. An example is the HealthPROMISE app which tracks patient reported QoL scores in IBD patients and provides decision support to physicians.[17] However, accurate e-monitoring tools for disease activity in IBD are yet to be developed. Previous efforts have aimed to develop PRO questionnaires by adjusting existing scores.[18-20] We aimed to identify the most optimal PRO score to use on an IBD disease-monitoring app. The best PROs were selected from an exhaustive list of PROs in a prospective cohort of IBD patients. Subsequently, the developed scores were tested prospectively in an independent cohort at three independent IBD centers.

Methods

Design

This was a prospective, observational study, which aimed to develop and validate a mHealth index (mHI) for CD and UC that accurately monitors IBD disease activity using PROs. The study consisted of two phases: a development phase and a validation phase. During the development phase the mHIs were developed using collected PROs and clinical disease activity indices. During the validation phase the developed mHIs were validated in an independent cohort.

Population

Development phase

IBD patients were identified during clinic visits between May 2013 and January 2014 at the University of California, Los Angeles (UCLA) Center for IBD. Patients with esophageal or anal CD involvement alone, patients with a pouch or stoma, and pregnant women were excluded. Eligible patients filled out disease-specific questionnaires assessing PROs of most common clinical disease activity indices (partial Mayo (pMayo), simple clinical colitis activity index (SCCAI), and modified Truelove and Witts index (MTWI) for UC; Harvey Bradshaw index (HBI) and Crohn's disease activity index (CDAI), including a 7-day diary prior to the visit for CD). Additionally, patients were asked to assess their symptoms and perceived disease activity using visual analogue scales (VAS). The PROs were categorized into 10 domains: stool frequency, abdominal pain, general wellbeing, urgency, stool consistency, rectal bleeding, fever, anorexia, nausea/vomiting, and perceived disease activity (*Table 2.1*).

During clinic visits, vital signs were measured and physicians collected the physician reported outcomes required for the clinical disease activity indices (*Table 2.1*). Hemoglobin (Hgb), hematocrit (Hct), white blood cell (WBC) count, platelets, albumin, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were requested. Furthermore, stool testing for calprotectin was requested either at the patient's preferred laboratory or using a free stool kit (Genova Diagnostics) picked up at the patient's home. A dedicated study nurse (E.K.) followed up with patients via phone or e-mail to ensure lab and stool tests were performed.

Validation phase

Eligible IBD patients were identified during clinic and endoscopy visits between April 2014 and March 2015 in three tertiary IBD referral centers (UCLA, USA; University of California, Irvine (UCI), USA; and Leiden University Medical Center (LUMC), The Netherlands). Patients who participated in the development phase of the study were excluded. For CD patients, the developed mHI-CD and HBI were completed during clinic visits; during endoscopic visits, the simple endoscopic score for CD (SES-CD) was additionally completed. For UC patients, the mHI-UC and pMayo were collected during clinic visits, and the Mayo endoscopic sub-score was additionally obtained during endoscopic visits. Patients at the LUMC, completed a Dutch version of the mHI-CD and mHI-UC. After translation to Dutch, the questionnaires were translated back to English by an independent translator; the Dutch questionnaire was then revised and re-tested. To assess sensitivity of the mHI to detect changes in clinical disease activity, a subset of patients was included a second time during scheduled follow-up visits. To assess test-test reliability, a subset of UCLA patients was asked to complete a second questionnaire at home after their clinic visit.

Definitions

For CD, clinical disease activity was defined as a HBI>4 or a CDAI>150. A change of ≥3 in HBI was considered a clinically relevant change.[21] Endoscopic disease activity was defined as an SES-CD>3. For UC, clinical disease activity was defined as a pMayo>2, a MTWI>3, or a

Domain	Question	CD	UC
1. Stool frequency	Number of liquid/very soft stools for each of the last 7 days	X	
	How many stools did you have yesterday during the day?	X	X
	How many stools did you have yesterday during the night?	X	X
	How many stools do you have normally during the day?	X	X
	How many stools do you have normally during the night?	X	X
2. Abdominal pain	Abdominal pain for each of the last 7 days (No / Mild / Moderate / Severe)	X	
	Abdominal pain (No / Mild / Moderate / Severe)		X
	Abdominal pain (No abdominal pain / With bowel actions / Continuous)	X	X
	Rate your abdominal pain on a scale from 0 to 10 (VAS)	X	X
3. General well-being	General well-being for each of the last 7 days (Very Well / Slightly below par / Poor / Very Poor / Terrible)		X
	General well-being (Very Well / Slightly below par / Poor / Very Poor / Terrible)	X	
	General well-being (Perfect / Very good / Good / Average / Poor / Terrible)		X
	Well-being (No impairment / Impaired, but able to continue activities / Activities reduced / Unable to work)	X	X
	Rate your well-being on a scale from 0-10 (VAS)	X	X
4. Urgency	Urgency of defecation (No urgency / Hurry / Immediate / Incontinence)	X	X
5. Stool consistency	Stool consistency (Normal or variably normal / Semi-formed / Liquid)	X	X
	Do you take opiates or lomotil/imodium for diarrhea?	X	X
	How often do you take anti-diarrheals? (0-10 VAS)	X	X
6. Rectal bleeding	What % of bowel movements contains visible blood? (None / Less than 50% / 50% or more / Blood alone)	X	X
	Amount of blood in stool (None / Trace / Occasionally frank (bright red) / Usually frank)	X	X
	How often do you experience rectal bleeding? (0-10 VAS)	X	X
7. Fever	Fever on each of the last 7 days	X	
8. Anorexia	Loss of appetite (Yes/No)	X	X
9. Nausea/ vomiting	Nausea and/or vomiting (Yes/No)	X	X
10. Disease activity	How well do you feel your disease is under control? (0-10 VAS)	X	X
11. Clinical markers	Temperature	X	X
	Weight and height	X	
	Pulse		X
	Abdominal tenderness		X
	Abdominal mass	X	
	Extra intestinal manifestations	X	X
	Physician global assessment of disease activity	X	X
	Hgb, Hct, WBC, platelets, albumin, CRP, ESR (blood) and calprotectin (stool)	X	X

Table 2.1. Collected patient reported outcomes (PROs) and clinical markers in CD and UC patients

SCCAI>2. A change of≥3 in the pMayo was considered a clinically relevant change.[19] Endoscopic disease activity was defined as a Mayo endoscopic subscore >1.

Ethical considerations
All patients consented to participate in this study. This study was approved by the IRBs of participating centers under the following protocol numbers: UCLA: IRB#13-000402; UCI: HS# 2014-1231; LUMC: P14.158.

Statistical analysis
Descriptive statistics were used for clinical characteristics and demographic information. Numeric values are presented as mean and standard deviation or median and range. SAS version 9.2 was used for statistical analyses.

Development phase
Univariate logistic regression was performed using disease activity (HBI>4 for CD or pMayo>2 for UC) as the dependent variable and the PROs as independent variables. For each of the PROs, different cut-offs were used, which roughly created linear associations between the groups and the chance of active disease. Because different PROs represented the same domain (*Table 2.1*), the variables with the highest Wald χ-square value for predicting clinical disease activity were selected within each domain for inclusion in the multivariate logistic regression models. If two variables within the same domain had a similar predictive value (difference between Wald χ-square values <0.5), both were tried in separate models unless the question type was less preferable. Because of usability on a mobile application VAS, yes/no, or numeric questions were preferred over categorical questions; within those, questions with less response options were preferred. Variables with a p-value >0.1 in the univariate analysis were omitted from subsequent analyses. Stepwise forward multivariate logistic regression was performed with clinical disease activity as the dependent variable and the selected PROs as independent variables. A significance level of $P<0.1$ was required for entry in the model and a significance level of $P<0.1$ to stay in the model. Several models were performed using different clinical disease activity indices to define clinical disease activity as the dependent variable.

Composite scores were created using the regression coefficients of independent predictors in the multivariate model. Spearman correlation coefficients were estimated between the newly developed mHIs and clinical disease activity indices. Receiver-operator characteristics (ROC) curves were used to assess the capability of the mHI to discriminate active versus non-active disease using different clinical disease activity indices, and the areas under the curves (AUC) were calculated. The composite score with overall highest AUC using different gold standards was selected.

Because the main aim of the developed score was to identify patients at risk for active disease, we defined the optimal cutoff for disease activity as a negative predictive value (NPV) of ≥95% and a sensitivity of ≥85% while maintaining maximum specificity. The overall prevalence of active disease was estimated at 22% based on cross sectional cohort data from UCLA.

Validation phase

To validate the mHI against clinical and endoscopic disease activity indices, the mHI-UC was compared to the pMayo and the endoscopic subscore of the Mayo; the mHI-CD was compared to the HBI and SES-CD. Spearman correlation coefficients between the scores were calculated and ROC curves to assess the ability to predict clinical and endoscopic disease activity were generated. To assess sensitivity to change, we compared patients who clinically improved, remained stable, and deteriorated. A Kruskal-Wallis test was used to compare groups. Test-retest reliability was assessed by the intra-class correlation coefficient (ICC). The performance of the VAS for patient-reported disease activity (DA-VAS) as single predictor for clinical and endoscopic disease activity was assessed as well.

Results

Development phase

In total, 219 patients (110 CD and 109 UC) were included in the development phase of the study (*Figure 2.1a, Table 2.2*). In 108 out of 110 CD patients the HBI was calculated, while the CDAI could only be calculated in 93 out of 110. The pMayo, SCCAI, and MTWI were calculated in all UC patients. Complete lab and stool tests were obtained from only 48% of patients. Despite intensive follow-up by a dedicated research nurse (E.K.), 39% of patients did not perform stool testing and 13% did not have labs drawn. Additionally, 14% of patients had blood drawn, but lab sets were incomplete due to protocol deviations.

Univariate logistic regression was performed for PROs and blood and stool tests (*Table 2.3 and 2.4*). Stool frequency, abdominal pain, general well-being, urgency, and patient-reported disease activity were all strong predictors for clinical disease activity in both CD and UC ($P<0.0001$). Incontinence was only present in 3% of patients and did not predict disease activity in either CD ($P=0.54$) or UC ($P=0.99$). In CD the use of anti-diarrheals was predictive for disease activity ($P=0.019$) but not in UC ($P=0.96$), while the VAS assessing frequency of anti-diarrheal use was a predictor for neither CD ($P=1.00$) nor UC ($P=0.26$). Rectal bleeding was a predictor for disease activity in both UC ($P<0.0001$) and CD ($P=0.019$). Anorexia was predictive in both CD ($P=0.019$) and UC ($P=0.0025$), while nausea and vomiting predicted only CD disease activity ($P=0.035$) and not UC disease activity ($P=0.14$). High CRP ($P=0.0009$), high ESR ($P=0.0022$), low Hgb ($P=0.022$), and low albumin ($P=0.034$) were predictors for clinical disease activity in CD. High calprotectin was not a significant predictor for CD disease activity ($P=0.054$), though calprotectin as continuous variable had predictive value ($P=0.011$). Low platelets ($P=0.98$), low Hct ($P=0.28$), and high WBC ($P=0.11$) were not predictive in CD (*Table 2.3*). In UC high CRP ($P=0.0067$), high calprotectin ($P=0.022$), high WBC ($P=0.013$), high ESR ($P=0.028$), and low Hct ($P=0.0047$) were all predictive for clinical disease activity. Low albumin ($P=0.98$) was not predictive for clinical activity in UC, though albumin as continuous variable was ($P=0.02$). Low platelets ($P=0.99$) and low Hgb ($P=0.13$) were not predictive for disease activity in UC, while Hgb as continuous variable ($P=0.032$) was (*Table 2.4*).

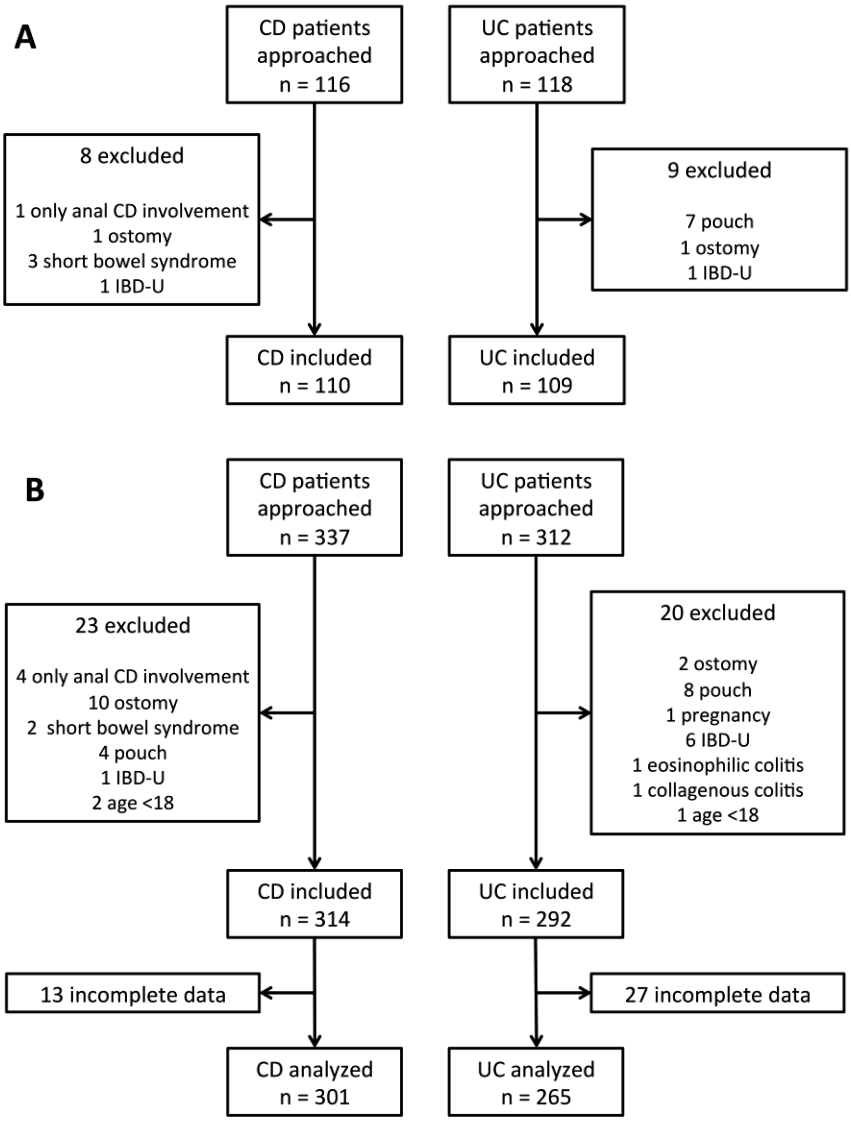

Figure 2.1 Inclusion flowcharts for development phase (a) and validation phase (b).

The most representative PROs were selected for inclusion in the multivariate regression model (*Table 2.3 and 2.4*). Because of low completion rates of lab testing despite intensive follow-up, lab tests were initially excluded from the multivariate analysis and score development. In CD four composite scores were evaluated (*Table 2.5*); In UC 11 composite scores were evaluated (*Table 2.6*). Addition of lab variables to the selected models decreased the sample size and therefore the power of the regression models; addition of the lab variables to the model did not result in inclusion of these variables in the models, because they did not reach the required significance level of $P<0.1$ for entry in the model.

	Development phase		Validation phase	
	CD	**UC**	**CD**	**UC**
n	110	109	301	265
Age (years), *median (range)*	33 (19-79)	35 (18-81)	33 (18-75)	42 (18-86)
Male, *n (%)*	56 (51)	57 (52)	144 (48)	132 (50)[a]
Smoking, *n (%)*	9 (8)	7 (6)[a]	19 (6)[c]	12 (5)[d]
Age at diagnosis (years), *median (range)*	24 (8-68)	28 (10-81)	25 (8-66)	29 (2-76)
Disease duration (years), *median (range)*	8 (0-46)	6 (0-52)	8 (0-52)	7 (0-59)
Surgical history, *n (%)*	48 (44)	1 (1)	132 (44)[b]	13 (5)[b]
Fistulizing disease (CD only), *n (%)*	5 (5)[a]	-	59 (20)[a]	-
Active disease (HBI>4 /pMayo>2), *n (%)*	32 (30)[a]	37 (34)	82 (27)	82 (31)

Table 2.2. Demographics of included patients in development and validation phase of the study.
[a]n=1 unknown; [b]n=2 unknown; [c]n=8 unknow; [d]n=9 unknown.

Table 2.3 and 2.4 on page 36 – 41.

Composite score development			AUC ROC curves		ρ	
Dependent variable	**Mo-del**	**Variables in composite scores***	**HBI**	**CDAI**	**HBI**	**CDAI**
HBI	1	V1.1; V3	0.981	0.912	0.903	0.739
	2	V1.2; V3; V10	0.956	0.898	0.750	0.702
CDAI	**1**	**V1.1; V3; V4; V10**	**0.951**	**0.963**	**0.837**	**0.830**
	2	V3; V4; V10	0.900	0.942	0.731	0.771

Table 2.5. Development and evaluation of composite scores for CD.
**see Table 2.3 for full details on each variable; V1.1 number of liquid/very soft stools per day; V1.2 total number of stools per day; V3 abdominal pain; V4 well-being VAS; V10 disease control VAS.*

Composite score development			AUC ROC curves			ρ		
Dependent variable	**Mo-del**	**Variables in composite scores***	**pMayo**	**SCCAI**	**MTWI**	**pMayo**	**SCCAI**	**MTWI**
pMayo	1, 2	V1.1; V3; V7; V8; V10	0.960	0.865	0.849	0.769	0.769	0.703
	1, 2[#]	V1.1; V3; V7; V10	0.957	0.879	0.883	0.797	0.803	0.762
	3	V1.2; V3; V7; V8; V10	0.964	0.908	0.890	0.808	0.812	0.748
	3[#]	**V1.2; V3; V7; V10**	**0.960**	**0.915**	**0.913**	**0.820**	**0.832**	**0.790**
	4	V1.2; V 4.2; V7; V10	0.956	0.920	0.909	0.809	0.838	0.787
SCCAI	1	V2; V4.1; V5; V7	0.872	0.974	0.896	0.711	0.907	0.836
	2, 4	V2; V3; V4.2; V5; V7; V10	0.904	0.971	0.883	0.765	0.911	0.810
	3	V1.2; V2; V4.1; V5; V7	0.885	0.981	0.923	0.721	0.914	0.869
MTWI	1	unbalanced model	-	-	-	-	-	-
	2	V1.1; V2; V6; V7; V8	0.928	0.879	0.937	0.801	0.806	0.855
	3	V1.2; V2; V4.1	0.880	0.907	0.984	0.712	0.797	0.933
	4	V1.2; V2; V4.2; V7; V8	0.906	0.894	0.950	0.777	0.810	0.866

Table 2.6. Development and evaluation of composite scores for UC.
**see Table 2.3 for full details on each variable; V1.1 and V1.2 number of stools per day; V2 number of stools at night; V3 abdominal pain VAS; V4.1 general well-being; V4.2 well-being VAS; V5 Urgency of defecation; V6 stool consistency; V7 rectal bleeding VAS, V8 Anorexia; V10 disease control VAS.*
[#]in these models loss of appetite was excluded as independent variable because of a clinically irrelevant negative value in the model

Domain	Variable	n	Cutoffs	MLE	SE	χ-sq	*P*	sel*	var
Stool frequency	**Number of liquid/very soft stools per day**	108	continuous	1.63	0.35	22.34	<.0001	-	
			0 / 1-3 / >3	3.49	0.73	23.11	<.0001	-	
			0 / 1-2 / >2	3.55	0.66	28.58	<.0001	1	V1.1
			0 / >0	3.36	0.77	19.10	<.0001	-	
	How many stools did you have yesterday during the day?	108	continuous	0.85	0.19	20.09	<.0001	-	
			0-1 / >1	2.00	0.65	9.53	0.0020	-	
	Number of stools more than normal per day	108	continuous	0.87	0.36	5.88	0.015	-	
			0 / >0	0.84	0.51	2.69	0.10	-	
	Total number of stools per day	108	continuous	0.97	0.20	22.75	<.0001	-	
			≤1 / >1	1.75	0.77	5.08	0.024	-	
			0-2 / >2	2.58	0.55	22.19	<.0001	-	
			0-1 / 2-4 / >4	2.64	0.58	20.79	<.0001	-	
			0-2 / 3-4 / >4	2.16	0.40	28.49	<.0001	2	V1.2
Stools at night	**How many stools did you have last night?**	108	continuous	0.88	0.26	11.59	0.0007	-	
			0 / >0	1.15	0.44	6.90	0.0086	-	
			0 / 1/ >1	0.99	0.30	11.01	0.0009	-	
			0 / 1-2 / >2	1.28	0.36	12.29	0.0005	1, 2	V2
Abdominal pain	**Abdominal pain (No - severe)**	108	No / Mild /Moderate / Severe	2.68	0.50	28.11	<.0001	-	
			No / Yes	3.72	0.62	35.35	<.0001	1, 2	V3
	Abdominal pain (No pain - continuous)	108	No abdominal pain / with bowel actions / continuous	1.52	0.31	23.97	<.0001	-	
	Abdominal pain VAS	108	continuous	0.51	0.10	24.99	<.0001	-	
			0-3 / >3, <8 / 8-10	2.02	0.41	24.17	<.0001	-	
			<3 / 3-6 / >6	1.94	0.39	25.03	<.0001	-	
General well-being	**General well-being (Very well - terrible)**	108	Very well Slightly below par / Poor / Very poor / Terrible	1.31	0.30	18.93	<.0001	-	
	Well-being VAS	108	continuous	0.47	0.11	18.44	<.0001	-	

*Table 2.3. CD variables, univariate logistic regression outcomes for prediction of active disease (HBI>4). CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, F: female, M: male, MLE: maximum likelihood estimate, SE: standard error WBC: white blood cell count. *variables selected for multivariate regression models (Table 2.5).*

Domain	Variable	n	Cutoffs	MLE	SE	χ-sq	*P*	sel*	Var
General well-being *(continued)*	**Well-being VAS *(continued)***		<4 / ≥4, <7 / ≥7	1.42	0.35	16.76	<.0001	-	
			≤2 / >2, <7 / ≥7	1.80	0.40	20.09	<.0001	1, 2	V4
	Well-being (No impairment - unable to work)	108	No impairment / Impaired but able to continue activities / Activities reduced / Unable to work	1.21	0.83	17.90	<.0001	-	
Urgency	**Urgency of defecation (No urgency - incontinence)**	108	No urgency / Hurry / Immediately / Incontinence	1.30	0.32	16.99	<.0001	1, 2	V5
			No Incontinence / Incontinence	0.88	1.43	0.38	0.54	-	
Stool consistency	**Stool consistency**	108	Normal or variably normal / Semi-formed / Liquid	2.09	0.48	19.06	<.0001	1, 2	V6
	Do you take opiates or lomotil/imodium for diarrhea?	108	No / Yes	1.22	0.52	5.47	0.019	-	
	Anti-diarrheals VAS	108	continuous	0.00	0.09	0.00	1.00	-	
Rectal bleeding	**Rectal bleeding VAS**	108	continuous	0.16	0.09	3.06	0.080	-	
			≤3 / >3	1.22	0.52	5.47	0.019	1, 2	V7
	What % of bowel movements contains visible blood?	108	None / <50% / ≥50% / Blood Alone)	0.36	0.34	1.08	0.30	-	
	Amount of blood in stool	108	None / Trace / Occasionally frank / Usually frank)	0.61	0.28	4.72	0.030	-	
Fever	**Did you have Fever yesterday?**	108	No / Yes	14.53	913.40	0.00	0.99	-	
Anorexia	**Loss of appetite**	108	No / Yes	1.04	0.45	5.51	0.019	1, 2	V8
Nausea/ vomiting	**Nausea and/or vomiting**	108	No / Yes	1.03	0.49	4.44	0.035	1, 2	V9
Disease activity	**Disease control VAS**	108	continuous	0.42	0.09	21.88	<.0001	-	
			≤3, >3, <7 / ≥7	1.60	0.32	24.41	<.0001	-	
			≤2, >2, <7 / ≥7	1.80	0.36	24.58	<.0001	1, 2	V10

Table 2.3 – continued. CD variables, univariate logistic regression outcomes for prediction of active disease (HBI>4).

Domain	Variable	n	Cutoffs	MLE	SE	χ-sq	*P*	sel*	var
Labs	**CRP (mg/dL)**	93	continuous	0.27	0.14	3.80	0.051	-	
			≤0.8 / >0.8	1.77	0.53	11.11	0.0009	-	
	Calprotectin (ug/g)	63	continuous	0.00	0.00	6.45	0.011	-	
			<163 / ≥163	1.22	0.63	3.71	0.054	-	
			<50 / ≥50	0.28	0.66	0.18	0.67	-	
	WBC(*10^3 cells/uL)	96	continuous	0.15	0.08	3.20	0.074	-	
			≤9.95 / >9.95	1.06	0.66	2.60	0.11	-	
	Albumin (g/dL)	94	continuous	-1.55	0.61	6.47	0.011	-	
			≥3.7 / <3.7	1.92	0.90	4.51	0.034	-	
	Platelets (*10^3 cells/uL)	96	continuous	0.00	0.00	1.43	0.23	-	
			≥143 / <143	15.17	770.20	0.00	0.98	-	
	ESR (mm/hr)	85	continuous	0.05	0.02	7.28	0.0070	-	
			≤22(F) or ≤10 (M) / >22 (F) or >10 (M)	1.62	0.53	9.38	0.0022	-	
	Hemoglobin (g/dL)	95	continuous	-0.10	0.14	0.59	0.44	-	
			>11.6 (F) or >13.5 (M) / ≤11.6 (F) or ≤13.5 (M)	1.15	0.50	5.24	0.022	-	
	Hematocrit	96	continuous	-3.34	5.39	0.38	0.54	-	
			>0.349 (F) or >0.385 (M) / ≤0.349 (F) or ≤0.385 (M)	0.61	0.57	1.15	0.28	-	

Table 2.3 – continued. CD variables, univariate logistic regression outcomes for prediction of active disease (HBI>4).

Domain	Variable	n	Cutoffs	MLE	SE	χ-sq	*P*	sel*	var
Stool frequency	**How many stools did you have yesterday during the day?**	109	Continuous	0.87	0.79	20.57	<.0001	-	
			<3 / 3-4 / 5-6 / 7-9 / >9	1.61	0.33	23.11	<.0001	-	
			<4 / 4-6 / >6	2.24	0.50	19.69	<.0001	-	
			<4 / 4-6 / >6	2.32	0.49	22.35	<.0001	-	
	Stools more than normal	109	Continuous model	0.99	0.33	9.23	0.0024	-	
			0 / 1-2 / 3-4 / >4	1.65	0.41	16.17	<.0001	-	
			0 / 1-2 / >2	1.78	0.41	19.18	<.0001	-	
	Total number of stools/day	109	Continuous	0.78	0.16	23.03	<.0001	-	
			<3 / 3-6 / >6	2.24	0.42	28.86	<.0001	-	
			0-4 / >4	3.57	0.62	32.79	<.0001	1, 2	V1.1
			0-2 / 3-4 / >4	1.95	0.34	32.46	<.0001	3, 4	V1.2
Stools at night	**How many stools did you have last night?**	109	Continuous	0.95	0.26	12.77	0.0004	-	
			0 / >0	1.48	0.43	11.79	0.0006	-	
			0 / 1-3 / >3	1.49	0.38	15.01	0.0001	1, 2, 3, 4	V2
Abdominal pain	**Abdominal pain (No - severe)**	109	No / Mild / Moderate / Severe	0.78	0.25	9.60	0.0019	-	
			No / Yes	1.47	0.45	10.62	0.0011	-	
	Abdominal pain (No - continuous)		No abdominal pain	1.02	0.30	11.44	0.0001	-	
	Abdominal pain VAS	109	Continuous	0.40	0.09	19.21	<.0001	-	
			<3 / ≥3, ≤6 / >6	1.75	0.37	21.84	<.0001	1, 2, 3, 4	V3
			0 / >0, ≤4 / >4	1.40	0.33	18.20	<.0001	-	
General well-being	**General well-being? (Very well - terrible)**	109	Very well / Slightly below par / Poor / Very Poor / Terrible	1.27	0.34	14.12	0.0002	-	
	General well-being (Perfect - terrible)	109	Perfect / Very good / Good / Average / Poor / Terrible	0.91	0.23	16.08	<.0001	1, 3	V4.1
	Well-being VAS	109	Continuous	0.43	0.11	15.30	<.0001	-	

*Table 2.4 UC variables, univariate logistic regression outcomes for prediction of active disease (pMayo >2). CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, F: female, M: male, MLE: maximum likelihood estimate, SE: standard error WBC: white blood cell count. *variables selected for multivariate regression models (Table 2.6).*

Domain	Variable	n	Cutoffs	MLE	SE	χ-sq	*P*	sel*	var
General well-being *(continued)*	**Well-being VAS *(continued)***	109	≤3 / >3	1.62	0.45	13.31	0.0003	-	
			≤3 / >3, ≤6 / >6	1.42	0.36	15.73	<.0001	2, 4	V4.2
	Well-being (No impairment - unable to work)	109	No impairment / Impaired but able to continue activities / Activities Reduced / Unable to work	1.14	0.36	15.93	<.0001	-	
Urgency	**Urgency of defecation**	109	No urgency / Hurry / Immediate / Incontinence	2.01	0.40	24.82	<.0001	-	
			No urgency / Hurry / Immediate	2.03	0.40	25.13	<.0001	1, 2, 3, 4	V5
			No Incontinence / Incontinence	14.13	826.90	0.00	0.99	-	
Stool consistency	**Stool consistency**	109	Normal or variably normal / Semi-formed / Liquid	2.13	0.46	21.68	<.0001	1, 2, 3, 4	V6
	Do you take opiates or lomotil/imodium for diarrhea?	109	No / Yes	-0.03	0.59	0.00	0.96	-	
	Anti-diarrheals VAS	109	Continuous	0.05	0.09	0.26	0.26	-	
Rectal bleeding	**Rectal bleeding VAS**	109	Continuous	0.59	0.11	27.82	<.0001	-	
			≤3 / >3	2.71	0.49	29.97	<.0001	-	
			<2 / ≥2, <5 / ≥5, <8 / ≥8	1.66	0.31	28.15	<.0001	1, 2, 3, 4	V7
	What % of bowel movements contains visible blood?	109	None / <50% / ≥50% / Blood Alone	2.84	0.59	22.89	<.0001	-	
			None / <50% / ≥50%	2.95	0.60	24.26	<.0001	-	
			None / >0%	3.86	1.04	13.76	0.0002	-	
	Amount of blood in stool	109	None / Trace / Occasionally frank / Usually frank	1.83	0.35	27.22	<.0001	-	
			None / Trace / More than a Trace	1.95	0.37	27.53	<.0001	-	
Anorexia	**Loss of appetite**	109	No / Yes	1.44	0.48	9.10	0.0025	1, 2, 3, 4	V8
Nausea/ vomiting	**Nausea and/or vomiting**	109	No / Yes	0.72	0.49	2.12	0.14	-	

Table 2.4 – continued. UC variables, univariate logistic regression outcomes for prediction of active disease (pMayo >2).

