Artificial intelligence and e-health for inflammatory bowel diseases: the quest to enhance patient experiences, outcomes and costs

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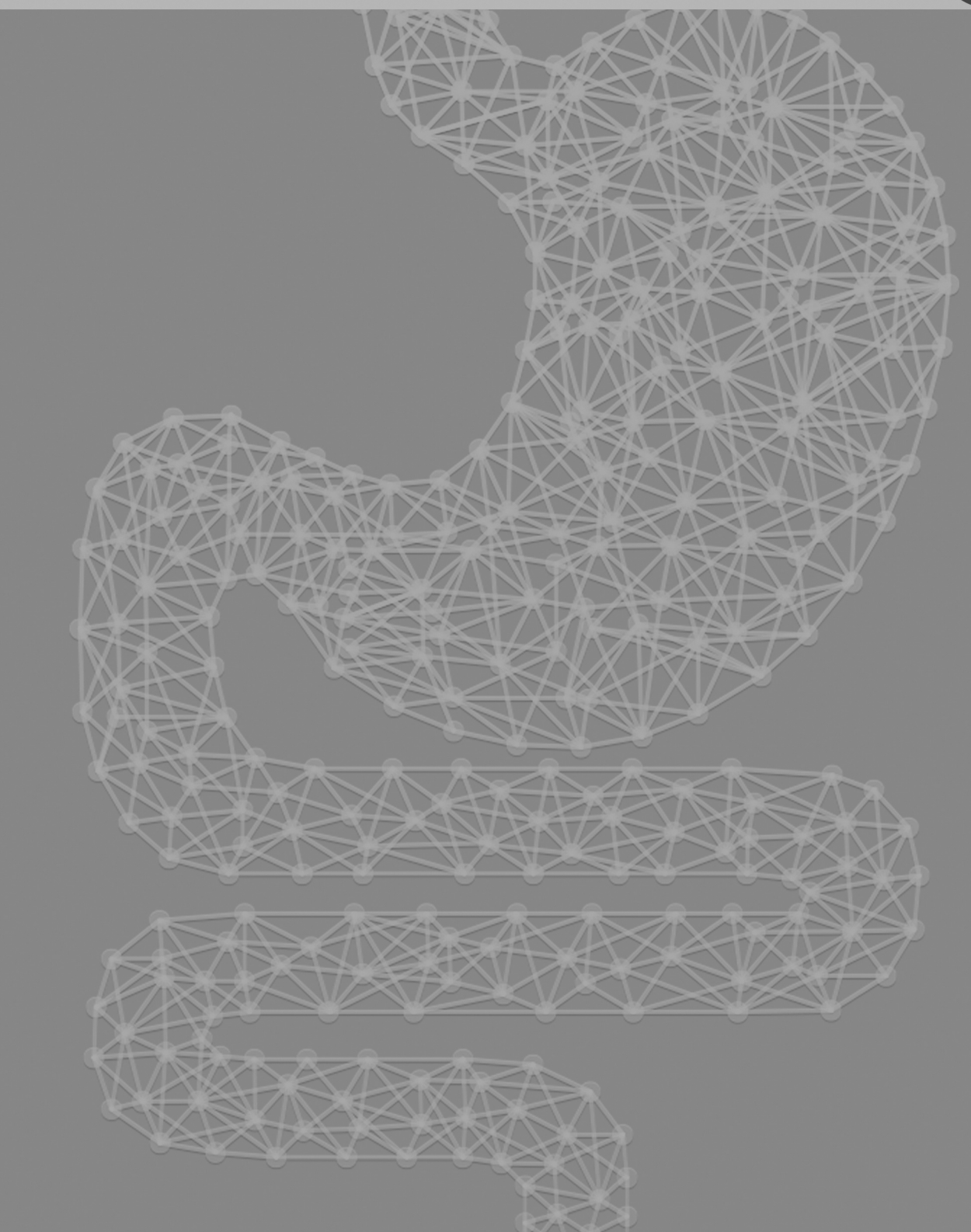
Part I: The Need for Innovation to Address the Economic and Psychosocial Impact of IBD



CHAPTER 2

Presenteeism in Inflammatory Bowel Diseases: a hidden problem with significant economic impact

