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Examination of the relationship between disease activity and patient reported outcome measures in an Inflammatory Bowel Disease cohort

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ABSTRACT

Background: The extent to which disease activity impacts on patient reported outcomes (PROs) is unclear.

Aims: The purpose of this study was to examine the relationship between disease activity and PROs.

Methods: Adult IBD patients attending a tertiary clinic from May to June 2015 were included. Assessment of disease activity (SCCAI, HBI), IBD knowledge (CCKNOW), medication adherence (MMAS8), psychological distress (HADS), work productivity (WPAI) and quality of life (IBDQ) was performed to investigate any correlations between disease activity and PROs.

Results: 81 participants were included: 49% female; 57% Crohn's Disease (CD); 38% ulcerative colitis (UC); 5% IBD-unclassified; median age 34. At least mild levels of depression were present in 21/81 (26%) of patients; 37/81 (46%)

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expressed some level of anxiety. A moderate-to-strong correlation was found between disease activity and depression in UC (*r*=0.84, p=0.002) but not in CD (*r*=0.53, p=0.29). Disease activity correlated with: overall work impairment due to health (*r*=0.85, p=0.001), health related impairment while working (*r*=0.76, p=0.02), and percentage of activity impaired due to health (*r*=0.83, p=0.002) in UC only.

Conclusions: Disease activity significantly affects mood and work productivity in patients with UC. Monitoring patients' ability to function and work, rather than minimizing disease activity alone, should become a routine part of IBD care.

Key words

Ulcerative Colitis

Crohn's Disease

Inflammatory bowel disease

Patient Reported Outcomes

Work Productivity

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INTRODUCTION

Inflammatory bowel diseases (IBD), comprising Ulcerative Colitis (UC) and Crohn's Disease (CD), are chronic and disabling diseases with an incidence rate of 30 per 100,000 people[1,2,3]. A complex interaction between genetic, environmental and immunoregulatory factors influence the development of the disease[4].

The focus of IBD care has recently shifted towards the management and prevention of disease activity, aiming for both clinical and endoscopic remission using a 'treat-to-target' approach to management[5]. Surrogate biomarkers of inflammation such as C-reactive protein (CRP) and fecal calprotectin (FC) have been used to non-invasively assess the presence of disease activity although their sensitivity for active disease is low, and dependent on disease subtype and disease location (CRP sensitivity for IBD 49%; FC sensitivity for IBD 88%)[6,7]. The impact of disease activity on patients' ability to function in their day-to-day lives is less well understood.

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Patient reported outcomes (PROs) are being increasingly recognized as important outcome measures in IBD trials because of the impact of IBD on the patient beyond the effects of disease activity alone[5,8,9]. PROs incorporate validated surveys that quantify patient reported qualitative data including assessments of anxiety and depression[10,11], work productivity measures[12], patient satisfaction[13], fatigue[14], quality of life (QoL)[11,12,15], and disability[16]. PROs can be used to determine efficacy of treatment insofar as how it impacts patients' ability to function[17]. PROs also enable generalization of results and comparison across different chronic disease states[18,19]. Despite the emerging interest in PROs, the extent to which disease activity impacts on PROs is unclear, and the interplay between different PROs, medication adherence and IBD knowledge requires further evaluation. Moreover, data are lacking on the relationship between disease activity and work productivity.

The purpose of this study was to explore the relationship between disease subtype, disease activity, and specific PROs in an IBD cohort.

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MATERIALS AND METHODS

A single center, prospective, cross-sectional analysis of IBD patient data from a large tertiary hospital in Melbourne, Australia was performed.

Participants

All patients aged 18 or over attending an adult IBD clinic at a metropolitan hospital in Melbourne, Australia between May and June 2015 were invited to participate. Patients were approached following arrival at the clinic by one of the study investigators if the patient had a clinical and/or radiological diagnosis of IBD and if they could communicate in English. The study was explained to each patient in detail and a patient information and consent form was provided to the patient. Participants could only participate once in the study and were ineligible if they presented to the IBD clinic more than once in the recruitment period.