Domain	Variable	n	Cutoffs	MLE	SE	χ-sq	*P*	sel*	var
Disease activity	**Disease control VAS**	109	Continuous	0.46	0.10	21.67	<.0001	-	
			≤3 / >3, <7, ≥7	1.44	0.31	21.37	<.0001	-	
			≤2 / >2, ≤5 / >5	1.82	0.36	25.86	<.0001	1, 2, 3, 4	V10
			≤2 / >2, <7 / ≥7	1.68	0.36	21.76	<.0001	-	
Labs	**CRP (mg/dL)**	91	continuous	1.03	0.42	5.87	0.015	-	
			≤0.8 / >0.8	1.50	0.55	7.35	0.0067	-	
	Calprotectin (ug/g)	70	continuous	0.00	0.00	4.31	0.038	-	
			<163 / ≥163	1.29	0.56	5.22	0.022	-	
			<50 / ≥50	1.96	0.80	6.06	0.014	-	
	WBC (*10^3 cells/uL)	93	continuous	0.20	0.08	5.91	0.015	-	
			≤9.95 / >9.95	1.39	0.56	6.19	0.013	-	
	Albumin (g/dL)	88	continuous	-1.52	0.66	5.39	0.02	-	
			≥3.7 / <3.7	14.36	610.50	0.00	0.98	-	
	Platelets (*10^3 cells/uL)	93	continuous	0.00	0.00	2.54	0.11	-	
			≥143 / <143	-12.66	805.50	0.00	0.99	-	
	ESR (mm/hr)	85	continuous	0.04	0.01	8.38	0.0038	-	
			≤22(F) or ≤10 (M) / >22 (F) or >10 (M)	1.04	0.47	4.81	0.028	-	
	Hemoglobin (g/dL)	93	continuous	-0.31	0.15	4.59	0.032	-	
			>11.6 (F) or >13.5 (M) / ≤11.6 (F) or ≤13.5 (M)	0.75	0.50	2.25	0.13	-	
	Hematocrit	93	continuous	-9.46	5.91	2.66	0.10	-	
			>0.349 (F) or >0.385 (M) / ≤0.349 (F) or ≤0.385 (M)	1.84	0.65	7.99	0.0047	-	

Table 2.4 – continued. UC variables, univariate logistic regression outcomes for prediction of active disease (pMayo >2).

For CD the selected composite score (*Table 2.7*) had an AUC of >0.95 for predicting clinical disease activity using both CDAI and HBI as gold standards (0.951 and 0.963, respectively). The Spearman correlation coefficients were 0.837 and 0.830, respectively (*Table 2.5*). The optimal cutoff for the mHI-CD to predict clinical disease activity was ≥5.5, resulting in a NPV of 96%, positive predictive value (PPV) of 63%, sensitivity of 88% and specificity of 85%. For UC the selected composite score (*Table 2.8*) had an AUC of >0.91 to predict disease activity using pMayo, SCCAI, and MTWI as gold standards (0.960, 0.915, and 0.913, respectively). The Spearman correlation coefficients were 0.820, 0.832, and 0.790, respectively (*Table 2.6*). The optimal cutoff for the mHI-UC to predict clinical disease activity was ≥4.99, resulting in a NPV of 97%, PPV of 72%, sensitivity of 89%, and specificity of 90%.

mHI-CD Questions	**Answer**	**Score**
Number of liquid/very soft stools/day	0 1-2 ≥3	0.0000 1.6983 3.3966
Abdominal pain	No Yes	0.0000 2.3868
Rate your well-being on a scale from 0 to 10 (0=worst, 10=best)	8 - 10 4 - 7 0 - 3	0.0000 2.1336 4.2672
How well do you feel your disease is under control (0=no disease activity, 10=worst disease activity)	0-2 3-6 7-10	0.0000 2.1175 4.2350
Total score (SUM)		

Table 2.7. Calculation of the mHI-CD

mHI-UC Questions	**Answer**	**Score**
How many stools did you have yesterday?	≤2 3 - 4 >4	0.0000 1.4428 2.8856
Rate your abdominal pain on a scale from 0 to 10 (0=none, 10=worst)	0 - 2 3 - 6 7 - 10	0.0000 1.0392 2.0784
How often do you experience rectal bleeding? (0=none, 10=always)	0 - 3 4 - 10	0.0000 2.2019
How well do you feel your disease is under control (0=no disease activity, 10=worst disease activity)	0 - 2 3 - 5 6 - 10	0.0000 1.7557 3.5114
Total score (SUM)		

Table 2.8. Calculation of the mHI-CD

Validation phase

A total of 301 CD patients (UCLA n=127; UCI n=82; LUMC n=92) and 265 UC patients (UCLA n=119; UCI n=67; LUMC n=79) were analyzed in the validation phase (*Figure 1b, Table 2.2*). For CD the Spearman correlation coefficient was 0.75 (P<0.0001) between HBI and mHI-CD, the AUC of the ROC for predicting clinical disease activity was 0.90, and a

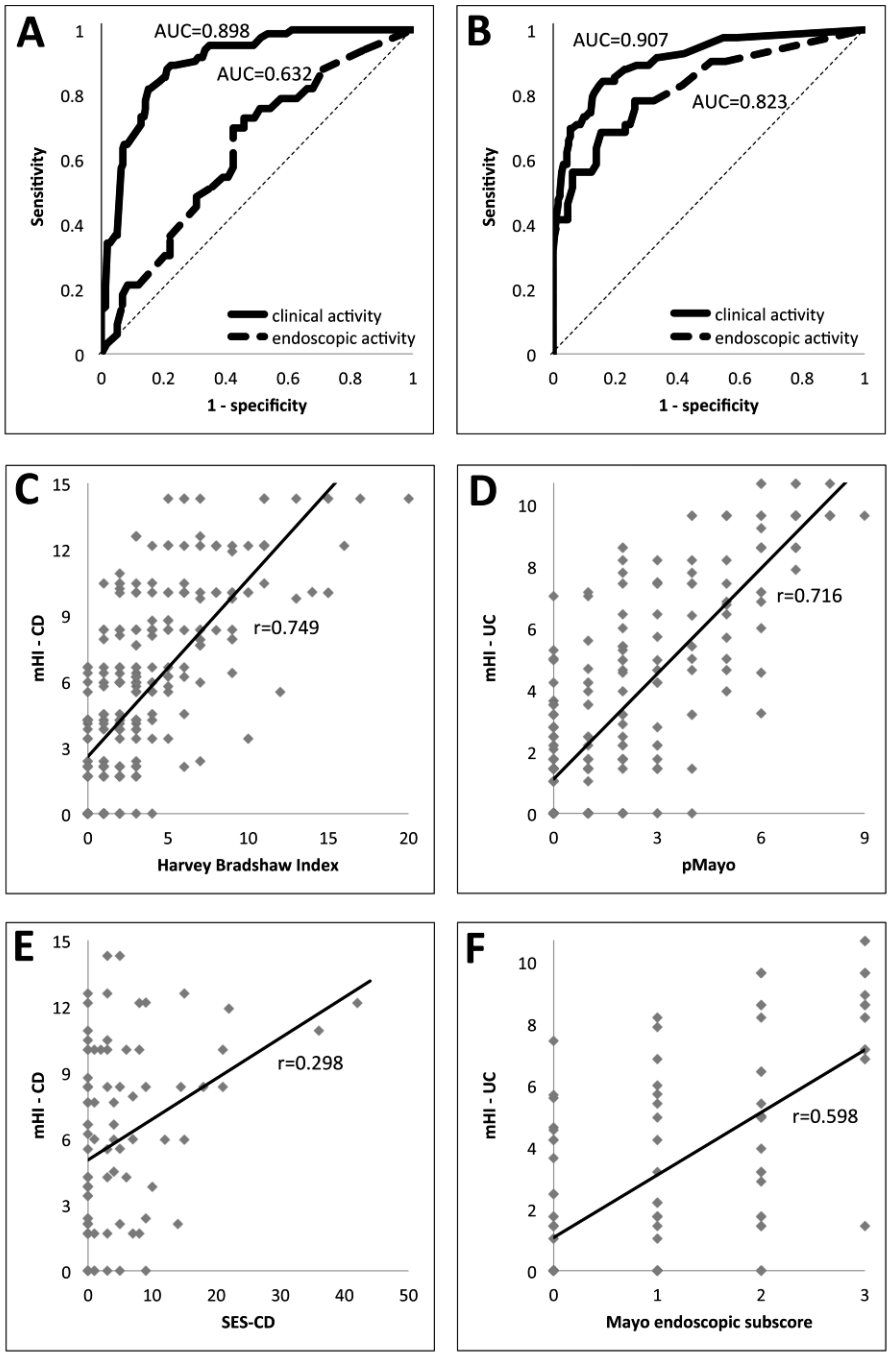

Figure 2.2 Performance of the developed mHI scores to detect disease activity in CD (a, c, e) and UC (b, e, f). ROC curves of the mHI to predict clinical and endoscopic disease activity (a+b), scatter plot of the mHI versus clinical disease activity scores (c+d) and endoscopic disease activity scores (e+f).

sensitivity of 94% and specificity of 67% were achieved using a cutoff of ≥5.5 (*Figure 2.2a and 2.2c*). To achieve the optimal NPV of 95% and sensitivity of 85%, the cutoff in this cohort would be ≥6.38, which would result in 85% sensitivity, 80% specificity, 95% NPV, and 55% PPV. The mHI-CD was poorly correlated with the SES-CD (ρ=0.30, *P*=0.0039), with an AUC of 0.63 (*Figure 2a and 2e*).

For UC the Spearman correlation coefficient was 0.72 (*P*<0.0001) between pMayo and mHI-UC, the AUC of the ROC for predicting clinical disease activity was 0.91, and a sensitivity of 73% and specificity of 90% specificity were achieved using a cutoff of ≥4.99 (*Figure 2.2b and 2.2d*). The optimal cutoff in this cohort would be ≥3.2, which would result in 85% sensitivity, 80% specificity, 95% NPV, and 55% PPV. The mHI-UC was strongly correlated with the Mayo endoscopic subscore (ρ=0.60, *P*<0.0001), with an AUC of 0.82 (*Figure 2.2b and 2.2f*).

Sensitivity to change was assessed in a subset of 50 CD patients and 44 UC patients. Median time between questionnaires was 46 days (range 2-352) for CD and 57.5 days (range 3-275) for UC. Four (8%) CD patients deteriorated, 31 (62%) had stable disease activity, and 15 (30%) improved. Of the UC patients, 5 (11%) deteriorated, 27 (61%) remained stable, and 12 (27%) improved. There was a significant difference in mHI between patients who clinically improved, remained stable, or worsened in both CD (*P*=0.0030) and UC (*P*=0.0025, *Figure 2.3a and 2.3b*). Test-retest reliability was assessed in a subset of 40 CD and 37 UC patients. The median time to second questionnaire completion was 21 hours (range 7-36) for the mHI-CD and 23 hours (range 11-144) for the mHI-UC. The ICC was 0.94 (confidence limits 0.89-0.97) for the mHI-CD and 0.94 (confidence limits 0.89-0.97) for the mHI-UC (*Figure 2.3c and 2.3d*).

One question in both the mHI-CD and the mHI-UC assessed patient reported disease activity using a VAS (DA-VAS). In CD patients (n=301) the DA-VAS had a Spearman correlation of 0.63 (*P*<0.0001) with the HBI, and the AUC for predicting clinical disease activity was 0.83 (compared to ρ=0.75 and AUC=0.90 for the full mHI-CD). The CD DA-VAS was weakly correlated with the SES-CD (ρ=0.21, *P*=0.040), and had an AUC to predict endoscopic disease activity of 0.59 (compared to ρ=0.30 and AUC=0.63 for the full mHI-CD). The DA-VAS was not significantly different between patients who deteriorated, remained stable, or improved (*P*=0.12). In UC patients (n=265) the DA-VAS had a Spearman correlation of 0.67 (*P*<0.0001) with the pMayo, and the AUC for predicting clinical disease activity was 0.86 (compared to ρ=0.72 and AUC=0.91 for the full mHI-UC). The UC DA-VAS was also correlated with the endoscopic component of the Mayo score (ρ=0.55, *P*<0.0001), and had an AUC to predict endoscopic disease activity of 0.79 (compared to ρ=0.60 and AUC=0.82 for the full mHI-UC). A significant difference between the DA-VAS of UC patients that deteriorated, remained stable, or improved was observed (*P*=0.0052).

Discussion

We developed two four-item questionnaires consisting solely of PROs for remote monitoring of IBD patients, which can be employed on mobile technology. The questionnaires were validated in a multi-center validation study and showed excellent characteristics to monitor clinical disease activity as well as symptom changes. As previously shown, UC clinical disease activity highly correlates with endoscopic disease activity, while correlation between CD symptoms and endoscopic findings is poor.[22]

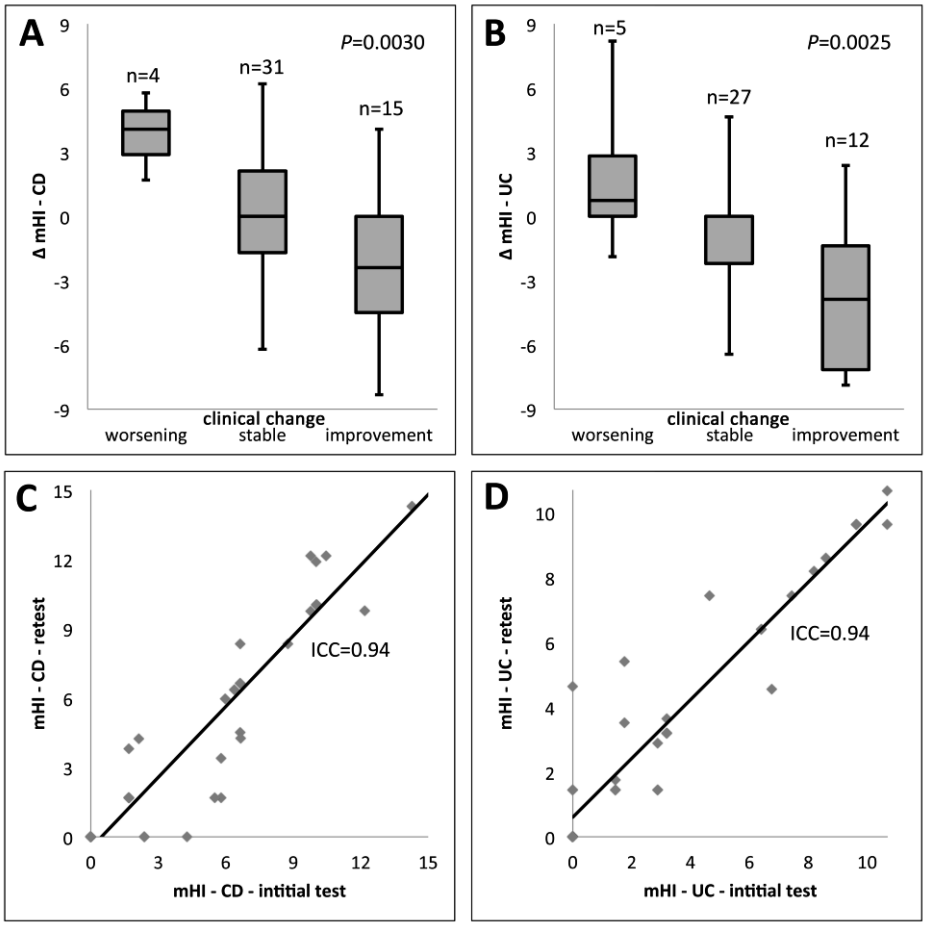

Figure 2.3. Sensitivity to change (a+b) and test-retest reliability (c+d) of the mHI-CD (a+c) and mHI-UC (b+d).

Although previous studies have aimed to identify PROs for disease monitoring either by adjusting existing questionnaires[18], or by using sub-components of existing questionnaires[19,20], we were able to prospectively identify PROs relevant for clinical disease monitoring and validate those in an independent cohort. Interestingly, patient reported disease activity was shown to be an independent predictor for clinical disease activity in both UC and CD patients, even after inclusion of common IBD symptoms such as

stool frequency and abdominal pain. Patient reported disease activity alone had a comparable performance to the complete mHI in both CD and UC for detecting clinical and endoscopic activity, though responsiveness to changes in disease activity was reduced in particular in CD patients.

A limitation of this study is the potential for recall bias in CDAI calculation. Though 7-day diary forms were sent out in advance, we did not log whether diaries were filled out daily of by recall. Additionally, in the validation cohort, optimal cutoffs of the mHI for detection of disease activity were higher than expected for CD and lower than expected for UC. This might be due to the reduction of questionnaire items from >20 PROs to just four, or due to differences in the patient population. The validation phase of the study most accurately represents the real-life situation. Therefore, we implemented the cutoff for optimal sensitivity and specificity as observed in the validation cohort in clinical practice.

This study was not primarily designed to evaluate correlations between PROs and endoscopic healing. In at-risk patients, clinical assessments remain warranted, which may lead to further endoscopic evaluation. This tool offers an optimal screening method to monitor and evaluate disease activity in and outside of clinical practice with a high NPV. The mHIs are currently implemented in the UCLA eIBD patient app (*Figure 2.4*) and automated messages are sent to a nurse coordinator when the mHI indicates disease activity.

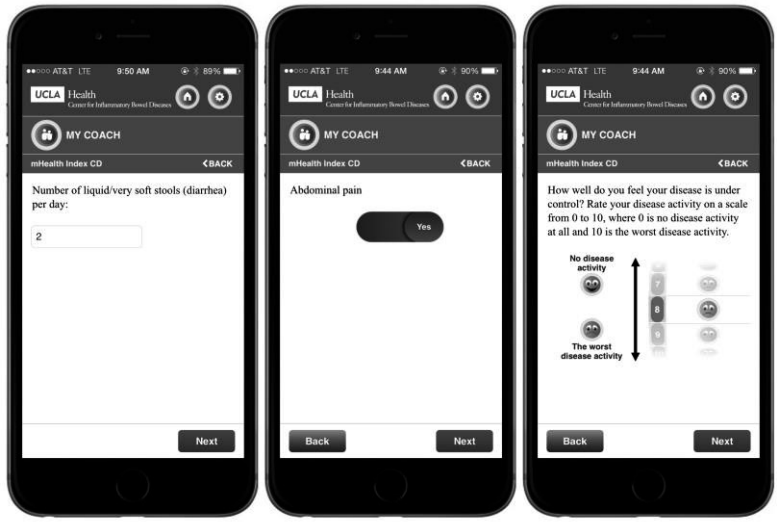

Figure 2.4. Screenshots of the mHI as implemented in the UCLA eIBD patient app available to patients treated at the UCLA IBD Center.

The calculation of the mHI is complex; however, simplifying the score would most likely result in loss of accuracy. Since the index is meant to be automated and implemented on digital platforms, we feel that using the more complex calculations is justified.

Cloud-based health technologies are predicted to revolutionize care delivery and patient engagement. Patients can participate in their care by signaling meaningful health outcomes during year-round monitoring. Barriers for more widespread implementation of mHealth in IBD care include policies affecting reimbursement and regulatory requirements[23], as well as privacy and security concerns.[1]

In summary, we developed the mHI-CD and mHI-UC for remote monitoring of CD and UC patients. The scores are specifically designed for implementation on a mobile application and are currently available to IBD patients treated at the UCLA Center for IBD. Prospective randomized studies will need to assess the effect of remote monitoring on disease control, QoL, patient satisfaction, and health care costs.

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Chapter 3.

Presenteeism in Inflammatory Bowel Diseases: A Hidden Problem with Significant Economic Impact

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Abstract

Background
Indirect costs associated with impaired productivity at work (presenteeism) due to inflammatory bowel disease (IBD) are a major contributor to health expenditures. Studies estimating indirect costs for IBD in the United States did not take presenteeism into account. We aimed to quantify work limitations and presenteeism and its associated costs in an IBD population to generate recommendations to reduce presenteeism and decrease indirect costs.

Methods
We performed a prospective study at a tertiary IBD center. During clinic visits, work productivity, work-related problems and adjustments, quality of life, and disease activity were assessed in patients with IBD. Work productivity and impairment were assessed in a control population as well. Indirect costs associated with lost work hours (absenteeism) and presenteeism were estimated, as well as the effect of disease activity on those costs.

Results
Of the 440 included patients with IBD, 35.6% were unemployed. Significantly more presenteeism was detected in patients with IBD (62.9%) compared with controls (27.3%, P=0.004), with no significant differences in absenteeism. Patients in remission experienced significantly more presenteeism than controls (54.7% versus 27.3%, respectively, P<0.01), and indirect costs were significantly higher for remissive patients versus controls ($17,766 per year versus $9,179 per year, respectively, P=0.03). Only 34.3% had made adjustments to battle work-related problems such as fatigue, irritability, and decreased motivation.

Conclusions
Patients with IBD in clinical remission still cope with significantly more presenteeism and work limitations than controls; this translates in higher indirect costs and decreased quality of life. The majority have not made any adjustments to battle these problems.

Introduction
A decrease in work productivity is commonly seen in patients suffering from chronic diseases.[1] This impairment is usually described in terms of presenteeism or absenteeism. Presenteeism is defined as the lost productivity that occurs when employees come to work but perform below par due to their illness. Absenteeism represents time missed from work due to their disease. Activity impairment is the effect of illness on regular everyday activities. The associated indirect costs are a major contributor to health expenditures. It was reported that 76% of medical costs in chronic diseases are due to indirect medical costs, of which 83% (63% of total costs) is due to presenteeism.[2]

The IBD are chronic, frequently progressive, conditions often with complications leading to disabilities.[3] The prevalence of Crohn's disease (CD) is 201 per 100,000 adults and 238

per 100,000 adults for ulcerative colitis (UC) in the U.S. population.[4] Impairment due to IBD has been shown to affect educational and employment prospects,[5-8] triggering a socioeconomic burden on the economy and the patient.[5,9] Patients with symptomatic IBD are less likely to have obtained a graduate or a professional degree than non-symptomatic patients.[10] Patients with IBD experience significant longer periods of unemployment[8] and have lower employment percentages[5-7]. Also, IBD-associated problems can result in job loss, missed school days, or reduced employment offers.[9] Even if patients with IBD do go to work, their productivity is frequently impaired because of diminished motivation, irritability, avoidance of social activities, and less participation during meetings.[11] Published estimates showed that 43% of employees with IBD need time off work due to the disease, averaging 7.2 days per employee with IBD per year.[12] This translates into a cost of $138 million per year for the U.S. The indirect cost of missed work time to IBD in 1998 or 1999 was more than $3.6 billion U.S. dollars (USD) or $5228 USD per person with IBD and symptoms.[10] Fortunately, more effective IBD therapies have resulted in improved health outcomes, which has been associated with improvements in employment status, hours worked, and productivity.[13-15]

So far, studies estimating the indirect costs for IBD in the U.S. did not take presenteeism into account.[16-19] Since presenteeism is the major contributor to indirect medical costs[2], the actual costs are probably underestimated. Therefore, in addition to confirming IBD work-related problems in a prospective, high volume, single IBD center study, we aimed to (1) quantify presenteeism, (2) determine its associated costs, and (3) generate recommendations to reduce presenteeism and thus lower indirect costs related to IBD.

Methods

Design and Population

We performed a prospective study at a tertiary IBD center in Los Angeles, California between March 2013 and February 2014. All included patients were above the age of 18 and participated in the Value-based Care Program[20] at the UCLA Center for Inflammatory Bowel Diseases. Consecutive patients were asked to participate in this study during clinic visits. In November 2013, a de-identified web-based questionnaire accessible through a 128-bit SSL encrypted link was sent out to patients who had not visited our clinic in the past year. Patients who could not be reached through e-mail were approached by telephone. Included patients were approached by e-mail to ask anyone they know (e.g. a family member or friend), above the age of 18 and without IBD, to serve as our control group. The study was approved by the UCLA IRB under protocol number 13-001507.

Questionnaires and Data Collection

The following questionnaires were administered: (1) the Work Productivity and Activity Impairment (WPAI)[21] questionnaire, (2) the short-IBD questionnaire for quality of life (QoL) assessment[22], and (3) disease activity (DA) scores (Harvey Bradshaw index for CD[23] and partial Mayo score for UC[24]). Additionally, we developed a work impact questionnaire based on the IMPACT[11] study to assess work-related problems. Finally, we included

questions about job-lock into the questionnaire (*Figure 3.1*). Job-lock is defined as the propensity of patients to stay in a job to retain insurance coverage. Data about race, ethnicity, initial symptoms, initial disease location, specific colon locations, fistula, extra-intestinal manifestations, disease duration, surgeries, smoking and alcohol use were collected from the medical charts.

Work Impact Questionnaire

1. What industry do you work in?
   - ☐ Real estate, renting, leasing
   - ☐ State and Local Government
   - ☐ Finance and insurance
   - ☐ Health/social care
   - ☐ Manufacturing
   - ☐ Retail trade
   - ☐ Wholesale trade
   - ☐ Federal Government
   - ☐ Information
   - ☐ Arts, entertainment
   - ☐ Construction
   - ☐ Waste services
   - ☐ Other services
   - ☐ Utilities
   - ☐ Mining
   - ☐ Corporate management
   - ☐ Education services
   - ☐ Agriculture
   - ☐ Other, please specify: ……

2. Who is currently providing you with health insurance?
   - ☐ Employer → proceed to next question
   - ☐ Other, please specify and proceed to question 5

     ……

3. Would you like to change your job?
   - ☐ Yes → proceed to next question
   - ☐ No → proceed to question 5

4. Is the risk of losing employer-provided health insurance your reason for not changing jobs?
   - ☐ Yes
   - ☐ No, please specify: ……

5. Have you been on disability in the past year? If yes please specify for how long
   - ☐ Yes, for …….. months → proceed to next question
   - ☐ No → proceed to question 7

6. What was the reason you were on disability?
   - ☐ Fatigue
   - ☐ Hospitalization/Surgery
   - ☐ Other, please specify: ……

7. Which of the following adjustments have you made in your work to avoid taking sick days off from work due to your IBD?
   - ☐ Working from home
   - ☐ Working part-time
   - ☐ Working flexible hours
   - ☐ Other: ……
   - ☐ I have not made any such adjustments
   - ☐ I do not have the possibility to make such an adjustment

Figure 3.1. The questionnaire used for data collection

8. If you have missed work due to your IBD, what was the reason? Check all that apply.
   - ☐ Hospital/emergency department visit
   - ☐ Doctor appointment
   - ☐ Incontinence or fear of incontinence
   - ☐ Abdominal pain or cramping
   - ☐ Fear of frequent stools or bowel movements interfering with work activities
   - ☐ Fear of frequent stools or bowel movements bringing attention to my condition from colleagues
   - ☐ Fatigue, and/or not enough energy to get through the day
   - ☐ Worry about gas pressure, discomfort
   - ☐ Worry/fear of potential for embarrassment
   - ☐ Rectal/anal pain or burning
   - ☐ Volume of blood in bleeding episode
   - ☐ I have never been absent from work due to IBD
   - ☐ Not applicable/other: …….

9. Have any of your superiors and/or colleagues complained or made unfair remarks about your performance at work in relation to your IBD?
   ☐ Yes ☐ No

10. Do you think you have been discriminated in the workplace as a direct consequence of your IBD?
    ☐ Yes ☐ No

11. How does IBD affect your performance at work
    - ☐ I am quiet or quieter during meetings
    - ☐ I cancel my attendance at meetings at the last minute
    - ☐ I do not participate in work social activities
    - ☐ I am irritable at work
    - ☐ I am less motivated in my work
    - ☐ My IBD does not affect my behavior at work
    - ☐ I am fatigued
    - ☐ Not applicable/other

How much do you agree with the following statements?

12. I believe that IBD has negatively affected my career path, opportunities for advancement, income and/or earning potential
    - ☐ Strongly agree
    - ☐ Agree
    - ☐ Neither agree nor disagree
    - ☐ Disagree
    - ☐ Strongly disagree

13. Because of my IBD, I have lost a job or had to quit /leave a job
    - ☐ Strongly agree
    - ☐ Agree
    - ☐ Neither agree nor disagree
    - ☐ Disagree
    - ☐ Strongly disagree

These questions were based on surveys and adapted for this study from the *European Federation of Crohn's and Ulcerative Colitis Associations* and *The National Association for Colitis and Crohn's Disease*.

Figure 3.1 – continued. The questionnaire used for data collection

Controls filled out a general health version of the WPAI and a modified version of the work impact questionnaire, assessing the effect of general health problems on work productivity. To classify patients by type of employment, we used the categorization of the U.S. Department of Labor Statistics.[25]

Definitions
The WPAI calculates absenteeism, presenteeism, and activity impairment independent of work status. Absenteeism is calculated based on the numbers of hours missed from work due to disease as a percentage of the total amount of hours worked in a week. Presenteeism and activity impairment are assessed on an 11-point Likert scale, where 0 was no effect of the disease, and 10 was full impairment due to disease. Prevalence of absenteeism, presenteeism, and activity impairment in our cohort were defined as any absenteeism, presenteeism, or activity impairment; no threshold was imposed. Job-lock is defined as not being able to change employment because of employer-provided health insurance and fear of loss of employee benefits. Remission of IBD was defined as a Harvey Bradshaw index of ≤4 for CD and a partial Mayo score ≤2 for UC, with higher scores indicating active disease.

Outcomes
Absenteeism, presenteeism, and work limitations were analyzed, and differences between patients with IBD and controls, patients with UC and CD, and patients with active disease and inactive disease were assessed. Absenteeism costs were estimated using the lost-wages method[26], which calculates absenteeism costs by multiplying the estimated number of workdays missed by the estimated average daily compensation for full-time employees and an average wage multiplier of 1.61[27]. Estimated daily earnings and benefits were defined as $31.93 per hour and based of the U.S. Department of Labor statistics.[25] To define a high and low salary group, we obtained the different hourly wages for the employment categories from the Department of Labor, patients who made more than $32 per hour were defined as the high salary group, whereas patients who made less than $32 per hour were defined as the low salary group. Presenteeism costs were calculated assuming the hours of decreased productivity as partially non-worked hours and multiplying them by the estimated average daily compensation and the average wage multiplier.