Inflammatory Bowel Diseases. 2015 Jul;21(7):1623-30

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Abstract

Objectives

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 in the U.S. did not take presenteeism into account. We aimed to quantify work limitations, and presenteeism and its associated costs in an IBD population order 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 IBD patients. 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 IBD patients 35.6% were unemployed. Significantly more presenteeism was detected in IBD patients (62.9%) compared to controls (27.3%) ($p=0.004$), with no significant differences in absenteeism. Patients in remission experienced significantly more presenteeism than controls (54.7% vs. 27.3%, respectively, $p<0.01$) and indirect costs were significantly higher for remissive patients versus controls ($17,766 per year vs. $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

IBD patients 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 inflammatory bowel diseases (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]. Symptomatic IBD patients are less likely to have obtained a graduate or a professional degree than non-symptomatic patients[10]. IBD patients 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 IBD patients 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 USA. The indirect cost of missed work time to IBD in 1998/1999 was more than $3.6 billion U.S. dollars 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[2] to indirect medical costs, 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 care 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 email were approached by telephone. Included patients were approached by email 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 (sIBDQ) for quality of life (QoL) assessment[22]; and 3) the disease activity scores 'Harvey-Bradshaw Index' for CD[23] and 'Partial Mayo Score' for UC[24]. Also, we developed a work impact questionnaire based on the IMPACT[11] study assessing work related problems. Finally, we included questions about 'job-lock' into the questionnaire (Supplementary figure 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.

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 United States 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 IBD patients and controls, UC and CD patients, and patients with active disease and inactive disease were assessed. Absenteeism costs were estimated using the "lost wages method"[26], which is defined as 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 for Labor Statistics (DoL)[25]. To define a high and low salary group, we obtained the different hourly wages for the employment categories from the DoL, patients that made more than $32/hour were defined as the high salary group, whereas patients that made less than $32/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 ANOVA 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 was analyzed using Microsoft Excel 2010 and SPSS 21.0.

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 IBD patients eligible for analysis. For a subset of 379 patients QoL and

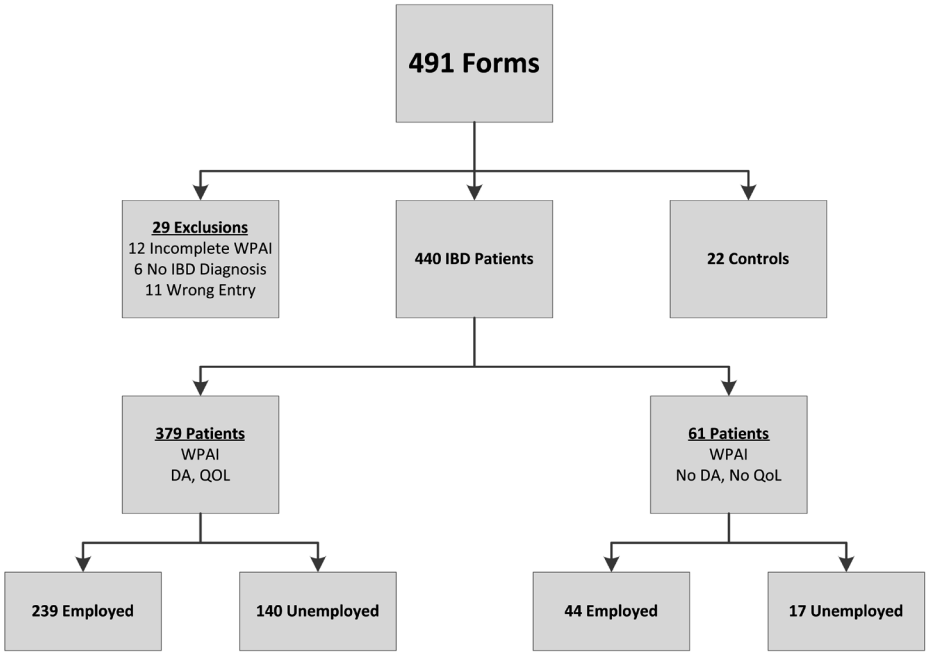

Figure 1. Study Flowchart

disease activity were assessed during the same clinic visit. In addition, a total of 213 patients filled out the work impact questionnaire. Disease activity and QoL scores were available for 152 of those. A total of 22 controls were included as a comparison (Figure 2.1).

