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The IBD-disk is a reliable tool to assess the daily-life burden of patients with inflammatory bowel disease

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Abbreviations: Crohn's disease: CD; ulcerative colitis: UC; inflammatory bowel disease: IBD; Groupe d'Etude Therapeutique des Affections du tube Digestif: GETAID; IBD-DI : Inflammatory Bowel Disease Disability Index: IBD-DI; International Classification of Functioning, Disability and Health: ICF Core Set; Receiver Operating Curve: ROC; World Health Organization: WHO.

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ABSTRACT

Introduction: The inflammatory bowel disease (IBD)-disk is a 10-item self-questionnaire that is used to assess IBD-related disability. The aim of the present study was to evaluate this tool in the assessment of IBD daily-life burden.

Patients and methods: A one-week cross-sectional study was conducted in 42 centres affiliated in France and Belgium. Patients were asked to complete the IBD-disk (best score: 0, worst score: 100) and a visual analogue scale (VAS) of IBD daily-life burden (best score: 0, worst score: 10). Analyses included internal consistency, correlation analysis and diagnostic performance assessment.

Results: Among the 2011 IBD outpatients who responded to the survey (67.8% of the patients had Crohn's disease), 49.9% were in clinical remission. The IBD-disk completion rate was 73.8%. The final analysis was conducted in this population (n= 1455 patients). The mean IBD-disk score and IBD daily-life burden VAS were 39.0 ± 23.2 and 5.2 ± 2.9, respectively. The IBD-disk score was well-correlated with the IBD daily-life burden VAS (r=0.67; p<0.001). At an optimal IBD-disk cut-off of 40, the area under ROC curve (AUROC) for high IBD daily-life burden (VAS>5) was 0.81 (CI95%: 0.79-0.83; p<0.001).

Conclusion: In a large cohort of patients, the IBD-disk score was well correlated with IBD daily-life burden, and it could be used in clinical practice.

Keywords: Crohn's disease; ulcerative colitis; inflammatory bowel disease; disability; patient-reported outcome.

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INTRODUCTION

Inflammatory bowel diseases (IBDs) are chronic inflammatory conditions that negatively affect various dimensions of daily life [1]. Therefore, new standards of care taking into account IBD-related disability and daily-life burden are increasingly being incorporated into clinical practice. According to the World Health Organization (WHO), disability is an umbrella term that includes impairments, activity limitations, and participation restrictions. An impairment is a problem with a bodily function or structure; an activity limitation is a difficulty encountered by an individual in executing a task or action; and a participation restriction is a problem experienced by an individual in achieving full involvement in life situations [2]. According to WHO, the burden of a disease is somewhat different to disability because it also covers death. As IBD is not considered to be a disease that reduces lifespan, the burden of IBD should directly correlate with IBD-related disability.

IBD can cause physical, psychological, familial and social impairment and self-administered questionnaires that assess patients' quality of life are often too restrictive for the assessment of disability [3–7]. To date, there is only one validated tool used to assess IBD-related disability: the IBD Disability Index (IBD-DI) [8,9]. Although the IBD-DI is a very informative questionnaire it has to be completed with the assistance of a trained nurse and it is time-consuming.

Based on the principles of the PSO-disk, a validated self-administered tool for assessing the burden of psoriasis [10–12], the IBD Connect group has developed the IBD-disk, a visual self-administered tool based on a Delphi consensus process to measure disability in patients with IBD[13]. Ten items were chosen to assess ten dimensions of disability including joint pain, abdominal pain, regulating defecation, interpersonal interactions, education and work, sleep, energy, emotions, body image and sexual functions [1,8,9]. The IBD-disk has been recently validated in the VALIDate Study, a multicentre French study including 447 patients in the baseline analysis[14]. In this study the IBD-disk has shown good correlation between IBD-disk and IBD-DI ($r = 0.75$, $p<0.001$). Reproducibility and internal consistency (Cronbach's $\alpha = 0.89$) were both excellent.

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Therefore, we aimed to assess in real life the correlation between the overall IBD-disk score and the IBD-disk subscores with the IBD daily-life burden taking into account disability during the last week in a larger cross-sectional study

PATIENTS AD METHODS

Study population

A cross-sectional survey was conducted in 42 tertiary centres in France and Belgium affiliated with the Groupe d'Etude Therapeutique des Affections Inflammatoires du tube Digestif (GETAID) in France and Belgium. The survey was conducted from November 26th to November 30th, 2018. Investigators asked consecutive adult outpatients with a confirmed diagnosis of IBD regardless of any other criteria to complete a standardized self-questionnaire that was given by their treating physicians or IBD nurse.

The study was conducted in accordance with the ethical principles expressed in the Declaration of Helsinki and the requirements of applicable French regulations. The patients' experience study was conducted through the French reference methodology, MR-004, and it was supervised by and registered with GETAID (registration number 2210131). All the authors had access to the study data and reviewed and approved the final manuscript.