Disease assessment and questionnaires

Following consent, each patient was provided with an iOS tablet, connected to the hospital's wireless internet system. Participants were asked to complete demographic data as well as several validated questionnaires relating to their IBD at the time of the study

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on the tablet. Participants with incomplete responses were contacted once by phone to complete the questionnaires from home.

Study data were collected and managed using REDCap (Research Electronic Data Capture), a secure, web-based application designed to support data capture for research studies[20]. A power calculation was not required due to the cross-sectional design of the study.

Clinical and demographic data

Demographic and clinical information was entered by the study investigators and included patient age, gender, smoking status, employment status, highest educational level, duration of IBD, type of IBD [UC, CD or IBD-unclassified (IBD-U)], disease extent, medication use and history of bowel surgery. Disease activity was self-assessed by the patient at the time of data collection and the severity was calculated according to validated clinical indices (remission if patient assessed Simple Clinical Colitis Activity Index (p-SCCAI) < 5; active disease if p-SCCAI ≥ 5 for UC or IBD-U; remission if Harvey Bradshaw Index (HBI) <5 for CD; active disease if HBI ≥ 5)[21,22]. Disease activity using the most recent biomarkers (CRP and FC) were documented by the study investigators at the time of the study. For UC, disease extent was coded as either proctitis (distal to the rectosigmoid junction), left sided colitis (distal to the hepatic flexure), or extensive colitis. For CD, disease stage was designated as ileal, colonic, or ileocolonic, with or without

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perianal disease, as per the Montreal classification system [23].

Patient reported outcomes and other study variables

IBD knowledge was assessed using the validated CC-KNOW and medication adherence was evaluated using the Morisky adherence scale (MMAS-8)[24,25]. Assessment of PROs included: the Hospital Anxiety and Depression Scale (HADS), a 14-item self-report questionnaire assessing levels of anxiety (seven items) and depression (seven items) over the past week, where a cut-off of 8 (or more) for each HADS subscale indicates mild to severe distress[26,27]; the Work productivity and activity impairment (WPAI) questionnaire to measure percentage of work time missed due to IBD, the percentage of impairment while working due to IBD, the overall work impairment due to IBD and the activity impairment due to IBD during the past 7 days[28], and; the Short Inflammatory Bowel Disease Questionnaire (S-IBDQ) to assess QoL[29].

Statistical analyses

Questionnaire data was exported onto the statistics software STATA (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP) for analysis. Only completed questionnaires were analyzed. Descriptive statistics were used for patient demographics and disease characteristics. Spearman's correlation was determined between the study variables: disease

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activity (clinical indices and biomarkers), IBD knowledge, medication adherence, depression and anxiety, work impairment and QoL. Bonferroni correction was used to keep the overall level of significance at a p value of 0.05 and exclude potential confounding demographic factors on the variables studied.

The study was reviewed and approved by the Hospital's Human Research Ethics Committee.

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RESULTS

Demographics

All patients (n=85) who were invited to participate met the inclusion criteria for the study and agreed to complete the study (100% participation rate). Eighty-one of the 85 participants (95%) completed all surveys. The responses from the four patients that did not complete all surveys were excluded from the study due to the incomplete dataset in each survey. The 81 participants included a similar number of males and females with a median age of 34 (SD 10.9, range 18-76). Forty-six (57%) patients had Crohn's Disease, 31 (38%) patients had UC and 4 (5%) patients had IBD-unclassified. Demographic and disease characteristics are displayed in Table 1.

Disease activity

Twenty-seven patients with CD (27/46; 59%) were in clinical remission according to the HBI at the time of the study. Fifteen (33%) patients had mild-to-moderate disease, and four (9%) had severe disease. Of the UC and IBD-U patients, 24/35 (68%) were in clinical remission according to the p-SCCAI at the time of the study; 10/35 (29%) had mild-to-moderate disease, and 1/35 (3%) had severe disease (Table 1). Seventy-five patients had a CRP tested within one week of the study, ranging from 0.3

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to 49.2. Only 18 patients had a FC performed within one week of the study. Due to the low numbers, the FC values were not included in the correlations.