Out of the 440 included IBD patients, 49.8% were male (Table 1). The median age was 37 years (range 18-83 years) 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, sex, smoking status, race, ethnicity and disease duration were observed between UC and CD patients. The median age at diagnosis for CD patients was slightly younger (24, range 8 - 68) then for UC patients (29, range 6 - 81) for UC patients (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 CD patients (33.5%) have undergone abdominal surgery then UC patients (9.1%) (P<.0001). No significant differences in gender, age, intoxications, race and ethnicity were observed between the IBD and the control group (Table 2). 13,6% of the controls had a chronic disease.

Table 2.1. Demographics of IBD population

N=440	CD N= 221		UC N= 219		P Value
Male sex % (no.)	49.8%	(110)	49.8%	(109)	1.000
Median Age (range)	36	(19-79)	40	(18-83)	0.174
Smoking % (no.)					0.782
- Current	- 8.1%	(18)	- 6.4%	(14)	
- Past	- 18.1%	(40)	- 19.2%	(42)	
- Never	- 73.8%	(163)	- 73.9%	(162)	
- Unknown	- N/A		- 0.5%	(1)	
Drinking% (no.)					0.014
- Yes	- 48%	(106)	- 59.4%	(130)	
- No	- 51.6%	(114)	- 40.5%	(88)	
- Unknown	- 0.4%	(1)	- 0.9%	(2)	
Median age at diagnosis (range)	24 yrs (8-68 yrs)		29 yrs (6-81)		0.002
Median disease duration (range)	8 yrs (0-52)		6.5 yrs (0-52)		0.115
Race					0.083
- American Indian or Alaska Native	- 0.9%	(2)	- 0.5%	(1)	
- Asian	- 5.9%	(13)	- 8.6%	(19)	
- Black or African American	- 5.4%	(13)	- 1.4%	(2)	
- Native Hawaiian	- 0.5%	(1)	- 0.0%	(0)	
- White	- 81.9%	(181)	- 81.4%	(180)	
- Unknown	- 5.4%	(11)	- 7.7%	(17)	
N=440	**CD N= 221**		**UC N= 219**		**P Value**
Ethnicity					0.552
- Hispanic or Latino	- 4.98%	(11)	- 6.36%	(14)	
- Not Hispanic or Latino	- 89.14%	(198)	- 90.00%	(197)	
- Unknown	- 5.88%	(12)	- 3.64%	(8)	
Medication use					0.000
- Biological therapy	- 37.6%	(83)	- 18.3%	(40)	
- Immunomodulators	- 18.6%	(41)	- 9.1%	(20)	
- Steroids	- 8.1%	(18)	- 13.7%	(30)	
- Other	- 29.9%	(66)	- 48.4%	(106)	
- No medication	- 5%	(11)	- 6.4%	(14)	
- Unknown	- 0.9%	(2)	- 4.1%	(9)	
Initial symptoms (1 or more)					
- Abdominal pain	- 69.7%	(153)	- 51.4%	(113)	0.000
- Diarrhea	- 26.7%	(59)	- 31.4%	(69)	0.216
- Rectal bleeding	- 33.5%	(72)	- 77.3%	(171)	0.000
- Weight loss	- 30%	(64)	- 18.6%	(41)	0.014
- Unknown	- 3.4%	(16)	- 9.1%	(19)	
Initial disease extent (1 or more)					
- Upper GI tract	- 3.4%	(15)			
- Small bowel excluding terminal ileum	- 15.8%	(35)			
- Terminal ileum	- 51.6%	(114)			
- Colon	- 49.3%	(109)			
- Unknown	- 14.9%	(33)			

Table 2.1. Continued

N=440	CD N= 221	UC N= 219	P Value
Disease extent			
- Cecum-ascending		- 16.1% (59)	
- Transverse-descending		- 44.4% (163)	
- Rectum		- 30.8% (113)	
- Unknown		- 14.6% (32)	
Fistula			
- % Fistula	- 23.2% (51)	- 2.8% (6)	0.000
- Peri-anal	- 12.3% (27)	- 1.4% (3)	0.000
- Enterocutaneous	- 3.2% (7)	- 0.5% (1)	0.068
- Other	- 10.5% (23)	- 0.9% (2)	0.000
- Unknown	- 0.5% (1)	- 1.8% (4)	
Extra-intestinal manifestations (EIM)			
- % EIM	- 20.5% (45)	- 8.8% (19)	0.001
- Eye	- 5% (11)	- 1.9% (4)	0.112
- Skin	- 4.5% (10)	- 1.9% (4)	0.173
- Joint	- 16.4% (36)	- 5.1% (11)	0.000
- PSC	- 1.4% (3)	- 1.9% (4)	0.487
- Other	- 1.4% (4)	- 0.5% (1)	0.315
Surgeries			
- Abdominal surgeries	- 33.5% (74)	- 9.1% (20)	0.000

