

PATIENT-REPORTED SYMPTOMS ARE THE SOLE INDEPENDENT PREDICTOR OF THE SOCIETAL BURDEN ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE: A CROSS-SECTIONAL STUDY

Authors: **Barbora Decker**^{1,2}, **Jan Tuzil**^{1,3}, **Milan Lukas**^{4,5}, **Karin Cerna**⁴, **Martin Bortlik**^{6,7,8}, **Barbora Turkova**¹, **Barbora Pilnackova**¹, **Tomas Dolezal**^{1,2}

¹Institute of Health Economics and Technology Assessment, Prague, Czech Republic

²Department of Pharmacology, Faculty of Medicine, Masaryk University, Brno, Czech Republic

³Department of Biomedical Informatics, First Faculty of Medicine, Charles University, Prague, Czech Republic

⁴IBD clinical and research center ISCARE a.s., Prague, Czech Republic

⁵Institute of Medical Biochemistry and Laboratory Medicine, General University Hospital and First Faculty of Medicine, Charles University, Prague, Czech Republic

⁶Gastroenterology Department, České Budějovice Hospital, České Budějovice, Czech Republic

⁷Department of Internal Medicine, Military University Hospital and First Faculty of Medicine, Charles University, Prague, Czech Republic

⁸Institute of Pharmacology, First Faculty of Medicine, Charles University, Prague, Czech Republic



Objectives

The societal burden of inflammatory bowel diseases (IBD) is not well documented in the literature, and further studies are needed to quantify these costs per disease state. This study aimed to estimate the societal burden and identify predictors of work productivity and activity impairment, productivity costs, and out-of-pocket costs related to IBD.

Methods

- A cross-sectional questionnaire-based study was performed among adult Czech patients with Crohn's disease (CD) and ulcerative colitis (UC).
- Inclusion criteria for data collection were verified diagnosis of CD/UC, study participation consent, and age ≥ 18 years. Only fully completed questionnaires were assessed; other exclusion criteria were not specified.
- The study was approved by the ethics committee of the clinical center ISCARE a.s. under the identifier 2021/1a and the ethics committee of the České Budějovice Hospital under the identifier 111/21.
- Participation in the study was voluntary and anonymous.
- The patients consented to personal data processing.
- Data were collected from 4/2021 to 3/2022 using electronic patient questionnaires.
- The disease severity was assessed by patients alone, i.e., patients reported the presence or absence of disease symptoms.
- The questionnaires collected data describing patient demographics and clinical characteristics, time spent on visits to the treatment centers and treatment-related lost productivity, social transfer costs, out-of-pocket expenditures, and a standardized Czech version of the WPPI (work productivity and activity impairment) questionnaire assessing absenteeism, presenteeism, and non-paid daily activities (1).
- Statistical analysis was performed in R and STATA version 13. Comparisons between groups were performed using the Mann-Whitney U-test and chi-square tests. The significance level was set at 0.05. Descriptive data analysis was performed for the whole population and the two subpopulations, i.e., with or without disease symptoms. Associations between different variables were assessed using multivariate linear regression.
- Productivity costs were assessed using a human capital approach (2).