Psychological wellbeing

Based on the HADS, at least mild levels of depression symptoms were present in 21 (26%) of patients, and 37 (46%) of patients expressed some level of anxiety on the day of study participation.

Patients with CD demonstrated a significantly greater level of depression and anxiety than patients with UC. Nine (9/35; 24%) patients with UC were assessed as having at least mild levels of depression. Sixteen (16/46; 35%) patients with CD had at least mild levels of depression. Twelve (12/35; 38%) patients with UC demonstrated at least mild levels of anxiety, whereas 25 (25/43; 58%) with CD demonstrated at least mild levels of anxiety.

There were no significant differences between males and females across depression scores; however, females were found to have significantly higher scores for anxiety than males. Eleven (11/36; 31%) females demonstrated some level of depression whereas 10

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(10/39; 26%) males demonstrated at least mild levels of depression. Twenty-three (23/36; 64%) females had some level of anxiety compared to 14 (14/39; 36%) males.

Correlations between disease activity and depression

A moderate-to-strong positive correlation was found between disease activity (p-SCCAI) and depression in UC (*r*=0.84, p=0.002) but not in CD (*r*=0.53, p=0.29) (Table 2 and 3). A low positive correlation was found between CRP and depression in CD (r=0.36, p=0.03) but not in UC (r=0.31, p=0.09).

Correlations between disease activity and anxiety

There was a moderate positive correlation between disease activity in UC (p-SCCAI) and anxiety (r=0.53) and between disease activity in CD (HBI) and anxiety (r=0.4-0.5) but it was only significant on univariate analysis (p=0.0029). There was no statistical significance after Bonferroni adjustment. There was a weakly positive correlation between anxiety and disease activity using CRP in UC (r=0.38, p=0.03) but not in CD (r=0.14, p=0.4).

Correlations between disease activity and other patient reported outcomes

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Disease activity (p-SCCAI) correlated positively with overall work impairment due to health (*r*=0.85, p=0.001), health related impairment while working (*r*=0.76, p=0.02), and percentage of activity impaired due to health (*r*=0.83, p=0.002) in UC only. Disease activity using CRP in CD demonstrated a weakly positive correlation with impairment while working due to health (r=0.57, p=0.003) and activity impairment due to health (r=0.4, p=0.026) but not in UC.

Neither patient knowledge nor medication adherence correlated with disease activity. Moreover, neither patient knowledge nor medication adherence correlated with level of psychological distress. QoL did not demonstrate a statistically significant correlation with disease activity nor did QoL correlate with psychological distress. Neither age, gender, smoking status, educational level nor employment status had an impact on disease activity, work impairment, medication adherence or QoL. Neither medication use (including the use of corticosteroids), duration of disease nor history of bowel surgery had an impact on QoL or psychological distress in our study.

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DISCUSSION

PRO measures have recently been thought to represent important outcome measures in clinical trials for IBD due to the great variability in the expression of symptoms from patient-to-patient. This study aimed to identify whether there were any relationships between disease activity, dependent variables (knowledge, medication adherence) and PROs. A significant positive relationship between disease activity (using clinical indices) and depression was identified in UC but not CD. This study has also demonstrated for the first time that there is a significant correlation between psychological distress and work impairment among patients with UC.

Health-related productivity has been increasingly recognized as an important component of the burden of illness associated with chronic diseases[30]. Health impairment often leads to work impairment in the form of both absenteeism and presenteeism (lost productivity that occurs when employees attend work but perform below par due to their illness) as assessed by the WPAI[30-32]. In our study, work impairment was positively associated with patients with active UC according to clinical indices, and associated with active CD based on elevated CRP, indicating that patients with active IBD are more restricted in their work productivity than those in clinical remission. Our findings are consistent with a Hungarian study that found significantly impaired work productivity in patients with active IBD with a 28% loss of work productivity[33]. It has also been shown that cost of care of

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IBD is largely influenced by a patient's ability to work[34]. Work productivity has been shown to correlate with QoL and disease activity in CD[35]. In this study we found a significant correlation between psychological distress and work impairment among patients with UC. Our data highlight the need to explore the factors associated with work productivity impairment in patients with UC beyond the impact of disease activity alone.