Employment

In total, 64.4% (283) of the total IBD cohort was employed and 35.6% (157) was not (Table 3). Supplementary Table 1 shows the industrial sectors in which patients were employed. Out of 62 unemployed patients that 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 controls were employed. There was no significant difference in employment rate between UC and CD patients (63.3% and 65.3%, respectively (p=0.67)). In the employed group 54.5% were male, while in the unemployed group only 41.4% were male (p=0.009). Activity impairment was present in 65% of the employed group, while 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<.001). No significant difference in disease activity was observed, with 24.3% active disease in the employed group versus 26.4% in the unemployed group (p=0.639).

Table 2.2. Demographics IBD patients versus controls

	IBD (n=440)		Controls N=(22)		P value
Male sex % (no.)	49.8%	(219)	54.5% (12)		0.662
Median Age (range)	37	(18-83)	37 (25-77)		0.439
Smoking % (no.)					0.908
- Current	- 7.3%	(32)	- 4.5%	(1)	
- Past	- 18.6%	(82)	- 18.2%	(4)	
- Never	- 73.9%	(325)	- 72.7%	(16)	
- Unknown	- 0.2%	(1)	- 4.5%	(1)	
Drinking% (no.)					0.085
- Yes	- 53.6%	(236)	- 72.7% (16)		
- No	- 45.7%	(201)	- 27.3% (6)		
- Unknown	- 0.7	(3)			
Race					0.379
- American Indian or Alaska Native	- 0.7%	(3)	- 4.5%	(1)	
- Asian	- 7.3%	(32)	- 9.1%	(2)	
- Black or African American	- 3.4%	(15)	-	(0)	
- Native Hawaiian	- 0.2%	(1)	-	(0)	
- White	- 82.0%	(361)	-	86.4% (19)	
- Unknown	- 6.4%	(28)	- N/A		
Ethnicity					0.785
- Hispanic or Latino	- 5.7%	(25)	- 4.5%	(1)	
- Not Hispanic or Latino	- 89.8%	(395)	- 95.5%	(21)	
- Unknown	- 4.5%	(20)	- N/A		

Work Productivity

Presenteeism and absenteeism were calculated in the employed patients (140 CD, 143 CD) and in 22 employed controls (Figure 2). No significant differences in absenteeism were observed between controls, UC and CD patients (13.6%, 22.4% and 20%, respectively). Significantly more presenteeism was detected in CD (61.4%) and UC patients (64.3%) compared to 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 to 14.4%, 54.7% and 62.7%, respectively, of patients in remission (p<.001). Absenteeism was similar between remissive patients and controls (14.4% and 13.6% respectively, p=1.000), while controls had significantly less presenteeism than remissive patients (27.3% and 54.7% respectively, p=0.022).

Table 2.3. Characteristics of employed versus unemployed IBD patients

Total (n=440)	Employed (n=283)	Unemployed (n=157)	P value
Median age (range)	36 (20-82)	41 (18-83)	0.094
Male gender %(n)	54.4% (154)	41.4% (65)	0.009
Disease type %(n)	49.5% CD(140) 50.5% UC (143)	51.6% CD (81) 48.4% UC (76)	0.670
Activity impairment %(n)	65.0% (184)	79% (124)	0.002
Active disease % (n) (n=379)	24.3% (58)	26.4% (37)	0.639
Mean QoL (SD) (n=379)	50 (SD 12)	44 (SD 15)	0.000

