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ORIGINAL PAPER

Work disability and productivity loss in patients with inflammatory bowel diseases in Hungary in the era of biologics

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Abstract

Background and aims To assess work disability (WD) rates in an inflammatory bowel disease (IBD) cohort involving patients with Crohn's disease (CD) or ulcerative colitis (UC) cohort and to identify possible clinical or demographic factors associated with WD. To our knowledge, this is the first study from Eastern Europe that has estimated indirect costs in IBD.

Methods Data from 443 (M/F: 202/241, CD/UC: 260/183, mean age: 35.5 (CD) and 40.5 (UC) years, biological drug exposure 31.2/11.5 %) consecutive patients were included. WD data were collected by questionnaire and the work productivity and activity impairment instrument. Disability pension (DP) rates in the general population were retrieved from public databases.

Results The overall DP rate in this IBD population was 32.3 %, with partial disability in 24.2 %. Of all DP events, 88.8 % were directly related to IBD. Overall, full DP was more prevalent in IBD (RR: 1.51, $p < 0.001$) and CD (RR: 1.74, $p < 0.001$) but not in UC compared to the general population and also in CD compared to UC (OR 1.57, $p = 0.03$). RR for full DP was increased only in young CD patients (RR_{<35 year olds}: 9.4; RR_{36–40 year olds}: 9.4 and 5.6,

$p < 0.01$ for both). In CD, age group, previous surgery, disease duration, frequent relapses, and the presence of arthritis/arthritis were associated with an increased risk for DP. Among employed patients, absenteeism and presenteeism was reported in of 25.9 and 60.3 % patients, respectively, leading to a 28 % loss of work productivity and a 32 % activity loss, and was associated with disease activity and age group. Average cost of productivity loss due to disability and sick leave with a human capital approach was 1,450 and 430 €/patient/year in IBD, respectively (total productivity loss 1,880 €/patient/year), the costs of presenteeism were 2,605 (SD = 2,770) and 2,410 (SD = 2,970) €/patient/year in CD and UC, respectively.

Conclusion Risk of DP was highly increased in young CD patients (sixfold to ninefold). Previous surgery and presence of arthritis/arthritis was identified as risk factors for DP. Work productivity is significantly impaired in IBD and is associated with high productivity loss.

Keywords UC · CD · Work disability · Productivity loss · Anti-TNF · Hungary

JEL Classification I190

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Introduction

Inflammatory bowel diseases (IBD), including primarily Crohn's disease (CD) and ulcerative colitis (UC), are chronic disabling gastrointestinal disorders with a variable disease course, but the majority of the patients eventually develop intestinal (penetrating or stricturing) or extraintestinal complications [1, 2].

This chronic and potentially debilitating disease course can represent a heavy burden for patients, impacting every aspect of the affected individual's life [3]. They account for substantial direct and indirect costs to the health care system and society. A large portion of the social costs associated with IBD are indirect and are associated with temporary or permanent work disability (WD) due to presenteeism, sick leave, or disability pension (DP). All of these are increasingly recognized as important negative outcomes.

In parallel, IBD treatment goals have evolved in the last ten years, with the advent of biological therapy [4]. A paradigm shift has occurred from merely treating symptomatic disease, toward the prevention of disease complications in patients with unfavorable prognostic factors; the latter being one of the main targets of current therapy. This prophylactic methodology potentially prevents hospitalizations and surgery [5], while also preserving quality of life and working ability—both recognized as important patient-centered outcome measures.

Work-disability rates of IBD patients vary considerably in the literature, with rates between 5.3 and 27.1 % reported [6–11]. Of note, the available studies were substantially different with regard to time periods, study design, definitions of disability, geographic area and patient cohorts. Additionally, there were differences in the social-security systems influencing possibly not only access to therapy but also employment and DP rates. Importantly, most studies were conducted in the pre-biologic era and very few studies included patient cohorts with a high exposure to biological (anti-tumour necrosis factor-alpha, anti-TNF) therapies [10].