High levels of depression and anxiety were found in our cohort, reinforcing the findings of previous studies which have demonstrated a high prevalence of psychological disorders in IBD patients[36]. In previous studies in IBD the rate of depression and anxiety during remission has been thought to be between 29-35% and as high as 80% during relapse[37-40]. In this study, levels of depression and anxiety correlated with disease activity using clinical indices in UC but not in CD. These findings are consistent with a study by Hauser *et al*. that also failed to demonstrate a correlation between depression and/or anxiety and disease activity in CD[41];. However, other studies have found contrary results[42]. In contrast to Hauser *et al*. we did find a correlation between psychological distress and disease activity in UC. Goodhand *et al*.[43] also reported that patients with active UC had higher rates of anxiety than those with inactive disease, although no significant correlation was found with depression. There was no correlation between depression or anxiety in patients with CD in the latter study[43]. The reasons for the lack of correlation between disease activity using clinical indices and psychological distress in CD in both Goodhand *et al's* and this

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study suggest that there are other drivers of psychological distress in patients with CD beyond disease activity alone. However, there is a paucity of evidence examining the differences in psychological distress amongst disease subtypes. Patients with CD have demonstrated higher levels of anxiety and depression with inactive disease[36] and therefore the change in psychological distress with active disease appears to be less pronounced. Further work is required to evaluate the factors that precipitate psychological distress in patients with IBD irrespective of disease activity.

We recognize that there are limitations associated with this study. In particular, the cohort of patients was from a single tertiary IBD center rather than a population-based cohort so may not be generalizable to other IBD populations. Although prospective, the study was cross-sectional and not longitudinal and was therefore not able to discern changes in PROs over time. Although it has been suggested that objective markers of disease activity such as FC may be able to help distinguish active disease from functional symptoms captured by PROs, this study did not evaluate FC in all patients, reflecting the relatively low uptake of FC by patients despite its known utility as a non-invasive biomarker. Although CRP did not correlate with clinical indices it did correlate with anxiety, depression and work impairment, confirming that raised inflammatory activity has a psychological and functional impact beyond disease activity measured by traditional clinical indices. Further study should be undertaken to assess the correlation between disease activity using clinical indices, PROS, CRP, FC and endoscopic activity. Due to the cross-

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sectional design of the study, data such as days off work due to illness as well as coping mechanisms were not collected. Furthermore, type of work was not captured which may influence work impairment. Additional PROs could have been collected such as the recently validated Disability Index[44]; however, time limitations during data collection limited the number of surveys used. Although our sample size was 81 patients, the subgroup analyses used smaller sample sizes, possibly limiting the ability to find significant correlations. Future studies could address these limitations by undertaking a prospective longitudinal study of consecutive IBD sample matched to a general population cohort. This would allow a larger sample size to be studied and enable an exploration of PROs in the context of dynamic alterations of disease activity within patients over time and potentially between PROs and disease activity based on clinical indices and objective markers of disease activity.

PROs inform clinicians about the functional impact of the disease on the patient. This study examined the relationship between PROs and disease activity and confirms that high levels of depression and anxiety exist in IBD. Disease activity appears to have a more significant impact on patients' level of psychological distress in UC than CD. Levels of psychological distress and work impairment are significant among patients with UC. The results of this study, together with incongruities identified in other studies, suggest that further work is required to understand the complex interaction between disease activity and PROs. Further

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work is required to discern the interaction between PROs over and above disease activity in order to find interventions that improve patients' ability to function.

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REFERENCES

1. Australia CsC. Interim Australian IBD Standards: Standards of healthcare for people with inflammatory bowel disease in Australia. 2015.