CD= Crohn's disease, UC= ulcerative colitis, QoL= Quality of life

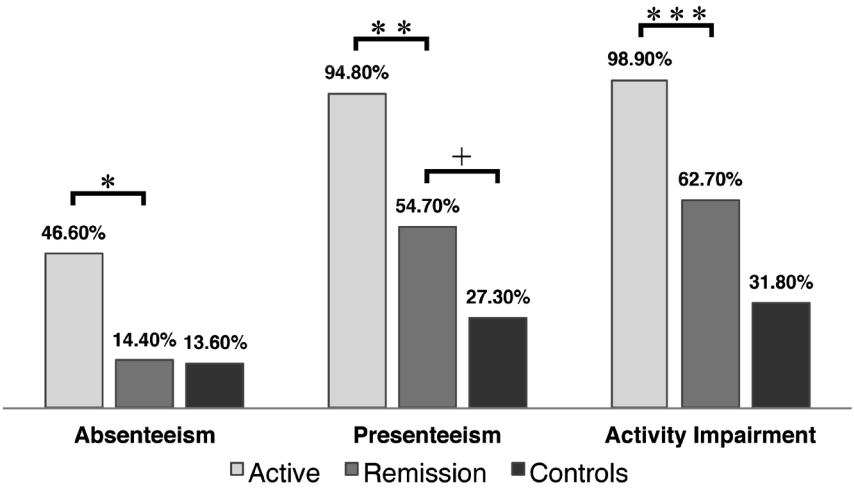

Figure 2. Prevalence of absenteeism, presenteeism, and activity impairment in controls and patients with IBD with active and inactive disease. *P < 0.01, **P < 0.01, ***P < 0.01, +P = 0.02.

Work Impact

Table 4 shows the limitations that IBD patients 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 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.
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 ($p=0.01$), felt more fatigued ($p<0.01$), 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 ($p<0.01$). We observed that patients who reported absenteeism or presenteeism felt more frequently stressed about taking time off work due to their disease, (78% and 49.6%, respectively, $p<0.01$) than those without absenteeism or presenteeism (27.2% and 15.6%, 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/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 $370.13/week for a full time employee ($P<0.01$).

Presenteeism accounted for the majority of costs, with 33.8% of total weekly compensation ($695.03/week) for active patients and 13.5% of total weekly compensation ($277.60/week) for remissive patients. Absenteeism accounted for 21.3% of total weekly compensation ($437.99/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 to controls ($p=0.029$). For controls average weekly indirect costs were estimated at 9.3% of total weekly compensation or $191.23/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). Furthermore, patients in remission who made more than $32/hour experienced absenteeism more frequently than those who made less than $32/hour (24.5% and 6.9% absenteeism, 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).

Table 4. An overview of limitations IBD patients experience at work divided by disease activity.

	Remissive patients (111)	Active Patients (41)	p value
Which of the following adjustments have you made in your work to avoid taking sick days off from work due to your IBD?			
1) Working from home	12.6% (14)	12.2% (5)	1.000
2) Working part-time	4.5% (5)	12.2% (5)	0.134
3) Working flexible hours	13.5% (15)	24.4% (10)	0.139
4) I have not made any such adjustments	55.9% (62)	34.1% (14)	0.028
5) I do not have the possibility to make such an adjustment	16.2% (18)	19.5% (8)	0.633
6) Other	7.2% (8)	4.9% (2)	1.000
If you have missed work due to your IBD, what was the reason? Check all that apply	**Remissive patients (111)**	**Active Patients (41)**	**p value**
1) Hospital/emergency department visit	19.8% (22)	14.6% (6)	0.638
2) Doctor appointment	36% (40)	25.9% (14)	0.829
3) Incontinence or fear of incontinence	4.5% (5)	12.2% (5)	0.134
4) Abdominal pain or cramping	17.1% (19)	31.7% (13)	0.072
5) Fear of frequent stools or bowel movements interfering with work activities	13.5% (15)	31.7% (13)	0.017
If you have missed work due to your IBD, what was the reason? Check all that apply	**Remissive patients (111)**	**Active Patients (41)**	**p value**
6) Fear of frequent stools or bowel movements bringing attention to my condition from colleagues	4.5% (5)	12.2 (5)	0.134
7) Fatigue, and/or not enough energy to get through the day	15.3% (17)	36.6% (15)	0.004
8) Worry about gas pressure, discomfort	6.3% (7)	9.8% (4)	0.489
9) Worry/fear of potential for embarrassment	3.6% (4)	19.5% (8)	0.003
10) Rectal/anal pain or burning	2.7% (3)	9.8% (4)	0.212
11) Volume of blood in bleeding episode	3.6% (4)	4.9%(2)	0.661
12) I have never been absent from work due to IBD	22.5% (25)	7.3% (3)	0.035