Several factors have been associated with temporary or permanent WD, including disease type [6, 9, 10], the activity or presence of complications [10, 11], gender [8, 9, 12], age [9, 10], surgery [7, 10], hospitalisations [7], quality of life [7, 12], and education level [6, 10]. In addition, only few studies outside clinical trials have assessed WD objectively by using validated questionnaires such as the work productivity and activity impairment (WPAI) instrument [13, 14]. Data are missing from Eastern Europe. The aim of the present study was to assess the DP and WD rates in an IBD cohort treated in two IBD biological centers in Hungary, with easy access and high exposure to anti-TNF therapy. In addition, we sought to estimate the costs of productivity loss in IBD and identify possible clinical or demographic factors associated with DP and WD.

Patients and methods

Patients

Four hundred and forty-three consecutive patients treated with IBD (M/F 202/241, CD/UC: 260/183, mean age at

Table 1 Clinical characteristics of patients with IBD

Characteristics	CD	UC
n	260	183
M/F	122/138	80/103
Age at presentation (years)*	26.3 (11.2)	30.0 (13.0)
Age at assessment (years)*	35.7 (11.3)	40.7 (14.1)
Disease duration (years)*	9.2 (7.1)	9.9 (9.7)
Location**		
L1	16.9 %	NA
L2	33.1 %	
L3	48.8 %	
L4 only	1.2 %	
L4	7.3 %	
Extent at diagnosis		
Proctitis	NA	9.9 %
Left-sided		48.9 %
Extensive		41.2 %
Behavior at diagnosis***		
B1	36.9 %	NA
B2	24.6 %	
B3	38.5 %	
Perianal disease	34.6 %	NA
Arthritis/arthralgia	34.6 %	24.6 %
Azathioprine therapy	64.3 %	36.3 %
Biological therapy	31.2 %	11.5 %
Resection/re-operation in CD or colectomy in UC	41.1/ 32.7 %	8.3 %

NA not applicable

* Mean (SD)

** Classification of CD by location of the disease: L1, terminal ileum; L2, colon; L3, ileocolonic disease L4: upper GI involvement

*** Classification of CD by disease behavior: B1, inflammatory phenotype without stricture formation and penetrating disease; B2, stricturing disease; B3, penetrating disease

onset: 26.3 (SD = 11.2) and 30.0 (SD = 13.0) years, duration: 9.2 (SD = 7.1) and 9.9 (SD = 9.7) years with at least 1-year disease with complete clinical follow-up were included from two specialized IBD centers providing biological therapy in Hungary. The clinical characteristics are presented in Table 1.

Methods

Diagnosis was based on the Lennard-Jones criteria [15]. Disease phenotype (age at onset, duration, location, and behavior) was determined according to the Montreal classification [16]. Medical records, including data regarding the presence of major extraintestinal manifestations (EIM), previous frequency of flare-ups (frequent flare-up: >1

clinical relapse/year [17]), previous surgical procedures (resections or perianal procedures), the presence of familial IBD, smoking habits, and perianal involvement, were determined by a thorough review of the patients' medical charts, which had been collected in a uniform format. Previous and concomitant medical therapy (steroid or immunosuppressive, previous biological therapy) and actual disease activity (in CD the Crohn's Disease Activity Index (CDAI [18]) and Harvey–Bradshaw Index (HBI [19]), and in UC the Colitis Activity Index (CAI or MAYO score [20]) were meticulously registered parallel with the administration of the questionnaires. Both centers were monitored for quality of care and regulation compliance by the National Health Insurance Fund Administration (Országos Egészségbiztosítási Pénztár, OEP) in June 2011.

Work disability data were collected by a questionnaire from September 2012 to September 2013. Questions included full or partial DP, actual and previous employment, unemployment and the WPAI questionnaire V2 for CD and UC [21, 22]. From 2012 the Hungarian pension system grants two types of subsidies for disabled patients: full DP (disability subsidy) and a temporary partial DP (rehabilitation subsidy), as assessed by the Hungarian Central Administration of National Pension Insurance (Országos Nyugdíjbiztosítási Főigazgatóság, ONYF). Data on full DP in the background population were retrieved from public databases (ONYF) [23, 24]. The 2010 national full DP rates (total and both gender and age-group specific rates were available) were used for comparison.

The central coordination and database management was completed at the 1st Department of Internal Medicine, Semmelweis University (by MDM, BDL and PLL). The study was approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (117/2012).