2. Wilson J, Hair C, Knight R, et al. High incidence of inflammatory bowel disease in Australia: a prospective population-based Australian incidence study. Inflammatory bowel diseases 2010;16:1550-6.

3. Burisch J, Jess T, Martinato M, Lakatos PL, EpiCom E. The burden of inflammatory bowel disease in Europe. Journal of Crohn's & colitis 2013;7:322-37.

4. Hanauer SB. Inflammatory bowel disease: epidemiology, pathogenesis, and therapeutic opportunities. Inflammatory bowel diseases 2006;12 Suppl 1:S3-9.

5. Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): Determining Therapeutic Goals for Treat-to-Target. The American journal of gastroenterology 2015;110:1324-38.

6. Mosli MH, Zou G, Garg SK, et al. C-Reactive Protein, Fecal Calprotectin, and Stool Lactoferrin for Detection of Endoscopic Activity in Symptomatic Inflammatory Bowel Disease Patients: A Systematic Review and Meta-Analysis. The American journal of gastroenterology 2015;110:802-19; quiz 20.

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Author Manuscript

7. Wright EK, Kamm MA, De Cruz P, et al. Measurement of fecal calprotectin improves monitoring and detection of recurrence of Crohn's disease after surgery. Gastroenterology 2015;148:938-47 e1.

8. Breitscheidel L, Stamenitis S. Using patient-reported outcome assessments in clinical practice and their importance in risk management. Journal of medical economics 2009;12:180-1.

9. Zittan E, Kabakchiev B, Kelly OB, et al. Development of the Harvey-Bradshaw Index-pro (HBI-PRO) Score to Assess Endoscopic Disease Activity in Crohn's Disease. Journal of Crohn's & colitis 2017;11:543-8.

10. McCormick M, Reed-Knight B, Lewis JD, Gold BD, Blount RL. Coping skills for reducing pain and somatic symptoms in adolescents with IBD. Inflammatory bowel diseases 2010;16:2148-57.

11. Elkjaer M, Shuhaibar M, Burisch J, et al. E-health empowers patients with ulcerative colitis: a randomised controlled trial of the web-guided 'Constant-care' approach. Gut 2010;59:1652-61.

12. Pedersen N, Elkjaer M, Duricova D, et al. eHealth: individualisation of infliximab treatment and disease course via a self-managed web-based solution in Crohn's disease. Alimentary pharmacology & therapeutics 2012;36:840-9.

13. Vasudevan A, Arachchi A, van Langenberg DR. Assessing patient satisfaction in inflammatory bowel disease using the QUOTE-IBD survey: a small step for clinicians, a potentially large step for improving quality of care. Journal of Crohn's & colitis 2013;7:e367-74.

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Author Manuscript

14. Norton C, Czuber-Dochan W, Bassett P, et al. Assessing fatigue in inflammatory bowel disease: comparison of three fatigue scales. Alimentary pharmacology & therapeutics 2015;42:203-11.

15. Cross RK, Cheevers N, Rustgi A, Langenberg P, Finkelstein J. Randomized, controlled trial of home telemanagement in patients with ulcerative colitis (UC HAT). Inflammatory bowel diseases 2012;18:1018-25.

16. Colombel JF. Measuring Disability in IBD: The IBD Disability Index. Gastroenterology & Hepatology 2013;9:300-2.

17. Acquadro C, Berzon R, Dubois D, et al. Incorporating the patient's perspective into drug development and communication: an ad hoc task force report of the Patient-Reported Outcomes (PRO) Harmonization Group meeting at the Food and Drug Administration, February 16, 2001. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research 2003;6:522-31.

18. Merolli M, Gray K, Martin-Sanchez F. Developing a framework to generate evidence of health outcomes from social media use in chronic disease management. Medicine 20 2013;2:e3.

19. Williet N, Sandborn WJ, Peyrin-Biroulet L. Patient-reported outcomes as primary end points in clinical trials of inflammatory bowel disease. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2014;12:1246-56 e6.

