High Impact of Pediatric Inflammatory Bowel Disease on Caregivers' Work Productivity and Daily Activities: An International Prospective Study

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Objectives To evaluate the longitudinal evolution of work productivity loss and activity impairment in caregivers of children with inflammatory bowel disease (IBD). We also evaluated the associations between these impairments, IBD-related factors, and caregivers' health-related quality of life (HRQOL) and estimated the indirect costs related to work absenteeism.

Study design Since January 2017, children with newly diagnosed IBD were enrolled prospectively in the Pediatric Inflammatory Bowel Disease Network for Safety, Efficacy, Treatment and Quality improvement of care study. The impact of pediatric-onset IBD on caregivers' socioeconomic functioning (work and daily activities) and HRQOL was assessed using the Work Productivity and Activity Impairment for caregivers questionnaire and the European Quality of Life Five Dimension Five Level questionnaire, at diagnosis and 3 and 12 months of age. Generalized estimating equation models were applied to evaluate outcomes longitudinally, adjusted for IBD type, disease activity, and child's age at diagnosis.

Results Up to July 2021, 491 children with IBD were eligible for analysis of caregivers' Work Productivity and Activity Impairment questionnaire. At diagnosis, the mean caregivers' employment rate was 78.4%; the adjusted mean work productivity loss was 44.6% (95% CI, 40.2%-49.0%), and the adjusted mean activity impairment was 34.3% (95% CI, 30.8%-37.7%). Work productivity loss and activity impairment significantly decreased over time and were associated with disease activity, but not with IBD type or child's age. Caregivers' HRQOL was associated with both impairments. Costs related to work absenteeism were at least €6272 ($7276) per patient during the first year after diagnosis.

Conclusions Caregivers of children with IBD experience significant impairments in work and daily activities, especially at diagnosis. The impact decreases thereafter and is associated with disease activity and caregivers' HRQOL. Work absenteeism results in high indirect costs. *(J Pediatr 2022;246:95-102)*.

Pediatric inflammatory bowel disease (IBD) impacts the physical, psychological, and socioeconomic functioning of patients and their caregivers. The incidence of this chronic relapsing-remitting disease, comprising Crohn's disease (CD), ulcerative colitis (UC), and IBD unclassified, is increasing.[1-3]

Studies in children with chronic diseases other than IBD have shown that a chronic disease has a substantial impact on the patient, their families, and working caregivers.[4] Children with a chronic disease often require additional care; this in turn affects the time available for employment or leisure activities for their caregivers.[5] Because school absence is higher in children and adolescents with IBD than in healthy children, this factor may force caregivers to miss work.[6-8] In addition, children with IBD have increased health service use, including

CD	Crohn's disease	IBD	Inflammatory bowel disease
COVID-19	Coronavirus disease 2019	LFS	Labor Force Survey
EU	European Union	PGA	Physician's global assessment
FPA	Friction period approach	UC	Ulcerative colitis
GEE	Generalized estimating equations	VAS	Visual analogue scale
		WPAI	Work Productivity And Activity Impairment
HRQOL	Health-related quality of life		

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Conference presentations: Portions of this study were presented as a poster during the European Crohn's and Colitis Organisation (ECCO) 2021 congress (virtual), July 8-10, 2021 and will be presented as an oral presentation at the European Society of Pediatric Gastroenterology, Hepatology and Nutrition meeting, June 22-25, 2022, Copenhagen, Denmark.

List of PIBD-SETQuality consortium members are available at www.jpeds.com (**Appendix 2**): Dan Turner, Gili Focht, Janneke Samsom, Gigi Veereman, Sibylle Koletzko, Annecarin Brückner, Arie Levine, Richard Russell, Anne Griffiths, Marina Aloi, Thomas Walters, and Michael Walker.

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diagnostic procedures, infusions of biologics, outpatient clinic visits, and other hospitalizations.[9,10]

Two studies have assessed the effect of pediatric IBD on caregivers' work status, productivity loss, or activity impairment; both reported high absence from work in caregivers of children with IBD.[11,12] However, these retrospective studies included patients with different disease stages and were not designed to evaluate IBD-related factors associated with the impairments.

This international prospective study aimed to assess the longitudinal evolution of work productivity loss and activity impairment in caregivers of children with IBD, to examine IBD-related factors associated with these impairments, and to estimate the indirect costs resulting from work productivity loss.

Methods

Data were obtained from the observational Pediatric Inflammatory Bowel Disease Network for Safety, Efficacy, Treatment and Quality improvement of care inception cohort study. In this prospective international study, children aged 0-18 years with newly diagnosed IBD were enrolled and followed longitudinally. Details on this cohort and its data collection have been published elsewhere.[13] At fixed time points, data on caregiver's socioeconomic functioning (work and daily activities) and health-related quality of life (HRQOL) was collected via questionnaires. Patients included in the inception cohort between January 1, 2017, and July 1, 2021, were eligible for this study. Patients were excluded if no questionnaire was returned at either baseline or any follow-up visit. No minimum follow-up was required.