Statistical Analysis
Descriptive statistics were provided for the results of the work impact questionnaire. Students' t tests and one-way analysis for variance tests were performed for continuous data, and Fisher's exact tests and chi-square tests for categorical data. The data were analyzed using Excel (Microsoft Office Excel 2010, Microsoft, Redmond, WA) and SPSS software (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY).

Results

Patients
A total of 469 patients filled out the WPAI questionnaire. Twenty-nine patients were excluded because 23 forms were filled out incorrectly, and 6 patients did not have confirmed IBD, which left 440 patients with IBD eligible for analysis. For a subset of 379 patients, QoL and DA were assessed during the same clinic visit. In addition, a total of 213

patients filled out the work impact questionnaire. DA and QoL scores were available for 152 of those. A total of 22 controls were included as a comparison (*Figure 3.2*).

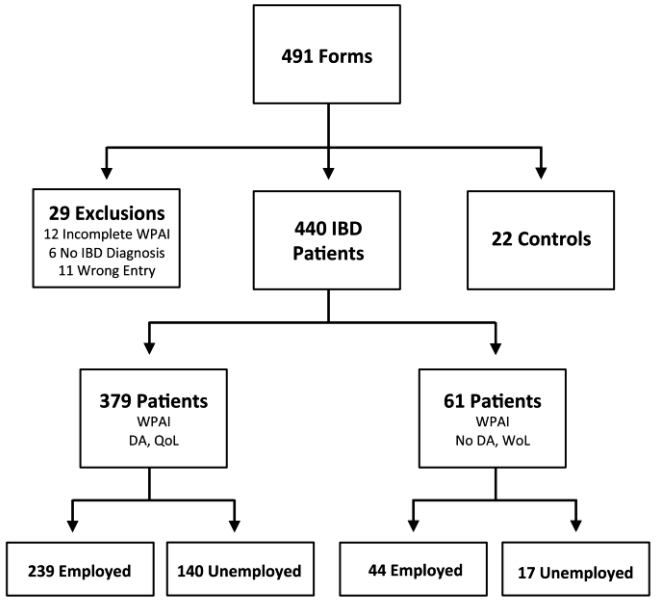

Figure 3.2. Study flowchart.

Out of the 440 included patients with IBD, 49.8% were male (*Table 3.1*). The median age was 37 years (range, 18-83 yr), and 73.9% had never smoked. The majority of the included patients (82%) were white, 7.3% were of Asian descent, and 3.4% were black or African American. In total, 50.2% (221) were diagnosed with CD and 49.8% (219) with UC. No significant differences in gender, smoking status, race, ethnicity, and disease duration were observed between patients with UC and CD. The median age at diagnosis for patients with CD was slightly younger (24; range, 8-68 year) than for patients with UC (29; range, 6-81 year) (P=0.002). Rectal bleeding was the most common presenting symptom in UC (77.3%) and abdominal pain the most common in CD (69.7%). As expected, more patients with CD (33.5%) have undergone abdominal surgery than patients with UC (9.1%) (P<0.0001). No significant differences in gender, age, intoxications, race, and ethnicity were observed between the IBD and the control group (*Table 3.2*); 13.6% of the controls had a chronic disease.

Employment

In total, 64.4% (283) of the total IBD cohort was employed and 35.6% (157) was not (*Table 3.3*). *Table 3.4* shows the industrial sectors in which patients were employed. Out of 62 unemployed patients who indicated a reason for being unemployed, 54.8% were retired or a student; 14.5% were on disability; 12.9% were homemakers (manager of the household); 4.8% could not work due to IBD; and 3.2% recently lost their job. All of our

Total (n=440)	**CD (n=221)**	**UC (n=219)**	***P***
Male gender, *n (%)*	110 (49.8)	109 (49.8)	1.000
Age (years), *median (range)*	36 (19-79)	40 (18-83)	0.174
Smoking, *n (%)*			0.782
- **Current**	18 (8.1)	14 (6.4)	
- **Past**	40 (18.1)	42 (19.2)	
- **Never**	163 (73.8)	162 (73.9)	
- **Unknown**	NA	1 (0.5)	
Drinking, *n (%)*			0.014
- **Yes**	106 (48)	130 (59.4)	
- **No**	114 (51.6)	88 (40.5)	
- **Unknown**	1 (0.4)	2 (0.9)	
Age at diagnosis (years), *median (range)*	24 (8-68)	29 (6-81)	0.002
Disease duration (years), *median (range)*	8 (0-52)	6.5 (0-52)	0.115
Race, *n (%)*			0.083
- **American Indian or Alaska Native**	2 (0.9)	1 (0.5)	
- **Asian**	13 (5.9)	19 (8.6)	
- **Black or African American**	13 (5.9)	2 (1.4)	
- **Native Hawaiian**	1 (0.5)	0 (0)	
- **White**	181 (81.9)	180 (81.4)	
- **Unknown**	11 (5.4)	17 (7.7)	
Ethnicity, *n (%)*			0.552
- **Hispanic or Latino**	11 (5.0)	14 (6.4)	
- **Not Hispanic or Latino**	198 (89.1)	197 (90.0)	
- **Unknown**	12 (5.9)	8 (3.6)	
Medication use, *n (%)*			0.000
- **Biological therapy**	83 (37.6)	40 (18.3)	
- **Immunomodulators**	41 (18.6)	20 (9.1)	
- **Steroids**	18 (8.1)	30 (13.7)	
- **Other medication**	66 (29.9)	106 (48.4)	
- **No medication**	11 (5.0)	14 (6.4)	
- **Unknown**	2 (0.9)	9 (4.1)	
Initial symptoms (1 or more), *n (%)*			
- **Abdominal pain**	153 (69.7)	113 (51.4)	0.000
- **Diarrhea**	59 (26.7)	69 (31.4)	0.216
- **Rectal bleeding**	72 (33.5)	171 (77.3)	0.000
- **Weight loss**	64 (29.0)	41 (18.6)	0.014
- **Unknown**	16 (3.4)	19 (9.1)	
Initial disease extent (1 or more), *n (%)*		NA	NA
- **Upper GI tract**	15 (3.4)		
- **Small bowel excluding terminal ileum**	35 (15.8)		
- **Terminal ileum**	114 (51.6)		
- **Colon**	109 (49.3)		
- **Unknown**	33 (14.9)		

Table 3.1. Demographics of IBD population. PSC: primary sclerosing cholangitis, NA: not applicable.

Total (n=440)	CD (n=221)	UC (n=219)	*P*
Disease extent, *n (%)*	NA		NA
- **Cecum-ascending**		59 (16.1)	
- **Transverse-descending**		163 (44.4)	
- **Rectum**		113 (30.8)	
- **Unknown**		32 (14.6)	
Fistula, *n (%)*			
All Fistula	51 (23.2)	6 (2.8)	0.000
- **Peri-anal fistula**	27 (12.3)	3 (1.4)	0.000
- **Enterocutaneous fistula**	7 (3.2)	1 (0.5)	0.068
- **Other fistula**	23 (10.5)	2 (0.9)	0.000
- **Unknown**	1 (0.5)	4 (1.8)	
Extra-intestinal manifestations, *n (%)*			
- **All extra-intestinal manifestations**	45 (20.5)	19 (8.8)	0.001
- **Eye**	11 (5.0)	4 (1.9)	0.112
- **Skin**	10 (4.5)	4 (1.9)	0.173
- **Joint**	36 (16.4)	11 (5.1)	0.000
- **PSC**	3 (1.4)	4 (1.9)	0.487
- **Other extra-intestinal manifestation**	4 (1.8)	1 (0.5)	0.315
Surgeries, *n (%)*			
- **Abdominal surgery**	74 (33.5)	20 (9.1)	0.000

Table 3.1 – continued. Demographics of IBD population. PSC: primary sclerosing cholangitis, NA: not applicable.

controls were employed. There was no significant difference in employment rate between patients with UC and CD (63.3% and 65.3%, respectively [*P*=0.67]). In the employed group, 54.5% were male, whereas in the unemployed group, only 41.4% were male (*P*=0.009). Activity impairment was present in 65% of the employed group, whereas in the unemployed group, this was 79% (*P*=0.002). Mean QoL was significantly higher in employed patients (QoL=50 [SD 12]) than in the unemployed patients (QoL=44 [SD 15]) (*P*=0.001). No significant difference in DA was observed, with 24.3% active disease in the employed group versus 26.4% in the unemployed group (*P*=0.639).

Work productivity

Presenteeism and absenteeism were calculated in the employed patients (140 CD, 143 CD) and in 22 employed controls (*Figure 3.3*). No significant differences in absenteeism were observed between controls, patients with UC and CD (13.6%, 22.4%, and 20.0%, respectively). Significantly, more presenteeism was detected in patients with CD (61.4%) and patients with UC (64.3%) compared with controls (27.3%) (*P*=0.004). Activity impairment was calculated as well, and similar patterns were observed with 63.6% and 66.4% activity impairment in CD and UC, respectively, and 31.8% for controls (*P*=0.007). The strongest impairment was observed in patients with active disease. Of these, 46.6% experienced absenteeism, 94.8% presenteeism, and 98.9% activity impairment, compared with 14.4%, 54.7%, and 62.7%, respectively, of patients in remission (*P*<0.001). Absenteeism was similar between remissive patients and controls (14.4% and 13.6%, respectively, *P*=1.000), whereas controls had significantly less presenteeism than remissive patients (27.3% and 54.7%, respectively, *P*=0.022).

Total (n=462)	**IBD (n=440)**	**Controls (n=22)**	***P***
Male gender, *n (%)*	219 (49.8)	12 (54.5)	0.662
Age (years), *median (range)*	37 (18-83)	37 (25-77)	0.439
Smoking, *n (%)*			0.908
- **Current**	32 (7.3)	1 (4.5)	
- **Past**	82 (18.6)	4 (18.2)	
- **Never**	325 (73.9)	16 (72.7)	
- **Unknown**	1 (0.2)	1 (4.5)	
Drinking, *n (%)*			0.085
- **Yes**	236 (53.6)	16 (72.7)	
- **No**	201 (45.7)	6 (27.3)	
- **Unknown**	3 (0.7)	NA	
Race, *n (%)*			0.379
- **American Indian or Alaska Native**	3 (0.7)	1 (4.5)	
- **Asian**	32 (7.3)	2 (9.1)	
- **Black or African American**	15 (3.4)	0 (0)	
- **Native Hawaiian**	1 (0.2)	0 (0)	
- **White**	361 (82)	19 (86.4)	
- **Unknown**	27 (6.1)	NA	
Ethnicity, *n (%)*			0.785
- **Hispanic or Latino**	25 (5.7)	1 (4.5)	
- **Not Hispanic or Latino**	395 (89.8)	21 (95.5)	
- **Unknown**	20 (4.5)	NA	

Table 3.2: Demographics of IBD patients versus controls. NA: not applicable.

Total (n=440)	**Employed (n=283)**	**Unemployed (n=157)**	***P***
Age (years), *median (range)*	36 (20-82)	41 (18-83)	0.094
Male gender, *n (%)*	154 (54.4)	65 (41.4)	0.009
Disease type, *n (%)*			0.670
- **CD**	140 (49.5)	81 (51.6)	
- **UC**	143 (50.5)	76 (48.4)	
Activity impairment, *n (%)*	184 (65.0)	124 (79.0)	0.002
Active disease (total n=379), *n (%)*	58 (24.3)	37 (26.4)	0.639
QoL (total n=379), *mean (SD)*	50 (12)	44 (15)	0.000

Table 3.3. Characteristics of employed versus unemployed IBD patients.CD: Crohn's disease; UC: ulcerative colitis; QoL: Quality of life.

Work impact

Table 3.5 shows the limitations that patients with IBD experienced at work. Most commonly reported limitations were fatigue (41.8% of patients), irritability (12.2%), and a decreased motivation (11.7%). The most frequent reasons to miss work were doctor appointments (39%), abdominal pain or cramping (24.4%), and hospital/emergency department visits (22.1%). Remarkably, only 34.3% were able to make work adjustments (e.g., telecommuting or flexible hours) to avoid taking time off due to their IBD. Stress or pressure when taking sick time off from work due to IBD was experienced by 37.1% of patients, 4.3% felt superiors and/or colleagues complained or made unfair remarks about their performance at work in relation to their IBD, and 5.3% felt that they were

discriminated in the workplace as a direct consequence of their IBD. Furthermore, 26.2% felt that IBD had negatively affected their career path, opportunities for advancement, income and/or earning potential. Also, 11.2% lost a job or had to quit a job because of IBD, job-lock was observed in 14% of patients, and 3.3% reported to have been on disability at some point in the past year.

Industry, *n (%)*	Total (n=213)
Arts, entertainment	38 (17.8)
Health/social care	33 (15.5)
Education services	24 (11.3)
Other services	23 (10.8)
Corporate management	18 (8.5)
Finance and insurance	15 (7.0)
Retail trade	15 (7.0)
Real estate, renting, leasing	10 (4.7)
Information	9 (4.2)
State and local government	7 (3.3)
Construction	5 (2.3)
Federal government	4 (1.9)
Other	4 (1.9)
Manufacturing	3 (1.4)
Utilities	2 (0.9)
Wholesale trade	2 (0.9)
Agriculture	1 (0.5)

Table 3.4. Patients by employment categories.

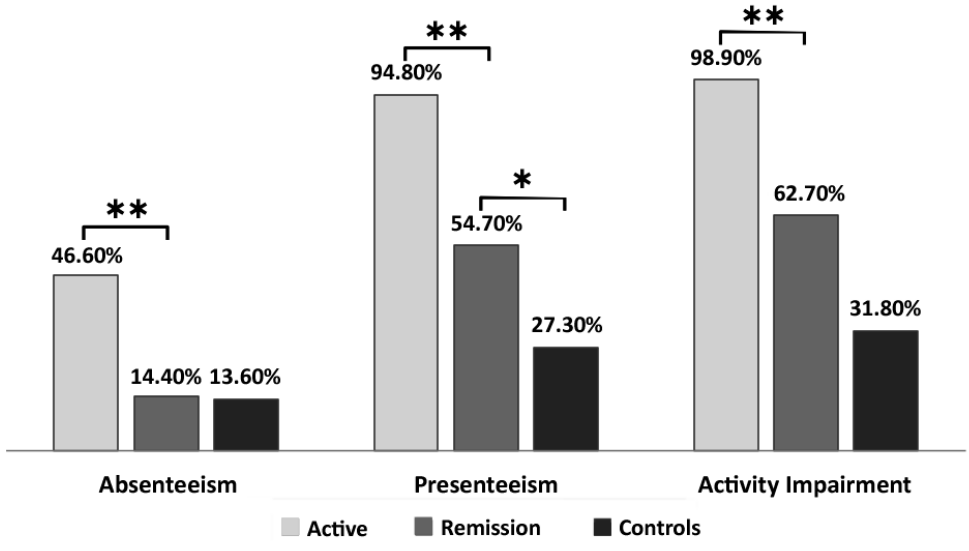

*Figure 3.3 Prevalence of absenteeism, presenteeism, and activity impairment in controls and IBD patients with active and inactive disease. *p=0.02; **p<0.001.*

	Remissive patients (n=111)	Active patients (n=41)	*P*
Which of the following adjustments have you made in your work to avoid taking sick days off from work due to your IBD? *n (%)*			1
- Working from home	14 (12.6)	5 (12.2)	.000
- Working part-time	45 (4.5)	5 (12.2)	0.134
- Working flexible hours	15 (13.5)	10 (24.4)	0.139
- I have not made any such adjustments	62 (55.9)	14 (34.1)	0.028
- I do not have the possibility to make such an adjustment	18 (16.2)	8 (19.5)	0.633
- Other	8 (7.2)	2 (4.9)	1.000
If you have missed work due to your IBD, what was the reason? Check all that apply. *n (%)*			
- Hospital/emergency department visit	22 (19.8)	6 (14.6)	0.638
- Doctor appointment	40 (36)	14 (25.9)	0.829
- Incontinence or fear of incontinence	5 (4.5)	5 (12.2)	0.134
- Abdominal pain or cramping	19 (17.1)	13 (31.7)	0.072
- Fear of frequent stools or bowel movements interfering with work activities	15 (13.5)	13 (31.7)	0.017
- Fear of frequent stools or bowel movements bringing attention to my condition from colleagues	5 (4.5)	5 (12.2)	0.134
- Fatigue, and/or not enough energy to get through the day	17 (15.3)	15 (36.6)	0.004
- Worry about gas pressure, discomfort			
- Worry/fear of potential for embarrassment	6 (6.3)	4 (9.8)	0.489
- Rectal/anal pain or burning	4 (3.6)	8 (19.5)	0.003
- Volume of blood in bleeding episode	3 (2.7)	4 (9.8)	0.212
- I have never been absent from work due to IBD	4 (3.6)	2 (4.9)	0.661
	25 (22.5)	3 (7.3)	0.035
How does IBD affect your performance at work? *n (%)*			
- I am quiet or quieter during meetings			
- I cancel my attendance at meetings at the last minute	6 (5.4)	5 (12.2)	0.168
- I do not participate in work social activities	6 (5.4)	3 (7.3)	0.703
- I am irritable at work			
- I am less motivated in my work	6 (5.4)	8 (19.5)	0.022
- My IBD does not affect my behavior at work	13 (11.7)	5 (12.2)	1.000
- I am fatigued	15 (13.5)	6 (14.6)	1.000
- Not applicable/other	31 (27.9)	2 (4.9)	0.002
	42 (37.8)	27 (65.9)	0.002
	29 (26.1)	5 (12.2)	0.081

Table 3.5. An overview of limitations patients with IBD experience at work, subdivided by disease activity.

Unsurprisingly, significant differences were observed between patients with active disease versus inactive disease. Active patients experienced more fear of frequent stools or bowel movements interfering with work activities (*P*=0.017), felt more fatigued (*P*=0.002), made more adjustments to avoid taking sick days off from work due their IBD (*P*=0.028), and

experienced more worry and fear of potential embarrassment at the workplace (*P*=0.003). We observed that patients who reported absenteeism or presenteeism felt more frequently stressed about taking time off work due to their disease (78% and 50%, respectively, *P*<0.01) than those without absenteeism or presenteeism (27% and 16%, respectively, *P*<0.01). Interestingly, patients who experienced absenteeism and presenteeism made work adjustments significantly more often (54% and 40%, respectively, *P*<0.01) than those without absenteeism or presenteeism (29% and 24%, respectively, *P*=0.02).

Indirect costs

We estimated that total indirect costs for active patients on average were $1133 per week, assuming an average hourly compensation of $31.93, a 40-hour work week, and a wage multiplier of 1.61. This equals 55.1% of the total weekly compensation. This was significantly more than patients in remission, whose total indirect cost was estimated to be 18% of the total weekly compensation or $370.13 per week for a full-time employee (*P*<0.01).

Presenteeism accounted for the majority of costs, with 33.8% of total weekly compensation ($695.03 per week) for active patients and 13.5% of total weekly compensation ($277.60 per week) for remissive patients. Absenteeism accounted for 21.3% of total weekly compensation ($437.99 per week) in active patients and 4.5% of total weekly compensation for patients in remission.

Indirect costs encountered for patients in remission were still significantly higher when compared with controls (*P*=0.029). For controls, average weekly indirect costs were estimated at 9.3% of total weekly compensation or $191.23 per week (for a full time employee). Average indirect cost associated with absenteeism were on average 4.8% of total weekly compensation or $98.70 per week, and costs associated with presenteeism were estimated at 4.6% of total weekly compensation or $94.59 per patient per week (*Figure 3.4*). Furthermore, patients in remission who made more than $32 per hour experienced absenteeism more frequently than those who made less than $32 per hour (24.5% and 6.9%, respectively, *P*=0.01). Presenteeism was similar in both salary groups (56.6% and 55.2%, respectively). Average total indirect costs were estimated at $789.58 in the high salary group and $114.47 in the lower salary group (*P*=0.03).

Discussion

"Without question, the single biggest force threatening U.S. workforce productivity, as well as health care affordability and QoL, is the impact of chronic conditions."[28] Indeed, the indirect costs of care are estimated to be approximately 76% of total cost of care.[2] This discussion has become especially relevant now that our daily clinical practice is faced with the transition from the fee-for-services model to the value-payment model to bend the cost curve. Tackling both direct and indirect costs will increasingly be placed on the agenda of the provider, especially in the management of costly chronic disease like IBD.

In this study, we found that employed patients with IBD, even when in complete clinical remission, still experienced decreased productivity significantly more frequently than healthy controls: 54.7% versus 27.3%, respectively (*P*=0.02). This translates into a sizable economic impact as reflected by the indirect costs for patients although they are in clinical remission (18% IBD versus 9.3% controls of total compensation per week [*P*=0.03]). Disturbingly, we found that patients continue to cope with limitations at work that cause a lower QoL and an increase in stress, absenteeism, and presenteeism. The majority, 65.7%, has not made any adjustments to combat these problems, most likely due to their inability to deal with complaints like fatigue or with aligning their doctors' appointments with their job demands.

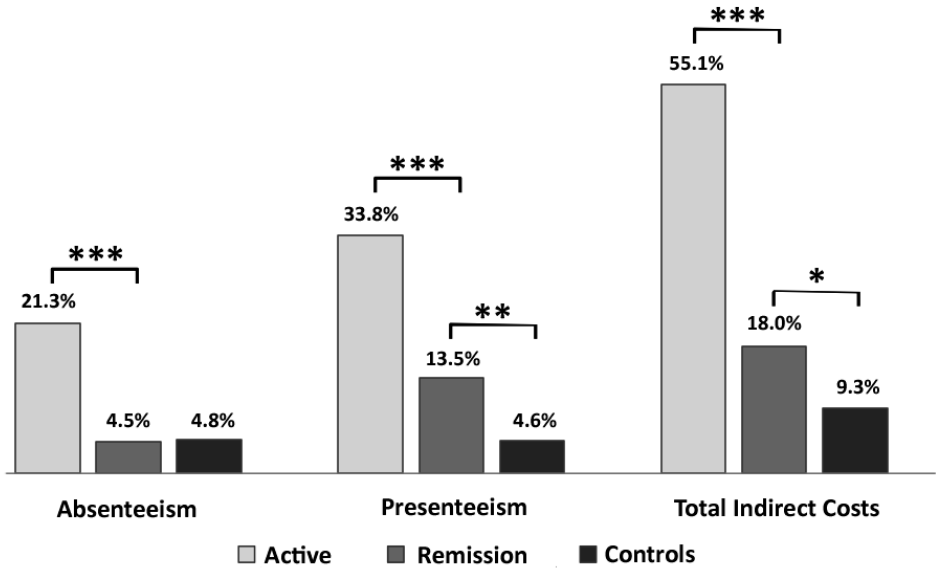

Figure 3.4. Indirect costs as a percentage of maximum weekly compensation for employees.
P*=0.03, ** *P*=0.02, * *P*<0.01.

Interestingly, we did not observe a significant difference in absenteeism between IBD patients and controls, respectively 21.2% (CD 20% and UC 22.4%) compared with 13.6% (*P*=0.399). This could be attributed to improved treatments, like biological therapy, inducing effective clinical remission and allowing patients to resume their work.[13-15,29] Other studies found comparable absenteeism percentages ranging from 18% to 36% for CD and 13% to 25% for UC.[1] Although the control population was small, differences for absenteeism, presenteeism, activity impairment, and indirect costs were significant.

A limitation of this study is that controls were identified through our patients with IBD, which could potentially lead to bias. However, it has been shown that caregivers of patient with chronic diseases usually tend to have reduced productivity compared with controls[9], which would suggest that this would only underestimate the measured effect. Furthermore, the included patients were selected in a tertiary care center, with

potentially more patients with difficult to treat disease. To limit the effect of this, we aimed to focus on the productivity of patients in clinical remission.

From a health economical perspective, it has been shown that presenteeism makes up for the majority of indirect costs.[2] This is the first report on indirect costs including presenteeism of patients with IBD in the U.S. Our cost model shows that indirect costs are significantly lower when patients with IBD enter a remissive state, dropping from $1333 per week when clinically active to $370 per week when in remission. A recent study from Hungary showed presenteeism costs of €2508 per patient per year, which translates to $3191 per patient per year,[30] that equals $66 per patient per week. This number is lower than our estimated $354 per patient per week. The difference can be explained by the average hourly wage that is lower in Hungary ($7) and the fact that we incorporated the average wage multiplier to correct for the variation in presenteeism cost among different kind of employment levels.

What can we, as caregivers, do to decrease presenteeism in patients with IBD in remission? First of all, it is important to note that patients themselves do not appear to make the necessary adjustments: only 34.3% were able to do so, which confirms results from a recent study that showed that only 40% of patients had made any adjustment.[11] Second, these patients continue to struggle with 3 types of problems: (1) persistent symptoms (e.g., fatigue, irritability, cramping), (2) lack of work motivation, and (3) missed workdays due to medical appointments. Third, we observed additional macroeconomic issues: (1) career stagnation, 26.2% felt that their disease had negatively affected their career and (2) job-lock, which was observed in 14% of patients. It has been reported that chronic illness reduces job mobility by about 40% those that rely on their employer coverage.[31] For IBD, this has not been studied previously.

Our recommendations therefore are divided into care provider recommendations and employer recommendations. Care providers (e.g., physicians, nurses, social workers, dieticians) will need to proactively discuss and propose employment-related adjustments tailored to the individual. They need to encompass mental support, nutritional support, wellness (e.g., fitness, yoga, meditation), and elimination of unnecessary tests, procedures, and medical appointments. Employer recommendations include job-coaching, an in depth discussion about career and work place related support measures. Surveys have shown that employees with chronic conditions are more likely to be highly satisfied with their jobs if they had high self-efficacy in managing their disease, perceive workplace support, and had less work limitations.[32] This would allow employers to make effective adjustments leading to a decrease of presenteeism.

In conclusion, this study shows that employed patients with IBD in clinical remission still have significant loss of work productivity that goes unnoticed in the majority of cases. The associated high indirect costs constitute a significant economic burden on health expenditures. A way to decrease indirect costs includes both care provider and employer interventions, ideally converging into an integrated approach. The development and

testing of practice guidelines and productivity enhancement tools will most likely have a meaningful and immediate impact.

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Chapter 4.

Patient Value Redefined for Inflammatory Bowel Diseases: A Choice Based Conjoint Analysis of Patients' Preferences

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Abstract

Introduction
Value-based health care is an upcoming field. The core idea is to evaluate care based on achieved outcomes divided by the costs. Unfortunately, the optimal way to evaluate outcomes is ill-defined. In this study we aim to develop a single, preference based, outcome metric for *patient value,* which can be used to quantify overall health value in inflammatory bowel disease (IBD) management.

Methods
IBD patients filled out a choice based conjoint (CBC) questionnaire in which patients chose preferable outcome scenarios with different levels of disease control (DC), quality of life (QoL), and productivity (Pr). A CBC analysis was performed to estimate the relative value of DC, QoL and Pr. A patient-centered composite score was developed which was weighted based on the observed preferences.

Results
We included 210 IBD patients. Large differences in individual preferences were observed. Increases from low to intermediate outcome levels were valued more than increases from intermediate to high outcome levels. Overall, QoL was more important to patients than DC or Pr. Individual *patient value* scores were calculated based on observed preferences. This score was significantly different from a score not weighted based on patient preferences, especially in patients with active disease.

Conclusion
We showed the feasibility of creating a single composite outcome metric for patient value in IBD using CBC. Including patient preferences in the score development significantly changed outcomes in patients with active disease. Therefore, we propose that success in health care should be measured using individual patient preferences, and that providers should be rewarded accordingly.

Introduction

Currently, a health care transformation of seismic proportions is unfolding, aimed to replace the broken fee-for-services model with new modalities, one of which is value-based health care (VBHC). Although VBHC is a relatively new concept in medicine with clearly defined principles[1], only few real-world models are currently available. Its key component is the quantification and continuous measurement of *health value* - the achieved health outcomes per the associated costs of care.[1] By means of demonstrating these health value metrics, a brand new framework for competition in the health care space is created. Providers are incentivized to improve individual health outcomes in a cost-effective manner. In addition, patients are able to compare provider performance to choose their care providers accordingly. Lastly, payers are able to choose provider

networks and health systems based upon performance, and they can direct their members in order to achieve the most optimal health outcomes and contain costs.

Inflammatory bowel diseases (IBD), which include Crohn's disease (CD) and ulcerative colitis (UC), are chronic, debilitating disorders characterized by inflammation of the gastrointestinal tract. IBD is thought to be caused by a dysregulated immune response in response to unknown environmental triggers in a genetically susceptible host.[2] IBD treatment is associated with significant costs, and large variations between clinical practices are observed.[3] Because of the chronic characteristic, the high costs, and the lack of consistency in treatment patterns, VBHC could greatly improve the value of IBD care.

The optimal health outcome on a patient level – *patient value* – is unfortunately ill-defined.[4] Several sets of quality measures have been developed in IBD. The American Gastroenterology Association (AGA) has developed a set of 8 process measures to estimate quality of care in IBD and is currently developing a set of outcome metrics[5]; the Crohn's and Colitis Foundation America developed a set of 10 process measures along with 10 outcome measures[6]. Optimal health outcomes from a patient perspective are not necessarily equivalent to those from a provider perspective. It is increasingly recognized that incorporating patient preferences into their associated treatment plan through a process called 'Shared Decision Making' (SDM) offers significant benefit to both patients' knowledge and patients' experience.[7] Additionally, patient reported outcomes (PROs) are increasingly recognized to be essential in evaluating a patients' health status. The US Food and Drug Administration (FDA) recently officially incorporated PROs as a measure of success in clinical trials.[8] The National Institute of Health (NIH) PRO Measurement Information System (PROMIS) project aims to develop databanks of PROs that allow comparisons of outcomes across multiple disease areas.[9] However, to our knowledge, nobody has aimed to quantify a single value measure based on patient preference.

Our recently launched VBHC program for IBD incorporated the VBHC principles of cost and outcome measurement within its care delivery infrastructure.[6] The IBD program designed the outcome measure Value-Quotient (vQ), which incorporates *patient value*, as well as the associated provider costs of care delivery, and medication. The key objective of this VBHC program is to annually increase individual vQs by increasing health outcomes at lower costs through interventions on the patient level (e.g. improve compliance, participation, wellness, job coaching, and education) and provider level (e.g. constant process innovation, cost awareness, medication choice, task shifting, and education).