Table 4. Continued

How does IBD affect your performance at work	Remissive patients (111)	Active Patients (41)	p value
1) I am quiet or quieter during meetings	5.4% (6)	12.2% (5)	0.168
2) I cancel my attendance at meetings at the last minute	5.4% (6)	7.3% (3)	0.703
3) I do not participate in work social activities	5.4% (6)	19.5% (8)	0.022
4) I am irritable at work	11.7% (13)	12.2% (5)	1.000
5) I am less motivated in my work	13.5% (15)	14.6% (6)	1.000
6) My IBD does not affect my behavior at work	27.9% (31)	4.9% (2)	0.002
How does IBD affect your performance at work	**Remissive patients (111)**	**Active Patients (41)**	**p value**
7) I am fatigued	37.8% (42)	65.9% (27)	0.002
8) Not applicable/other	26.1% (29)	12.2% (5)	0.081

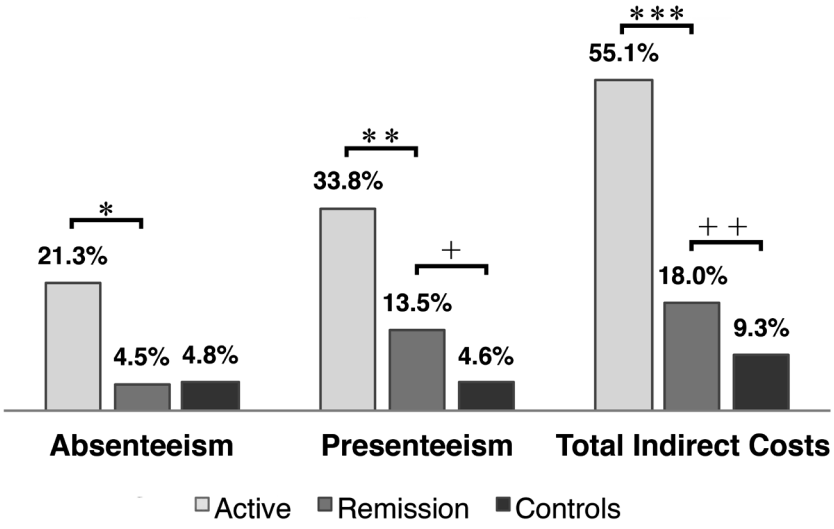

Figure 3. Indirect costs as a percentage of maximum weekly compensation for employees. *P < 0.01, **P < 0.01, ***P < 0.01, +P = 0.02, ++P < 0.03.

Discussion

"Without question, the single biggest force threatening U.S. workforce productivity, as well as health care affordability and quality of life, 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 in order 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 IBD patients, even when in complete clinical remission, still experienced decreased productivity significantly more frequently than healthy controls: 54.7% vs. 27.3%, respectively (P=0.02). This translates into a sizable economic impact as reflected by the indirect costs for patients even though they are in clinical remission (18% IBD vs. 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 in order 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.

Interestingly, we did not observe a significant difference in absenteeism between IBD patients and controls, respectively 21.2% (CD 20%, UC 22,4%) compared to 13.6% (P=0.399). This could be attributed to improved treatments, like biologic therapy, inducing effective clinical remission and allowing patients to resume their work[13-15,29]. Other studies found comparable absenteeism percentages ranging from 18-36% for CD and 13-25% 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 IBD patients, 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 to 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 IBD patients in the United States. Our cost model shows that indirect costs are significantly lower when IBD patients enter a remissive state, dropping from $1333/week when clinically active to $370/week when in remission. A recent study from Hungary showed presenteeism costs of €2508/patient/year which translates to $3191/patient/year[30], that equals $66/patient/week. This number is lower than our estimated $354/patient/week. The difference can be explained by the average hourly wage which 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 care givers, do to decrease presenteeism in IBD patients 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]. Secondly, these patients continue to struggle with three types of problems: 1) persistent symptoms (e.g. fatigue, irritability, cramping); 2) lack of work motivation; and 3) missed work days due to medical appointments. Thirdly, we observed additional macro-economic 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 pro-actively 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 IBD patients 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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Supplementary

Supplementary Figure 1

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. Do you experience stress or pressure when taking sick time off from work due to your IBD?