Outcome Measures

Socioeconomic Functioning of Caregivers. The impact of the child's IBD on caregivers' socioeconomic functioning was assessed using the Work Productivity and Activity Impairment (WPAI) questionnaire, a validated questionnaire for which a caregiver's version for children with IBD had been developed (**Appendix 1**; available at www.jpeds.com).[14] The caregivers were made up of parents (biological, adoptive, or step-parents), foster parents, or relatives who looked after the child. The WPAI survey consists of 6 questions and uses a recall period of 7 days. Caregivers had to indicate if they were employed, how many hours they worked during the past 7 days, and how many hours they missed. For hours of missed work, they were asked to indicate whether this was due to their child's IBD or other reasons, such as vacation. In addition, employed caregivers were asked to report to which extent (scale of 0-10) their child's IBD influenced their working productivity. The primary outcome measures owing to the child's IBD included: absenteeism, presenteeism, and work productivity loss (for calculations, see **Appendix 1**).[15] Absenteeism was defined as the percentage of work time missed. Presenteeism was defined as the percentage of impairment while working. Work productivity loss was defined as the percentage of overall work impairment. All caregivers also reported to what extent (scale of 0-10), their child's IBD affected their ability to perform regular daily activities, such as household tasks, shopping, childcare, exercising, or studying, excluding their job. Activity impairment was defined as the percentage of those affected daily activities.

The WPAI questionnaire was completed at the time of diagnosis (baseline), then at 3 and 12 months after diagnosis. Questionnaires were completed during the study visit at the hospital or sent to patients' home addresses directly after the visit and returned. Questionnaires were completed by 1 or both parents, depending on the setting and caregivers' preference. This practice varied between visits for individual patients. Data from each completed WPAI questionnaire were analyzed separately, without averaging data if both caregivers completed the questionnaire. If only 1 caregiver completed the questionnaire, we conservatively assumed only 1 caregiver was affected by the child's disease. To investigate potential bias, a sensitivity analysis was performed to compare WPAI outcome measures between those visits where 1 caregiver completed the questionnaire and those where both caregivers completed the questionnaire. In another sensitivity analysis, we aimed to investigate the impact of the coronavirus disease 2019 (COVID-19) pandemic on work productivity loss and activity impairment. To do so, we compared work productivity losses for visits dated before and visits dated after March 11, 2020, which was the date the World Health Organization officially declared the COVID-19 outbreak a pandemic.

HRQOL. Caregivers' HRQOL was assessed using the European Quality of Life Five Dimension Five Level (EQ-5D-5L) questionnaire, a standardized instrument that measures health status in terms of 5 dimensions, using a 5-level scale.[16] Respondents also rated their own overall health status on a visual analogue scale (VAS) from 0 to 100. The EQ-5D-5L questionnaire was available in all necessary translations for centers participating in the inception cohort.

HRQOL scores (VAS score divided by 10) were obtained for each EQ-5D-5L questionnaire separately, and averaged if both caregivers had completed this questionnaire. These averages were then coupled with the WPAI data of each individual caregiver, corresponding with the patient's visit.

Clinical Data Collection

Baseline demographics and clinical data were collected routinely during hospital visits simultaneously with the distribution of questionnaires. Disease activity was scored at each visit, using the Pediatric Ulcerative Colitis Activity Index or the Weighted Pediatric Crohn's Disease Activity Index, and was categorized into 3 groups (remission, mild, moderate to severe) using validated cut-offs of these scores (**Appendix 1**).[17,18] At baseline, disease location and extent,

disease behavior, and the presence of perianal disease were classified according to the Paris classification (**Appendix 1**).[19]

Statistical Analyses

Continuous data were presented as mean and SD/CI or median and IQR. Data obtained from the WPAI questionnaire were presented as means, irrespective of distribution, because means rather than medians are of fundamental interest in health economics evaluations.[20] The frequencies of categorical variables were compared using the χ^2 test or Fisher exact test. All statistical tests were 2 sided and a P value of less than .05 was considered statistically significant.

Unadjusted estimates of mean employment rate, absenteeism, presenteeism, work productivity loss, and activity impairment were calculated for each visit based on all available questionnaires using generalized estimating equations (GEE) models, while accounting for disease duration (0, 3, or 12 months) and IBD type (CD or UC/IBD unclassified). A GEE model is a semiparametric model that allows repeated measurements per patient and does not require a normal distribution of the outcome. Based on the lowest quasi likelihood under independence model criterion, we selected a first-order autoregressive correlation structure and used robust variance estimators. These GEE models were also applied to calculate the adjusted estimates, by correcting for disease duration, IBD type, child's age at diagnosis, and disease activity (remission, mild, or moderate to severe). Possible interactions between IBD type and disease duration and between disease activity and disease duration were tested in these models. To investigate HRQOL, we included in these models caregivers' average HRQOL, as measured by the VAS. Data were analyzed using SPSS Statistics for Windows, version 25.0 (IBM) and R statistics, version 4.0.3 (R Core Team).

Employment details (eg, employment rate, weekly work time) at baseline were compared with employment details of the European Union (EU) in 2019, using a 1-sample t test. EU employment details were obtained from Eurostat, using the EU Labor Force Survey data.[21] The EU employment rate represent unemployed persons as percentage of the labor force.