Although patient value is difficult to define, a reasonable assumption is that most patients value a high level of disease control (DC) with preservation of their quality of life (QoL) and ability to perform daily activities, including (work) productivity (Pr). In collaboration with IBD patient focus groups, the initial design around patient value therefore consisted of a combination 1) DC, 2) QoL, and 3) Pr.[10] Critical to both the evaluation and the constant improvement of this VBHC program is an improved understanding on how patients value various outcomes in this value-based care program and how they relate to each other. Incorporating these values in the constant redesign of the program may

ultimately result in clinical, reimbursement, and policy decisions that better reflect patient preferences. Aligning the value-based care program with patient preferences can potentially increase its effectiveness by improving adoption of, satisfaction with, and adherence to its coordinated care scenarios.

Different methods are available to quantify value to consumers, which can roughly be divided into revealed and stated preference methods.[11] Revealed preference methods derive preferences from actual market data, whereas stated preference methods refer to data obtained through questionnaires in which preferences are elicited. Value is preferably assessed through revealed methods, but direct data are often hard to obtain. Stated preference methods for measuring preference have been developed to facilitate this process. One form of a stated preference is choice based conjoint analysis (CBC), in which consumers are asked to choose from a set of products or outcomes. Using conjoint analysis, the value to customers of different components of a product can be assessed.[11] Although the cost component is difficult to include in the health care setting, the relative preferences for outcomes (components) can still be determined. Conjoint analysis has been used progressively in health research, mostly in the setting of SDM processes.[11] In this study we aim to quantify the relative importance of each of the '*patient value'* components: DC, QoL, and Pr using a CBC analysis for IBD patients and use this to construct a single, preference based, PRO metric for IBD health value.

Methods

Study design
This is a prospective study evaluating patient preferences in disease outcomes using a CBC questionnaire and analysis. Relative importance for DC, QoL, and Pr was assessed for each participant. Data was collected using an online questionnaire using SSI web, version 8.3.8, Sawtooth Software (Orem, UT).

Population and data collection
Patients with an established IBD diagnosis were approached by email and supplied with a unique code to login to the computerized questionnaire. Patients were recruited between December 2014 and April 2015. The questionnaire started with a set of PROs assessing current symptom level, and self-reported DC, QoL, and Pr using 10-point Likert scales. The last 10 questions involved CBC questions eliciting patient preference for each of these three disease outcomes. The design of the questions was selected based on a pilot study including 12 patients that chose the most optimal questionnaire design (*Figure 4.1*). Additional characteristics including age, gender, disease duration, age at diagnosis, surgical history, and medication use were extracted from medical records.

Definitions
To assess and compare disease activity we utilized the mobile health index (mHI) for CD (mHI-CD) and UC (mHI-UC), which were calculated based on the reported symptom levels. These validated score assess clinical disease activity utilizing solely PROs.[12] For CD the mHI

includes the number of liquid stools, abdominal pain (yes/no), general well-being, and self-assessed disease control; a score of ≥6.38 indicates active disease. The mHI-UC includes stool frequency, abdominal pain, rectal bleeding, and self-assessed disease control; a score of ≥3.2 indicates active disease.

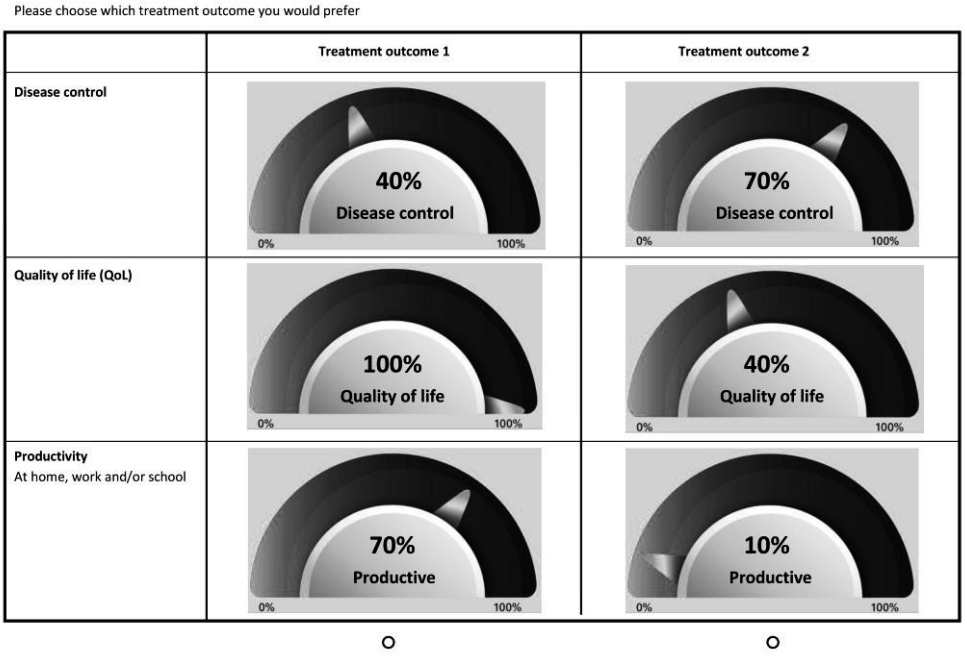

Figure 4.1. Example of CBC question soliciting patients' preference for the three different attributes: disease control, quality of life, and work productivity. Each patient answers 10 CBC questions and is asked to choose the most preferable scenario for each of those ten

Conjoint analysis

A CBC analysis was performed to assess the relative value that patients attribute to the 3 individual components of patient value: DC, QoL, and Pr. CBC is a decomposition method, which estimates the individual value of an attribute based on the overall value of a scenario containing multiple attributes.[11] Three attributes were evaluated: DC, QoL, and Pr. For each attribute the worth of 4 levels were evaluated:

I. **Disease control**; 10%, 40%, 70%, or 100% of disease control
II. **Quality of Life**; 10%, 40%, 70%, or 100% of quality of life
III. **Productivity**; 10%, 40%, 70%, or 100% of productivity

Each participating patient was asked to fill out a set of 10 CBC questions. Every question showed two scenarios including all three attributes (i.e. DC, QoL, and Pr), with different attribute levels (i.e. 10%, 40%, 70%, or 100%) shown in each scenario (*Figure 4.1*). In each question patients were asked to choose their most preferable scenario. Questions in which one scenario has better outcomes for all three attributes than the second scenario

were not included in the questionnaires (i.e. in all questions a trade-off between at least one attribute versus the other needed to be made).

Calculations of patient value
We defined overall *patient value* on a scale from 0-100 where 100 means the highest possible patient value and 0 the lowest patient value possible. Individual value scores were calculated using individual outcomes and weights for DC, QoL, and Pr. To estimate DC we used the mHI, for QoL and Pr self-reported values using Likert-scales. Weights were assigned based on the individual importances derived from the CBC analysis. These weights add up to 100% per definition. For any decrease in DC, QoL, or Pr, the percentage decrease (relative to the maximum decrease) was calculated and subtracted from 100; relative to the individual weights. We also calculated patient value using arbitrary weights for DC, QoL, and Pr, which are more closely aligned with physician practice: DC 60%, QoL 20%, and Pr 20% importance.

Statistical analysis
Patients that completed all CBC questions were included in the analysis. A Hierarchical Bayes (HB) model was used to estimate individual part worth utilities (i.e. preference scores) for each of the attribute levels. All questions were included in the HB model. Constraints were included in the model stating that 100% DC/QoL/Pr is better than 70%, 70% better than 40%; and 40% better than 10% for each of the three attributes. For estimation of preferences 10,000 iterations of the model were used for convergence of the model, another 10,000 cycles were run for estimation of part-worth utilities.

Part worth utilities were normalized to allow comparison of importances between patients across all three attributes. Part worth utilities are scaled on an arbitrary scale. To estimate the importance of improving from one level to another (i.e. improving from 40% QoL to 70% QoL), utility scores of the respective levels were subtracted. To assess the overall importance of each of the attributes (i.e. DC, QoL, and Pr), for each attribute the part worth utility of the 100% level is subtracted by the part-worth utility of the 10% level. The relative difference between those three values determines the importance of each of the attributes. Based on the individual patient's highest preference, patients were assigned to one of three groups: 1) DC preference; 2) QoL preference; 3) Pr preference. Self-reported DC, QoL, Pr, and symptoms, as well as clinical characteristics such as gender, age, disease duration, age at diagnosis, and previous surgeries were compared between groups. Pearson Chi-squared and Fisher exact test were used to compare categorical data; Wilcoxon Mann-Whitney tests were used to compare non-parametric data. A Wilcoxon Signed Rank Sum test was performed to compare paired observations of patient value scores calculated using different weightings.

The target inclusion number was 250 patients. To collect 1,000 representations per main level effect, a sample size of 200 patients is sufficient, taking into account that each respondent answers 10 questions, each comparing two scenarios.[13] Assuming an 80% completion rate, 250 participants need to be included. SSI web, version 8.3.8, Sawtooth Software (Orem, UT), and SAS version 9.4 (Cary, NC) were used for the analysis.

Ethical considerations

This study was approved by the University of Los Angeles, California Institutional Review Board under protocol number IRB#14-001308. All included patients consented to participate in this study.

Results

In total, 227 patients filled out the questionnaire. After exclusion of 17 incomplete questionnaires, 210 patients were included in the final analysis. The median time to finish the first CBC question was 40 (IQR 28-58) seconds, the second 19.5 (IQR 15-30.5) seconds, and for the next questions the median time gradually decreased to 10-12 seconds per question for the last 5 questions (*Figure 4.2*). Of the patients that finished all CBC questions, 107 (51%) had CD, 6 had (3%) indeterminate colitis (IC), and 97 (46%) had UC. For 14 (6%) of included patients only self-reported measures were available because no consent to look up medical information in the medical chart was acquired. Of the remaining 196 patients, 96 (49%) was male, and the median age was 40 years (range 20-83). The median age at diagnosis was 29 years (range 0-55), and 59 (30%) had an abdominal surgery for IBD in the past (*Table 4.1*). Of the participating CD patients, 26% had active disease; for UC this was 31%. In total 16 (8%) were using oral corticosteroids at the time of the study, 82 (42%) were using biologics, 85 (33%) were using immunomodulators and 76 (39%) were using 5-ASA.

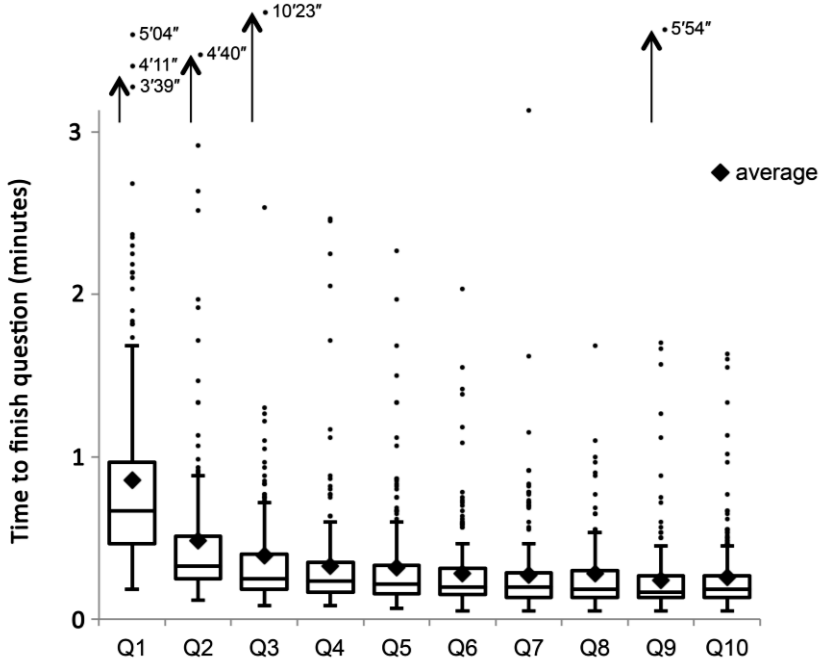

Figure 4.2 Average and median time to complete CBC questions

		Maximum preference group			
	all	**Disease control**	**Quality of life**	**Productivity**	***P***
n (% of total)	210	63	115	32	
Male gender, *n (%)*	96 (49)	26 (43)	51 (48)	19 (66)	0.13
Diagnosis, *n (%)*					0.19
- **Crohn's disease**	107 (51)	30 (48)	57 (50)	20 (62.5)	
- **Indeterminate colitis**	6 (3)	0 (0)	6 (5)	0 (0)	
- **Ulcerative colitis**	97 (46)	33 (52)	52 (45)	12 (37.5)	
Age, *median (range)*	40 (20-83)	39 (21-71)	38 (20-83)	47 (23-80)	0.21
Age at diagnosis, *median (range)*	29 (7-81)	30 (14-69)	27 (7-81)	36 (16-75)	0.037
Disease duration, *median (range)*	7 (0-55)	6 (1-47)	7 (0-55)	6 (0-40)	0.36
months in program, *median (range)*	42 (6-96)	43 (9-91)	41 (6-96)	43 (13-91)	0.22
Smoking, *n (%)*					0.53
- **Current**	7 (4)	3 (5)	3 (3)	1 (3)	
- **Never**	143 (76)	44 (77)	80 (78)	19 (66)	
- **Past**	39 (21)	10 (18)	20 (19)	9 (31)	
Alcohol use, *n (%)*	110 (63)	32 (58)	63 (66)	15 (58)	0.53
Medication use, *n (%)*					
- **5ASA**	76 (39)	27 (45)	41 (39)	8 (28)	0.29
- **immunomodulators**	65 (33)	21 (35)	38 (36)	6 (21)	0.29
- **biologics**	82 (42)	25 (42)	44 (42)	13 (45)	0.95
- **ciprofloxacin/ metronidazole**	1 (1)	1 (2)	0 (0)	0 (0)	0.46
- **budesonide**	10 (5)	2 (3)	6 (6)	2 (7)	0.67
- **systemic corticosteroids**	16 (8)	6 (10)	7 (7)	3 (10)	0.63
- **rectal corticosteroids**	8 (4)	3 (5)	4 (4)	1 (3)	0.89
Surgical history, *n (%)*					
- **abdominal surgery**	59 (30)	17 (28)	34 (32)	8 (28)	0.85
- **perianal surgery**	12 (6)	2 (3)	8 (7)	2 (7)	0.59
Anatomy, *n (%)*					
- **ileostomy**	2 (1)	1 (2)	1 (1)	0 (0)	1.00
- **IPAA**	7 (4)	2 (3)	4 (4)	1 (3)	1.00
Perianal disease, *n (%)*	12 (6)	1 (2)	8 (8)	3 (10)	0.15
Patient reported outcomes, *median (range)*					
- **disease activity VAS**	2 (0-10)	2 (0-10)	2 (0-10)	2 (0-10)	0.95
- **quality of life decrease VAS**	1.5 (0-10)	1 (0-10)	2 (0-10)	2 (0-9)	0.98
- **productivity decrease VAS**	1 (0-10)	1 (0-10)	1 (0-10)	1 (0-8)	0.73
Active disease*, *n (%)*	59 (29)	21 (34)	28 (25)	10 (31)	0.41
Characteristics CD patients					
Disease location, *n (%)*					0.52
- **L1**	27 (30)	4 (15)	16 (33)	7 (44)	
- **L2**	14 (15)	5 (19)	7 (14)	2 (13)	
- **L3**	48 (53)	16 (62)	25 (51)	7 (44)	
- **L4**	2 (2)	1 (4)	1 (2)	0 (0)	
Upper GI involvement, *n (%)*	6 (6)	1 (4)	3 (6)	2 (12)	0.62

*Table 4.1 Demographics and disease characteristics of included patients, and by preferred outcome. *Active disease defined as mHI-CD≥6.38 or mHI-UC≥3.2.*

		Maximum preference group			
	all	**Disease control**	**Quality of life**	**Produc-tivity**	***P***
Characteristics CD patients *(cont'd)*					
Disease behavior, *n (%)*					0.61
- **B1**	57 (59)	17 (61)	32 (62)	8 (47)	
- **B2**	29 (30)	7 (25)	14 (27)	8 (47)	
- **B3**	8 (8)	2 (7)	5 (10)	1 (6)	
- **B2+B3**	3 (3)	2 (7)	1 (2)	0 (0)	
Patient reported outcomes, *median (range)*					
- **liquid stools/day**	1 (0-20)	1 (0-15)	1 (0-20)	1.5 (0-6)	0.64
- **well-being VAS**	8 (0-10)	8 (0-10)	8 (4-10)	8 (5-10)	0.84
- **abdominal pain present, *n(%)***	35 (33)	9 (31)	21 (37)	5 (25)	0.60
mHI-CD*, *median (range)*	3.6 (0-14.3)	3.4 (0-14.3)	3.8 (0-12.2)	4.5 (0-10.0)	0.95
active disease*, *n (%)*	28 (26)	9 (31)	14 (25)	5 (25)	0.80
Characteristics UC/IC patients					
Disease extent, *n (%)*					0.84
- **E1**	26 (28)	10 (32)	13 (25)	3 (30)	
- **E2**	33 (36)	9 (29)	21 (41)	3 (30)	
- **E3**	33 (36)	12 (39)	17 (33)	4 (40)	
Patient reported outcomes, *median (range)*					
- **n stools/day**	3 (0-15)	2 (0-12)	3 (0-15)	2.5 (1-9)	0.87
- **abdominal pain VAS**	1 (0-8)	1 (0-7)	1 (0-8)	1 (0-6)	0.87
- **rectal bleeding VAS**	1 (0-10)	0 (0-8)	1 (0-9)	1 (0-10)	0.70
mHI, *median (range)*	1.4 (0-10.7)	1.4 (0-9.6)	1.4 (0-10.7)	2.1 (0-9.6)	0.97
active disease*, *n (%)*	31 (31)	12 (36)	14 (25)	5 (42)	0.36

Table 4.1 – continued. *Demographics and disease characteristics.*

The HB estimation showed that on average, an increase in QoL from 10% to 40% was perceived as very valuable: twice as valuable as an increase in QoL from 40% to 70%, and 3.9 times more valuable than an increase in QoL from 70% to 100% (*Figure 4.3, Table 4.2*). Similarly, increasing QoL from 10%-40% was valued 1.4 times as important as increasing DC from 10%-40%, and 2.3 times as important as increasing Pr from 10%-40%. Increases in DC were on average less valued by patients than increases in QoL, and increases in Pr were less valued than increases in QoL. Across the three attributes, patients assigned on average 34% importance (SD 19) to DC, 42% importance (SD 16) to QoL, and 24% importance (SD 17) to Pr.

Patient preferences for DC, QoL and Pr vary widely across patients (*Figure 4.4*). Overall, preference for DC ranged from 4%-87%, QoL from 7%-78%, and Pr from 1%-79%. In total, 63 patients (30%) had a stronger preference for DC than for QoL or Pr; 32 (15%) had a stronger preference for Pr than for QoL or DC; and 115 (55%) preferred improvements in QoL over improvements in Pr or DC (*Table 4.3)*. No significant differences in baseline

demographics, medical history, current medication use, and current disease state were observed (*Table 4.1*).

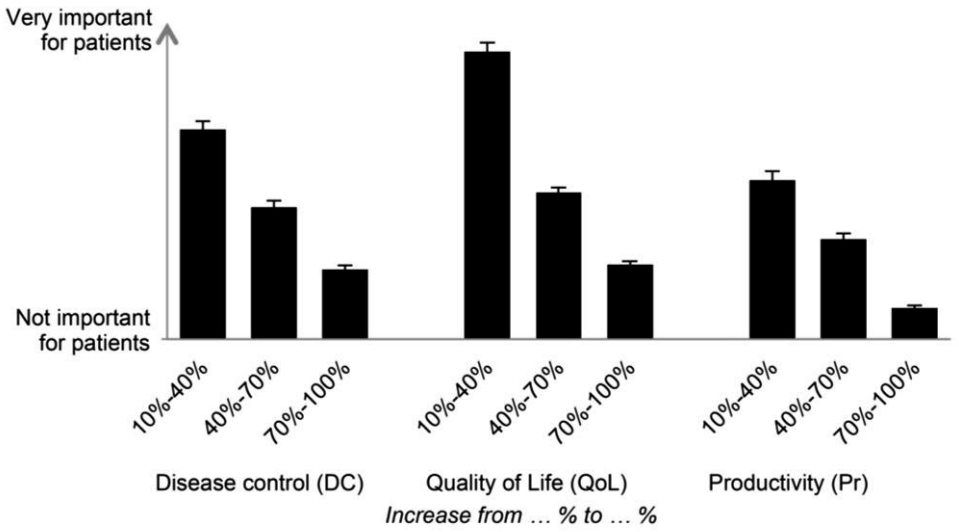

Figure 4.3 The importance patient assign to increasing DC, QoL, and Pr with 30% at different thresholds. Increasing any of the three attributes rom 10-40% is valued more than increases from 40%-70% and increases from 70%-100%. Increases in QoL are valued more than similar increases in DC and Pr. The y axis represents importances, which are directly related to the differences in utility scores between two levels (e.g. utility score of 40% DC minus the utility score of 10% DC). Utility scores do not have units, are scaled arbitrarily, and can generally not be compared between studies. Therefore, the y-axis does not have units, but the relative size of the bars can be compared (e.g. a bar twice as high means twice as important).

	increase in		
Increase from-to	**Disease control**	**Quality of life**	**Productivity**
10%-40%	52 (2)	71 (2)	39 (2)
40%-70%	33 (2)	36 (1)	25 (1)
70%-100%	17 (1)	18 (1)	8 (1)

Table 4.2. Differences between zero-centered utility scores between attribute levels separated for DC, Qol, and productivity. Utility scores do not have units, are scaled arbitrarily, and can generally not be compared between studies. Therefore, the differences do not have units and are scaled arbitrarily as well. However, relative differences between the numbers can be compared (i.e. if a difference is twice as much as another difference, it means that difference is twice as important).

Next, the individualized *patient value* component of the vQ was calculated for all patients, which was weighted based on an individual patient's preference. The average patient value score was 76 (SD 24) for CD patients, and 79 (SD 23) for UC/IC patients. When calculating patient value using a static weight of 60% DC, 20% QoL, and 20% Pr for all patients, the average score was 74 (SD 24) for CD and 78 (SD 23) for UC/IC, which is on average 1.4 (SD 6.2) point lower than using the personalized method in CD (*P*=0.067) and 1.0 (SD 6.4) points lower in IC/UC (*P*=0.25). Overall, 14 (14%) of CD patients had a change of >10 points in their patient value score, as well as 14 (14%) UC/IC patients.

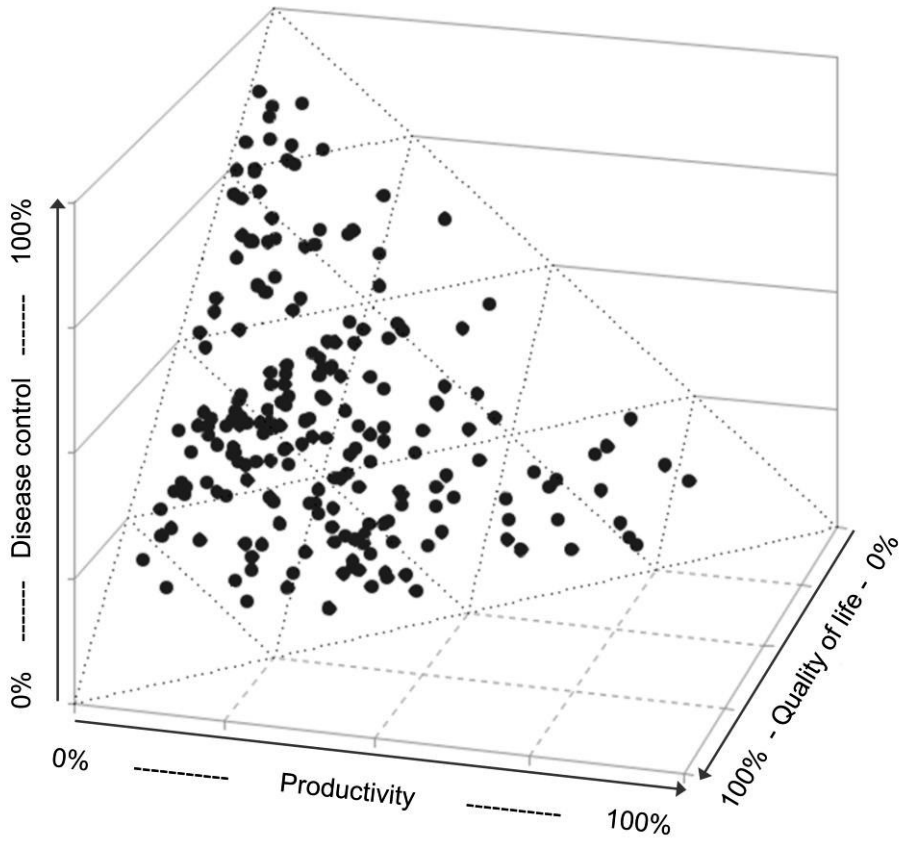

Figure 4.4 Individual patient preferences for DC, QoL, and Pr.

	all	Maximum preference group		
		Disease control	Quality of life	Producti-vity
n	210	63	115	32
% importance of vQ component, *mean (SD)*				
- **disease control (DC)**	34 (19)	58 (14)	25 (10)	18 (9)
- **quality of life (QoL)**	42 (16)	27 (10)	54 (9)	28 (9)
- **productivity (Pr)**	24 (17)	15 (10)	21 (10)	54 (12)
Total	100%	100%	100%	100%

Table 4.3. Average importances of DC, QoL, and Pr in each preference group.

When comparing score changes based on the disease state, we found that for CD patients in remission the score decreased by 0.2 (SD 4.9) points from 86 (SD 14) when using the personalized score to 86 (SD 14) when using the static score (P=0.75), while for CD patients with active disease the score significantly decreased from 47 (SD 21) using the personalized method to 42 (SD 16) using the static method (P=0.0095). Similarly, in UC and IC patients in remission the score increased by 0.6 (SD 4.6) points from 89 (SD 14)

when using the personalized score to 90 (SD 11) when using the static score (*P*=0.27), while for patients with active disease the score decreased from 57 (SD 25) using the personalized method to 52 (SD 22) using the static method (*P*=0.0028, *Table 4.4*, *Figure 4.5*). This resulted in a change of more than 10 points in the patient value score in 32% of patients with active disease in both CD and UC/IC.

Diagnosis	disease state	n	patient value - personalized *mean (SD)*	patient value - static *mean (SD)*	Wilcoxon Rank Sum *P*	>10 points change in patient value *n (%)*
CD	**All**	106	76 (24)	74 (24)	0.0669	14 (14)
	Inactive	78	86 (14)	86 (14)	0.7487	5 (6)
	Active	28	47 (21)	42 (16)	0.0095	9 (32)
UC/IC	**All**	101	79 (23)	78 (23)	0.2479	14 (14)
	Inactive	70	89 (14)	90 (11)	0.2706	4 (6)
	Active	31	57 (25)	52 (22)	0.0028	10 (32)

Table 4.4. Differences between personalized method of calculating patient value and the static scoring using 60% weight for DC and 20% weight for QoL and Pr per disease type and disease state.

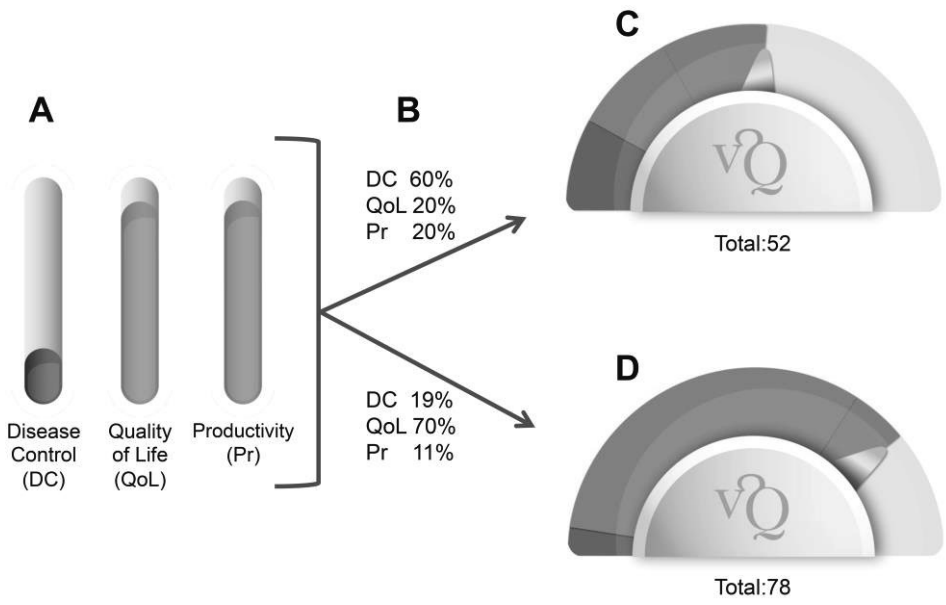

Figure 4.5. Difference between a patient-preference weighted outcome score versus the pre-defined static outcome score. Example of outcomes of a UC patient with active disease, using the measured DC, QoL, and Pr (A), when different weightings (B) are applied. The total patient value score is 52 when it is calculated using the static weightings (C), and 78 when it is calculated using the patients' preferred weightings (D).

Discussion

In this study we developed and tested a method to assess patient value quantitatively in a single outcome metric for IBD. We showed a wide variability in patient preferences for

disease outcomes; patients' preferences were on average more heavily weighted on QoL, in contrast to traditional outcome metrics in which the focus is more heavily weighted on DC. This reaffirms the importance of SDM, and the incorporation of individualized treatment goals in the treatment plan. Interestingly, patient preferences were not linearly correlated with increases in DC, QoL, or Pr; increases from 10%-40% were judged to be more important than increases from 40%-70%, which in turn was perceived to be more important than increases from 70% to full DC, QoL, or Pr. This pattern was consistently observed across all three outcomes. On the other hand, no clinical characteristics could be identified that predict patient preferences.

Because individual patients' goals differed widely across patients we propose to measure outcomes accordingly. Instead of using a static composite score, we propose that composite scores should be weighted based on individual patient preferences. We showed the feasibility of constructing a single composite outcome metric using individual patient preferences. Indeed, outcomes were very different when using a patient preference weighted outcome metric, especially in patients with active disease. This concept is not limited to the metrics established in this Center; but conjoint analysis could be used to weigh and measure different sets of outcome metrics as well.

Limitations of this study are that there is a potential for sampling error and respondent bias because of the recruitment strategy through email and the setting in a tertiary IBD referral center. Furthermore, QoL, DC, and Pr are strongly correlated with each other. However, regardless of these correlations, we showed that weighting these outcomes could result in significantly different outcomes. A major strength of this study is that to our knowledge this is the first attempt to quantify a single composite outcome metric based on patient preference using conjoint analysis. This is a proof of concept that CBC can be used for the purpose of quantifying a single patient-centered outcome metric, which could be used directly to fill in the *patient value* portion of the *value equation*.