This article is protected by copyright. All rights reserved.

20. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. Journal of biomedical informatics 2009;42:377-81.

21. Bennebroek Evertsz F, Nieuwkerk PT, Stokkers PC, et al. The patient simple clinical colitis activity index (P-SCCAI) can detect ulcerative colitis (UC) disease activity in remission: a comparison of the P-SCCAI with clinician-based SCCAI and biological markers. Journal of Crohn's & colitis 2013;7:890-900.

22. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet 1980;1:514.

23. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut 2006;55:749-53.

24. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical care 1986;24:67-74.

25. Wardle RA, Mayberry JF. Patient knowledge in inflammatory bowel disease: the Crohn's and Colitis Knowledge Score. European journal of gastroenterology & hepatology 2014;26:1-5.

26. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta psychiatrica Scandinavica 1983;67:361-70.

Author Manuscript

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27. Knowles SR, Wilson JL, Connell WR, Kamm MA. Preliminary examination of the relations between disease activity, illness perceptions, coping strategies, and psychological morbidity in Crohn's disease guided by the common sense model of illness. Inflammatory bowel diseases 2011;17:2551-7.

28. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. PharmacoEconomics 1993;4:353-65.

29. Irvine EJ, Zhou Q, Thompson AK. The Short Inflammatory Bowel Disease Questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn's Relapse Prevention Trial. The American journal of gastroenterology 1996;91:1571-8.

30. Prasad M, Wahlqvist P, Shikiar R, Shih YC. A review of self-report instruments measuring health-related work productivity: a patient-reported outcomes perspective. PharmacoEconomics 2004;22:225-44.

31. Hemp P. Presenteeism: at work--but out of it. Harv Bus Rev 2004;82:49-58, 155.

32. Goetzel RZ, Long SR, Ozminkowski RJ, Hawkins K, Wang S, Lynch W. Health, absence, disability, and presenteeism cost estimates of certain physical and mental health conditions affecting U.S. employers. J Occup Environ Med 2004;46:398-412.

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Author Manuscript

33. Mandel MD, Balint A, Lovasz BD, et al. Work disability and productivity loss in patients with inflammatory bowel diseases in Hungary in the era of biologics. The European journal of health economics : HEPAC : health economics in prevention and care 2014;15 Suppl 1:S121-8.

34. Reilly MC, Gerlier L, Brabant Y, Brown M. Validity, reliability, and responsiveness of the work productivity and activity impairment questionnaire in Crohn's disease. Clinical therapeutics 2008;30:393-404.

35. Feagan BG, Reilly MC, Gerlier L, Brabant Y, Brown M, Schreiber S. Clinical trial: the effects of certolizumab pegol therapy on work productivity in patients with moderate-to-severe Crohn's disease in the PRECiSE 2 study. Alimentary pharmacology & therapeutics 2010;31:1276-85.

36. Mikocka-Walus A, Knowles SR, Keefer L, Graff L. Controversies Revisited: A Systematic Review of the Comorbidity of Depression and Anxiety with Inflammatory Bowel Diseases. Inflammatory bowel diseases 2016;22:752-62.

37. Mittermaier C, Dejaco C, Waldhoer T, et al. Impact of depressive mood on relapse in patients with inflammatory bowel disease: a prospective 18-month follow-up study. Psychosomatic medicine 2004;66:79-84.

38. Andrews H, Barczak P, Allan RN. Psychiatric illness in patients with inflammatory bowel disease. Gut 1987;28:1600-4.

39. Addolorato G, Capristo E, Stefanini GF, Gasbarrini G. Inflammatory bowel disease: a study of the association between anxiety and depression, physical morbidity, and nutritional status. Scandinavian journal of gastroenterology 1997;32:1013-21.

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40. Mikocka-Walus A, Pittet V, Rossel JB, von Kanel R, Swiss IBDCSG. Symptoms of Depression and Anxiety Are Independently Associated With Clinical Recurrence of Inflammatory Bowel Disease. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2016;14:829-35 e1.