Statistical methods

Descriptive statistics were calculated and variables were tested for normality using Shapiro–Wilk's W -test. The χ^2 -test and χ^2 -test with Yates correction and logistic regression analysis were used to assess the association between categorical clinical variables, and DP. The Mann–Whitney U -test, Spearman Rank Order correlation and the Kruskal–Wallis test were used to test the association between categorical variables, disease activity, and WPAI. Kaplan–Meier survival curves were plotted to determine probability of full DP.

We calculated the productivity loss due to disability with the human capital approach and friction cost method [25, 26], the productivity loss due to sick leave, the total productivity loss and the cost of presenteeism. For calculating disability-related productivity loss, we multiplied the

number of missed months due to disability per patient by the average monthly gross salary. We didn't distinguish full and partial disability in neither methods. The maximum calculated duration in human capital approach and friction cost method were 12 and six months, respectively. For calculating sick-related costs, we multiplied the average missed working hours/patient/week by the average gross hourly wage and the number of weeks in a year. The total productivity loss is the sum of these two components. For the estimation of the cost of presenteeism [27], we multiplied the average hours worked per week by the presenteeism score. The resulting lost hours due to presenteeism were multiplied by the average gross hourly wage and the number of weeks in a year. Data were retrieved from the databases of the Hungarian Central Statistical Office (KSH) for calculating the Hungarian average monthly gross salary and average gross hourly wage in 2013, including employment taxes (1.001 and 5.96 €, respectively). We assumed a maximum 40 h working week. The official Hungarian retirement ages (62 years for both genders) were used for the calculation. For currency conversion 300HUF = 1€ was assumed. Variables with $p < 0.1$ were included in multivariate testing. A p value < 0.05 was considered significant. For statistical analysis, SPSS® 20.0 was used.

Results

The patient characteristics are consistent with the previous IBD center-based cohorts (Table 1). The mean disease duration was 9–10 years. Almost 50 % of CD patients had extensive disease, and a complicated phenotype was observed in 63.1 %, while perianal involvement was observed in 34.6 %. Consequently, the need for immunosuppressives (64.3 %) or anti-TNFs (31.2 %) was frequent. At the time of the assessment 28.5 % of patients had active disease (CDAI > 150), while 15.2 % of patients had moderate-to-severe disease activity (CDAI > 220) with a mean CDAI of 113 (SD = 125) and HBI of 3.6 (SD 3.8). Similarly, in UC more than 41 % of patients had extensive location with a frequent use of immunosuppressives (36.3 %) or anti-TNFs (11.5 %). At the time of the assessment 24.6 % of patients had active disease with a mean partial Mayo score (pMAYO > 3) of 2.3 (SD 2.6).

Frequency of and risk factors for disability pension

The overall DP rate in this IBD population was 32.3 % with partial DP in 24.2 %. Of all DP events, 88.8 % were directly related to IBD. Of those patients with DP, 79 % (77.8 % with full DP) did work before the DP. For those

Table 2 The frequency and risk for disability pension (DP) according to the age groups in inflammatory bowel diseases (IBD) and Crohn's disease (CD) compared to the gender and age-matched background population

Age groups	Total DP (%)	Full DP (%)	OR ^b for full DP (95 % CI) ^b
IBD			
18–35	17.7	3.5	9.41 (4.54–19.5) [#]
36–40	33.7	8.2	5.60 (2.75–11.4) [#]
41–45	54.8	14.3	5.28 (2.52–11.1) [#]
46–50	38.7	6.5	1.25 (0.33–4.76)
51–62	59.6	21.0	1.34 (0.81–2.21)
CD			
18–35	21.6	4.5	12.2 (5.59–26.7) [#]
36–40	45.3	11.3	7.79 (3.67–16.6) [#]
41–45	68.0	20.0	7.4 (3.38–16.2) [#]
46–50	46.7	13.3	1.29 (0.19–8.56)
51–62	52.0	24.0	1.54 (0.76–3.08)