In conclusion, we showed that the definition of value matters in the evaluation of treatments. It is important to measure the right outcomes that are important to patients. We propose that success – on an individual patient level, as well as on a system level – should be defined based on individualized patient value, which incorporates the preferences of the patient. Moreover, these metrics should be included in provider scorecards and adopted into value based insurance designs. Where previous proposals have sought to include SDM process measures into reimbursement policies[14], we propose to include provider incentives for annually increasing a patient-centric value metric which incorporates patients' individual preferences. By striving for this, SDM needs to become an inherent part of patient treatment, and overall health care will be more patient focused and outcome driven.

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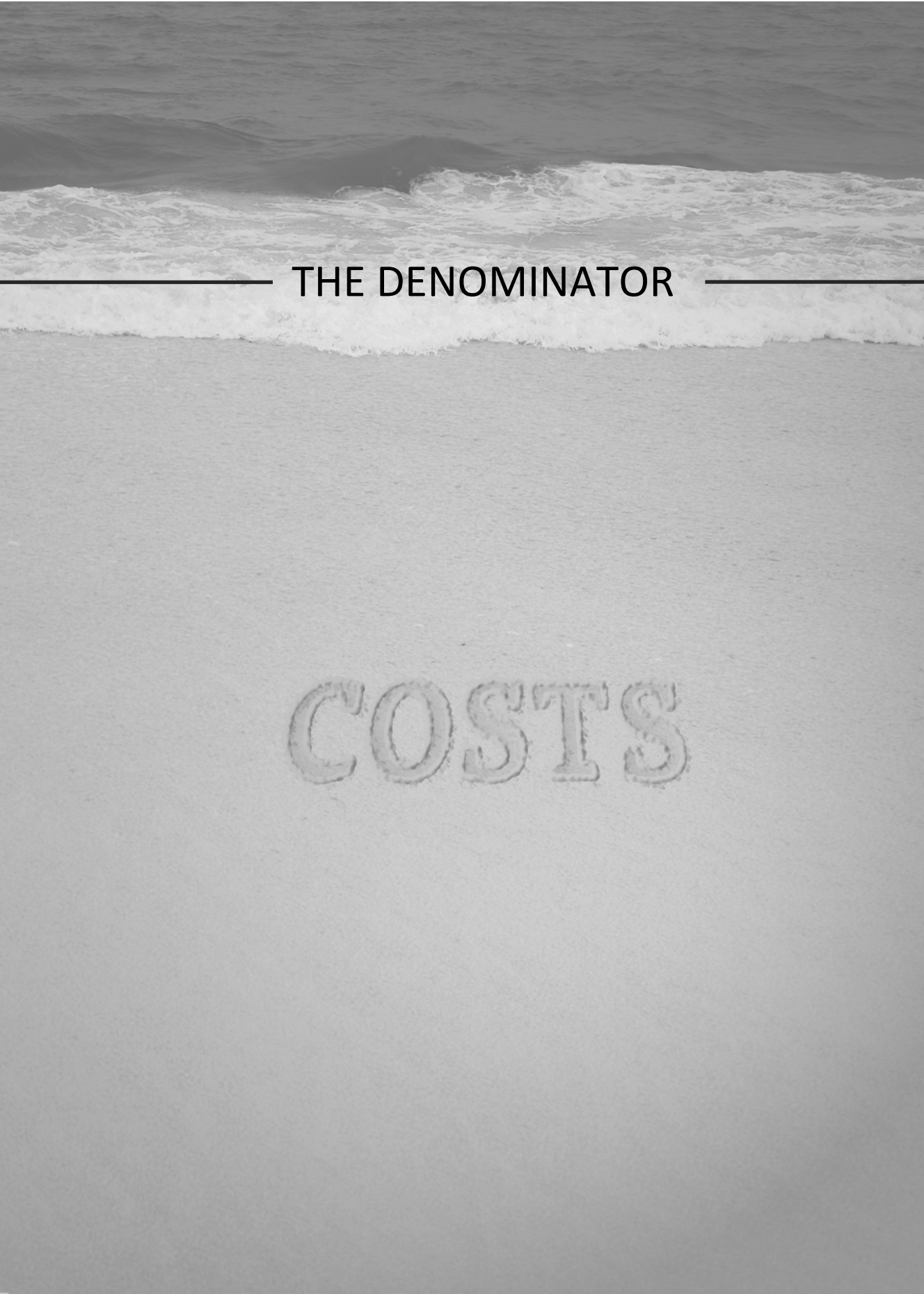
THE DENOMINATOR
COSTS

Chapter 5.

A Nationwide 2010-2012 Analysis of U.S. Health Care Utilization in Inflammatory Bowel Diseases

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Abstract

Background
Implementation of the 2010 Affordable Care Act (ACA) calls for a collaborative effort to transform the U.S. health care system toward patient-centered and value-based care. In order to identify how specialty care can be improved we mapped current U.S. health care utilization in inflammatory bowel diseases (IBD) patients using a national insurance claims database.

Methods
We performed a cross-sectional study analyzing U.S. health care utilization in 964,633 IBD patients between 2010 and 2012 using insurance claims data, including pharmacy and medical claims. Frequency of IBD-related care utilization (medication, tests, treatments) and their charges were evaluated. Subsequently, outcomes were put into the framework of current U.S. guidelines to identify areas of improvement.

Results
A disproportionate usage of aminosalicylates (42%) in Crohn's disease (CD), frequent corticosteroid use (46%, with 9% long-term users), and low rates of corticosteroid-sparing drugs (thiopurines 15%; methotrexate 2.7%) were observed. Markers for inflammatory activity such as CRP or fecal calprotectin were not commonly used (8.8% and 0.13%, respectively). Although infrequently used (11%), anti-TNFα antibody therapy represents a major part of observed IBD charges.

Conclusions
This analysis shows 2010-2012 utilization and medication patterns of IBD health care in the U.S., and suggests that improvement can be obtained through enhanced guidelines adherence.

Introduction
The current U.S. health care system is suffering from a variety of clinical and economic inefficiencies.[1-3] While the focus of debates on these challenges may vary, such as excessive administration, non-adherence to guidelines, overutilization of resources, uncoordinated care, and broad-based preventive failures, there is an emerging consensus that the U.S. health care system as currently implemented, with a persistent disconnect between high spending levels and discernible improvements in patient outcomes, is not sustainable.

IBD are prototypic chronic diseases, affecting around 1.4 million adults and children in the U.S. The estimated annual disease-attributable direct costs are largely driven by hospital costs and medication, especially biological therapy.[4,5] Like most chronic diseases, IBD care is beset with wide practice variations[6], provider expertise differentials (primary and specialty), and a limited evidence base for basic, let alone integrated, standards of care and quality of care.[7] Fragmentation and duplication of services, suboptimal follow-up, and

a lack of transparency in adherence to guidelines, particularly in regard to overuse and misuse of drugs, could as well contribute to the high spending in IBD care.

We conducted a 2010-2012 insurance claims analysis encompassing 964,633 IBD patients. The primary study objective was to assess U.S. health care utilization in IBD patients on a national level, to establish a detailed understanding of current practices in IBD management. The secondary objective was to analyze charges encountered for different aspects of IBD management and assess their relative contribution to total IBD related health care costs.

Methods

Claims derived care analysis

We conducted a retrospective analysis of U.S. IBD pharmacy and medical claims data, between 2010 and 2012, from Source Healthcare Analytics LLC (SHA). The data represent a significant proportion of all U.S. medical and pharmacy claims enabling quantitative/qualitative assessments of IBD-related practices and costs. Only fully adjudicated claims by both payers and providers were included. IBD patients were identified as having ≥1 medical claim with one of the International Classification of Diseases (ICD)-9 codes for CD (555.x) or ulcerative colitis (UC) (556.x) between 04/2010 and 03/2012. Patients with diagnosis codes for both UC and CD were excluded from the disease specific analyses. We analyzed medical claims for patient identifiers, demographics, procedure details, charge, date, and physician information. Pharmacy claims for IBD specific drugs (*Table 5.1*) were analyzed for patient identifiers, demographics, prescription details, charge, date, insurance, and physician information. A summary of the claims data capture process is shown in *Figure 5.1*. Heat maps were generated based on UC and CD pharmacy claim counts in different U.S. regions, by physician 3-digit zip codes, divided by the assumed population sizes of these regions.

Drug group	Included drugs
Aminosalicylates	mesalamine, sulfasalazine, balsalazide, olsalazine
Antibiotics	metronidazole, ciprofloxacin
Local acting corticosteroids	budesonide
Systemic corticosteroids	prednisone, methylprednisolone
Immunomodulators	azathioprine, mercaptopurine, cyclosporine, methotrexate
Biologics	adalimumab, certolizumab pegol, infliximab, natalizumab

Table 5.1. IBD related medication sorted by drug group

Medications were categorized into 6 groups of ascending potency: 1) aminosalicylates; 2) antibiotics; 3) budesonide; 4) systemic corticosteroids; 5) immunomodulators; and 6) biologic therapy (*Table 5.1*). We determined the number of unique patients using these drugs between 2010 and 2012. Biologics, in particular i.v. infliximab and i.v. natalizumab, are commonly charged as medical claims, which were therefore included as well. For each drug group, the percentage prescribed by gastroenterologists was calculated. To determine concomitant medication use, we analyzed prescription rates in 3-month

timeframes. In addition, we calculated the percentage of patients using corticosteroids for more than 105 consecutive days. To quantify the volume of patients discontinuing immunomodulators or biologics, we defined stopping as not receiving a refill within 30 days after the end date of the last prescription.

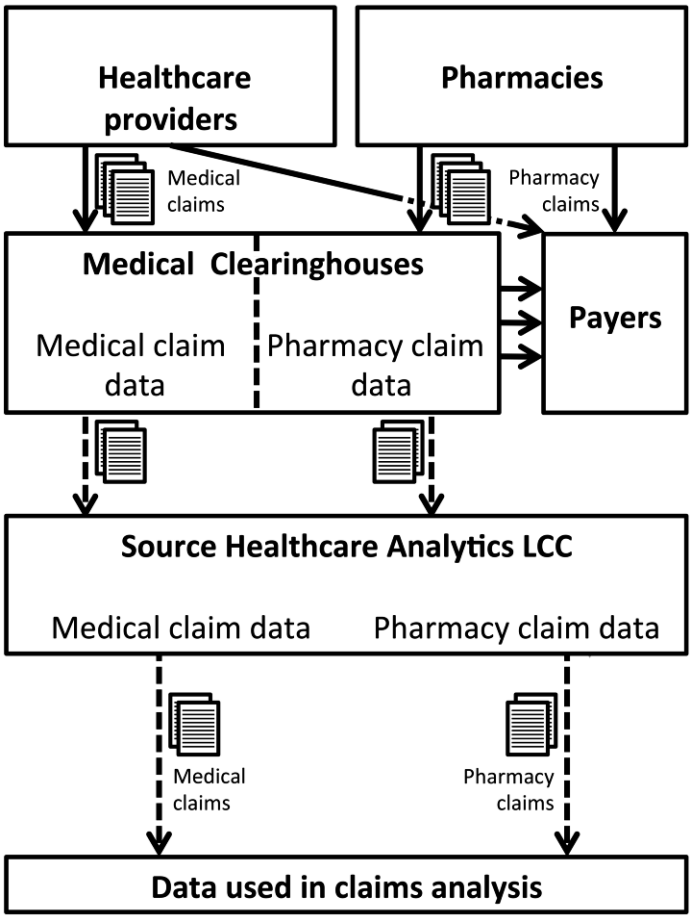

Figure 5.1. Origin of the data sets. Medical claims and pharmacy claims are submitted by providers either directly to the payer or, more commonly, this process is outsourced to medical clearinghouses that subsequently process the claims and submit the claims to payers. Source Healthcare Analytics has access to a considerable amount of these claims data. We queried this database, based on diagnosis codes and specific medications.

For the analysis of IBD-related procedures and tests, total claim counts, unique patient counts, and charges were extracted from the medical claims data set. IBD-related procedures were defined based on a pre-defined set of Current Procedural Terminology (CPT) and Healthcare Common Procedure Coding System (HCPCS) codes summarized in *Table 5.2*. The included CPT codes cover gastrointestinal surgical procedures, anesthesia, and medical procedures; laboratory, pathology, and radiological procedures; and codes

for evaluation and management. In addition, we included CPT category 2 codes for IBD specific quality measures[8] and CPT category 3 codes for gastrointestinal procedures. The included HCPCS level II codes were A-codes for stoma care, B-codes for (par)enteral therapies, and J-, C-, and S-codes for IBD-specific drugs (*Table 5.2*).

	codes	**explanation**
CPT codes category I		
Anesthesia	00700 – 00882	abdomen
Surgery	43200 – 43278 44360 – 44397 45300 – 45392 46600 – 46615	endoscopies
	44005 – 44346 44500 – 44701 44900 – 45190 45395 – 45999 49000 – 49084	intestinal surgeries
	46020 – 46500 46700 – 46899	peri-anal surgeries
Radiology	70010 – 76499	diagnostic imaging
	76506 – 76999	diagnostic ultrasound
	77001 – 77032	radiologic guidance
Pathology & Laboratory	80047 – 80076	organ or disease-oriented panels
	80500 – 80502	consultations clinical pathology
	81000 – 81099	urinalysis
	82000 – 84999	chemistry
	85002 – 85999	hematology & coagulation
	87001 – 87999	microbiology
	88300 – 88399	surgical pathology
Medical procedures	90465 – 90474	immunization administration for vaccines/toxoids
	90476 – 90749	vaccines, toxoids
	91000 – 91299	gastroenterology
	96360 – 96549	hydration, therapeutic, prophylactic, diagnostic injections & infusions, and chemotherapy & other highly complex drug or highly complex biologic agent administration
Evaluation and management	99201 – 99215	office/other outpatient services
	99217 – 99220	hospital observation services
	99221 – 99239	hospital inpatient services
	99241 – 99255	consultations
	99281 – 99288	emergency dept. services
	99291 – 99292	critical care services
CPT codes category II		
	1036F	current non-tobacco user
	3095F	DXA results
	4037F	influenza vaccine ordered and administered

Table 5.2. Included IBD-related CPT and HCPCS codes in the analysis of the medical claims data set.

	codes	explanation	
CPT codes category III			
	4040F	pneumococcal vaccine administered or previously received	
	0184T	excision of rectal tumor, transanal microsurgical approach	
	0227T	anoscopy high resolution with biopsies	
HCPCS level II			
A-codes	A4361 – A4427 A5051-A5063 A5082-A5093		ostomy supplies (excluding urinary ostomy)
B-codes	All		enteral and parenteral therapy
J-, C-, and S- codes	J0135, J0718, J0744 J1020 – J1040, J1094, J1100, J1700 – J1720, J1745, J2323, J2650, J2920, J2930, 7030 – J7130, J7500 – J7502, J7506 – J7510, J7515, J7516, J8540, J8610, J9250, J9260, C8957, C9249, C9279, C9283, C9399, S0173		IBD related drugs and infusion fluids

Table 5.2 – continued. Included IBD-related CPT and HCPCS codes in the analysis of the medical claims data set

Charge analysis

Since neither costs nor reimbursement rates are publicly known, costs in this study refer to claims-related charges and were utilized to assess the relative contribution of different medications and procedures to total IBD-related charges. Patient identifiers, and thus information regarding diagnoses, were only available for a subset of all pharmacy claims; therefore, de-identified claims for IBD-related medications prescribed by gastroenterologists were also collected for charge estimations. For each claim, physician and insurance information, prescription details, charges, and claim month were obtained. We corrected for the subset of IBD patients that is not managed by gastroenterologists, using the proportion of IBD medication prescribed by non-gastroenterologists in the IBD patient-identified pharmacy claims data set. To assess the charges of IBD-related procedures and tests, the medical claims data set was used. For claims without a charge, the average of charges per procedure with a known charge was used.

Guidelines-derived care analysis

We critically appraised and summarized all available U.S. guidelines, medical position statements, and technical reviews from the American College of Gastroenterology (ACG) and the American Gastroenterological Association (AGA). Where different sets of guidelines disagreed on specific management decisions, the most conservative measure was used in our analysis. The guidelines-derived data sets were structured in a way that would enable comparison with the claims-derived data analysis.

Statistical analysis

Our descriptive statistics consist of patient and physician demographics, medication and medical resources utilization, and charges. All outcomes were analyzed for all patients

with a diagnosis of IBD, and per diagnosis specifically (UC vs. CD). All statistical analyses were performed on the SHA-retrieved data sets using SAS software, version 9.2.

Results

Claims-derived care analysis

Between 2010 and 2012, a total of 964,633 IBD patients was identified: 501,718 CD patients (52%) and 529,788 UC patients (55%); 7% had a diagnosis code for both UC and CD. The mean age of the study population was 50.8 (SD 18.1) years (CD 48.3 [SD 18.3] years, UC 52.6 [SD 17.7] years), and 44% was male (43% CD and 45% UC). In the pharmacy claims dataset a total of 413,334 IBD patients was identified that had at least 1 pharmacy claim for IBD related medication; 39% of these claims were processed by commercial insurers, 30% by a pharmacy benefit manager, 14% by Medicare, 6% by Medicaid, 8% by an employer group, and 3% paid cash (*Table 5.3*). Geographical heat maps that show the relative amount of claims per 3-digit zip code area are provided in *Figure 5.2* for CD and UC.

Insurance	IBD total	CD	UC
Unique patients	413,334	221,912	227,203
Cash	3%	3%	3%
Commercial	39%	39%	40%
Employer Group	8%	7%	8%
Medicaid	6%	7%	5%
Medicare	14%	14%	14%
Pharmacy benefit manager	30%	29%	30%

Table 5.3. Payer analysis of pharmacy claims

Pharmacy claims analysis

Table 5.4 summarizes observed use of IBD medication, subdivided for CD and UC. In our study population, 62% of UC patients and 42% of CD patients used aminosalicylates. In total, 32% of all aminosalicylate claims were prescribed for CD patients. Antibiotics were used by 21% of patients with UC, and 25% with CD, and corticosteroids were used in 46% of IBD patients (CD 47%, UC 44%). Long-term use of corticosteroids was observed in 8.8% of patients (19% of all corticosteroid users) within the study period. Concomitant use of corticosteroid sparing medication, i.e., immunosuppressives, was low (15% used thiopurines concomitant with corticosteroids, 2.7% used methotrexate) (*Table 5.5*). In total, 18% of patients used thiopurines (CD 21%, UC 12%), 2.6% methotrexate, and 0.2% cyclosporine. Of UC patients receiving thiopurines, 59% continued the use of aminosalicylates; for methotrexate this was 31%. We observed that 54% of patients who used immunomodulators stopped, of whom 73% restarted again. The number of CD patients who used infliximab, adalimumab, certolizumab pegol, or natalizumab was 6.0%, 9.2%, 2.5%, and 0.1%, respectively; for UC patients, these rates were 2.1%, 1.3%, 0.2%, and 0%, respectively. Of patients taking biologics, 48% stopped, of whom 74% restarted. The majority of biologics (69%), immunomodulators (63%), aminosalicylates (64%), and

budesonide (69%) were prescribed by gastroenterologists. Non-gastroenterologists specialists prescribed most of the corticosteroids (70%) and antibiotics (71%).

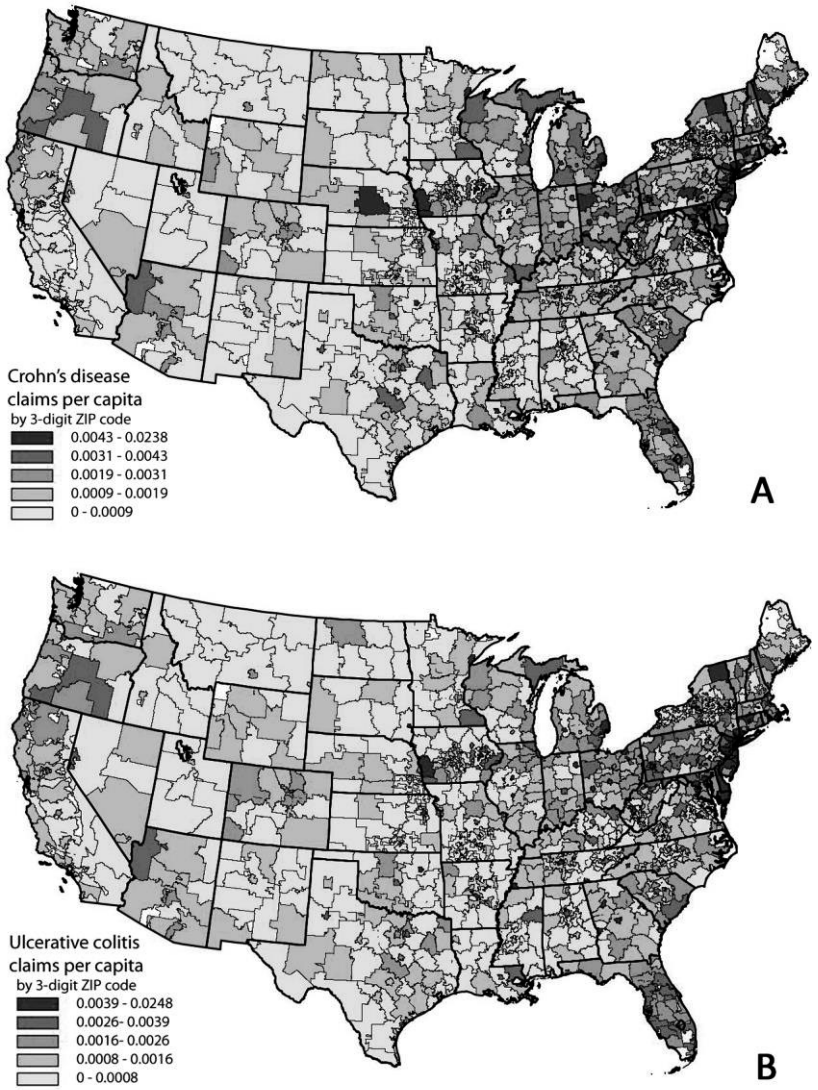

Figure 5.2. Heat map of the U.S., reflecting the number of Crohn's disease (a) and ulcerative colitis (b) patient claims per provider zip code over the number of individuals registered at that zip code

Medical claims analysis

A total of 12,374,156 medical claims were identified between 2010 and 2012, covering 6,405 different claim codes. Of these codes 1,750 (27%) were IBD-related, corresponding with 9,818,429 claims (79% of the total claims). The most common claims were 15-minute

office visit (684,790 claims), 25-minute office visit (641,367 claims), complete blood count (514,459 claims), venipuncture (513,527 claims), and colonoscopy with biopsies (467,980 claims).

	IBD	CD	UC
Aminosalicylates	53.1%	42.1%	62.3%
Antibiotics	23.5%	25.2%	20.7%
Budesonide	8.0%	12.0%	3.7%
Systemic corticosteroids	46.3%	47.0%	44.4%
Long term corticosteroids	8.8%	8.3%	8.4%
Thiopurines	17.5%	21.3%	12.3%
Methotrexate	2.6%	3.4%	1.6%
Cyclosporine	0.2%	0.2%	0.2%
Biologics	11.0%	16.8%	3.5%

Table 5.4. Percentage of IBD/CD/UC patients using IBD drugs between 2010 and 2012.

Table 5.5 on page 96.

The average rate of annual outpatient clinic visits was 94%, emergency department (ED) visits 11%, hospitalizations 6.5%, and surgeries 2.8% (*Table 5.6*). The rate of outpatient clinic visits was higher for CD (97%) compared to UC (74%). Annual colonoscopy rates were 25% for CD and 34% for UC. The annual rate of imaging (ultrasound, magnetic resonance imaging [MRI], or computed tomography [CT] abdomen/pelvis) was 18%, of complete blood count 32%, and of liver enzyme tests 20% Annual rates of inflammatory activity assessment using biomarkers were as follows: C-reactive protein (CRP) 8.8%, erythrocyte sedimentation rate (ESR) 9.7%, fecal calprotectin 0.13%, fecal lactoferrin 0.13%, and fecal leukocytes 0.32%. During the study period 1.0% of patients underwent a dual-energy x-ray absorptiometry (DXA) scan. Determination of the rate of thiopurine methyltransferase (TPMT) testing and thiopurine metabolites did not result in reliable results, because multiple CPT codes are used for these tests and these CPT codes are also used for other tests. The annual observed rate of tuberculosis (TB) skin or quantiferon tests, recommended for screening in patients starting with biological treatment, was 0.8%, and of hepatitis B screening 0.8%, and annual rates of influenza and pneumococcal vaccinations were 1.8% and 0.5%, respectively. However, many of those might not be billed for independently.

Charges

Annual U.S. medical claim charges for IBD patients were in total $4.6 billion, of which 86% ($3.9 billion) were directly related to IBD care. The medical claim with the highest share in these charges was infliximab (35%), followed by colonoscopy with biopsies (4.6%) and intravenous infusion of chemotherapy/biologics (3.5%). Furthermore, in total 22% of the IBD related medical claim charges were related to endoscopies and surgeries (including pathology and anesthesia charges), 13% to physician consultation services, and 9% were for laboratory tests (*Figure 5.3a*). Patients with a diagnosis code for CD had on average higher annual charges and more claims (mean annual charge of $5,004 with 6 claims on average) compared to UC patients (mean annual charge of $2,381, with 3 claims on

average). Annual IBD related pharmacy claims were estimated to account for a total of $2.9 billion annually. In total 54% of those were for aminosalicylates (of which 32% for CD patients) and 21% for biologics (*Figure 5.3b*).

	IBD	CD	UC
ED visit	10.7%	15.1%	4.5%
Outpatient visit	93.8%	97.4%	74.2%
Hospitalization	6.5%	7.6%	4.3%
Endoscopy total	42.0%	34.1%	44.2%
- **Upper GI endoscopy**	- 5.8%	- 6.2%	- 4.7%
- **Colonoscopy**	- 31.3%	- 25.0%	- 33.9%
IBD related surgery total	2.8%	3.3%	1.6%
- **resection colon/ileocecal**	- 1.1%	- 1.2%	- 0.8%
- **fistula/abscess surgery**	- 0.6%	- 0.9%	- 0.1%
CBC	32.5%	39.5%	18.6%
CRP	8.8%	11.2%	4.1%
ESR	9.7%	12.0%	4.8%
Liver enzymes	20.4%	24.9%	11.4%
Fecal calprotectin	0.1%	0.2%	0.1%
Fecal lactoferrin	0.1%	0.1%	0.1%
Fecal leukocytes	0.3%	0.3%	0.3%
Influenza vaccination*	1.8%	1.9%	1.3%
Pneumococcal vaccination*	0.5%	0.5%	0.4%
Hepatitis B vaccination*	0.1%	0.2%	0.1%
TB screen*	0.8%	1.1%	0.4%
Hepatitis B screening*	0.8%	1.0%	0.4%
US/MRI/CT abdomen/pelvis	18.1%	22.6%	11.3%
DXA scan	0.6%	0.8%	0.3%

*Table 5.6. Observed average annual rate for hospital visits, endoscopies, surgeries, laboratory investigations, and imaging. CD: Crohn's disease, CBC: complete blood count, CRP: C-reactive protein, CT: computed tomography, DXA: Dual-energy X-ray absorptiometry scan, ED: emergency department, ESR: erythrocyte sedimentation rate, GI: gastro-intestinal tract, IBD: inflammatory bowel diseases, MRI: magnetic resonance imaging, TB: tuberculosis, UC: ulcerative colitis, US: ultrasound. *Might not be billed for independently.*

Guidelines-derived care analysis

We identified seven guidelines/medical position statements published between 2003 and 2010 with recommendations relevant for IBD care; four by the American Gastroenterological Association (AGA)[9-12] (all accompanied by technical reviews[13-16]), and three by the American College of Gastroenterology (ACG)[17-19]. Four focused on IBD management[10,12,17,18], two on colorectal cancer screening[9,19], and one on osteoporosis management in gastrointestinal diseases[11]. None of the guidelines offered detailed recommendations on the annual frequency of clinic visits, lab visits, and endoscopies, with the exception of colorectal screening protocols. Extracted care recommendations from all guidelines are summarized in *Table 5.7*.

An overview of expected rates of medication and medical resource utilization according to guidelines versus the observed rates is provided in *Tables 5.8 and 5.9*, respectively. Summarized, we found that although aminosalicylate treatment is not recommended in

CD patients, 42.1% of CD patients were prescribed aminosalicylates during the 2-year study period, which alone accounts for at least 17% of total pharmacy charges. Metronidazole and ciprofloxacin, indicated for treatment of pouchitis in UC, active fistulizing disease in CD, and to treat infectious complications, were prescribed to 23% of patients. However, the claims data did not allow a more detailed analysis on indications for antibiotic use.