Survey instrument

A 4-page, self-administered questionnaire was designed to examine the demographics of the patients, type of IBD, history of surgical treatment of IBD, working status, duration of IBD and current IBD-related treatment (Supplementary Figure S1). An IBD-disk was included in the survey and included a 0-10 visual analogue scales (0 = absolutely disagree; 5 = neither agree nor disagree; 10 = absolutely agree or maximal disability) assessing each component of the IBD-related disability during

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the last week : joint pain, abdominal pain, body image, education and work, emotions, energy, interpersonal interactions, regulating defecation, sexual function, and sleep (Figure S1). The overall IBD-disk score was calculated as the sum of its 10 components, ranging from 0 to 100. The questionnaire also included two VASs to assess the IBD daily-life burden and overall health (0 = worst; 10 = perfect). Burden scales have been used to study the burden of many chronic diseases, such as Crohn's disease, celiac disease, irritable bowel syndrome, diabetes and congestive heart failure (14–20). IBD activity was determined by patient self- assessment (yes or no).

Correlation of the overall IBD-disk score with IBD daily-life burden

A simple linear correlation analysis using Pearson's correlation coefficient was applied to test the correlation between the overall IBD-disk score and IBD-disk subscores with the IBD daily-life burden scale. Outliers were detected using a graphical method by excluding values 1.5-fold over the standard deviation. A correlation was considered significant if the Pearson correlation coefficient r was strictly superior to 0.5. Discrimination of models was assessed by the C-statistic (Area Under the ROC Curve). The C-statistics of the models were applied to assess the accuracy of detecting a high IBD daily-life burden (score >5).

Reliability

Cronbach's α coefficient (> 0.7) and corrected item-total correlations (> 0.4) were used to assess the internal consistency of the overall IBD-disk score. Cronbach's α coefficient with a one-at-a-time deletion procedure was used to assess the impact of the items on the internal consistency of the overall IBD-disk score.

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The overall IBD-disk score was calculated for the overall study population and compared according to the patients' characteristics using a Mann-Whitney test or an ANOVA test followed by a Tukey test for post hoc analysis.

Statistical analysis

The data are expressed as numbers (%) for qualitative data and as the means ± standard deviations (SDs) or medians [interquartile ranges] for quantitative data. Qualitative variables were compared using Chi² test or Fisher's exact test, and quantitative variables were compared using the Mann-Whitney test or an ANOVA test followed by a Tukey test for post hoc analysis. The normality of the distribution was verified using the Kolmogorov-Smirnov test, Shapiro-Wilk test and visual inspection. A result was considered significant if the p value less than 0.05. All the statistics were calculated using SPSS Statistics v23® software.

RESULTS

Study population

During the one-week study period, 2011 outpatients with IBD (47% male; median age of 40.0 [29.0-52.0] years) were included in the 42 centres. The median number of patients recruited at each centre was 46.5 (24.0-63.0). The characteristics of the study population are listed in Table 1. Briefly, 67.8% of the patients had Crohn's disease (CD), and 32.2% had ulcerative colitis (UC). The median duration of IBD was 10.5 [4.5-18.5] years. The majority of the patients were treated with biological agents, including anti-TNF in 56.0%, vedolizumab in 11.1% and ustekinumab in 6.6%; 78.6% of the patients were treated with biological agents alone, and 21.4% of the patients were treated with biological agents in combination with an immunomodulator. According to the patient global assessment, 49.1% of the patients considered themselves to be in clinical remission.

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Overall IBD-disk score and IBD-disk subscores correlation and reliability

Among the 2011 participants, 1484 (73.8%) patients fully completed the 10 items of the IBD-disk score, 220 (10.9%) completed ≥6 items and 307 (15.3%) completed <6 items. Considering every items of the IBD-disk questionnaire separately, the completion rate of any item was > 80% (Table 2). The IBD-disk questionnaire was considered easy to complete by 1571 (88.4%) patients.

After removing 29 outliers, complete IBD-disk scores with all subscores were assessable in 1455 patients. The overall IBD-disk score and subscores are presented in Table 2. The mean complete IBD-disk score was 39.3 ± 23.0, and the subscores from its components ranged from 2.4 (interpersonal interactions) to 5.7 (energy). The proportions of patients with significant disability (subscore > 5) in each dimension of IBD-related disability are presented in table S2.

Cronbach's alpha coefficient calculated with the overall IBD-disk score was 0.89, and this value calculated with the subscores was between 0.87 and 0.89. One-at-a-time deletion of subscores confirmed the contribution and the unidimensionality of the 10 subscores (Cronbach's alpha coefficient between 0.87 and 0.89) (Table 3). All the corrected item-total correlations were > 0.4.

Assessments of IBD daily-life burden and overall health with the VAS were available for 1927 (95.8%) and 1952 (97.1%) patients, respectively. The mean IBD daily-life burden and overall health scores were 5.2 ± 2.9 and 6.6 ± 2.2, respectively.

The correlation between the complete IBD-disk score and IBD daily-life burden VAS was r = 0.67 (p < 0.001) and was inversely correlated with the overall health score (r = −0.64, p < 0.001). Analysis of the IBD-disk subscores revealed inconsistent correlations; four subscores (regulating defecation, abdominal pain, work and study, and energy) had

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correlations with IBD daily-life burden that were over 0.5, and six other subscores had correlations that were lower than 0.5, ranging between 0.299 and 0.491 (Table 4).