All of the frequency and risk values are negative in subgroup UC

[#] $p < 0.001$

^a Odds-ratio

^b vs controls

patients with partial- or full-DP, 63.5 and 32.2 %, respectively, felt that they could work. Fifty percent of patients with partial DP had a part time job. The probability of full DP in IBD at 5, 10, and 15 years from diagnosis was 6.0, 9.1 and 12.1 %, respectively, while in CD it was 6.2, 9.7 and 15.0 % (Fig. 1). Overall, full DP was more prevalent in IBD (8.1 %, RR: 1.51, $p = 0.016$) and CD (9.2 %, $p = 0.009$) but not in UC (6.6 %, $p = 0.56$) compared to the background population (5.5 %). The full DP rate was higher in CD compared to UC (OR 1.57, 95 % CI 1.04–2.38, $p = 0.038$). The partial and full DP rates in IBD increased gradually parallel with the age groups (from 17.7 % in the <35-year-olds to 59.6 % in the 51–62 year-olds). The RR for full DP was highest in patients with an age <35 years and 36–40 years (RR: 9.4 and 5.6, $p < 0.01$), while patients over 46 years of age had no increased RR (Table 2). In a sensitivity analysis, DP cases not related to IBD were excluded. All associations remained the same in both IBD (RR_{IBD<35 years}: 9.4, 95 % CI 4.5–19.5, RR_{IBD36–40 years}: 4.8, 95 % CI 2.1–10.9, RR_{IBD41–45 years}: 4.4, 95 % CI 1.7–11.3, $p \leq 0.001$ for all) and CD patients (RR-s were unchanged for patients younger than 46 years old).

In CD, age group ($p < 0.001$), previous surgery or colectomy (OR 4.48, 95 % CI 2.86–7.02), long disease duration (OR 3.06, 95 % CI 2.02–4.62), frequent relapses (OR 1.59; 95 % CI 1.03–2.46) and the presence of arthritis or arthralgia (OR 3.66, 95 % CI 2.37–5.64) but not disease phenotype, exposure to steroids, or the need for

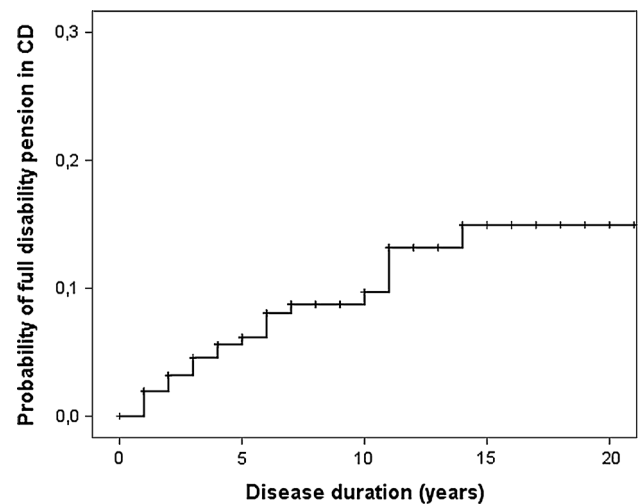


Fig. 1 Frequency of full disability pension (DP) in Crohn's disease (CD) according to disease duration

Table 3 Factors associated with DP in patients with CD in logistic regression analysis

	<i>p</i>	Odds ratio	95 % CI
Age decade	<0.001	1.47	1.22–1.77
Long (>10 years) disease duration	0.07	1.66	0.96–2.85
Frequent (>1/year) relapses	0.18	1.44	0.84–2.47
Arthritis/arthralgia	<0.001	3.41	1.98–5.89
Previous surgery	<0.001	5.40	3.10–9.41

azathioprine or biological were associated with increased risk for DP in univariate analysis. The association for age group, previous surgery and arthritis or arthralgia remained significant in a logistic regression analysis (Table 3).

Work productivity and activity impairment in inflammatory bowel diseases

We calculated productivity loss outcomes in the 212 full-time or part-time employed patients. Overall, absenteeism and presenteeism was reported in 25.9 % and 60.3 % patients, respectively. Absenteeism [8.5 % (SD 22.8 %) and 11.7 % (SD 26.1 %)], presenteeism [27.6 % (SD 28.1 %) and 24.5 % (SD 28.4 %)], activity loss [33.9 % (SD 29.4 %) and 31.0 % (SD 31.2 %)] and work productivity loss [28.8 % (SD 29.4 %) and 27.6 % (SD 31.8 %)] as assessed by missing days was not different in CD and UC patients. In contrast, it was significantly different according to IBD activity (26.9 % of IBD patients reported IBD activity at WPAI assessment according to CDAI or partial Mayo score, Fig. 2) in all patients as well as in CD and in UC separately (data not shown). Similarly, previous surgery or colectomy was associated with all parameters