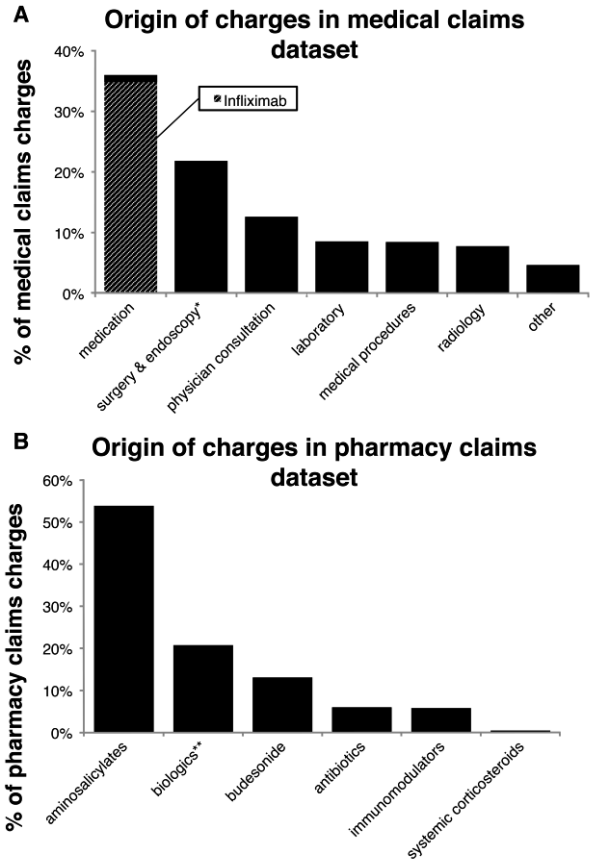

Figure 5.3. Origin of charges in medical claims dataset (a) and pharmacy claims dataset (b).
**includes anesthesia and pathology.*
***The majority of infliximab and natalizumab charges is charged as a medical claim and is therefore not included in this graph*

Corticosteroid-sparing medication was used sparsely in conjunction with corticosteroid therapy (15% thiopurines, and 2.7% methotrexate), while long-term corticosteroid use was observed in 9% of patients. Though 9% of patients used corticosteroids for more than 105 days consecutively, only 1% underwent a DXA scan. Furthermore, we found a low use of surrogate biomarkers for assessment of inflammation such as CRP and/or fecal calprotectin (8.8% and 0.13%, respectively).

	aminosalicylates			systemic corticosteroids			thiopurines			methotrexate			biologics*		
concomitant drug use	**IBD total**	**CD**	**UC**	**IBD total**	**CD**	**UC**	**IBD total**	**CD**	**UC**	**IBD total**	**CD**	**UC**	**IBD total**	**CD**	**UC**
aminosalicylates	x	x	x	34%	25%	42%	42%	30%	59%	25%	20%	31%	13%	11%	24%
systemic corticosteroids	15%	15%	15%	x	x	x	19%	16%	22%	29%	25%	35%	13%	11%	16%
thiopurine	14%	17%	12%	15%	15%	13%	x	x	x	3%	4%	2%	10%	10%	9%
methotrexate	1%	1%	1%	3%	3%	2%	0%	0%	0%	x	x	x	3%	3%	5%
biologics*	2%	3%	1%	4%	6%	1%	4%	5%	1%	10%	12%	5%	x	x	x

Table 5.5. Concomitant drug use. Percentages of patients on drug A (columns) concomitantly using drug B (rows).
**Because this analysis was performed using pharmacy claims and infliximab is mostly charged as a medical claim, infliximab use is underestimated in this analysis.*

	UC	**CD**	**Extra recommendations**
Aminosalicylates	Remission induction and maintenance[18] in mild – severe disease activity	Minimally effective for remission induction, not effective for maintenance[17]	
Antibiotics	Only recommended for pouchitis, no benefit for luminal disease[18]	Benefit for luminal disease not demonstrated, recommended for Crohn's fistula[17]	
Budesonide	Not recommended[10]*	Mild – moderate activity, Maximally 3[10] - 6[17] months	
Oral corticosteroids	Remission induction in mild – severe disease activity; not recommended for maintenance[10,18]	Mild – severe remission induction, not maintenance[10,17]	- DXA scan if use exceeds 3 months[10,11,17,18] - Calcium and vitamin D for high-risk patients[11,17,18]
IV corticosteroids	Remission induction for moderate to severe disease[10,18]	Remission induction for moderate to severe disease[10,17]	

Table 5.7. Recommendations in US guidelines for medical treatment of IBD and on necessity of IBD specific procedures. CBC: complete blood count, CD: Crohn's disease, CRC: colorectal carcinoma, CRP: C-reactive protein, DXA: Dual-energy X-ray absorptiometry scan, ESR: erythrocyte sedimentation rate, IV: intravenous, TB: tuberculosis, TPMT: thiopurine methyltransferase, UC: ulcerative colitis
** Substantial evidence for topical budesonide in distal UC, not approved in US however.*

	UC	CD	Extra recommendations
Thiopurines	Maintenance and as adjunctive to corticosteroids during induction of remission[10,18]	Maintenance and as adjunctive to corticosteroids during remission induction[10,17]	- CBC: Initially 1x/1-2 weeks, then 1x/3 months[10,17,18] - Liver enzymes routinely[10,18] - TMPT genotype/phenotype before initiation[10,17,18] - Metabolites to monitor compliance and metabolization not routinely recommended[10,17,18]
Methotrexate	Not recommended[10,18]	Remission induction and maintenance therapy if initiated during remission induction[10,17]	- CBC: routinely[10,17] - liver enzymes: routinely / every 4-8 weeks[10, 17]
Cyclosporine A	Remission induction of severe disease[10,18]	Remission induction of severe disease[10,17]	
Infliximab	Remission induction and maintenance of moderate to severe disease activity[10,18]	Remission induction and maintenance of moderate to severe disease activity[10 17]	- TB screening (skin test or quantiferon) before initiation[10,17,18] - Hepatitis B screening before initiation[18]
Adalimumab	-	Remission induction and maintenance of moderate to severe disease activity[17]	- TB screening (skin test or quantiferon) before initiation[17]
Certolizumab pegol	-	Remission induction and maintenance of moderate to severe disease activity[17]	- TB screening (skin test or quantiferon) before initiation[17]
Natalizumab	-	Remission induction and maintenance of moderate to severe disease activity[17]	- TOUCH program (mandatory)[17]
Overall disease specific	Screening colonoscopy for CRC every 1-3 year, start 8 years after diagnosis[9,18,19]	Fecal leukocytes, calprotectin or lactoferrin, orosomucoid, ESR, or CRP to confirm intestinal inflammation[17]	- Annual influenza vaccine and pneumococcal vaccine every 3-5 year if using immunosuppressive therapy[18]

Table 5.7 – continued. Recommendations in US guidelines for medical treatment of IBD and on necessity of IBD specific procedures.

Medication	Guidelines	Expected	Observed
Aminosalicylates	Recommended for UC, not/minimally effective for CD	No aminosalicylates for CD	42.1% in CD
Ciprofloxacin/ metronidazole	Only recommended for pouchitis or fistula	Unknown	23.5%
Budesonide	Recommended for UC not for CD	No budesonide in UC	3.7% budesonide in UC
Corticosteroids	For induction of remission, no long term use	No long term use	9% long term use
Immunomodulators/ Biologics	Recommended for corticosteroid sparing	46.3% used corticosteroids	15% of corticosteroid users used concomitant thiopurines, 2.7% methotrexate. In total 11.0% biologics use.

Table 5.8. Expected medication use according to guidelines compared with observed values. CD: Crohn's disease, UC: ulcerative colitis.

Procedures	Guidelines	Expected	Observed
Colonoscopy	Screening colonoscopy for UC 1x/1-3year 8 years after diagnosis	UC patients >8yr after diagnosis: 33.3% annual colonoscopy	UC patients: 33.9% annual rate
Surrogate activity markers	Fecal calprotectin, lactoferrin, calprotectin, ESR, orosomucoid or CRP		Annual rates: calprotectin: 0.1%; lactoferrin: 0.1%; fecal leukocytes: 0.3%; CRP: 8.8%; ESR: 9.7%
DXA scan	Patients >3 months corticosteroids	9% of patients ≥1 episode of long term corticosteroids	1.0% of patients
Complete blood count	Patients on thiopurines: initially 1x/1-2 weeks, then 1x/3 month, on methotrexate: routinely.	Patients on immunomodulators per quarter: 8.7% thiopurines, 1.1% methotrexate	8.1% 3-monthly rate. (32.5% annual rate)
Liver enzymes	Patients on thiopurines/methotrexate: routinely / every 1-2 months	Patients on immunomodulators per quarter: 8.7% thiopurines, 1.1% methotrexate	3.4% 2-monthly rate (20.4% annual rate)

Table 5.9. Expected rates of tests and procedure in the data set according to guidelines, compared with the observed values. CRP: C-reactive protein, DXA: Dual-energy X-ray absorptiometry scan, ESR: erythrocyte sedimentation rate, UC: ulcerative colitis.

Discussion

In this study we report on U.S. health care utilization in IBD patients, and found unexpected discrepancies with U.S. guidelines. This was demonstrated by a disproportionate rate of aminosalicylate use in CD, common corticosteroid use (including long-term), and a low rate of corticosteroid-sparing drugs. In addition, we found only infrequent usage of surrogate biomarkers such as CRP and/or fecal calprotectin.

IBD-related health expenditures are among the highest in the U.S. health care system.[20] A 2012 study based on patient-reported expenditures from 556 IBD patients estimated annual IBD-related costs in the U.S. to be $2.9 billion[20], while another claims analysis of 19,420 IBD patients estimated annual disease-attributable direct costs to be $6.3 billion[21]. Although we were not able to access actual costs in our study, we were able to assess the relative contribution of the different facets of IBD treatment to total IBD-related charges. We identified biologics to be a major cost component in IBD care, although their use was restricted to only 11% of IBD patients in the observation period. Aminosalicylates accounted for 54% of pharmacy claim charges, while 32% of the prescriptions were prescribed for CD patients, which is not supported by current guidelines.

Medical insurance claims databases are increasingly used in health outcomes research, and these data present both opportunities and limitations.[22] A major advantage is that claims are anonymous, plentiful, and available in electronic format. Limitations include the focus of claims on reimbursement, which is not designed for research purposes; no health outcomes or treatment goals are available, diagnoses cannot be formally confirmed, and medical utilization without insurance coverage, such as influenza vaccinations at the workplace, is not captured. Also, because only claims processed through medical clearinghouses could be captured in our data set, we were likely not able to capture all U.S. IBD patients, a fraction of claims for the identified patients might not have been included, and no reimbursement rates were available.

An insurance claims analysis including 19,420 IBD patients by Kappelman *et al*[5] found much higher utilization rates because of more stringent inclusion criteria, thereby excluding patients with a mild disease phenotype, patients whom our study aimed to include. In contrast, utilization rates reported in a Northern California study analyzing 8,787 IBD patients were very similar to our observations, except for the number of outpatient visits (*Table 5.10*). [23] This study also reported a decline in prolonged steroid exposure from 14% in 1998-1999 to 9% in 2004-2005 annually in CD, and interestingly, an increase in UC from 11% to 14%. Infliximab use increased from 1% to 5% in CD and from <0.1% to 0.4% in UC.[23] Our results are in line with these findings and confirm that similar patterns are observed on a national level.

The observed discrepancies between guidelines and observed care could be explained in different ways. The New England Health Institute identified four major barriers to guideline adherence.[24]

1) The current payment system is problematic, because we pay for volume of procedures rather than for outcomes;

2) a lack of information technology (IT) systems is a barrier because physicians often have insufficient access to guidelines at the point of care and because IT does not yet adequately support clinical decision-making;
3) the culture, beliefs, and habits of physicians could be barriers because many doctors receive little or no comparative feedback on their performance; and
4) the current process of development of guidelines presents an obstacle to adherence. In particular, the lack of transparency in guideline development leads to a lack of trust among physicians, while guidelines themselves often lack sufficient flexibility and relevance to clinical practice; many guidelines do not reflect the complexity and context in which real-world clinical decisions must be made.[24]

		Our analysis	Herrinton *et al.*[29]	Kappelman *et al.*[10]
Hospitalizations	**CD**	7.6%	8%	27%
	UC	4.3%	5%	19%
Surgeries	**CD**	3.3%	3.5%	5.4%
	UC	1.6%	0.6%	3.6%
Endoscopies	**CD**	34%	-	41%
	UC	44%	-	52%
ER visits	**CD**	15%	-	36%
	UC	4.5%	-	15%
Outpatient visits	**CD**	97%	220%	1030%
	UC	74%	180%	921%

Table 5.10. Annual utilization rates for CD and UC patients compared with a utilization study by Herrinton et al[29] and Kappelman et al[10].

In summary, in our claims data set of 964,633 IBD patients, unprecedented in size, we found relevant discrepancies between daily care and guideline recommendations on a national level. The guidelines themselves, in this case for a prototypic chronic disease, need to be assessed and updated to enable development of optimal care-pathways that are both clinically and economically efficacious. Future research will need to show the effect of improved guidelines on adherence, quality of care and cost-effectiveness.

Disclosures

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Chapter 6.

Value-Based Health Care for Inflammatory Bowel Diseases: The Impact on Health Care Utilization

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Abstract

Background
Value-based health care is thought to be the solution that will improve quality and decrease costs in health care. Many hospitals are implementing programs based on this strategy, but rigorous scientific reports are still lacking. Here, we present the first-year outcomes of a value-based health care program for inflammatory bowel disease (IBD) management which focused on highly coordinated care, task differentiation of providers and continuous home monitoring.

Methods
IBD patients treated within a value-based health care program were identified in an administrative claims database from a commercial insurer allowing comparisons to matched controls. Health care utilization including visits, hospitalizations, tests, and medications were compared between groups.

Results
In total, 173 IBD program patients were identified of which 100 were matched to 499 controls. Significantly more biomarker testing was performed in the value-based health care group. Numerically less surgeries, hospitalizations, emergency department visits, and imaging were observed. More biologics were used, while both short- and long-term corticosteroid use was decreased.

Conclusion
These are the first results of the first year of a value-based health care program for inflammatory bowel disease management. Significantly more preventative measures were performed, while corticosteroid use, ED visits, and hospitalizations decreased.

Introduction
Globally, health care costs are inflating without necessarily leading to better outcomes.[1] In order to increase quality and bend the cost curve, the introduction of value-based health care (VBHC) is thought to be inevitable.[2] Conceptually, VBHC is focused around the idea of introducing value in care by dividing achieved health outcomes over the amount of dollars spent. Key components of VBHC are measuring outcomes and costs, and making subsequent changes in the care delivery processes accordingly. To facilitate this process, a coordinated care infrastructure is thought to be of major importance.[3,4] Many institutions are currently adopting components of VBHC in clinical practice. Unfortunately, rigorous scientific reports on the outcomes of these approaches are currently lacking.

IBD management accounts for significant health care costs. While initially the main cost driver in IBD was hospitalizations, with the introduction of the newer biologics, medication has also become a dominant cost driver.[5] This poses a difficult dilemma since the most effective medication is oftentimes also the most expensive. This underlines the importance of delivering the right care at the right time to the right patient in order to

fully optimize value for each individual patient. Care coordination programs for IBD have been implemented in a variety of centers across the world, though reported outcomes are very sparse.[6] The Royal Adelaide Hospital in Australia introduced a chronic care model in 2008 which included nurse case managers, scheduled follow-up phone calls for symptomatic patients, and standardized protocols for blood test monitoring, which resulted in a decrease in IBD related hospitalizations[7]. The effect of remote disease monitoring has been studied by a variety of programs as well, such as the Danish Constant-Care system for ulcerative colitis (UC), which was shown to reduce relapse duration whereas the total number of recognized relapses increased.[8] Similarly, the UC-HAT tele-monitoring system showed no improvement in quality of life or disease activity, and many patients discontinued using the system.[9] A meta-analysis assessing six remote monitoring interventions found a trend towards improvements in quality of life and a reduced number of office visits, but showed no significant reduction in relapses or hospitalizations.[10]

The University of California, Los Angeles (UCLA) Center for IBD has implemented a VBHC Program which instituted its first version on February 1st, 2012. The program was designed around the concepts of value-based health care, including regular monitoring of meaningful health outcomes and the implementation of coordinated care pathways focusing on improving value for patients.[4] Nine care pathways based on patients' disease activity and treatment regimen were implemented, which include scheduled clinic visits, labs, and home monitoring (*Table 6.1*). Task differentiation was introduced, with specified tasks for administration, IBD nurses, and IBD specialists. Furthermore, at any time patients could reach out with questions to a specialized IBD nurse through email with a response time of <24 hours during weekdays.

Disease state	Medication	Total duration	Office visit	Labs	Home monitoring
Active	**Antibiotics** **5ASA/SPS**	6 weeks	Week 6	Week 6	Every 2 weeks
	Corticosteroids **Biologicals**	6 weeks	Week 6	Every 2 weeks	Every 2 weeks
Remission	**5ASA/SPS** **No medication**	continuous	Annual	2x/year	Every 2 months
	Immunomodulator **Biological** **Combination therapy**	continuous	2x/year	Every 2 months	Every 2 months

Table 6.1. Care scenarios implemented at the UCLA Center for Inflammatory Bowel Diseases in 2012.

Patient participation was achieved in part by completing health outcomes questionnaires in the out-of-hospital setting. During the initial year of the UCLA IBD Program hardcopy questionnaires were provided to patients during clinic visits and patients were asked to return these questionnaires at predefined time points by mail, fax or scanned by email, which were subsequently evaluated by a specialized IBD nurse. E-mail reminders were

sent, which also included an interactive pdf. During subsequent stages, a supporting IT infrastructure enabling outcome collection and reporting was developed and implemented in 2013; a patient-facing mobile application which improves usability for patients was implemented in 2014.[11] These questionnaires consisted of a modified Harvey Bradshaw Index for Crohn's disease (CD) patients and a modified partial Mayo score for UC patients and were used to assess patients' symptoms in between clinic visits.

This study aims to assess the impact of the first phase of the VBHC program (2012) on health care utilization and medication use in IBD patients. One of the key components of VBHC is the assessment of health care expenditure. In order to allow for a meaningful utilization assessment we chose to analyze our performance based on insurance claims data extracted from a commercial payer database, which captures the entire spectrum of health related utilization and pharmacy use. This allowed us to assess utilization patterns within as well as outside of our own facility, and to compare patients treated according to the VBHC program to a matched control group.

Methods

Design

We performed a prospective case-control study assessing health care utilization patterns in IBD patients treated at the UCLA Center for IBD compared to patients not treated at UCLA for their IBD, by using an administrative claims database of Anthem California. We performed an intention-to-treat (ITT) analysis including all patients that enrolled in the UCLA IBD Center program, and a per-protocol (PP) analysis including only patients that were continuously treated at UCLA for at least one year. Additionally, health care utilization was assessed longitudinally in the UCLA IBD Center cohort before and after enrollment in the UCLA IBD Center.

Population

Administrative claims that were fully processed and paid by Anthem California were obtained between January 2012 and December 2013. Patients that visited the UCLA IBD Center between February 2012 (opening of the UCLA IBD Center) and December 2012 were included in the analysis. Patients who entered in 2013 were not included to ensure one year follow-up in the database. Data from 2012 was used as index-data, 2013 data was used as outcome data. Matched controls with at least one IBD related visit with a non-UCLA gastroenterologist between February and December of 2012 were identified and matched 5:1 based on patient characteristics in 2012 using the greedy method[12]. Patients were matched based on age (+/- 10), IBD subtype (+/- 0.3 for UC claims/total IBD claims), adjusted Charleston comorbidity index[13] (+/- 2), and relapse rate (+/- 1) in 2012. Because relapse rate could only be measured if pharmacy claims were available for analysis, patients were also fully matched based on pharmacy claims coverage in 2012.

Outcomes in 2013 were compared between groups. Only patients that were covered for medical claims for at least 80% of the year in both 2012 and 2013 were included. Patients

aged 65 years and older were excluded because these patients are eligible for Medicare coverage and the data is likely to be incomplete for these patients.

For the PP analysis, we included only patients that visited the UCLA IBD Center at least once in 2012 and once in 2013 without any IBD related visits with a gastroenterologist elsewhere. Patients were matched to a control population with at least one non-UCLA gastroenterologist visit for IBD in 2012 and one in 2013, without any IBD related gastroenterologist visits at UCLA.

Lastly, a longitudinal analysis was performed including UCLA IBD patients with at least one visit at the UCLA IBD Center. Health care utilization and medication use during the year prior to the first UCLA IBD Center visit was compared to the year thereafter, excluding the day of the first visit. Patients with no IBD related claims in the year prior to entering the program were excluded to ensure only patients with an established diagnosis were included in the study. Only patients that were covered for medical claims from a full year before to a full year after the first UCLA IBD visit were included.

Outcomes
IBD related claims were defined as a claim with an International Classification of Diseases (ICD)-9 diagnosis code 555.x or 556.x. IBD subtype was determined based on whether the majority of IBD related claims was for CD (555.x) or UC (556.x). IBD related utilization was identified using Current Procedural Terminology (CPT) codes (*Table 6.2*). Additionally, office visits needed to be accompanied with ICD-9 code 555.x or 556.x in the primary or secondary ICD-9 field. Office visits with a gastroenterologist were identified using the provider's registered specialty. A UCLA IBD Center visit was defined as an IBD related visit at UCLA with one of the gastroenterologists associated with the UCLA IBD Center.

IBD related ED visits were defined as any visit with ED as the place of service with the most frequent primary ICD-9 for an IBD related complaint (*Table 6.3*). IBD related hospitalizations were identified as having at least 2 subsequent days with inpatient hospital as the place of service and at least 10% of claims with an ICD-9 code 555.x or 556.x, or including an IBD related surgery during the hospitalization. If the Diagnosis-related group (DRG) associated with the hospital stay was not related to IBD (*Table 6.4*) the hospitalization was not considered related to IBD. Medication related to IBD was identified based on the generic name. Because biologics, particularly infliximab and natalizumab, are frequently billed as a medical claim, Health Care Common Procedure Coding System (HCPCS) codes for those drugs were included as well (*Table 6.5*). Relapses were identified based on newly started steroids, newly started biologics, or an acute IBD related surgery. Newly started steroids were defined as a new prescription starting at least 14 days after the end of the last one; for biologics this was defined as a new prescription starting at least 30 days after the end of the last one.

Type of utilization	CPT codes	Description
Office visit	99201 – 99205 99211 – 99215 99241 – 99245	Office or outpatient visit for new patients Office or outpatient visit for established patients Consultations: Office and outpatient
Colonoscopy	45330 – 45392 44388 – 44397	Sigmoidoscopy and colonoscopy procedures (rigid and flexible) Colonoscopy via stoma
Upper endoscopy	43200 – 43202 43235, 43239	Upper GI endoscopies with/without biopsies. Excluding interventional procedures/EUS
Surgery	44005 – 44346 44602 – 44701 45000 – 45190 45395 – 45999 46020 – 46060 46270 – 46288 49000 – 49084	Incisional and resectional procedures of bowel, intestinal transplant procedures, colon resection procedures, laparoscopic enterolysis, laparoscopic and open enterostomy procedures Open repair procedures intestine , other intestinal procedures Open and transrectal procedures of rectum Laparoscopic and closed procedures of rectum, open repairs of rectum Surgical incision of anus - setons and abscess drainage Resection of anal fistula Exploratory drainage procedures: abdomen/peritoneum
Acute surgeries		All surgeries except - open repair procedures intestine (44602 – 44680) - removal seton (46030)
Complete blood count	80050, 80055, 85004, 85025 – 85027	General health panel, obstetric panel CBC with and without Diff
Liver enzyme tests	80050, 80053, 80076 84460, 84450	General health panel, CMP hepatic function panel AST/ALT
C-reactive protein	86140	
Sedimentation rate (ESR)	85651, 85652	
Stool calprotectin	83993	
C. difficile stool test	87230, 87324 87493, 87803	Toxin or antitoxin assay, enzyme immunoassay, probe technique, immunoassay with direct optical observation
X-ray	72170 – 72190 74000 – 74022 74240 – 74260 74270 – 74280	Pelvis Abdomen Intestines Intestines
CT scan	72192 – 72194 74150 – 74170 74176 – 74178 74261 – 74263	Pelvis Abdomen Abdomen & Pelvis Intestines
MR scan	72195 – 72197 74181 – 74183	Pelvis Abdomen
Ultrasound	76700 – 76705	Abdomen

Table 6.2. IBD related utilization

Code(s)	Explanation
555.*	Regional enteritis
556.*	Ulcerative Enterocolitis
558.9	Other and unspecified noninfectious gastroenteritis and colitis
560.8*	Other specified intestinal obstruction
560.9	Unspecified intestinal obstruction
565.*	Anal fissure and fistula
566	Abscess of anal and rectal regions
567.21	Acute generalized peritonitis
567.22	Peritoneal abscess
567.29	Other suppurative peritonitis
567.89	Other specified peritonitis
567.9	Unspecified peritonitis
568.0	Peritoneal adhesions (postoperative) (post infection)
569.2	Stenosis of rectum and anus
569.3	Hemorrhage of rectum and anus
569.41	Ulcer of anus and rectum
569.42	Anal or rectal pain
569.49	Other specified disorders of rectum and anus
569.5	Abscess of intestine
569.6*	Colostomy and enterostomy complications
569.7*	Complications of intestinal pouch
569.81	Fistula of intestine, excluding rectum and anus
569.82	Ulceration of intestine
569.83	Perforation of intestine
569.89	Other specified disorder of intestine
569.9	Unspecified disorder of intestine
578.1	Blood in stool
578.9	Hemorrhage of gastrointestinal tract, unspecified
579.2	Blind loop syndrome
579.3	Other and unspecified postsurgical nonabsorption
579.8	Other specified intestinal malabsorption
579.9	Unspecified intestinal malabsorption
787.91	Diarrhea
789.0*	Abdominal pain
789.3*	Abdominal or pelvic swelling mass or lump
789.4*	Abdominal rigidity
789.6*	Abdominal tenderness
789.9	Other symptoms involving abdomen and pelvis

Table 6.3. ICD-9 codes for IBD related complaints

DRG	Type	Description
326	Surg	Stomach, esophageal & duodenal proc w mcc
327	Surg	Stomach, esophageal & duodenal proc w cc
328	Surg	Stomach, esophageal & duodenal proc w/o cc/mcc
329	Surg	Major small & large bowel procedures w mcc
330	Surg	Major small & large bowel procedures w cc
331	Surg	Major small & large bowel procedures w/o cc/mcc
332	Surg	Rectal resection w mcc
333	Surg	Rectal resection w cc
334	Surg	Rectal resection w/o cc/mcc
335	Surg	Peritoneal adhesiolysis w mcc
336	Surg	Peritoneal adhesiolysis w cc
337	Surg	Peritoneal adhesiolysis w/o cc/mcc
344	Surg	Minor small & large bowel procedures w mcc
345	Surg	Minor small & large bowel procedures w cc
346	Surg	Minor small & large bowel procedures w/o cc/mcc
347	Surg	Anal & stomal procedures w mcc
348	Surg	Anal & stomal procedures w cc
349	Surg	Anal & stomal procedures w/o cc/mcc
356	Surg	Other digestive system o.r. Procedures w mcc
357	Surg	Other digestive system o.r. Procedures w cc
358	Surg	Other digestive system o.r. Procedures w/o cc/mcc
371	Med	Major gastrointestinal disorders & peritoneal infections w mcc
372	Med	Major gastrointestinal disorders & peritoneal infections w cc
373	Med	Major gastrointestinal disorders & peritoneal infections w/o cc/mcc
377	Med	G.i. Hemorrhage w mcc
378	Med	G.i. Hemorrhage w cc
379	Med	G.i. Hemorrhage w/o cc/mcc
385	Med	Inflammatory bowel disease w mcc
386	Med	Inflammatory bowel disease w cc
387	Med	Inflammatory bowel disease w/o cc/mcc
388	Med	G.i. Obstruction w mcc
389	Med	G.i. Obstruction w cc
390	Med	G.i. Obstruction w/o cc/mcc
391	Med	Esophagitis, gastroent & misc digest disorders w mcc
392	Med	Esophagitis, gastroent & misc digest disorders w/o mcc
393	Med	Other digestive system diagnoses w mcc
394	Med	Other digestive system diagnoses w cc
395	Med	Other digestive system diagnoses w/o cc/mcc
856	Surg	Postoperative or post-traumatic infections w o.r. Proc w mcc
857	Surg	Postoperative or post-traumatic infections w o.r. Proc w cc
858	Surg	Postoperative or post-traumatic infections w o.r. Proc w/o cc/mcc
862	Med	Postoperative & post-traumatic infections w mcc
863	Med	Postoperative & post-traumatic infections w/o mcc
864	Med	Fever
870	Med	Septicemia or severe sepsis w mv 96+ hours
871	Med	Septicemia or severe sepsis w/o mv 96+ hours w mcc

Table 6.4. DRGs related to IBD.

DRG	Type	Description
872	Med	Septicemia or severe sepsis w/o mv 96+ hours w/o mcc
917	Med	Poisoning & toxic effects of drugs w mcc
918	Med	Poisoning & toxic effects of drugs w/o mcc
919	Med	Complications of treatment w mcc
920	Med	Complications of treatment w cc
921	Med	Complications of treatment w/o cc/mcc
922	Med	Other injury, poisoning & toxic effect diag w mcc
923	Med	Other injury, poisoning & toxic effect diag w/o mcc
947	Med	Signs & symptoms w mcc
948	Med	Signs & symptoms w/o mcc
949	Med	Aftercare w cc/mcc
950	Med	Aftercare w/o cc/mcc
951	Med	Other factors influencing health status

Table 6.4 – continued. DRGs related to IBD.

Drug type	Included drugs / CPT codes
5ASA	mesalamine, sulfasalazine, balsalazide, olsalazine
antibiotics	metronidazole, ciprofloxacin
budesonide **corticosteroids**	budesonide prednisone, methylprednisolone, hydrocortisone, prednisolone, dexamethasone
thiopurines **methotrexate**	azathioprine, mercaptopurine, methotrexate
adalimumab **infliximab** **certolizumab pegol** **natalizumab**	adalimumab / J0135 infliximab / J1745 certolizumab pegol / J0718, C9294 natalizumab / J2323, Q4079

Table 6.5. Drugs included in the analyses.

Statistical analysis

The average number of IBD related office visits, ED visits, hospitalizations, procedures, labs, and imaging studies as well as the number of patients using IBD related medications in 2013 were compared between groups. IBD medication use was compared if patients were covered for pharmacy claims in the observation period.

In the ITT and PP analyses, the Fisher's exact test was used for categorical data and the Wilcoxon-Mann-Whitney test for continuous data. Differences in IBD subtype in the demographics section were assessed using Chi-square tests. In the longitudinal study, a Wilcoxon signed-rank test was used for continuous data and a McNemar's test for categorical data. A Bonferroni correction for multiple testing was carried out. A *P* value smaller than 0.05/33=0.00015 was considered statistically significant.

Ethical considerations

This study was approved by the University of Los Angeles, California Institutional Review Board under protocol number #15-001120.

Results

Intention to treat analysis

In total 173 IBD patients were identified within the Anthem database that visited the UCLA IBD Center at least once in 2012. Of those, 16 were excluded from further analyses because they were aged 65 years or older and 57 patients were excluded because they were not covered for medical claims throughout index and analysis year (*Figure 6.1*). This resulted in inclusion of a total of 100 UCLA IBD patients that were matched to 499 non-UCLA patients. Mean age in both groups was 39 (SD 11.6 for UCLA patients, 11.4 for controls). In the UCLA group 46% had UC versus 47% in the control group, and the average Charlson comorbidity index was 0.50 (SD 1.30) in the UCLA group versus 0.46 (1.19). There were no significant differences in baseline utilization and relapses in the index year between both groups. Numerically, we observed 32% less ED visits, 21% less hospitalizations, and 24% more office visits in UCLA IBD patients in the index year (*Table 6.6*).