Figure 1. Flow diagram

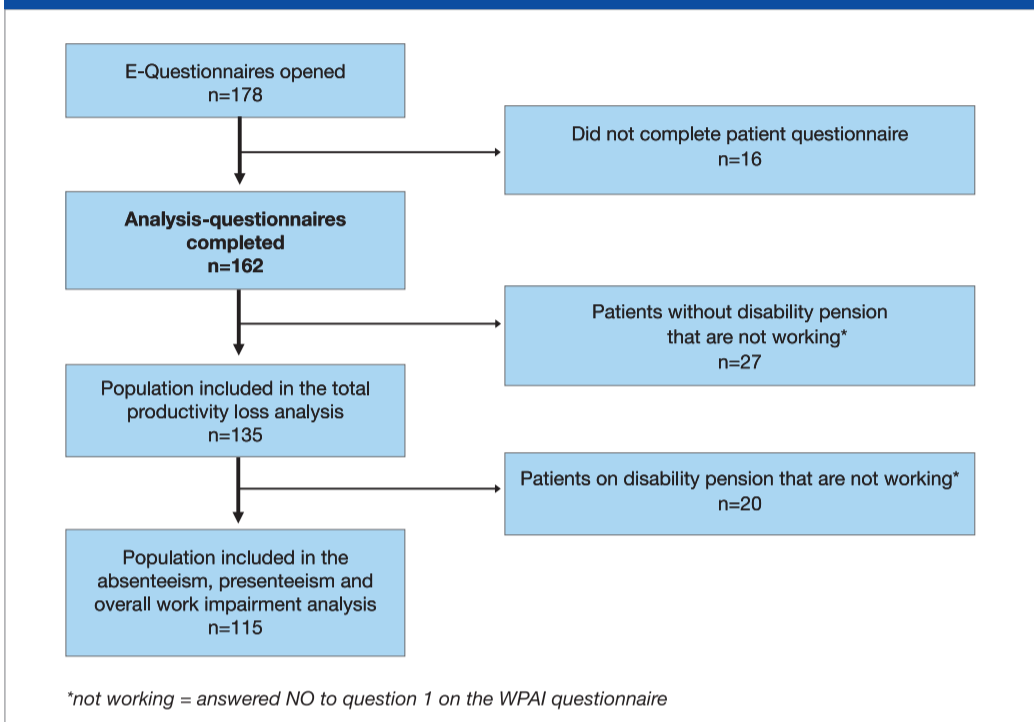


Figure 2. Patient-reported percentage of impairment in work productivity and daily activities according to the disease activity in patients with IBD

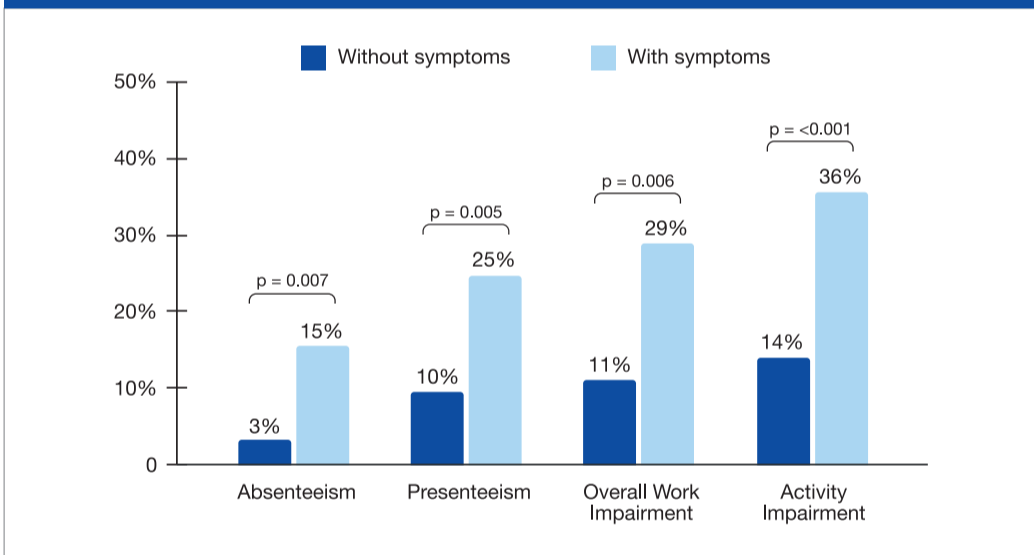


Table 1. Patient characteristics

	Total (N=162)	Patient-reported remission (N=123)	Patient-reported active disease (N=39)	p-value*
Crohn's disease, n (%)	105 (65%)	82 (67%)	23 (59%)	0.381
Female, n (%)	94 (58%)	69 (56%)	25 (64%)	0.377
Mean age, y (SD)	41.22 (13.07)	41.67 (13.04)	39.77 (13.20)	0.365
Disease duration, y (SD)	13.16 (8.72)	13.27 (8.22)	12.78 (10.50)	0.430
Mean age at presentation, y (SD)	27.58 (10.08)	27.58 (10.14)	27.57 (10.07)	0.928
Mean age at diagnosis, y (SD)	29.00 (10.40)	29.05 (10.65)	28.83 (9.67)	0.972
Mean BMI, kg/m ² (SD)	25.29 (4.68)	25.46 (4.86)	24.76 (4.06)	0.460
Smoking, n (%)	17 (10%)	11 (9%)	6 (15%)	0.126
Presence of complications, n (%)	34 (21%)	19 (15%)	15 (38%)	0.002

*Differences between groups were assessed using Mann-Whitney and Chi-square tests.