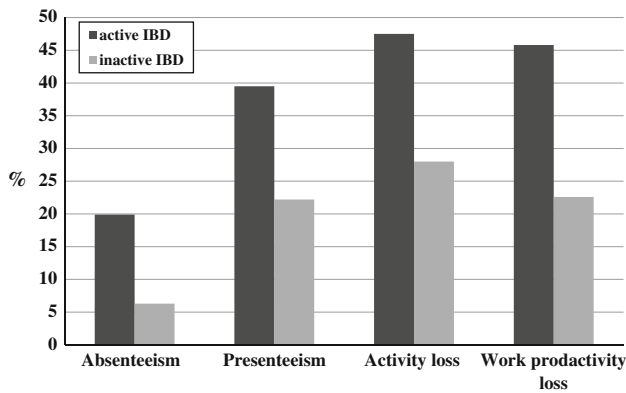


Fig. 2 Absenteeism, presenteeism, activity loss and work productivity loss according to the disease activity in patients with IBD

($p_{\text{absenteeism}} = 0.003$, $p_{\text{presenteeism}} = 0.04$, $p_{\text{activity loss}} = 0.06$ and $p_{\text{work productivity loss}} = 0.026$) (Table 4).

In addition, presenteeism ($p = 0.03$) and activity loss ($p < 0.001$) was associated with age groups by Kruskal–Wallis test as well as presenteeism ($p = 0.001$ for both). Activity loss ($p < 0.001$) and work productivity loss ($p = 0.02$ and $p = 0.001$) were associated with long disease duration and presence of arthritis/arthritis.

Productivity loss due to disability and sick leave, the cost of presenteeism

The average cost of productivity loss due to disability with human capital approach was 1,450 (SD = 3,905) €/patient/year in IBD. In CD, the cost was 1,545 (SD = 4,010) €/patient/year, while it was 1,310 (SD = 3,740) €/patient/year in UC. There was no significant difference between the two subgroups ($p = 0.505$). We calculated the productivity loss due to disability with the friction cost method as well. Only one patient became eligible for DP in the last six months before data collection. Due to this, the average cost was 11.3 (SD = 240) €/patient/year. The average number of missed working hours was 1.39 (SD = 5.87) hours/patient/week and the average cost of productivity

loss due to sick leave was 430 (SD = 1,820) €/patient/year in IBD. The number of missed working hours in CD and UC were mean 1.28 (SD = 5.64) and 1.56 (SD = 6.20) hours/patient/week, leading to sick-leave related costs of mean 395 (SD = 1,750) and 485 (SD = 1,920) €/patient/year, respectively. There was no significant difference in sick-leave related costs between the two subgroups ($p = 0.576$).

The total productivity loss with the human capital approach was 1,880 (SD = 4,310) €/patient/year in IBD. In CD, the total productivity loss was 1,940 (SD = 4,375) €/patient/year, while it was 1,795 (SD = 4,220) €/patient/year in UC. The total productivity loss with the friction cost method was 445 (SD = 1,835) €/patient/year in IBD.

The average hours worked in CD and UC were 30.42 (SD = 13.84) and 31.73 (SD = 13.24) hours/patient/week, respectively. The lost hours due to presenteeism were mean 8.40 (SD = 8.93) and 7.77 (SD = 9.58) hours/patient/week, while the costs of presenteeism were 2,605 (SD = 2,770) and 2,410 (SD = 2,970) €/patient/year in CD and UC, respectively. There was no significant difference between the two subgroups ($p = 0.455$).

Discussion

The main finding of the present study was a sixfold to ninefold increased risk for DP in young patients CD despite easy access and high percentage of biological therapy in these patients in this consecutive IBD cohort treated in specialized IBD centers. In addition, absenteeism and presenteeism were frequent among full or part time employed patients (25.9 % and 60.3 % respectively) with the latter becoming more common with age. Besides age, factors associated with DP or WD were previous surgery, long disease duration, and arthralgias/arthritis.