Indirect Costs

Indirect costs of productivity loss by absenteeism were calculated by the human capital approach, which takes the patient's perspective and calculates productivity costs as the product of those hours lost with the hourly wage. Based on the 2015 Dutch guideline for health economic evaluations, costs related to 1 hour of productivity loss were €34.75 ($41.35).[22] Costs were calculated in Euros and converted to US dollars, using the currency of October 4, 2021 (€1 = $1.16). A detailed description and example of calculating indirect costs is presented in **Appendix 1**. Indirect costs of presenteeism were not calculated, as most national guidelines generally do not include practical instruments to generate productivity costs owing to presenteeism.[23]

Ethics Statement and Informed Consent

The Pediatric Inflammatory Bowel Disease Network for Safety, Efficacy, Treatment and Quality improvement of care study was first approved by the institutional ethics committee of the Erasmus Medical Center in Rotterdam, the Netherlands, and subsequently by all other relevant ethics committees for each center. Written informed consent was obtained by caregivers or legal guardians of study participants and, when appropriate according to national regulations, by patients themselves.

Results

During the study period, 658 patients from 29 centers (23 European centers) were enrolled. Of these, 99 patients were not eligible for analyses of the WPAI questionnaire because there was no available questionnaire translation for the language spoken by the caregiver (n = 26), questionnaires were not used at the site (n = 23), or the patient was recruited before the introduction of the WPAI questionnaire at the site (n = 50). The remaining 559 patients were eligible for this study (**Table I**; available at www.jpeds.com).

For 491 patients (87.8%), at least 1 questionnaire was returned by either 1 or both caregivers during the study period. The number of completed questionnaires per country is presented in **Table II** (available at www.jpeds.com). In total, 1033 questionnaires were returned at 856 visits, indicating that, for 20.6% of the visits, both caregivers completed the questionnaire. At baseline, 67.4% of patients had at least 1 questionnaire completed by either 1 or both caregivers (**Table III**; available at www.jpeds.com), similar to the completion rate of all follow-up visits combined (63.1%; P = .10).

Patient and IBD Characteristics

CD was diagnosed in 292 patients (60%), of whom 62% had moderate-to-severe disease activity at baseline (**Table IV**). The median age at IBD diagnosis was 13.6 years (IQR, 11.0-15.2). There were no significant differences in age at diagnosis (P = .15) or disease activity (P = .09) between children with CD and those with UC/IBD unclassified.

Employment Status

At the time of diagnosis, 78.7% (95% CI, 74.5%-82.3%) of caregivers who had completed the questionnaire were employed (**Table V**). This rate is significantly lower than the employment rate in the EU (93.3%; P < .001).[24] The adjusted mean employment rate at baseline was 78.4%, similar to that at 3 months (76.7%; P = .54) or at 12 months (77.5%; P = .78) (**Tables VI** and **VII**; available at www.jpeds.com). Employment rates were independent of IBD type (P = .18), disease activity at the time of assessment (P = .33), and the child's age at diagnosis (P = .67) (**Table VI**).

Table IV. Baseline demographics and clinical disease characteristics of pediatric IBD study population

Patient characteristics	CD (n = 292; 59.5%)	UC/IBD unclassified (n = 199; 40.5%)	Total (n = 491)
Male sex	178 (61.0)	111 (55.8)	289 (58.9)
Age at diagnosis, years	13.7 (11.4-15.1)	13.2 (10.3-15.2)	13.6 (11.0-15.2)
Paris classification*			
Location (L)/extent (E)	L1-66 (24.8)	E1-15 (8.9)	
	L2-40 (15.0)	E2-34 (20.2)	
	L3-154 (57.9)	E3-20 (11.9)	
	L4-6 (2.3)	E4-99 (58.9)	
Disease behavior (B)	B1-215 (82.7)	n/a	
	B2/B3-45 (17.3)		
Perianal disease (P)	53 (19.3)	n/a	
Disease activity			
None/remission†	15 (5.2)	12 (6.1)	27 (5.6)
Mild	93 (32.5)	62 (31.5)	155 (32.1)
Moderate	93 (32.5)	82 (41.6)	175 (36.2)
Severe	85 (29.7)	41 (20.8)	126 (26.1)
Induction treatment			
EEN	166 (56.8)	n/a	
Corticosteroids	49 (16.8)	105 (52.8)	
5-ASA	6 (2.1)	76 (38.2)	
Upfront anti-TNF	56 (19.2)	14 (7.0)	
Other	15 (5.1)	4 (2.0)	

5-ASA, 5-aminosalicylic acid; *anti-TNF*, anti-tumor necrosis factor; *EEN*, exclusive enteral nutrition; *n/a*, not applicable.
Values are number (%) or median (IWR). Baseline characteristics of all pediatric patients with IBD included in the study, eligible for analysis of the WPAI questionnaire for caregivers.
*L1, terminal ileal ± limited cecal disease; L2, colonic disease; L3, ileocolonic disease; L4, isolated upper disease; E1, proctitis; E2, left-sided (distal to splenic flexure); E3, extensive (proximal to splenic flexure); E4, pancolitis; B1, nonstricturing, nonpenetrating behavior; B2, stricturing behavior; B3, penetrating behavior.
†There were 27 patients who had disease activity scores within the remission range at diagnosis. Those were mainly patients with few symptoms or patients without symptoms the week before assessment. Missing values for each variable were: disease activity n = 8 (6 CD, 2 UC/IBD unclassified); location/extent n = 57 (26 CD, 31 UC/IBD unclassified); disease behavior n = 32; and perianal disease n = 17.