Table 2. Productivity, and out-of-pocket costs in patients with/without IBD symptoms

	Total (SD)	Patient-reported remission (SD)	Patient-reported active disease (SD)	Difference [95% CI]	p-value*	Adjusted difference [95% CI]**	p-value adjusted**
Productivity costs (A), €/year	1,158 (3,593)	475 (824)	3,183 (6,694)	-2,709 [-4,159; -1,259]	0.009	-2,953 [-4,513; -1,392]	0.000
Productivity costs (P), €/year	2,132 (3,413)	1,874 (3,284)	2,897 (3,727)	-1,024 [-2,470; 422]	0.146	-1,336 [-2,889; -217]	0.091
Productivity costs (WI; A+P), €/year	3,290 (5,111)	2,348 (3,589)	6,081 (7,512)	-3,732 [-5,802; -1,662]	0.016	-4,289 [-6,518; -2,061]	0.000
Total productivity costs (A+P+D), €/year	7,649 (9,002)	6,002 (7,636)	12,345 (10,902)	-6,352 [-9,689; -3,015]	0.001	-6,626 [-10,051; -3200]	0.000
Out-of-pocket costs, €/year	559 (608)	469 (509)	844 (791)	-375 [-589; -162]	0.001	-397 [-622; -172]	0.001

*Differences between groups were assessed using Mann-Whitney and Chi-square tests.

**adjusted for age, disease duration, gender, BMI, IBD type and smoking history

Results

- We analyzed data from 162 questionnaires (CD: n=105, UC: n=57). The complete flow diagram is shown in **Figure 1**.
- Patient demographics and clinical characteristics are described in **Table 1**. There were no significant differences in patient characteristics in the subgroup with/without disease symptoms.
- The results, along with the corresponding p-values, are summarized in **Figure 2** and **Table 2**:
 - The overall work impairment reached 15.4%; 11.2% vs. 28.8% without/with self-reported symptoms (p=0.006) (**Figure 2**).
 - Daily activity impairment was 19.3%; 14.1% vs. 35.6% (p<0.001) (**Figure 2**).
 - The disability pension rate was 27.8%; 22.8% vs. 43.6% (p=0.011).
 - The total loss of productivity due to absenteeism, presenteeism and disability summed up to 7,649 €/patient/year overall, 6,002 and 12,354 €/patient/year without/with self-reported symptoms, respectively (p=0.001) (**Table 2**).
 - Out-of-pocket costs amounted to 559 €/patient/year overall, 469 vs. 844 €/patient/year without/with self-reported symptoms, respectively (p<0.001) (**Table 2**).
- Differences in productivity and out-of-pocket costs between patients without/with self-reported symptoms remained significant even after adjustment to other characteristics.
- According to the multivariate linear regression analysis, self-reported symptoms (i.e., disease activity) were the only independent predictor of patient productivity and costs (p<0.001). Age, disease duration, gender, IBD type, smoking, and BMI had no measurable impact.

Conclusion

Strengths:

- The strength of the study lies in the large sample and diversity of self-reported outcomes.
- Another major strength was the self-assessment study design, reflecting disease characteristics from the patients' perspective and eliminating interviewer bias.
- The adjusted differences are comparable to the crude estimates. We showed that no other measured parameter apart from self-reported symptoms predicts the costs.

Limitations:

- Patient answers might be influenced by recall, response or social desirability bias. Patient responses were not validated with medical records or clinical examinations.
- Another limitation might be sampling bias since all patients were treated in highly specialized IBD centers. Nevertheless, patient characteristics were consistent with previous IBD center-based cohorts as well as a global systematic analysis of IBD patients (3,4).
- Another possible limitation lies in the cross-sectional study design itself. The goal was to describe the correlation between multiple variables, but we can only speculate on its causality. Various confounders could have distorted our reported correlations, i.e., third factors not captured by the study.

This study revealed a high societal burden of IBD and a significant association of work disability, daily activity impairment, disability pension, and out-of-pocket costs with patient-reported disease symptoms. The results indicate that induction and maintenance of remission in all participants with active disease can lower indirect costs by more than half.

References

- Reilly MC, Zbrozek AS, Duker EM. The validity and reproducibility of a work productivity and activity impairment instrument. *Pharmacoeconomics*. 1993 Nov;4(5):353-65. • 2. Hout WB van den. The value of productivity: human-capital versus friction-cost method. *Ann Rheum Dis*. 1999;58(1):89-91. Available from: https://ard.bmj.com/content/58/Suppl_1/89
- Michael MD, Bálint A, Lovász BD, Gulácsi L, Strbák B, Golovics PA, et al. Work disability and productivity loss in patients with inflammatory bowel diseases in Hungary in the era of biologics. *Eur J Health Econ*. 2014 May 1;15(1):121-8. Available from: <https://doi.org/10.1007/s10198-014-0603-7> • 4. Alatab S, Sepanlou SG, Ikuta K, Vahedi H, Bisignano C, Safiri S, et al. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol*. 2021;5(1):17-30. Available from: [https://www.thelancet.com/journals/langas/article/PIIS2468-1253\(19\)30333-4/abstract](https://www.thelancet.com/journals/langas/article/PIIS2468-1253(19)30333-4/abstract)

Corresponding author: barbora.decker@valueoutcomes.cz