☐ Yes

☐ No

☐ Not applicable/don't know

8. 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
☐ I have not made any such adjustments
☐ I do not have the possibility to make such an adjustment
☐ Other: .....

.....

9. 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: .....

.....

10. 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

11. Do you think you have been discriminated in the workplace as a direct consequence of your IBD?

☐ Yes ☐ No

12. 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?

13. I believe that IBD has negatively affected my career path, opportunities for advancement, income and/or earning potential

☐ Strongly agree ☐ Disagree
☐ Agree ☐ Strongly disagree
☐ Neither agree nor disagree

14. Because of my IBD, I have lost a job or had to quit /leave a job

☐ Strongly agree ☐ Disagree
☐ Agree ☐ Strongly disagree
☐ Neither agree nor 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.*

Supplementary Table 1. Comparing the characteristics of responders to the non-responders.

N=560	Responders N=440		Non-responders N= 140		P Value
% Crohn's disease % Ulcerative colitis	50.2% (221) 49.8% (219)		51.4% (72) 48.6% (68)		0.804
Male sex % (no.	49.8% (219)		57.1% (80)		0.129
Median Age (range)	37 (18-83)		38 (19-83)		0.454
Median age at diagnosis (range)	26 yrs (6-81 yrs)		26 yrs (0-80)		0.166
Median disease duration (range)	7 yrs (0-52 yrs)		8 yrs (1-53 yrs)		0.447
Race - American Indian or Alaska Native - Asian - Black or African American - Native Hawaiian - White - Unknown	 - 0.7% - 7.3% - 3.4% - 0.2% - 82.0% - 6.4%	 (3) (32) (15) (1) (361) (28)	 - N/A - 3.6% - 2.1% - N/A - 69.3% - 25%	 (0) (5) (3) (0) (97) (35)	0.656
Ethnicity - Hispanic or Latino - Not Hispanic or Latino - Unknown	 - 5.7% - 89.8% - 4.5%	 (25) (395) (20)	 - 6.4% - 70.7% - 22.9%	 (9) (99) (32)	0.369
Initial symptoms (1 or more) - Abdominal pain - Diarrhea - Rectal bleeding - Weight loss - Unknown	 - 65.7% - 31.6% - 60% - 25.9% - 8%	 (266) (128) (243) (105) (35)	 - 57% - 66.1% - 58.7% - 19.8% - 13.6%	 (69) (80) (71) (24) (19)	 0.082 0.000 0.000 0.172
N=560	**Responders N=440**		**Non-responders N= 140**		**P Value**
Initial disease extent (1 or more) - Upper GI tract - Small bowel excluding terminal ileum - Terminal ileum - Colon - Unknown	 - 4.1% - 9.5% - 31.2% - 78.6% - 16.1%	 (15) (35) (115) (290) (71)	 - N/A - 7.8% - 34.3% - 78.4% - 27.1%	 (0) (8) (35) (80) (38)	 0.039 0.610 0.546 0.972
Disease extent (1 or more) - Cecum - Ascending - Transverse - Descending-sigmoid - Rectum - Unknown	 - 22% - 9.3% - 21.2% - 41.3% - 39.3% - 12%	 (85) (36) (82) (160) (152) (53)	 - 17.1% - 13.7% - 15.4% - 36.8% - 31.6% - 16.4%	 (20) (16) (18) (43) (37) (23)	 0.256 0.173 0.168 0.375 0.134
Fistula - % Fistula - Peri-anal - Enterocutaneous - Other	 - 13.1% - 6.9% - 1.8% - 5.7%	 (57) (30) (8) (25)	 - 11.4% - 5.7% - 0.7% - 5.7%	 (16) (8) (1) (8)	 0.605 0.624 0.058 0.988
Surgeries - Abdominal surgeries	 - 24.6%	 (97)	 - 34.3%	 (48)	 0.027

Supplementary Table 2. Percentages of presenteeism in the patient population, with and without a treshold.

% of presenteeism	All employed patients (n=283)	Employed patients in Remission (n=181)	Controls (n=22)	P value Employed vs. Controls
No treshold	62,9%	54,7%	27,3%	
20% treshold	43,5%	30,9%	18,2%	0.03

Supplementary Table 3. Patients split up by employment categories

Industry	N	%
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%
Total	213	100%