Absenteeism, Presenteeism, and Work Productivity Loss at the Time of Diagnosis

The average weekly work time of caregivers in our study (37.2 hours) is similar to that of employed persons in the EU (37.1 hours; $P = .19$).[25] However, employed caregivers worked on average 24.0 hours per week (95% CI, 22.1-26.1) at the time of diagnosis (Table V), after missing on average 10.5 hours (95% CI, 9.0-12.0) in the past 7 days owing to their child's IBD and 2.7 hours (95% CI, 1.7-3.6) owing to other reasons. The unadjusted mean absenteeism rate was 32.0%, unadjusted mean presenteeism 34.7%, and unadjusted mean work productivity loss was 51.2%, all not significantly different between caregivers of children with CD and UC/IBD unclassified.

Predictors of Absenteeism, Presenteeism, and Work Productivity Loss

Absenteeism, presenteeism, and work productivity loss significantly decreased over time (Figure 1, A-C, Tables VI and VII). Adjusted mean work productivity loss for caregivers of children with IBD was 44.6% at diagnosis. This impairment significantly decreased afterwards, to 27.8% 3 months after diagnosis and 24.2% 12 months after diagnosis ($P < .001$). Differences between work productivity loss at 3 months and 12 months were not significant ($P = .21$). Evaluation of predictors of work productivity loss is described in Table VI. More severe disease activity at the time of assessment was significantly associated ($P < .001$) with increased work productivity

Table V. Unadjusted employment rate and work-related outcomes of caregivers of children with IBD at time of IBD diagnosis

Outcomes	CD (n = 292)	UC/IBD unclassified (n = 199)	Total (n = 491)	*P* value
No. of completed questionnaires	283	182	465	
Employment rate	76.5 (71.4-81.0)	80.7 (75.0-85.3)	78.7 (74.5-82.3)	.21
Hours worked in the past 7 days	23.7 (21.5-25.9)	24.4 (21.8-27.0)	24.0 (22.1-26.1)	.64
Hours missed owing to the child's IBD	10.3 (8.7-11.8)	10.7 (8.7-12.7)	10.5 (9.0-12.0)	.64
Absenteeism	32.0 (27.5-36.5)	31.8 (26.9-36.6)	31.9 (27.8-35.9)	.93
Presenteeism	34.7 (30.4-38.9)	33.2 (28.3-38.1)	33.9 (30.1-37.8)	.57
Work productivity loss	51.5 (46.6-56.4)	51.0 (45.3-56.6)	51.2 (46.8-55.6)	.87

Data are unadjusted means (95% CI). Unadjusted means were calculated using the GEE models, accounting for only IBD diagnosis and disease duration. *P* values are for comparison between CD and UC/IBD unclassified. Missing values at baseline for each outcome were 0 for employment rate, 13 for absenteeism (5 CD, 8 UC/IBD unclassified), 15 for presenteeism (8 CD, 7 UC/IBD unclassified), 20 for work productivity loss (9 CD, 11 UC/IBD unclassified).

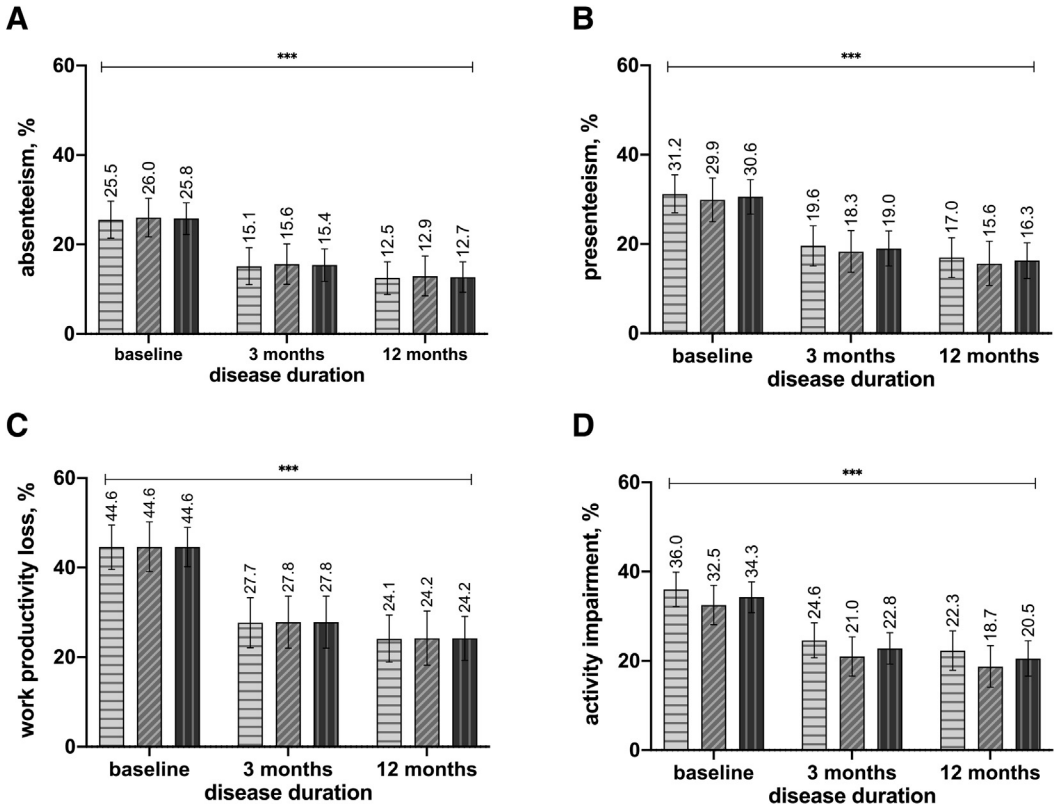

Figure 1. Caregivers' absenteeism, presenteeism, work productivity loss, and activity impairment by their child's IBD disease duration. **A,** Absenteeism (absence from work), **B**, Presenteeism (reduced productivity while at work), **C,** Work productivity loss (overall work impairment), and **D,** Activity impairment of caregivers of children with IBD, at time of diagnosis, and 3 months or 12 months after diagnosis, presented per IBD type. Bars indicate adjusted means (95% CI). Adjusted means were calculated using a GEE model, accounting for IBD diagnosis, age at diagnosis, disease activity, and disease duration as predictors. ***$P < .001$. P values are for the predictor variable disease duration in the GEE model.