Full and partial DP rates identified in our study were, to some extent, different from recent reports from Europe and North America. In one of the landmark population-based study from the IBSEN cohort [9], the frequency of full DP

Table 4 Correlation between absenteeism, presenteeism, activity loss, work productivity loss and disease activity in Crohn’s disease (CD) and ulcerative colitis (UC)

	CD				UC	
	CDAI index		HBI index		pMAYO index	
	Coefficient	p value	Coefficient	p value	Coefficient	p value
Absenteeism	0.22	0.01	0.35	<0.001	0.45	<0.001
Presenteeism	0.21	0.007	0.39	<0.001	0.51	<0.001
Activity loss	0.36	<0.001	0.39	<0.001	0.37	<0.001
Work productivity loss	0.30	<0.001	0.48	<0.001	0.60	<0.001

Spearman Rank Order correlation, CDAI Crohn’s disease activity index, HBI: Harvey–Bradshaw index, pMAYO partial Mayo score

was 18.8 % in IBD after 10-years' disease duration in 518 patients during follow-up. The DP rate was 8.5 % in an earlier report after five years [8]. Rates were not different in CD and UC, but an approximately twofold risk was reported in females, and was even higher in patients receiving steroids 1-year after diagnosis. However, this cohort dated back to the pre-biologic era, with only very limited biologic exposure. Interestingly, the rate of full-DP unrelated to IBD was exceedingly high in UC. Relative risks for UC related DP rates were not calculated.

Somewhat contrastingly, in a report from the South Limburg cohort in 2000 [6], authors reported a 13 % and 24 % risk for full DP in UC and CD, respectively, with an 8–14 % partial-DP rate after a median 7 years' disease duration in 680 IBD patients. Rates in this cohort were similar in males and females, but were associated with young age at onset and higher educational level. DP rates were lower in a recent nationwide IBD cohort ($n = 2,282$) from the Netherlands [10]. In this cohort, patients had a high exposure to biologicals (CD: 33.3 % and UC: 9.5 %), and reported full-DP or partial-DP rates were 18.8 % and 8 %, respectively, in CD, and 9.5 % and 5.4 %, respectively, in UC after median disease duration of 16 and 14 years. Overall, RR was increased over the background population. Factors associated with DP were higher age, low education, depression, chronic back pain, joint manifestations and disease-related risk factors such as penetrating disease phenotype. In addition, steroid use was associated with DP in UC.

In the present study, in a CD cohort with similar high exposure to anti-TNFs, the probability of full DP was increased only in CD, with a cumulative probability of 9.7 % and 15 %, respectively, at ten and 15 years from diagnosis. Both partial-DP and full-DP rates increased with age. In contrast, the relative risk of DP was increased only in patients younger than 46 years of age, and was associated with previous surgery and arthritis/arthritis, but not gender, disease phenotype, exposure to steroids, immunosuppressives or anti-TNFs. A similar age-dependent increase in disability rates was also reported in the IBSEN cohort and a recent report from the Swiss IBD cohort [11]. In the latter, DP rates increased from 2 % to 23 % in CD and from 3 % to 7 % in UC in the >25–35 to >55 years-olds in the 1,187 patients after a median of ten and seven years of follow-up, respectively.

Similar rates were recently reported from the Manitoba IBD cohort from Canada [14]. WD rates were 19 % in CD and 11 % in UC ($p < 0.05$), as assessed by the Work and Social Adjustment Scale (WSAS). Disability was associated with long-term active disease and depression but not IBD-related surgeries or hospitalizations. Finally, only a 5.3 % permanent WD rate was reported from an IBD center cohort ($n = 737$, duration 13.8 years) from the US

[7]. Patients reporting low quality of life (OR 12.4), or requiring multiple surgeries (OR 7.09) or hospitalizations (OR 2.76) were identified to be at risk for CD-related WD in a subcohort of 185 patients.