41. Hauser W, Janke KH, Klump B, Hinz A. Anxiety and depression in patients with inflammatory bowel disease: comparisons with chronic liver disease patients and the general population. Inflammatory bowel diseases 2011;17:621-32.

42. Tribbick D, Salzberg M, Ftanou M, et al. Prevalence of mental health disorders in inflammatory bowel disease: an Australian outpatient cohort. Clinical and experimental gastroenterology 2015;8:197-204.

43. Goodhand JR, Wahed M, Mawdsley JE, Farmer AD, Aziz Q, Rampton DS. Mood disorders in inflammatory bowel disease: relation to diagnosis, disease activity, perceived stress, and other factors. Inflammatory bowel diseases 2012;18:2301-9.

44. Leong RW, Huang T, Ko Y, et al. Prospective validation study of the International Classification of Functioning, Disability and Health score in Crohn's disease and ulcerative colitis. Journal of Crohn's & colitis 2014;8:1237-45.

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TABLES

Table 1 Patient demographics and disease characteristics

Patient characteristics	**Number of patients** (Total n = 81)	**%**[†]
Age (years), mean (SD; range)	34 (10.9; 18,76)	-
Gender, %		
Male	41	51
Female	40	49
Smoking status		
Current smoker	10 (7 CD, 3 UC)	12
Ex-smoker	31	38
Never smoked	40	49
Highest education level		
Master's degree or PhD	3	4
Bachelor's degree	24	30
Certificate or diploma	27	33

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High school or equivalent	21	26
Did not complete high school	6	7
Employment status		
Working full-time	39	48
Working part-time	16	20
Student	14	17
Unemployed	12	15
IBD Subtype		
UC	31	38
CD	46	57
IBD-U	4	5
Phenotype		
UC		
Proctitis	3	10
Left-sided	11	35
Pancolitis	17	55
CD		

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Ileal	9	20
Colonic	7	15
Ileocolonic	19	41
Perianal disease (in isolation or in combination with luminal disease)	11	24
Disease activity at time of study according to clinical indices		
UC and IBD-U		
Remission	24	68
Mild-to-moderate	10	29
Severe	1	3
CD		
Remission	27	59
Mild-to-moderate	15	33
Severe	4	9
C-Reactive Protein		
UC and IBD-U		

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<5 mg/L	22	69
5 mg/L or greater	10	31
CD		
<5 mg/L	25	64
5 mg/L or greater	14	36
Fecal calprotectin		
UC and IBD-U		
<100 µg/g	8	89
100 µg/g or greater	1	11
CD		
<100 µg/g	5	56
100 µg/g or greater	4	44

SD, standard deviation; IBD, inflammatory bowel disease; UC, ulcerative colitis; CD, Crohn's disease; IBD-U, inflammatory bowel disease-unclassified

HADS-Anxiety/Depression: < 7 = mild distress, 8-10 = moderate distress, >11 = severe distress †% may not add to 100% due to rounding

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Table 2 Spearman Correlations (and Significance Values) and Descriptive Values of Disease Variables and Patient Reported Outcomes for patients with Crohn's Disease