loss (**Figure 2**, A, **Table VIII**; **Table VII** available at www.jpeds.com). No significant differences were observed between caregivers of children with UC/IBD unclassified and CD ($P = .97$). Age at IBD diagnosis was not associated with absenteeism, presenteeism, or work productivity loss (**Table VI**).

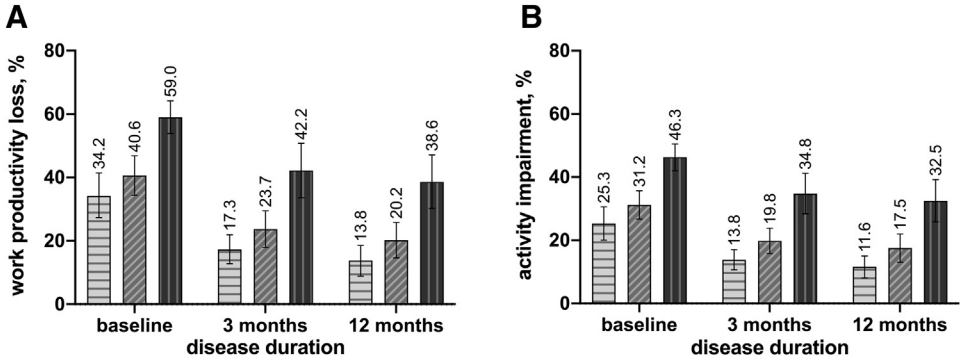

Figure 2. Caregivers' work productivity loss and activity impairment by their child's IBD disease duration and disease activity. **A,** Work productivity loss (overall work impairment) and **B,** Activity impairment of caregivers of children with IBD, according to disease duration and disease activity. Bars indicate adjusted means (95% CI). Adjusted means were calculated using a GEE model, accounting for IBD diagnosis, age at diagnosis, disease activity, and disease duration as predictors.

Indirect Costs

The estimated annual costs related to absenteeism during the first year after diagnosis were at least €6272 ($7276) per patient: €5990 ($6949) for children with CD and €6538 ($7584) for children with UC/IBD unclassified (Table VII).

Activity Impairment

At the time of diagnosis, caregivers had an average activity impairment related to their child's IBD of 34.3% (Figure 1, D). This impairment decreased to 22.8% at 3 months and 20.5% at 12 months after diagnosis, both significantly lower than at baseline ($P < .001$). There were no significant differences between caregivers of children with CD and UC/IBD unclassified ($P = .97$). Higher disease activity was associated with increased activity impairment ($P < .001$), irrespective of disease duration. Mean activity impairment for each disease activity by disease duration is presented in Figure 2, B and Table VIII.

Association with HRQOL

The mean caregiver HRQOL, as measured by the VAS, at time of diagnosis was 8.05/10 (Figure 3; available at www.jpeds.com). HRQOL was not associated with disease duration ($P = .52$) or IBD type ($P = .75$), but was associated with the child's age at diagnosis ($P = .009$) and disease activity ($P = .004$). When including HRQOL as predictor of work productivity loss, we found an independent association between caregivers' HRQOL and work productivity loss ($\beta = -0.368$; 95% CI, −0.593 to −0.143; $P = .001$). Similarly, caregivers' HRQOL was independently associated with activity impairment ($\beta = -0.307$; 95% CI, −0.464 to −0.150; $P < .001$).

Sensitivity Analyses

The reported work productivity losses owing to the child's IBD were lower during the COVID-19 pandemic than before (28.4% vs 34.8%; $P = .02$). Caregivers' activity impairment owing to the child's IBD were similar before and during the pandemic ($P = .11$). Work productivity loss was higher for those visits where only 1 caregiver had completed the questionnaire than for those visits where both caregivers had completed the questionnaire ($P = .03$), with mean rates of 47.0% (95% CI, 42.0%-51.9%) vs 41.0% (95% CI, 35.7%-46.3%) at baseline.