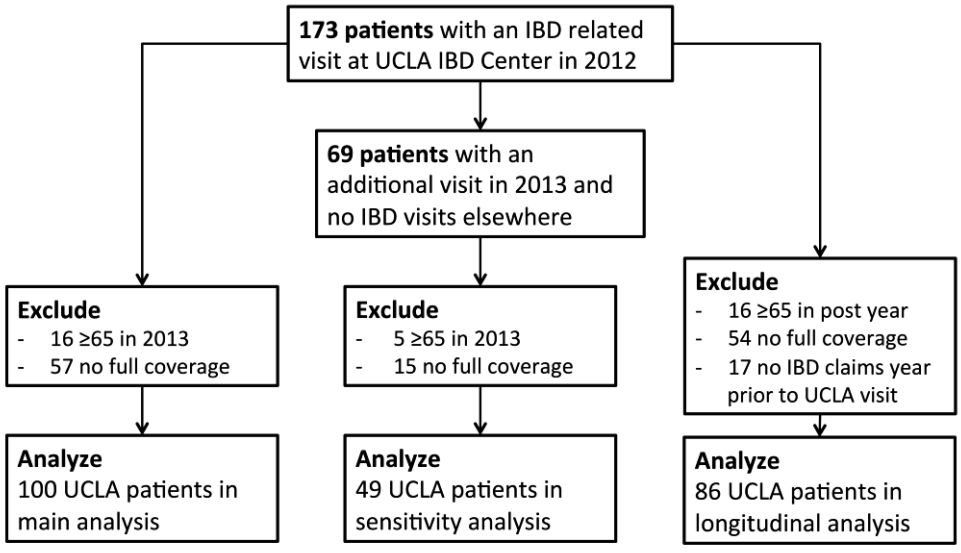

Figure 6.1. Inclusion flowchart.

In the ITT analysis we observed more than twice as much biomarker testing in the UCLA group, with an increase in CRP, ESR, and calprotectin testing of 116% (P=0.00003), 116% (P<0.00001), and 199% (P=0.00006), respectively. No significant differences in other IBD related health care utilization or medication use were observed. However, numeric reductions of more than 50% were observed for ED visits (58%), hospitalizations (57%), upper endoscopies (74%), and abdominal ultrasounds (60%) (*Table 6.7*). Furthermore, we observed 58% less systemic corticosteroid use, 80% less long-term corticosteroid use, 68% more topical corticosteroid use, 231% more methotrexate use, and 73% more adalimumab use in UCLA patients (*Table 6.8*).

Baseline characteristics of included patients	UCLA patients (n=100)	Non-UCLA patients (n=499)	*P*
Age (years), *avg (SD)*	39 (12)	39 (11)	0.99
IBD subtype, *n (%)* - **Ulcerative colitis** - **Crohn's disease**	 46 (46) 54 (54)	 232 (47) 268 (53)	0.94
Charlson comorbidity score in 2012, *avg (SD)*	0.50 (1.30)	0.46 (1.19)	0.91
days with IBD related claims in 2012, *avg (SD)*	8.8 (8.9)	7.8 (10.1)	0.20
Office visits in 2012, *avg (SD)*	4.1 (4.3)	3.3 (2.9)	0.19
ED visits in 2012, *avg (SD)*	0.21 (0.61)	0.31 (1.29)	0.25
Hospitalizations in 2012, *avg (SD)*	0.11 (0.51)	0.14 (0.43)	0.12
Surgeries in 2012, *avg (SD)*	0.06 (0.37)	0.07 (0.33)	0.36
Relapses in 2012*, *avg (SD)*	0.86 (1.22)	0.83 (1.19)	0.91
Insured for pharmacy claims in 2013, *n (%)*	375 (75)	68 (68)	0.14

Table 6.6. Baseline demographics and IBD related utilization in index year (2012) for patients included in the ITT analysis.
**only patients with insurance plans that covered prescription drugs were included in this assessment (UCLA n=77, non-UCLA n=384).*

IBD related utilization in 2013, *average (SD)*	UCLA (n=100)	Non-UCLA (n=499)	Δ	*P*
Office visits	2.9 (3.0)	2.6 (3.6)	+14%	0.10
Office visits with gastroenterologist	1.6 (1.5)	1.6 (2.0)	-0.8%	0.32
ED visits	0.11 (0.35)	0.26 (1.79)	-58%	0.91
Hospitalizations	0.05 (0.22)	0.12 (0.50)	-57%	0.40
Colonoscopies	0.42 (0.57)	0.38 (0.60)	+11%	0.34
Upper endoscopies	0.020 (0.141)	0.078 (0.30)	-74%	0.064
Surgeries	0.050 (0.261)	0.056 (0.292)	-11%	0.86
Complete blood count	2.7 (3.0)	2.6 (3.7)	+3.7%	0.65
Liver enzyme tests	2.4 (2.9)	2.2 (3.3)	+6.9%	0.66
C-reactive protein	1.47 (1.95)	0.68 (1.4)	+116%	0.00003
Sedimentation rate (ESR)	1.46 (1.96)	0.68 (1.35)	+116%	<.00001
Stool calprotectin	0.15 (0.386)	0.050 (0.275)	+199%	0.00006
***C. difficile* stool test**	0.15 (0.44)	0.10 (0.43)	+44%	0.10
X-ray	0.23 (0.96)	0.27 (1.92)	-15%	0.46
CT scan	0.17 (0.47)	0.29 (1.06)	-41%	0.69
MR scan	0.08 (0.273)	0.066 (0.332)	+21%	0.25
Ultrasound	0.03 (0.171)	0.074 (0.277)	-60%	0.13
Relapses*	0.59 (1.02)	0.59 (1.28)	+1.7%	0.50

Table 6.7.Health care utilization in matched UCLA and non-UCLA patients included in the ITT analysis.
**only patients with insurance plans that covered prescription drugs were included in this assessment (UCLA n=68, non-UCLA n=375).*

Medication use in 2013, *n (%)*	UCLA (n=68)	Non-UCLA (n=375)	Δ	*P*
Any IBD related medication	60 (88.2)	300 (80.0)	+10%	0.13
Topical 5-ASA	7 (10.3)	42 (11.2)	-8.1%	1.00
Oral 5-ASA	30 (44.1)	177 (47.2)	-6.5%	0.69
Metronidazole/ciprofloxacin	12 (17.6)	53 (14.1)	+25%	0.46
Topical corticosteroids	7 (10.3)	23 (6.1)	+68%	0.20
Budesonide	6 (8.8)	31 (8.3)	+6.7%	0.81
Systemic corticosteroids	8 (11.8)	106 (28.3)	-58%	0.0039
Long term corticosteroids	1 (1.5)	27 (7.2)	-80%	0.10
Thiopurines	23 (33.8)	95 (25.3)	+34%	0.18
Methotrexate	3 (4.4)	5 (1.3)	+231%	0.11
Biologics	26 (38.2)	102 (27.2)	+41%	0.080
- **adalimumab**	16 (23.5)	51 (13.6)	+73%	0.043
- **infliximab**	10 (14.7)	51 (13.6)	+8.1%	0.85
- **certolizumab pegol**	0 (0)	9 (2.4)	-100%	0.37
- **natalizumab**	0 (0)	0 (0)	0%	1.00

Table 6.8. Number of patients using IBD medication in matched UCLA and non-UCLA patients in the ITT analysis.

Per protocol analysis

In total, 49 UCLA IBD patients were included in the PP analysis (*Figure 6.1, Table 6.9*), which were matched to 245 control patients. Increases in biomarker testing were confirmed with an observed 161% increase in CRP testing ($P<0.00001$), 134% increase in ESR testing ($P=0.00007$), and 344% increase in calprotectin testing ($P=0.00011$). No significant differences in health care utilization or medication use were detected between the two groups. The observed numeric differences were confirmed in the PP analysis, with slightly higher effect sizes: 75% less ED visits, 89% less hospitalizations, 79% less upper endoscopies, and no ultrasounds in the UCLA group. In addition, we observed 57% less CT scans and 64% less abdominal X-rays in UCLA patients. Finally, no IBD surgeries were observed in the UCLA group. Similar trends were observed in medication use as well with a 61% reduction in corticosteroid use, as well as long-term corticosteroid use, and 68% more rectal corticosteroid use. Additionally, 76% less budesonide use was observed in this cohort. More than 4 times as many UCLA patients used methotrexate compared to controls, and 41% more patients used adalimumab. The number of relapses was 48% less in UCLA patients (*Figure 6.2 and 6.3, Tables 6.10 and 6.11*).

Baseline characteristics of included patients	UCLA (n=49)	Non-UCLA patients (n=245)	*P*
Age avg (SD)	39 (12)	40 (12)	0.95
IBD subtype n (%) - **Ulcerative colitis** - **Crohn's disease**	 21 (43) 28 (57)	 106 (43) 139 (57)	0.96
Charlson comorbidity score in 2012 avg (SD)	0.47 (1.10)	0.44 (1.09)	0.85
days with IBD related claims in 2012 avg (SD)	7.7 (8.3)	8.7 (10.2)	0.47
Office visits in 2012 avg (SD)	3.6 (3.1)	3.4 (2.8)	0.89
ED visits in 2012 avg (SD)	0.16 (0.59)	0.51 (3.0)	0.11
Hospitalizations in 2012 avg (SD)	0.12 (0.63)	0.19 (0.57)	0.09
Surgeries in 2012 avg (SD)	0.061 (0.429)	0.065 (0.332)	0.45
Relapses in 2012* avg (SD)	0.86 (1.34)	0.84 (1.28)	0.94
Insured for pharmacy claims in 2013 n (%)	33 (67)	179 (73)	0.42

*Table 6.9. Baseline demographics and IBD related utilization in index year (2012) for patients included in the PP analysis. *only patients with insurance plans that covered prescription drugs were included in this assessment (UCLA n=37, non-UCLA n=185).*

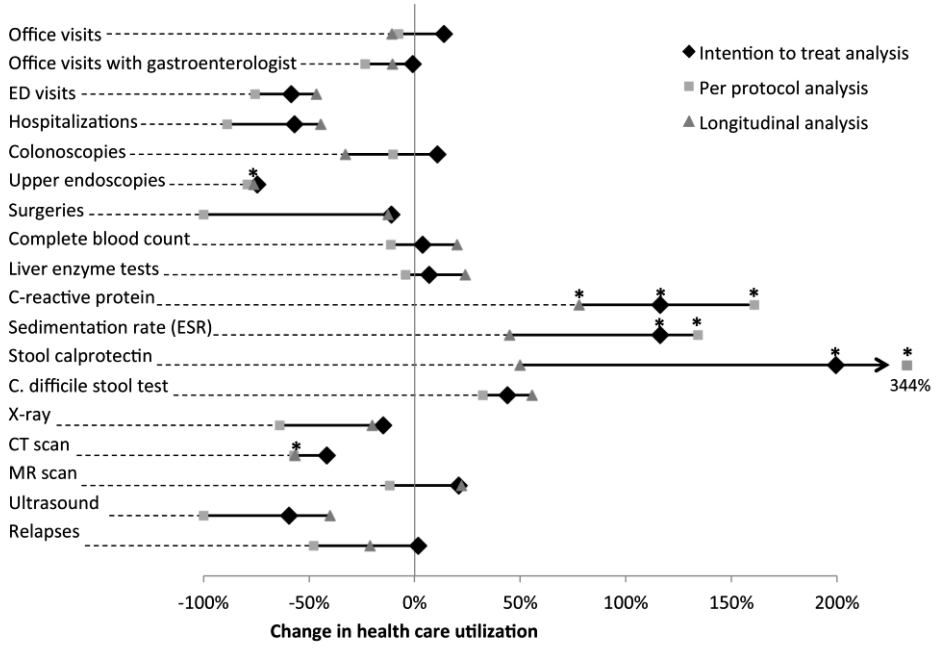

*Figure 6.2. Change in health care utilization in IBD patients treated at the UCLA IBD Center compared to controls (ITT analysis and PP analysis), and compared to the year before enrollment at the UCLA IBD Center in a longitudinal cohort. *P<0.0015*

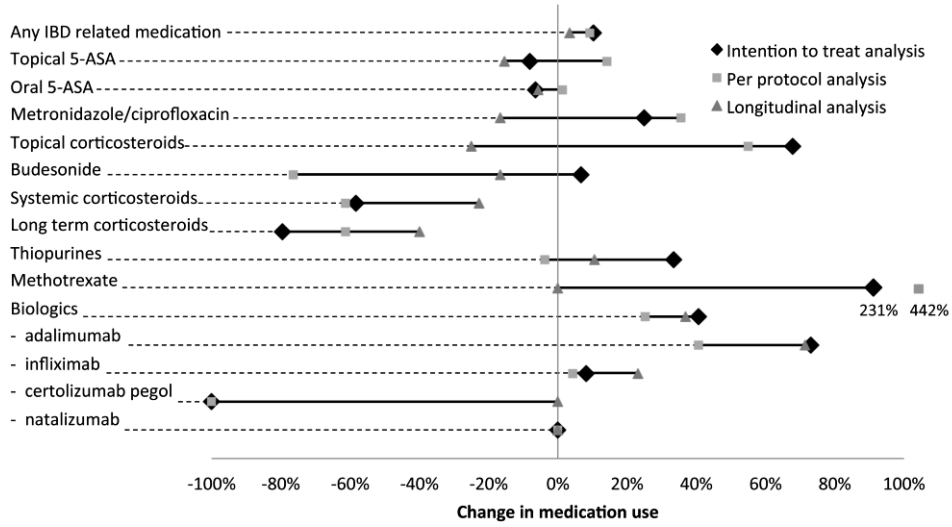

Figure 6.3. Change in medication use in IBD patients treated at the UCLA IBD Center compared to controls (ITT analysis and PP analysis), and compared to the year before enrollment at the UCLA IBD Center in a longitudinal cohort.

IBD related utilization in 2013, *average (SD)*	**UCLA (n=49)**	**Non-UCLA (n=245)**	**Δ**	***P***
Office visits	2.9 (2.4)	3.1 (2.7)	-8%	0.41
Office visits with gastroenterologist	1.7 (0.8)	2.2 (1.8)	-23%	0.057
ED visits	0.16 (0.43)	0.67 (5.20)	-75%	0.52
Hospitalizations	0.020 (0.143)	0.184 (0.68)	-89%	0.064
Colonoscopies	0.43 (0.54)	0.48 (0.67)	-10%	0.91
Upper endoscopies	0.020 (0.143)	0.098 (0.36)	-79%	0.15
Surgeries	0 (0)	0.045 (0.226)	-100%	0.15
Complete blood count	2.9 (2.8)	3.3 (5.4)	-11%	0.99
Liver enzyme tests	2.7 (2.8)	2.8 (4.8)	-4%	0.73
C-reactive protein	1.98 (2.02)	0.76 (1.33)	+161%	<.00001
Sedimentation rate (ESR)	1.82 (2.02)	0.78 (1.39)	+134%	0.00007
Stool calprotectin	0.163 (0.373)	0.037 (0.228)	+344%	0.00011
***C. difficile* stool test**	0.18 (0.53)	0.14 (0.49)	+32%	0.42
X-ray	0.16 (0.62)	0.45 (2.72)	-64%	0.91
CT scan	0.20 (0.54)	0.48 (2.46)	-57%	0.85
MR scan	0.061 (0.242)	0.069 (0.285)	-12%	0.99
Ultrasound	0 (0)	0.11 (0.33)	-100%	0.015
Relapses*	0.36 (0.86)	0.70 (1.28)	-48%	0.089

Table 6.10. Health care utilization in matched UCLA and non-UCLA patients included in the PP analysis.
**only patients with insurance plans that covered prescription drugs were included in this assessment (UCLA n=33, non-UCLA n=179).*

Medication use in 2013, *n (%)*	UCLA (n=33)	Non-UCLA (n=179)	Δ	*P*
Any IBD related medication	30 (90.9)	149 (83.2)	+9.2%	0.43
Topical 5-ASA	4 (12.1)	19 (10.6)	+14%	0.76
Oral 5-ASA	17 (51.5)	91 (50.8)	+1.3%	1.00
Metronidazole/ciprofloxacin	7 (21.2)	28 (15.6)	+36%	0.45
Topical corticosteroids	4 (12.1)	14 (7.8)	+55%	0.49
Budesonide	1 (3.0)	23 (12.8)	-76%	0.14
Systemic corticosteroids	4 (12.1)	56 (31.3)	-61%	0.034
Long term corticosteroids	1 (3.0)	14 (7.8)	-61%	0.48
Thiopurines	11 (33.3)	62 (34.6)	-3.8%	1.00
Methotrexate	2 (6.1)	2 (1.1)	+442%	0.12
Biologics	12 (36.4)	52 (29.1)	+25%	0.41
- **adalimumab**	7 (21.2)	27 (15.1)	+41%	0.44
- **infliximab**	5 (15.2)	26 (14.5)	+4.3%	1.00
- **certolizumab pegol**	0 (0)	5 (2.8)	-100%	1.00
- **natalizumab**	0 (0)	0 (0)	0%	1.00

Table 6.11. Number of patients using IBD medication in matched UCLA and non-UCLA patients in the PP analysis.

Longitudinal analysis

In total 86 UCLA patients were included in the longitudinal analysis (*Figure 6.1*). Biomarker testing using CRP increased with 78% (*P*=0.0025), the number of upper endoscopies decreased by 76% (*P*=0.00075), and the number of CT scans decreased by 57% (*P*=0.0028). No significant differences in other outcomes were observed between the year before and after enrollment in the UCLA IBD Program. Numerically, there was an increase in biomarker testing using ESR or calprotectin (45% and 50%, respectively) and MR scans (22%), and a decrease in the average number of ED visits (46%), hospitalizations (44%), surgeries (13%), ultrasounds (40%), and abdominal X-rays (20%). The number of relapses was 21% less after enrollment. Corticosteroid use decreased by 23%, long-term corticosteroids use by 44%, budesonide use by 17%, and topical corticosteroid use by 25% after enrollment in the UCLA IBD Program. No changes in methotrexate use were observed before and after enrollment in the UCLA IBD Program. Overall 37% more patients used biologics after enrollment, with a 70% increase in adalimumab use and 23% increase in infliximab use (*Figure 6.2 and 6.3*, *Table 6.12 and 6.13*).

Discussion

These are the first results of a novel and developing VBHC program for IBD management. We show evidence that patients treated in this VBHC program, which incorporated 1) constant monitoring of health outcomes; 2) highly coordinated care pathways; 3) patient education; and 4) task differentiation between providers, undergo more preventative monitoring then matched control patients and undergo less IBD related tests. This reflects the highly preventative nature of this program in contrast to the often observed reactive nature of current IBD care.[14] Since this study only included Anthem members, and it only reports on the first development stage of the program, the size of the study population is relatively small and no significant differences in health care utilization or medication use were observed. However, it is highly promising that we did consistently observe trends

towards less ED visits, hospitalizations, surgeries, upper endoscopies, and most imaging tests, as well as less corticosteroid use (including long term corticosteroid use), and more biologics use.

IBD related utilization, ***average (SD)***	**pre-UCLA (n=86)**	**post-UCLA (n=86)**	**Δ**	***P***
Office visits	3.9 (4.2)	3.5 (3.9)	-11%	0.23
Office visits with gastroenterologist	2.0 (1.9)	1.8 (1.9)	-11%	0.15
ED visits	0.33 (0.83)	0.17 (0.60)	-46%	0.055
Hospitalizations	0.21 (0.53)	0.12 (0.56)	-44%	0.13
Colonoscopies	0.64 (0.78)	0.43 (0.62)	-33%	0.056
Upper endoscopies	0.29 (0.53)	0.07 (0.26)	-76%	0.00075
Surgeries	0.093 (0.33)	0.081 (0.382)	-13%	0.78
Complete blood count	3.1 (3.3)	3.8 (3.5)	+20%	0.087
Liver enzyme tests	2.6 (2.9)	3.2 (2.8)	+24%	0.021
C-reactive protein	1.2 (1.9)	2.2 (2.4)	+78%	0.0025
Sedimentation rate (ESR)	1.5 (2)	2.2 (2.3)	+45%	0.023
Stool calprotectin	0.09 (0.33)	0.14 (0.54)	+50%	0.69
***C. difficile* stool test**	0.1 (0.38)	0.16 (0.46)	+56%	0.47
X-ray	0.29 (0.91)	0.23 (0.95)	-20%	0.76
CT scan	0.53 (1.17)	0.23 (0.7)	-57%	0.0028
MR scan	0.1 (0.31)	0.13 (0.4)	+22%	0.59
Ultrasound	0.12 (0.52)	0.07 (0.26)	-40%	0.55
Relapses*	0.85 (0.99)	0.67 (1.05)	-21%	0.20

*Table 6.12. Health care utilization in UCLA patients before and after enrollments in UCLA IBD program.*only patients with insurance plans that covered prescription drugs were included in this assessment (n=67).*

Medication use in 2013, ***n (%)***	**pre-UCLA (n=67)**	**Post-UCLA (n=67)**	**Δ**	***P***
Any IBD related medication	59 (88.1)	61 (91.0)	3.4%	0.73
Topical 5-ASA	13 (19.4)	11 (16.4)	-15%	0.75
Oral 5-ASA	35 (52.2)	33 (49.3)	-5.7%	0.77
Metronidazole/ciprofloxacin	18 (26.9)	15 (22.4)	-17%	0.66
Topical corticosteroids	8 (11.9)	6 (9.0)	-25%	0.73
Budesonide	6 (9.0)	5 (7.5)	-17%	1.00
Systemic corticosteroids	22 (32.8)	17 (25.4)	-23%	0.33
Long term corticosteroids	5 (7.5)	3 (4.5)	-40%	0.63
Thiopurines	19 (28.4)	21 (31.3)	11%	0.75
Methotrexate	3 (4.5)	3 (4.5)	0%	1.00
Biologics	19 (28.4)	26 (38.8)	37%	0.016
- **adalimumab**	7 (10.4)	12 (17.9)	71%	0.063
- **infliximab**	13 (19.4)	16 (23.9)	23%	0.45
- **certolizumab pegol**	0 (0)	0 (0)	0%	1.00
- **natalizumab**	0 (0)	0 (0)	0%	1.00

Table 6.13. Number of UCLA patients using IBD medication before and after entering the UCLA IBD Center.

Oftentimes it takes many years before these types of care redesign programs come to full fruition since there are many initial hurdles to overcome. First, this program was not designed and executed as a research project but as an implementation project which requires more institutional involvement and change management among all stakeholders. Since the medical community is traditionally most resistant to change, it may require a multitude of years before programs like ours to truly flourish. Second, the largest resistance to VBHC programs is the current fee-for-service (FFS) payment system, which does not incentivize the use of a VBHC program. The current payment system incentivizes quantity as opposed to quality care, and does not reimburse for many essential care components such as email communication. Third, a major upfront investment is required for successful implementation of a VBHC program, including the vital development of a secure IT infrastructure and mobile application. Consistently, typical Accountable Care Organizations (ACO) - i.e. provider groups that take accountability for both outcomes and costs in a specified patient population - experienced great difficulty performing in their first years. ACOs can qualify for shared savings payments through the Medicare Shared Savings Program (MSSP) by successfully reducing total spending and reporting quality measures. However, only 22% of ACOs that began participating in the MSSP in 2012 or 2013 qualified for shared savings.[15] Typically, ACOs are far less influencing the care delivery process compared to our VBHC programs. Due to unprecedented institutional support we were able to implement this program despite the challenges described and we expect to continue to report its advances throughout the years. We encourage the various groups invested in VBHC to publish early reports of their programs in order to establish a basis for best practices and further growth and improvements.

Limitations of this study include that numeric differences in baseline utilization between the two groups were observed, including 32% less ED visits and 21% less hospitalizations, despite matching on baseline demographics including relapse rate, disease type, comorbidities, and age. Therefore, we might have overestimated the observed reduction in ED visits (58%) and hospitalizations (57%). We did not have access to objective health outcomes in this study due to the use of an insurance claims database. Despite the limitations of the dataset, we did observe large numeric differences in health care utilization, in three different analyses (i.e. ITT, PP, and longitudinal analysis). As expected, the PP analysis showed larger numeric differences in health care utilization than the ITT analysis. This is in concordance with the fact that these patients continued to receive care at UCLA, while the ITT analysis also included patients with no follow-up visits at UCLA and/or patients with concomitant visits elsewhere.

The observed reduction in hospitalizations is in accordance with the results of the chronic care model at the Royal Adelaide Hospital in Australia[7]. In contrast, this study found numerically more corticosteroid use in the chronic care group as well as more immunomodulators. Consistent with other programs[10] utilizing remote monitoring, we could not confirm a reduction in relapse rate, possibly due to the fact that more relapses are identified using remote monitoring approaches. In contrast to these programs, we did not consistently observe a reduction in office visits but did observe a trend towards fewer hospitalizations.

In order to bend the cost curve and improve care quality in IBD, VBHC is thought to be the most certain path going forward. Due to the initial phase of the UCLA IBD Program analyzed and reported here, many components of a full VBHC Program were not implemented yet. In 2013 an electronic system was implemented, which enables patients to view their care scenarios, easily communicate with a dedicated IBD nurse through messaging, and fill out electronic home monitoring questionnaires. Furthermore, this electronic system enables internal outcome reporting. In 2014 a mobile application (eIBD, available through iTunes and Google Play Store) was launched to facilitate this process even further, which to date has been used by almost 200 IBD patients. The mobile health index (mHI), a validated score consisting of 4 patient reported outcomes, was developed for implementation on the app.[16] This score improves the accuracy of home monitoring as well as allows for continuous outcome monitoring, which is of utmost importance in a VBHC program. Future research will address the effects of these implementations because the current dataset does not include the necessary follow up for these analyses.

Summarized, this is the first comprehensive utilization analysis of a VBHC program for IBD management. Despite the limitations of this study we feel this study gives a first insight in the effects of a comprehensive VBHC approach in IBD. More intense disease activity monitoring was confirmed and positive trends were observed, including trends towards fewer ED visits, fewer hospitalizations, and less corticosteroid use.

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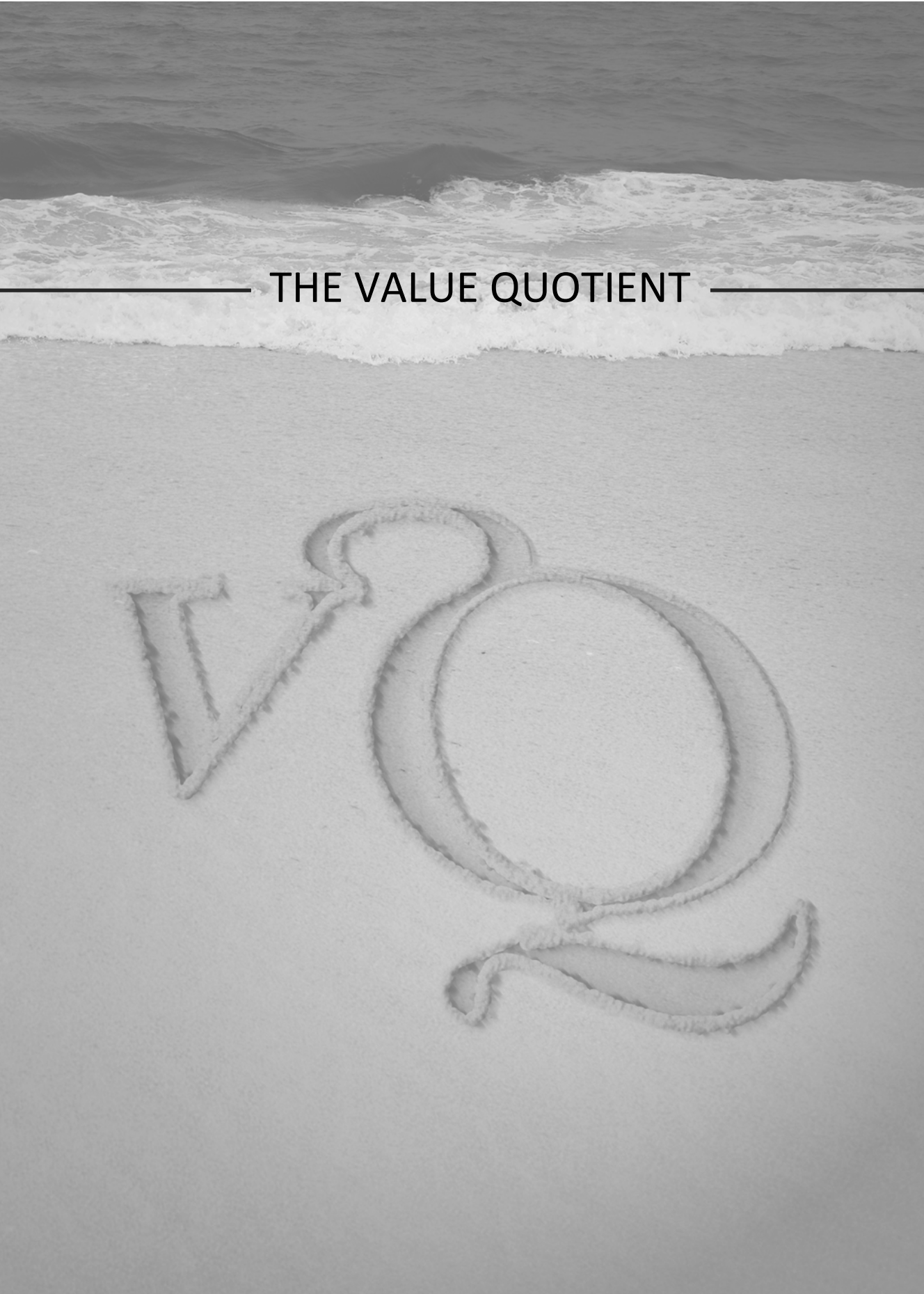
THE VALUE QUOTIENT



Chapter 7.

Summary, General Discussion, and Future Perspectives

Summary
Value based health care (VBHC) is thought to be the solution to fix the health care crisis. Health care costs are increasing globally, and restructuring of our payment system may be the most promising solution. The key concept of VBHC is to evaluate care by the health value obtained: the achieved health outcomes divided by the encountered costs.[1,2] By rewarding high value care, an incentive is created to reduce costs and improve quality. However, in order to fairly reward value, value needs to be clearly defined. This value definition is an essential component for a well-functioning VBHC system.

Chapter 1 discusses in depth the key components of VBHC, and the applicability in IBD management. The three key components discussed are 1) measuring the right outcomes and the associated costs of care; 2) reporting those outcomes and comparing them to outcomes from other providers; and 3) improve care delivery accordingly in a coordinated care infrastructure which supports the implementation of these changes. A fourth component – a value based insurance system, in which value of care is rewarded rather than volume of care – is essential to drive this cycle of improvement. While the number of programs incorporating key-components of VBHC is rapidly growing, the evidence supporting these concepts is still limited to date.[3] This thesis explores the first part of this VBHC framework in IBD – the development, implementation, and measurement of outcome measures relevant for the evaluation of IBD care – and evaluates the efficacy of an IBD specific VBHC program implemented at the University of California, Los Angeles (UCLA).