	Disease Severity (HBI)	**C-Reactive Protein**	**Medication Adherence**	**Quality of Life**	**Depression**	**Anxiety**	**IBD Knowledge**	**% of Work time missed due to IBD**	**% of Impairment while working due to IBD**	**Overall work impairment due to IBD**
C-Reactive Protein	0.12 (>0.05)	-								
Medication Adherence	-0.08 (>0.05)	0.17 (>0.05)	-	-	-	-	-	-	-	-
Quality of Life	-0.03 (>0.05)	0.31 (>0.05)	-0.3 (>0.05)	-	-	-	-	-	-	-
Depression	0.53 (>0.05)	**0.36** (0.03)	0.08 (>0.05)	-0.22 (>0.05)	-	-	-	-	-	-
Anxiety	0.27 (>0.05)	0.14 (>0.05)	0.32 (>0.05)	-0.39 (>0.05)	0.56 (>0.05)	-	-	-	-	-
IBD Knowledge	0.004 (>0.05)	0.24 (>0.05)	0.04 (>0.05)	0.17 (>0.05)	-0.04 (>0.05)	0.15 (>0.05)	-	-	-	-
% of Work time missed due to IBD	0.33 (>0.05)	0.26 (>0.05)	-0.01 (>0.05)	-0.07 (>0.05)	0.52 (>0.05)	0.20 (>0.05)	-0.22 (>0.05)	-	-	-
% of Impairment while working due to IBD	0.42 (>0.05)	**0.57** (0.003)	0.09 (>0.05)	-0.42 (>0.05)	0.51 (>0.05)	0.35 (>0.05)	0.001 (>0.05)	**0.65** (0.02)	-	-
Overall work impairment due to IBD	0.45 (>0.05)	0.22 (>0.05)	0.08 (>0.05)	-0.41 (>0.05)	0.52 (>0.05)	0.38 (>0.05)	-0.03 (>0.05)	**0.72** (0.002)	**0.99** (< 0.001)	-
Activity Impairment due to IBD	0.35 (>0.05)	**0.41** (0.03)	0.15 (>0.05)	-0.48 (>0.05)	0.58 (>0.05)	0.4 (>0.05)	0.11 (>0.05)	**0.62** (0.05)	**0.88** (<0.001)	**0.88** (<0.001)

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Table 3 Spearman Correlations (and Significance Values) and Descriptive Values of Disease Variables and Patient Reported Outcomes for patients with Ulcerative Colitis

	Disease Severity (p-SCCAI)	**C-Reactive Protein**	**Medication Adherence**	**Quality of Life**	**Depression**	**Anxiety**	**IBD Knowledge**	**% of Work time missed due to IBD**	**% of impairment while working due to IBD**	**Overall work impairment due to IBD**
C-Reactive Protein	-0.05 (>0.05)	-								
Medication Adherence	0.28 (>0.05)	0.31 (>0.05)	-	-	-	-	-	-	-	-
Quality of Life	-0.15 (>0.05)	0.24 (>0.05)	-0.03 (>0.05)	-	-	-	-	-	-	-
Depression	**0.84** (0.001)	0.31 (>0.05)	0.32 (>0.05)	-0.16 (>0.05)	-	-	-	-	-	-
Anxiety	0.53 (>0.05)	**0.38** (0.03)	-0.12 (>0.05)	-0.80 (>0.05)	0.64 (0.31)	-	-	-	-	-
IBD Knowledge	-0.34 (>0.05)	0.07 (>0.05)	0.06 (>0.05)	-0.05 (>0.05)	-0.24 (>0.05)	-0.18 (>0.05)	-	-	-	-
% of Work time missed due to IBD	0.58 (>0.05)	0.29 (>0.05)	-0.24 (>0.05)	-0.14 (>0.05)	0.53 (>0.05)	0.72 (>0.05)	-0.45 (>0.05)	-	-	-
% of Impairment while working due to IBD	**0.76** (0.02)	0.02 (>0.05)	0.10 (>0.05)	-0.19 (>0.05)	**0.76** (0.02)	0.4 (>0.05)	-0.17 (>0.05)	0.48 (>0.05)	-	-
Overall work impairment due to IBD	**0.85** (0.001)	0.15 (>0.05)	0.13 (>0.05)	-0.11 (>0.05)	**0.79** (0.008)	0.51 (>0.05)	-0.22 (>0.05)	0.67 (>0.05)	**0.93** (< 0.001)	-
Activity Impairment due to IBD	**0.83** (0.002)	0.13 (>0.05)	0.31 (>0.05)	-0.07 (>0.05)	**0.80** (0.006)	0.49 (>0.05)	0.11 (>0.05)	0.48 (>0.05)	**0.86** (<0.001)	**0.90** (<0.001)

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