Discussion

This prospective study documented the substantial impact of pediatric IBD on caregivers' work status and daily activities, with 25.8% absence from work and 30.6% decreased productivity at work for caregivers of children with IBD at the time of diagnosis. Three months after diagnosis, the work productivity loss is nearly one-halved, and stabilizes thereafter up to 1 year. In a drug trial in children with UC, caregivers' overall work impairment decreased by 25% and 30% at 3 months and 1 year, respectively, after the child started adalimumab treatment, thus showing a trend similar to our findings.[26] Stawowczyk et al, using the same WPAI questionnaire, reported an absenteeism of 20.8% and presenteeism of 35.3% at baseline.[12] Both studies included children in various stages of the disease. Another retrospective study found that caregivers of children with CD had 214.4 annual hours of work loss compared with 169.6 hours for controls, indicating an absenteeism of 20.9% that might be attributed to the IBD.[11] These findings demonstrate that the impact on caregivers' work status is greatest at the time of diagnosis and during active disease, but that it remains important throughout the course of the disease. This finding is similar in other chronic childhood diseases. For example, a study assessing caregiver burden of children with uncontrolled asthma reported work impairment of similar magnitude.[27] Similar to our finding that there is 1.5- to 3.0-fold higher productivity loss in children with moderate-to-severe disease activity (compared with those in remission), parents of patients with cystic fibrosis reported higher work productivity losses during exacerbations (54%) than during well disease states (28%).[28] Stawowczyk et al also reported differences in productivity losses between parents of children with active IBD and those with inactive IBD (50% vs 26%; $P = .02$).[12]

Productivity losses owing to absenteeism are associated with significant costs, estimated to be at least €6272 ($7276) per patient in the first year after diagnosis. The literature on costs in children with IBD is scarce.[29] Annual absenteeism costs reported in 3 other studies ranged from €902 ($1046) to €1154 ($1339), lower than in our study.[11,12,30] This could be explained by the fact that these cross-sectional studies did not calculate costs specifically for the first year after diagnosis, the year with the highest cost. Additionally, in our study, Dutch labor costs related to 1 hour productivity loss were used for calculations, which are relatively high. In contrast, we have been conservative because we corrected for the unemployment rate in our population and took into account only 1 value of absenteeism per patient to calculate costs, thereby ignoring possible costs for the second caregiver. We used this method because those caregivers who completed the questionnaire might be the ones accompanying the child to the hospital and, therefore, are most likely be the ones with the greatest impact on work productivity.

Having a child with IBD might have an impact on the employment rate, as supported by the higher unemployment rate in our study (21.6%) than the general unemployment rate in the EU (6.7%).[21] Similarly, in a Dutch prospective study, employment rates were lower in parents of children with chronic diseases (52% worked >20 hours work per week) than in those of healthy children (66% worked >20 hours work per week; $P < .01$).[5] Kuhlthau et al also showed that having a child with a chronic condition was negatively associated with parental employment (paternal OR, 0.81; maternal OR, 0.84).[31] Considering the high unemployment rate at baseline and the fact that the employment rate did not change over time, this outcome could suggest that there had been a change in the employment rate before diagnosis. In contrast, the high unemployment rate in our

study could be an overestimation owing to reporting bias. In a sensitivity analysis, caregivers' employment rates of those patients that had the questionnaire returned by only 1 caregiver were indeed lower than of those that had the questionnaire returned by both caregivers (76.1% vs 82.8% at baseline; $P = .04$).

Disease activity was strongly associated with work productivity loss, irrespective of disease duration. Caregivers of children with IBD experience parenting distress, most commonly within the emotional distress domain.[32,33] This distress is related to disease activity and recent flares, and can reduce HRQOL.[34] In addition to reducing HRQOL, this factor can lead to work productivity loss, increasing psychological problems in caregivers. The ability of caregivers to identify coping mechanisms might decrease the impact of having a child with chronic disease on their work status. Current treatment strategies are predominantly focused on the patients' medical and psychological functioning, with less consideration of family functioning. A family-centered approach could support caregivers in dealing with having a child with a chronic disease and so decrease the impact on their daily lives.

This study has several strengths. It is a large population of children with IBD in whom caregivers' socioeconomic status was evaluated, with a relatively high response rate. The prospective nature and standardized data collection enabled us to assess the WPAI at identical follow-up moments for each patient, while accounting for detailed clinical data. Another important strength was the use of validated questionnaires, allowing us to compare our results with studies in other chronic diseases in children.

One of the limitations of this study is that the WPAI questionnaire uses a recall period of 7 days, excluding the day of assessment, which is often the day of a hospital visit for regular follow-up or treatment. This practice could underestimate the impairments, but that would even further strengthen our findings of a big impact. Because caregivers were not asked to report who completed the questionnaire, we were not able to perform a paired analysis, forcing us to make some assumptions, such as combining the average HRQOL of 2 caregivers with outcomes of a single WPAI questionnaire. Additionally, the data were not obtained systematically from both caregivers, which could have introduced bias, but was a practical approach to improve response rates of questionnaires. Work productivity losses were indeed lower if both parents completed the questionnaire, possibly suggesting that caretaking responsibilities come down to 1 caregiver, with the other caregiver's daily life being less affected. We did not collect detailed information of some relevant demographic or socioeconomic variables, such as household situation, marital status, parental age, employment type, or caregiver educational level and income. Finally, we did not assess childcare dependency and additional family burden or explore the role of emotional support from others. Future studies should investigate the main reasons for work productivity loss and include other variables to assess how these influence socioeconomic functioning of caregivers of children with IBD.

This study implies that the care burden of caregivers of children with IBD needs more attention. Family-centered comprehensive care could help mitigate this burden. This work might improve HRQOL and decrease work productivity loss and disease-associated indirect costs. ■

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Data Statement

Data sharing statement available at www.jpeds.com.