Significantly, less data are available on temporary WD in IBD outside clinical trials. In addition, most studies had only a semiquantitative assessment of WD. Earlier studies reported an association between overall WD, employment status and quality of life (HRQL and SF36) [8, 12]. In a recent study by the Swiss group, authors investigated frequency and predictors of temporary WD. Temporary WD was reported in one-fifth of IBD patients at enrollment (median disease duration of ten years in CD and seven years in UC) and in 12–13 % during the 13-month prospective follow-up. Predictors for days absent and temporary WD in CD were gender, disease duration, disease activity, C-reactive protein level, smoking, depression, presence of fistulas, EIM, and the use of immunosuppressants or steroids. In UC it was associated with gender, age, disease duration, disease activity, and the use steroids or antibiotics. In addition, in a very recent Australian study [13], authors assessed healthcare utilization, cost, and work-related impairment in patients with UC. Similar to the present study, WD was determined by the WPAI questionnaire. WPAI was associated with quality of life assessed by Assessment of Quality of Life—8-Dimension (AqoL-8D), EuroQol 5-dimension, 5-level (EQ-5D-5L), the disease-specific Inflammatory Bowel Disease Questionnaire (IBDQ). In concordance with previous studies, quality-of-life measures were associated with disease severity. In addition, disease activity was identified as the main driver of health care costs and the predictor for impairment in work productivity and daily activities. Of note, the close correlation between WPAI and disease activity suggests that WPAI assessment can be used as a patient reported activity measure. Overall, UC patients reported substantial UC-related impairment on all four categories of the WPAI, with the greatest level of impairment (30.9 %) in daily activities other than work. In contrast, mild disease activity was associated with moderate impairment only. Similarly, disease activity was identified as the main predictor for all four items of the WPAI. However, in contrast to the previous study we failed to identify significant differences in the WPAI outcomes between mild and moderate-to-severe patients in either UC (pMayo mild = 3–4, moderate to severe >4) or CD (CDAI mild: 151–220, moderate to severe >220), however, both were significantly different from the patients in remission ($p < 0.02$ for presenteeism, work productivity loss and activity loss in CD and $p < 0.01$ for all comparisons for UC by Mann–Whitney U test between patients in remission and different disease activity and $p < 0.001$ by Kruskal–Wallis test for the whole group).

This is the first time that costs for productivity loss in IBD have been estimated from an Eastern European country. Average cost of productivity loss due to disability and sick leave with human capital approach was 1,450 and 430 €/patient/year, respectively, (total productivity loss was 1,880 €/patient/year, which represents a high economic burden, especially compared to the monthly gross salary. These figures are comparable from that reported in other chronic inflammatory diseases, e.g., psoriatic arthritis (PsA) or rheumatoid arthritis (RA) from the same region or compared to the monthly gross salaries. For instance, in Hungary, the total indirect cost was 2,660 €/patient/year in PsA, 4,240 €/patient/year in RA, whilst in the Netherlands productivity loss of RA was 5,545 €/patient/year and 8,605 €/patient/year in Finland (costs were recalculated with prices from 2013 and with the actual exchange rates for the comparison) [28–33].

The authors are aware of possible limitations of the present study. The study investigated a referral IBD population treated in two specialized IBD centers and results may not be generalizable to population-based and non-IBD center cohorts. In addition, some possible confounders (e.g., highest education level) were not assessed, as there was a change in the reimbursement policy of anti-TNFs in Hungary in 2008. After 2008, the anti-TNF use has become more widespread with easier and earlier use in CD and UC patients with poor prognostic factors. However, in the present cohort, a significant proportion of patients may have received anti-TNFs according to the earlier reimbursement strategy only at a later disease stage, thereby the therapeutic approach was suboptimal. This may have influenced the association between anti-TNFs and the DP outcome. In contrast, the strengths of this study include vigorous prospective data collection and a detailed definition of the clinical phenotypes. In addition, the centers included apply an accelerated treatment and monitoring strategy in IBD patients and so the step-up to anti-TNFs is far quicker compared to community centers. Our calculation likely overestimates the actual cost of presenteeism, due to lack of standardization of evaluation of productivity costs we have to be very cautious in the interpretation of these results [34], and further research is needed.

In conclusion, in this contemporary IBD cohort with a high exposure to anti-TNFs, the risk of DP was highly increased in only young CD patients (sixfold to ninefold). Previous surgery and presence of arthritis/arthralgia was identified as risk factor for DP. Work productivity is significantly impaired in IBD, and it is associated with age and disease activity.

Conflict of interest The authors do not have any competing interest.

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