Inflammatory bowel diseases (IBD), consisting of Crohn's disease and ulcerative colitis, are chronic inflammatory diseases of the intestines. IBD is thought to be caused by environmental triggers, which lead to a dysregulated immune response in a susceptible host.[4] IBD are chronic, lifelong diseases, which affect around 1.4 million Americans. IBD treatment is associated with significant costs, which were traditionally mostly driven by hospitalizations, and more recently by the newer biological therapies.[5,6] The UCLA Center for IBD has implemented a VBHC program in 2012, which incorporates the key concepts of VBHC. The program is based on a coordinated care infrastructure and is supported by a designated IT platform with a patient app. Patients are treated by pre-defined evidence-based care pathways, in which health outcomes are measured frequently while IBD related health care utilization is tracked. The in-house developed UCLA eIBD mobile app allows patients to view their treatment plan, update medications, participate in eLearning, and communicate directly with a specialized IBD nurse. Additionally, wellness programs tailored for IBD patients are available. To assess the treatment results of individual patients, and to assess overall performance, the UCLA IBD Center developed the outcome metric *value quotient* (*vQ*). The *vQ* is calculated by dividing obtained *patient value* by the associated costs. *Patient value* is defined as a combination of disease control, quality of life, and (work) productivity.[9] In **Chapter 2, 3, and 4** the development and evaluation of IBD specific outcome metrics to assess *patient value* are discussed, while **Chapter 5 and 6** focus on the measurement of health care utilization in IBD care as a proxy for costs. Additionally, we discuss indirect costs related to IBD in **Chapter 3**.

As discussed in **Chapter 1**, quality of care can be assessed on multiple levels using structure, process, or outcome measures.[10] Structural measures assess the availability of resources in a care delivery setting such as the number of beds in a hospital. Process measures evaluate key processes in health care delivery and can be helpful for internal process improvement. However, process measures do not measure what is ultimately important to the patient: the achieved outcomes. Therefore, outcome measures are increasingly recognized to be the most important metrics to assess. The evaluation of care using outcome metrics should incorporate outcomes in three tiers: 1) the achieved level of health and quality of life, 2) the level of discomfort during the recovery process, and 3) the sustainability of the achieved outcomes; regardless of the processes leading to these outcomes.[11] Which outcomes are important to measure remains ill-defined, but patient reported outcomes are increasingly recognized to be important. The IBD Center strives to measure *patient value* regularly, to get an in-depth view on the obtained results in all three tiers. While clinical outcome scores can be evaluated during clinic visits, remote monitoring of outcomes using patient reported measures is essential to ensure regular evaluation of patients' health statuses. In **Chapter 2** we developed a score for remote monitoring of IBD disease activity that patients can use on a mobile app. We assessed how well different patient reported outcomes predict clinical disease activity using multivariable logistic regression. Two composite-scores were developed, one for Crohn's disease and one for ulcerative colitis patients. Both scores consist of four patient reported questions that accurately predict clinical disease activity. This tool is now implemented in the UCLA eIBD app and allows for year-round monitoring of patient reported outcomes in the out-of-clinic setting.

In **Chapter 3** we assessed the prevalence of reduced work productivity in IBD patients. Reductions in work productivity can be categorized as absenteeism or presenteeism. Absenteeism refers to missed work hours due to for example sickness, or doctor's visits. Presenteeism refers to reduced productivity while at work. We showed that absenteeism rates are significantly higher in patients with active disease (47%) than in patients with remissive disease (14%). Similarly, more presenteeism was observed in patients with active disease (95%) than in patients in remission (55%). No difference in absenteeism rates was observed between patients in remission and healthy controls (both 14%). However, patients in remission still experience significantly higher rates of presenteeism (55%) than healthy controls (27%). The most common reported cause for reduced productivity was fatigue (42%), and only 34% of patients were able to make adjustments in their work schedule to avoid taking time off.[12]

To further quantify the *patient value* component of the *vQ*, we assessed patient preference for the three outcomes incorporated in the *vQ*: disease control, quality of life, and productivity, in **Chapter 4**. Using a choice-based conjoint analysis we showed that there is a large variation in individual preferences between patients. Overall, quality of life is perceived to be more important than both disease control and productivity, and increases from low outcome levels to intermediate outcome levels are valued more than increases from intermediate to high levels. Furthermore, we constructed a composite *patient value* metric weighted based on observed patient preferences for disease

outcome (i.e. quality of life outcomes were weighted more heavily than disease control outcomes if a patient valued quality of life more than disease control). Use of these patient-centric *patient value* scores resulted in significantly different outcomes, both on the individual patient level, and on the aggregate provider level. Incorporation of patient preferences in the treatment plan, a process called shared decision making, has been shown to increase both patients' knowledge as well as the patients' experience.[13] Because of the importance of shared decision making and the observed differences in the observed *patient value* metric when incorporating patients' preferences, we suggest that physicians should be rewarded accordingly in value-based insurance designs.

To quantify the complete *vQ*, costs need to be assessed as well. In **Chapter 1** different methods to estimate costs are discussed. Charges, the amounts listed on hospital bills that are charged to the insurance, are most readily available. However, charges often correlate poorly with the actual reimbursements which in turn don't correlate well with the actual costs of care.[14] To truly understand the costs of care, a method called time driven activity based costing (TDABC) can be used. This technique assigns costs, based on the time and materials required, to each step in the process. TDABC has successfully been shown to measure costs and identify waste in care processes.[15] While TDABC offers a good solution to estimate costs of specific processes of care, it is hard to assess overall costs in care due to the time intensive nature of the development of TDABC models. Therefore, we chose to focus on health care utilization instead. Utilization data can be obtained from payer databases, hospital databases, or medical clearing houses. We developed methods to extract meaningful utilization patterns using insurance claims and applied those in **Chapter 5 and 6**. Next to the direct costs, indirect costs should eventually be incorporated in the *vQ* as well. It has been shown that indirect costs due to losses in work productivity represent a major percentage of overall health care related costs.[16] In **Chapter 3** we confirmed high indirect costs in IBD as well, mostly due to presenteeism.[12]

In **Chapter 5**, US health care utilization in IBD care is evaluated in depth using an insurance claims analysis. Using a database with 964,633 IBD patients, we showed that utilization patterns are inconsistent with current guideline-based recommendations. We showed that 42% of Crohn's disease patients are managed using aminosalicylates, which are shown to be non-effective in this population while accounting for 54% of prescription drug costs in IBD management. Additionally, 46% of patients were shown to use corticosteroids, of which 9% used corticosteroids for more than 90 consecutive days. Nonetheless, corticosteroid sparing medications were prescribed infrequently, in contrast to current guideline-based recommendations. Lastly, we observed only infrequent usage of biomarker testing for disease control.[7] Non-adherence to guidelines, leading to underuse of necessary care and overuse of unnecessary care, is known to be a major contributor to excessive health care costs in the US.[8] In **Chapter 5** we confirmed that overutilization and underutilization are significant problems in IBD management as well, which indicates that implementation of VBHC components in IBD management could highly increase the value of IBD care.

To facilitate the care delivery process and allow for structural implementation of improvements, a coordinated care infrastructure is important. Additionally, a coordinated care infrastructure can facilitate the routine collection of outcome measures in a systematic manner. In **Chapter 1** different models for care coordination are explored. Positive results have been shown for disease-specific infrastructures[17] as well as for population health infrastructures such as the U.S. patient-centered medical home[18] and primary care based systems[19]. For IBD specifically only one evaluation of a coordinated care infrastructure has been published, in which a reduction in hospitalizations and costs after implementation was shown.[20] In **Chapter 6** we evaluated the UCLA IBD Center's VBHC infrastructure by comparing patients treated at the UCLA IBD Center to a matched control population of patients treated by gastroenterologists elsewhere. We found significantly more biomarker testing and numeric reductions in the number of ED visits, hospitalizations, surgeries, upper endoscopies, and radiology tests in UCLA patients. Additionally, UCLA patients received more biologics and less short and long term corticosteroids, which is thought to result in better long term outcomes.

Finally, in order to promote VBHC, physicians will need to be reimbursed for delivering high value. A large variety of insurance designs have been developed that incentivize either cost savings, such as capitated payments and shared saving contracts, or that incentivize high quality care, such as pay for performance programs. More recently, insurance designs rewarding the combinations of high quality and low costs have been implemented, such the U.S. Accountable Care Organization model. The reported results of these programs are mixed and the number of reports is still very limited.[21] Generally, value-based insurance designs can target physicians or patients by reimbursing high value care more generously than low value care, which is discussed in depth in **Chapter 1.** Additionally, in **Chapter 4** a method to incorporate patient preference in reimbursement strategies is discussed.

General discussion and future perspectives

The essence of VBHC is to improve patients' outcomes at lower costs. This thesis attempts to construct the *value quotient (vQ)* for IBD: a metric for value which incorporates *patient value*, defined as a combination of disease control, quality of life, and productivity in the numerator, and divides it by the associated IBD-related costs in the denominator. In this thesis we showed the feasibility of monitoring clinical disease control remotely using a mobile app, we showed the impact of IBD on work productivity, and we developed a patient-centric composite score that incorporates all three outcomes as well as individual patient preferences. However, metrics for long term outcomes still need to be incorporated in the *vQ*. Although ideally this would be done by measuring disease outcomes long-term, this is not practical for short-term improvements. Process measures that are associated with long term outcomes and that are well-grounded in the medical literature offer a feasible short term alternative. Future research is needed to assess which process measures would be appropriate in this context, and to develop a quantifiable way to include these in the *vQ*.

The cost component of the *vQ* can be split into direct and indirect costs. Though in this thesis no direct costs were estimated in dollar amounts, we did develop and apply methods to assess health care utilization in IBD. To fully quantify the *vQ*, methods to reliably and efficiently estimate direct costs need to be developed. TDABC offers a very in depth view of costs associated with care, but is a very time intensive method that needs to be repeated for every process involved in care delivery. Utilization-based cost-models based on published costs could be a more practical approach. The development of a procedure database with TDABC-derived cost estimations would be of major value to facilitate further research in this field. Indirect costs are another major contributor to disease-associated costs. We were able to estimate indirect costs and showed that presenteeism is the major cause of indirect costs in IBD. This suggests that incorporation of rehabilitation and work-integration strategies in IBD care could vastly improve the value of care. Future research needs to be done to identify successful interventions that improve work productivity.

Full VBHC implementation requires benchmarking of outcome and costs data, and subsequent improvement of the care processes, which can be facilitated by value-based insurance contracting. This thesis adds to the still limited evidence-base for VBHC, by showing preliminary results of a VBHC program specifically designed for IBD. Although the scientific evidence is limited, a VBHC approach might be the only option to safeguard the existence of a sustainable and accessible health care system, given the growing costs of care globally. The challenge will be to find the ways to most effectively improve value in clinical practice.

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ADDENDUM

Nederlandse samenvatting (Dutch summary)

Samenvatting en perspectief
Value based healthcare (VBHC) – in het Nederlands te vertalen als 'op waarde gebaseerde zorg' – is een potentiële oplossing voor de financiële crisis in de gezondheidzorg. Wereldwijd nemen de kosten voor gezondheidszorg toe, en een anders georganiseerde financiering lijkt daar een goede oplossing voor te kunnen bieden. Het belangrijkste idee achter VBHC is dat zorg wordt beoordeeld en vergoed op basis van de waarde die geleverd wordt: de behaalde resultaten gedeeld door de gemaakte kosten.[1,2] Het vergoeden van hoogwaardige zorg is een drijfveer om de kosten te verlagen en de kwaliteit te verbeteren. Om de waarde van de zorg objectief te kunnen belonen, moet die waarde wel scherp gedefinieerd worden. Die waardedefinitie is een essentiële component van een VHBC-systeem.

Hoofdstuk 1 van dit proefschrift behandelt in detail de belangrijkste componenten van een VBHC-systeem, en de toepasbaarheid van VHBC op de behandeling van inflammatoire darmziekten (IBD). De drie belangrijkste componenten zijn: 1) het meten van de resultaten van de zorg en de daaraan verbonden kosten; 2) het rapporteren van de resultaten en kosten en het vergelijken daarvan met die van andere zorgaanbieders; en 3) het verbeteren van de zorg aan de hand van de resultaten en kosten in een gecoördineerd zorgsysteem dat de implementatie van verbeteringen faciliteert. Een vierde element, een *value-based insurance* systeem – ofwel een op waarde gebaseerd verzekeringssysteem – waarin zorg vergoed wordt op basis van de behaalde waarde in plaats van op basis van het geleverde volume, is essentieel om deze verbeteringscyclus in stand te houden. Hoewel het aantal ziekenhuizen dat onderdelen van VBHC implementeert wereldwijd snel groeit, is het bewijs dat deze concepten ook echt werken nog zeer beperkt.[3] Dit proefschrift focust op de eerste component van dit VBHC-kader specifiek voor IBD-gerelateerde zorg – de ontwikkeling en implementatie van resultaatindicatoren relevant voor IBD – en evalueert de effectiviteit van een VBHC-programma voor IBD bij de Universteit van Califonia in Los Angeles (UCLA).

Inflammatoire darmziekten (IBD) – de ziekte van Crohn en colitis ulcerosa – zijn chronische ontstekingsziekten van de darmen. De gangbare opvatting is dat IBD veroorzaakt wordt door onbekende omgevingsfactoren, die leiden tot een ongecontroleerde immuunreactie bij patiënten die daar een aanleg voor hebben.[4] IBD is een chronische, levenslange ziekte, die bij ongeveer 1,4 miljoen Amerikanen is vastgesteld. Behandeling van IBD gaat gepaard met aanzienlijke kosten, die van oudsher vooral werden veroorzaakt door ziekenhuisopnames, en meer recent vooral door nieuwe biologische therapieën.[5,6] Het IBD Centrum van UCLA is in 2012 een VBHC programma begonnen, waarin de belangrijkste concepten van VBHC zijn opgenomen. Het programma is ontwikkeld rondom een gecoördineerd zorgsysteem en wordt ondersteund door een speciaal ontwikkeld IT-platform met een mobiele app voor patiënten. Patiënten worden behandeld volgens vastgelegde zorgpaden op basis van recente inzichten en richtlijnen. In het systeem wordt de gezondheidsstatus van patiënten regelmatig gemeten, en wordt het

aantal IBD-gerelateerde doktersbezoeken, laboratoriumonderzoeken en behandelingen bijgehouden. Via de bij UCLA ontwikkelde eIBD mobiele app kunnen patiënten hun behandelplan bekijken, veranderingen in hun medicijngebruik registreren, deelnemen aan interactief onderwijs, en rechtstreeks communiceren met een gespecialiseerde IBD-verpleegkundige. Tevens zijn er wellness-programma's beschikbaar, specifiek ontwikkeld voor IBD patiënten. Om de resultaten van de zorg voor individuele patiënten, en daarnaast die van het programma in totaal te beoordelen, heeft het UCLA IBD Centrum de *value quotient* (*vQ*) ontwikkeld. De *vQ* wordt berekend door de verkregen *patient value* – de waarde van de resultaten voor de patiënt – te delen door de bijbehorende kosten. *Patient value* wordt gedefinieerd als een combinatie van de mate waarin de ziekte onder controle is, de kwaliteit van leven, en de (arbeids)productiviteit.[9] In de **hoofdstukken 2, 3 en 4** wordt de ontwikkeling en de evaluatie van IBD-specifieke resultaatindicatoren voor *patient value* besproken, terwijl de **hoofdstukken 5 en 6** gericht zijn op het meten van het zorggebruik in IBD als een benaderingsmethodiek voor de gemaakte kosten. De indirecte kosten van IBD bespreken we in **hoofdstuk 3**.

De kwaliteit van zorg kan vanuit meerdere niveaus worden gemeten met behulp van structuur-, proces- of resultaatindicatoren.[10] Structuurindicatoren meten de beschikbare middelen in een zorgomgeving, zoals het aantal bedden in een ziekenhuis. Procesindicatoren meten de implementatie van belangrijke processen in de gezondheidszorg en kunnen goed worden gebruikt voor interne procesverbetering. Procesindicatoren meten echter niet wat uiteindelijk van belang is voor de patiënt: de resultaten. Daarom worden resultaatindicatoren in toenemende mate het belangrijkste geacht om the evalueren. De evaluatie van zorg op basis van resultaatindicatoren kent drie verschillende aspecten: 1) de mate van gezondheid en kwaliteit van leven die bereikt is; 2) de mate van ongemak tijdens het herstelproces; en 3) de duurzaamheid van de behaalde resultaten, ongeacht hoe deze resultaten behaald worden.[11] Hoe de resultaten bepaald moeten worden is onduidelijk, maar *patient reported outcomes* – ofwel resultaten die door de patiënt gerapporteerd worden – worden steeds belangrijker gevonden. Het UCLA IBD Centrum streeft ernaar om de *patient value* frequent te meten, en zo goed zicht op de resultaten op alle drie aspecten te krijgen. Klinische resultaten kunnen tijdens doktersbezoeken worden geëvalueerd, maar het op afstand monitoren van zorgresultaten door middel van *patient reported outcomes* is essentieel om een frequente evaluatie van de gezondheidsstatus van patiënten te waarborgen. In **hoofdstuk 2** hebben wij een index voor het op afstand monitoren van de IBD ziekteactiviteit ontwikkeld, die patiënten kunnen gebruiken op een mobiele app. We hebben onderzocht hoe goed verschillende *patient reported outcomes* de klinische ziekteactiviteit van de ziekte voorspellen met behulp van multivariabele logistische regressie. Twee indices werden ontwikkeld, één voor patiënten met de ziekte van Crohn en één voor patiënten met colitis ulcerosa. Beide indices zijn gebaseerd op vier door de patiënt te beantwoorden vragen, die de klinische activiteit van de ziekte nauwkeurig voorspellen. Deze index is nu geïmplementeerd in de UCLA eIBD patiënten app en zorgt voor continue monitoring door het meten van *patient reported outcomes* in de thuis-situatie.

In **hoofdstuk 3** onderzochten we de vermindering van de arbeidsproductiviteit van IBD-patiënten. Verlaging van arbeidsproductiviteit kan worden gecategoriseerd als ziekteverzuim of als presenteïsme. Ziekteverzuim betreft gemiste werkuren als gevolg van bijvoorbeeld ziekte of doktersbezoeken. Presenteïsme verwijst naar verminderde productiviteit tijdens het werk. We lieten zien dat het ziekteverzuim significant hoger is bij patiënten met ziekteactiviteit (47%) dan bij patiënten met met goed gecontroleerde IBD (14%). Evenzo was er meer presenteïsme bij patiënten met actieve ziekte (95%) dan bij patiënten in remissie (55%). Er was geen verschil in verzuimpercentages tussen patiënten in remissie en de gezonde controlegroep (14% beide). Wel trad bij patiënten in remissie aanzienlijk meer presenteïsme op (55%) dan bij de gezonde controlegroep (27%). De meest genoemde oorzaak van verminderde productiviteit was vermoeidheid (42%). Verder was slechts 34% van de patiënten in staat om aanpassingen te maken in hun werkschema om ziekmelding te voorkomen.[12]

Om de *patient value* component van de *vQ* verder te kwantificeren, onderzochten wij in **hoofdstuk 4** de voorkeur van patiënten voor de drie onderdelen van de *vQ*: de mate waarin de ziekte onder controle is, de kwaliteit van leven en de productiviteit. Met behulp van een conjoint analyse hebben we laten zien dat er grote variatie is tussen patiënten in hun individuele voorkeuren. Over het algemeen wordt kwaliteit van leven door patiënten als belangrijker ervaren dan ziektecontrole of productiviteit. Daarnaast wordt een verbetering van een laag naar een gemiddeld niveau als belangrijker ervaren dan een verbetering van een gemiddeld naar een hoog niveau. Vervolgens hebben we een nieuwe resultaatindicator voor *patient value* gecreëerd, met gewichtsfactoren afhankelijk van de gemeten voorkeuren van de individuele patiënt (bijvoorbeeld wanneer een patiënt kwaliteit van leven als belangrijker ervaart dan ziektecontrole, dan krijgt kwaliteit van leven een hoger gewicht). Het gebruik van deze patiëntgerichte score voor *patient value* resulteerde in significant andere resultaten, zowel op het niveau van de individuele patiënt als op het niveau van de zorgverlener. Het is bekend dat het meenemen van patiëntvoorkeuren in een behandelplan – *shared decision making* – leidt tot meer ziekte-inzicht bij, en een prettiger ervaren behandeling door de patiënt.[13] Gezien dit belang van *shared decision* making en gezien de waargenomen verschillen in de *patient value* wanneer patiëntenvoorkeur hierin wordt opgenomen, stellen wij voor artsen ook op basis hiervan te beoordelen en te honoreren in *value based insurance designs*.

Om de *vQ* volledig te kwantificeren, moeten ook de kosten worden gemeten. In **hoofdstuk 1** worden verschillende methodes besproken om zicht te krijgen op deze kosten. Gemakkelijk te verkrijgen zijn de facturen die door de ziekenhuizen aan de verzekeraar en patiënt worden gestuurd. De factuurbedragen correleren in de V.S. echter vaak slecht met de daadwerkelijke vergoedingen, die op hun beurt niet goed correleren met de werkelijke kosten van de zorg.[14] Om echt inzicht te krijgen in de kosten van de zorg kan de methode van *time-driven activity-based costing* (TDABC) worden gebruikt. Deze techniek kent kosten toe aan elke stap in het zorgproces, gebaseerd op de tijd en het materiaal die voor elke stap nodig zijn. TDABC kan met succes kosten meten en inefficiënties in het zorgproces aantonen.[15] Hoewel TDABC een goede oplossing kan zijn voor het berekenen van de kosten van specifieke processen, is het moeilijk om door

middel van deze methode de totale kosten van de zorg te berekenen omdat het ontwikkelen van TDABC modellen erg tijdrovend is. Daarom hebben wij ervoor gekozen om ons te concentreren op het meten van de hoeveelheid geleverde zorg als een indicator voor de kosten. Gegevens over de hoeveelheid geleverde zorg zijn beschikbaar via databases van verzekeraars, ziekenhuizen en financiële intermediairs in de gezondheidszorg. Wij hebben methodes ontwikkeld om in dit soort data patronen te onderkennen die medisch gezien betekenisvol zijn. In **hoofdstuk 5 en 6** passen wij deze toe. Naast de directe kosten, moeten ook indirecte kosten uiteindelijk worden meegenomen in de kwantificatie van de *vQ*. Het is bekend dat indirecte kosten als gevolg van verlies van arbeidsproductiviteit een groot percentage uitmaken van de totale kosten van de gezondheidszorg.[16] In **Hoofdstuk 3** bevestigen wij dat dit ook in de IBD-zorg het geval is, wat met name te wijten is aan presenteïsme.[12]

In **hoofdstuk 5** evalueren we het gebruik van gezondheidszorg voor IBD in de V.S. door middel van een analyse van verzekeringsclaims. Met behulp van een database met 964.633 IBD-patiënten hebben we aangetoond dat de huidige zorgpatronen strijdig zijn met de actuele richtlijnen. We lieten zien dat 42% van de patiënten met de ziekte van Crohn wordt behandeld met aminosalicylaten, hoewel deze bewezen ineffectief zijn voor deze populatie, maar wel verantwoordelijk voor 54% van de kosten van voorgeschreven IBD-medicatie. Ook lieten wij zien dan 46% van de patiënten corticosteroïden gebruikten, waarvan 9% meer dan 90 opeenvolgende dagen. Desondanks bleek het gelijktijdig gebruik van steroïd-sparende medicatie laag, wat wederom tegenstrijdig is met de richtlijnen. Ten slotte bleek dat biomarker-testen voor het monitoren van ziektecontrole weinig gebruikt worden.[7] Het niet-naleven van richtlijnen, wat leidt tot onderbenutting van noodzakelijke zorg en overmatig gebruik van onnodige zorg, levert een belangrijke bijdrage aan de excessieve kosten van de gezondheidszorg in de V.S..[8] In **hoofdstuk 5** bevestigen wij dat ook in de IBD-zorg zowel overgebruik als onderbenutting belangrijke problemen zijn, wat aangeeft dat het invoeren van VBHC-componenten in IBD de waarde van IBD-zorg sterk kan verhogen.

Om de zorgverlening te vergemakkelijken en verbeteringen structureel door te voeren is een gecoördineerd zorgsysteem belangrijk. Bovendien vergemakkelijkt een dergelijk systeem het routinematig en systematisch verzamelen van resultaten. In **hoofdstuk 1** worden verschillende modellen voor zorgcoördinatie besproken. Positieve resultaten zijn aangetoond in systemen voor specifieke ziektebeelden[7] en in gezondheidszorgsystemen op nationaal niveau, zoals het *patient-centered medical home* (PCMH) in de V.S.[18] en andere systemen gebaseerd op eerstelijns zorg[19]. Specifiek voor IBD is er slechts één publicatie over een gecoördineerd zorgsysteem, waarin minder ziekenhuisopnamen en lagere kosten werden gemeten na implementatie.[20] In **hoofdstuk 6** evalueerden wij de resultaten van het bij het UCLA IBD Centrum geïmplementeerde systeem. Patiënten van het UCLA IBD Centrum werden vergeleken met een controlegroep van patiënten van andere gastro-enterologen. Bij UCLA-patiënten vond significant meer laboratoriumonderzoek plaats met biomarkers, maar zij hadden een geringer aantal bezoeken aan de spoedeisende hulp, ziekenhuisopnames, operaties, gastroscopieën en radiologisch onderzoek. Daarnaast kregen UCLA patiënten meer biologische medicatie en

minder korte en lange termijn corticosteroïden, wat aannemelijkerwijs betere resultaten oplevert op de lange termijn.

Om VBHC verder te bevorderen, zullen artsen moeten worden gehonoreerd voor het leveren van hoogwaardige zorg. Verscheidene verzekeringsmodellen zijn ontwikkeld die verschillende componenten van *value* belonen. Sommige modellen stimuleren kostenbesparingen, bijvoorbeeld door de zorgverlener niet meer te honoreren boven een bepaald bedrag of door de winst te delen tussen de verzekeraar en zorgverlener. Andere modellen stimuleren de zorgkwaliteit, zoals programma's waarin zorgverleners extra vergoedingen krijgen wanneer ze aan bepaalde kwaliteitseisen voldoen. Meer recent zijn er verzekeringsmodellen geïmplementeerd die de combinatie van hoge kwaliteit én lage kosten belonen, zoals in het *Accountable Care Organization* model in de V.S. – een model waarin meerdere partijen in de zorgverlening gedeelde verantwoordelijkheid nemen voor zowel resultaten als kosten van de zorg. De eerste resultaten van deze *value-based insurance designs* zijn gemengd en er is nog weinig over gepubliceerd.[21] In het algemeen kunnen *value-based* contracten zich richten op zowel artsen als patiënten door hoogwaardige zorg ruimer te vergoeden dan laagwaardige zorg, wat besproken is in **hoofdstuk 1**. De in **hoofdstuk 4** besproken methode waarmee de voorkeur van de patiënt gemeten wordt, kan opgenomen worden in deze verzekeringsmodellen.

Algemene discussie en toekomstperspectieven

De essentie van VBHC is het verbeteren van patiëntgerichte resultaten tegen lagere kosten. Dit proefschrift heeft als doel de *value quotient* (*vQ*) voor IBD te construeren: een breuk met in de teller *patient value*, gedefinieerd als een combinatie van de mate waarin de ziekte onder controle is, de kwaliteit van leven en (arbeids)productiviteit, en in de noemer de bijbehorende IBD-gerelateerde kosten. In dit proefschrift lieten wij zien dat het haalbaar is om ziekteactiviteit op afstand te monitoren met behulp van een mobiele app, we toonden de impact aan van IBD op arbeidsproductiviteit, en we ontwikkelden een score die alle drie aspecten van *patient value* meeneemt met gewichtsfactoren passend bij de individuele voorkeuren van de patiënt. Statistieken van resultaten op lange termijn moeten echter nog in het *vQ* worden opgenomen. Idealiter zou dit gebeuren door *patient value* over langere tijd te meten. Voor verbeteringen op korte termijn is het meten van resultaten op lange termijn echter niet praktisch. Procesindicatoren, waarvan we op basis van de medische literatuur mogen aannemen dat zij geassocieerd zijn met resultaten op lange termijn, zouden een haalbaar alternatief kunnen zijn. Verder onderzoek is nodig om te beoordelen welke procesindicatoren bruikbaar zijn voor dit doel, en om een methode te ontwikkelen om deze indicatoren kwantitatief in de *vQ* op te nemen.

De kostencomponent van de *vQ* kan worden opgesplitst in directe en indirecte kosten. Hoewel in dit proefschrift geen directe kosten in dollars zijn bepaald, hebben we wel methodes ontwikkeld om de hoeveelheid IBD-zorg nauwkeurig te meten. Om de *vQ* volledig te kwantificeren moeten methodes worden ontwikkeld waarmee we die directe kosten betrouwbaar en efficiënt kunnen schatten. TDABC biedt een goed inzicht in

zorgkosten, maar is een tijdrovende werkwijze die moet worden herhaald voor elk proces in de zorgverlening. Kostenmodellen die zijn gebaseerd op de hoeveelheid geleverde zorg vormen een meer praktische aanpak. Niettemin zou de ontwikkeling van een database met kosten van afzonderlijke werkprocessen gebaseerd op TDABC van grote waarde zijn voor verder onderzoek op dit gebied. Indirecte kosten vormen een ander belangrijk onderdeel van ziekte-gerelateerde kosten. We konden indirecte kosten schatten en toonden aan dat presenteïsme de belangrijkste oorzaak is van indirecte kosten in IBD. Dit suggereert dat de integratie van revalidatie en reïntegratie op de werkvloer de waarde van de zorg sterk kan verbeteren. Toekomstige studies zullen moeten uitmaken wat succesvolle interventies zijn die de arbeidsproductiviteit verhogen.

Volledige VBHC implementatie vereist vergelijking van de resultaten en de kosten tussen verschillende zorgverleners, en verbetering van de zorgprocessen aan de hand daarvan. Meer innovatie hierin kan worden gestimuleerd door het invoeren van *value based insurance* contracten. Dit proefschrift draagt bij aan de nog beperkte bewijsvoering voor VBHC, door het tonen van de voorlopige resultaten van een VBHC programma speciaal ontworpen voor IBD. Hoewel het wetenschappelijk bewijs beperkt is, denken wij dat VBHC een kansrijke optie is om een duurzaam en toegankelijk gezondheidszorgsysteem te waarborgen, gezien de toenemende kosten van de zorg wereldwijd. De uitdaging zal zijn om de meest effectieve manieren te vinden om de waarde van zorg in de dokterspraktijk te verbeteren.

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List of Publications

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