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Table I. Number of recruited pediatric patients with IBD per participating center, eligible for analysis of caregivers' WPAI questionnaire

Countries	Center	No. of recruited patients (%)
France	Necker–Enfants Malades Hospital, University of Paris Descartes, Paris	35 (6.3)
Israel	Wolfson Medical Center, Holon	14 (2.5)
Israel	Shaare Zedek Medical Center, Jerusalem	21 (3.8)
Israel	Schneider Children's Medical Center of Israel, Petach Tikva	3 (0.5)
Italy	Sapienza University Hospital, Rome	33 (5.9)
Japan	National Center for Child Health and Development, Tokyo	15 (2.7)
Malaysia	University of Malaya Medical Center, Kuala Lumpur	11 (2.0)
The Netherlands	Erasmus Medical Center – Sophia Children's Hospital, Rotterdam	84 (15.0)
The Netherlands	Medisch Spectrum Twente, Enschede	12 (2.1)
The Netherlands	Rijnstate Hospital, Arnhem	6 (1.1)
The Netherlands	Jeroen Bosch Hospital, Den Bosch	7 (1.3)
The Netherlands	Amsterdam University Medical Center, Amsterdam	24 (4.3)
Serbia	University Children's Hospital, Belgrade	20 (3.6)
UK	Royal London Hospital, London	67 (12.0)
UK	Alder Hey Children's Hospital, Liverpool	28 (5.0)
UK	Royal Hospital for Sick Children, Edinburgh	14 (2.5)
UK	Royal Hospital for Children Glasgow, Glasgow	22 (3.9)
UK	Birmingham Women's and Children's Hospital, Birmingham	25 (4.5)
UK	Sheffield Children's Hospital, Sheffield	21 (3.8)
UK	Oxford Children's Hospital, Oxford	46 (8.2)
UK	Royal Free Hospital, London	10 (1.8)
UK	Nottingham Children's Hospital, Nottingham	11 (2.0)
UK	Royal Devon and Exeter Hospital, Exeter	7 (1.3)
UK	University College Hospital, London	6 (1.1)
UK	King's College, London	17 (3.0)
Total		559

Frequencies of children with IBD recruited for the PIBD-SETQuality inception cohort study between January 2017 and July 2021, eligible for analysis of the WPAI for caregivers' questionnaire. Frequencies are depicted for all participating centers.

Table II. Number of completed WPAI questionnaires by caregivers of children with IBD, presented per country

Countries	Patients with ≥1 completed questionnaire (% of total)	No. of visits with ≥1 completed questionnaire (% of country visits)	Total No. of available questionnaires (% of total)
France	26 (5.3)	44 (54.3)	47 (4.5)
Israel	32 (6.5)	60 (66.7)	81 (7.8)
Italy	32 (6.5)	56 (84.8)	67 (6.5)
Japan	15 (3.1)	35 (94.6)	35 (3.4)
Malaysia	11 (2.2)	20 (80.0)	27 (2.6)
The Netherlands	102 (20.8)	189 (59.8)	269 (26.0)
Serbia	20 (4.1)	42 (100)	81 (7.8)
UK	253 (51.5)	410 (62.0)	426 (41.2)
Total	491	856	1033

The table shows the total number of children with IBD with ≥1 completed WPAI questionnaire by caregivers, the total number of visits with ≥1 completed WPAI questionnaire by a caregiver per country, and the total number of available WPAI questionnaires by caregivers, presented per country.

Table III. Number of completed WPAI questionnaires by caregivers of children with IBD, presented per visit

Visits	Patients with available questionnaire at the visit (% completion rate per visit)	Questionnaire completed by 1 parent (% of patient with visit)	Questionnaire completed by both parents (% of patient with visit)	Total number of completed questionnaires (% of total No. of questionnaires)
Visit 0 (baseline)	377 (67.4)	289 (51.7)	88 (15.7)	465 (45.0)
Visit 2 (3 months)	271 (58.8)	219 (47.5)	52 (11.3)	323 (31.3)
Visit 4 (12 months)	208 (69.8)	171 (57.4)	37 (12.4)	245 (23.7)
Total	856	679	177	1033

The table shows the number of completed WPAI questionnaires by caregivers of pediatric patients with IBD per visit, presented as number of pediatric patients with ≥1 completed questionnaire and total number of completed questionnaires.

Table VI. Predictors of employment rate, absenteeism, presenteeism, work productivity loss, and activity impairment of caregivers of children with IBD

Predictors	Employment rate	Absenteeism	Presenteeism	Work productivity loss	Activity impairment
IBD diagnosis	.82	.84	.60	.97	.12
Age at IBD diagnosis	.18	.19	.73	.37	.20
Disease activity	.67	.001	.001	.001	.001
Disease duration	.32	.001	.001	.001	.001
IBD diagnosis × Disease duration (interaction term)	n.s.	n.s.	n.s.	n.s.	n.s.
Disease activity × Disease duration (interaction term)	n.s.	n.s.	n.s.	n.s.	n.s.

n.s., not significant.

Table demonstrating *P* values for predictors of employment rate, absenteeism (absence from work), presenteeism (reduced productivity while at work), work productivity loss (overall work impairment), and activity impairment of caregivers of children with IBD. *P* values were obtained by fitting GEE models for each outcome, while accounting for IBD diagnosis, child's age at IBD diagnosis, disease duration, and disease activity as predictors.

Table VII. Caregivers' employment rate, absenteeism, presenteeism, work productivity loss, activity impairment, and costs related to absenteeism, represented by child's IBD disease duration and IBD type

	Baseline			3 months			12 months		
Outcomes	**CD**	**UC/IBD unclassified**	**Total**	**CD**	**UC/IBD unclassified**	**Total**	**CD**	**UC/IBD unclassified**	**Total**
Employment rate	76.1 (70.3-81.1)	80.6 (74.6-85.4)	78.4 (73.8-82.4)	74.2 (67.9-79.7)	79.0 (72.2-84.4)	76.7 (71.3-81.3)	75.1 (68.4-80.7)	79.7 (72.4-85.4)	77.5 (71.6-82.4)
Absenteeism	25.5 (21.4-29.7)	26.0 (21.7-30.3)	25.8 (22.2-29.3)	15.1 (11.0-19.3)	15.6 (11.1-20.1)	15.4 (11.7-19.0)	12.5 (8.8-16.1)	12.9 (8.5-17.4)	12.7 (9.3-16.1)
Presenteeism	31.2 (27.0-35.5)	29.9 (25.0-34.8)	30.6 (26.7-34.4)	19.6 (15.1-24.1)	18.3 (13.7-23.0)	19.0 (15.1-22.9)	17.0 (12.5-21.4)	15.6 (10.7-20.6)	16.3 (12.3-20.3)
Work productivity loss	44.6 (39.6-49.5)	44.6 (39.1-50.2)	44.6 (40.2-49.0)	27.7 (22.1-33.3)	27.8 (22.0-33.6)	27.8 (22.8-32.7)	24.1 (18.9-29.4)	24.2 (18.2-30.3)	24.2 (19.3-29.1)
Activity impairment	36.0 (32.2-39.9)	32.5 (28.1-36.9)	34.3 (30.8-37.7)	24.6 (20.7-28.5)	21.0 (16.6-25.4)	22.8 (19.3-26.3)	22.3 (17.9-26.7)	18.7 (14.1-23.4)	20.5 (16.6-24.5)
Costs related to absenteeism*	n/a	n/a	n/a	€2122 ($2462)	€2302 ($2670)	€2217† ($2572)	€3868 ($4487)	€4236 ($4914)	€4055† ($4704)

n/a, not applicable.

Caregivers' employment rate, absenteeism (absence from work), presenteeism (reduced productivity while at work), work productivity loss (overall work impairment), and activity impairment at time of diagnosis, and 3 months or 12 months after diagnosis, represented per IBD type. Data are adjusted means (95% CI). Adjusted means were calculated using GEE models, accounting for IBD diagnosis, age at diagnosis, disease activity, and disease duration as predictors.

*Costs were calculated for month 0-3 and month 3-12 separately (details of methodology described in the **Supplemental Methods**).

†Absenteeism costs for caregivers of patients with IBD from diagnosis to 3 months after diagnosis were calculated as follows: (25.8 + 15.4)/2/100% × 13 (weeks) × 30.4 (hours per week) × 34.75 × 0.784 (employment rate at baseline) × 1 (parent). Absenteeism costs for IBD patients' caregivers from 3 to 12 months after diagnosis were calculated as follows: (12.7/100%) × 39 (weeks) × 30.4 (hours per week) × €34.75 × 0.775 (employment rate at 12 months) × 1 (parent).

Table VIII. Caregivers' work productivity loss and activity impairment, represented by child's IBD disease duration and disease activity

Times	Remission	Mild	Moderate to severe
Work productivity loss			
Baseline	34.2 (27.3-41.1)	40.6 (34.4-46.8)	59.0 (53.9-64.2)
3 months	17.3 (12.8-21.9)	23.7 (17.9-29.5)	42.2 (33.6-50.8)
12 months	13.8 (8.9-18.6)	20.2 (14.6-25.8)	38.6 (30.2-47.1)
Activity impairment			
Baseline	25.3 (20.0-30.6)	31.2 (26.7-35.7)	46.3 (42.0-50.5)
3 months	13.8 (10.6-17.0)	19.8 (15.8-23.8)	34.8 (28.4-41.2)
12 months	11.6 (8.1-15.0)	17.5 (13.0-22.0)	32.5 (25.8-39.2)

Data are adjusted means (95% CI). Adjusted means were calculated using a GEE model, accounting for IBD diagnosis, age at diagnosis, disease activity, and disease duration as predictors.

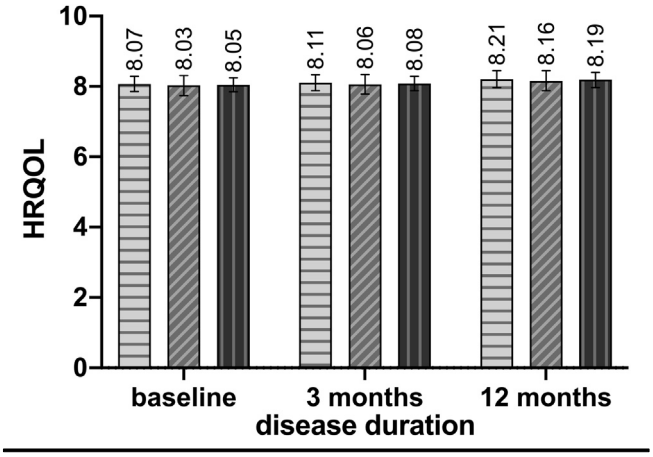

Figure 3. HRQOL of caregivers of children with IBD, as measured on a VAS, according to disease duration and IBD type. Bars indicate adjusted means (95% CI). Adjusted means were calculated using a GEEs model, accounting for IBD diagnosis, age at diagnosis, disease activity, and disease duration as predictors.