The diagnostic performance of the overall IBD-disk score in predicting a high IBD daily-life burden (> 5) was evaluated using a receiver operative curve showing a C-statistic of 0.81 [0.79-0.83] ($p < 0.001$) with an optimal threshold for the overall IBD-disk score > 40 (Figure 3).

DISCUSSION

Taking into account IBD-related disability requires validated tools. In the present study, we assessed the performance and internal consistency of the IBD-disk questionnaire in a large population of outpatients with IBD to predict high IBD-related daily-life burden. Our study population encompassed a wide range of patients with long-lasting disease, requirements of immunomodulators and biological agents and a history of intestinal resection, namely, a population highly relevant to the field of patient-reported outcomes (PRO). We demonstrated there was a good correlation of the overall IBD-disk score with IBD daily-life burden. The overall IBD-disk score disclosed a diagnostic performance of 0.81 [0.79-0.83] to predict high IBD daily-life burden > 5 with an optimal threshold for the overall IBD-disk score > 40.

IBD is a severe, chronic, progressive disease that causes disability and impacts patients' daily-lives [21]. The development of biological agents has changed the paradigm of management of IBD from focusing on physician-reported clinical outcomes to implementing mucosal and/or transparietal healing and patient-reported outcomes [22,23]. PROs are divided into two categories: those that measure disease activity from the patients' perspective and those that assess IBD-related disability. Although most of the current studies are focusing on PRO measurement of clinical activity, we chose to focus on those that assess IBD-related disability by using the IBD-disk questionnaire. Indeed

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disability remains poorly studied in IBD compared to other inflammatory diseases such as rheumatoid arthritis, multiple sclerosis or psoriasis [11,24–27].

It should be emphasized that quality of life and disability are two distinct concepts that should both be studied independently [3]. Disability is an objective description, unlike quality of life which is the patient's subjective perception regarding a loss of function. For those reasons, we chose to use an auto-administered questionnaire to assess different components of disability and the IBD daily-life burden scale as a reference of IBD-related disability instead of quality-of-life scores such as the Short-IBD questionnaire or other tools built by physicians and not patients to assess IBD-related disability [1,8,28].

Assessing a tool for IBD-related disability requires clarity, readability and comprehensiveness of the questionnaire as well as a high completion rate of the whole questionnaire [29,30]. Indeed, it is not conceivable to focus on the small subset of patients who are willing to complete a complex questionnaire or only those who understand the whole questionnaire or specific items. In the present study, the IBD-disk questionnaire was considered easy to complete by 88.4% of patients. Furthermore, the full completion rate for the 10 items of the IBD-disk was 73.8%. It is important to mention that the IBD-disk we used in this study shows some deviations from the original IBD-disk which is a VAS-scale ranging from 0 (absolutely disagree) to 10 (absolutely agree). Le Berre et al. chose to adapt the scale from 0 (absolutely no complaint) to 10 (maximal complaint). We also use this modified version of the IBD-disk since it has been validated in a large cohort with a 80%-completion rate (447 patients out of 559)[14] It should be noted that such deviation have been previously demonstrated as non-inferior to the original model in other similar studies.[31,32] We also did not find any difference in the overall IBD-disk score and IBD-disk subscores between patients with CD and UC patients with mild but significant differences for and abdominal pain, emotions, body image subscores, confirming that both disease induce a similar level of disability[9,33].

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IBD-related disability is a multidimensional concept that includes six main domains: body functions and structures, activities and participation and personal and environmental factors [1]. The IBD-DI and the IBD-disk questionnaire were developed focusing mostly on three domains, bodily functions (abdominal pain, sleep, energy, emotions, joint pain, body image and sexual functions), activities and participation (regulating defecation, interpersonal interactions and work and study) [8,13]. The IBD-DI is an exhaustive questionnaire that evaluates different aspects of IBD-related disability. The IBD-DI is not self-administered and could lead to discrepancies between the patients' experience and the perception of a physician [34,35]. As such, it is mostly used in clinical trials settings [13]. It should be emphasized that the IBD-DI is based on a 0 to 4 Likert scale and does not include sexual functions which is an important component of disability. Moreover, the IBD-DI includes the number of daily liquid stools which is more related to the clinical activity of IBD [36,37]. In the present study, we confirmed that a self-administered questionnaire, such as IBD-disk, that assess all of the components of disability on a wider scale of severity was also reliable and was easy to complete. However, we have to highlight the lack of a direct comparison between IBD-disk and IBD-DI in our study.

We also need to highlight some limitations of the present study. The recruitment was mainly conducted in tertiary IBD centres with an obvious recruitment bias, and more than two-thirds of the included patients were treated with biological agents. However, this limitation is counterbalanced by the size of our study population, which included a large panel of patients with varied IBD history, demographics and treatment. We did not assess the reliability of the overall IBD-disk score due to the absence of repeated IBD-disk questionnaire administration. However, we thought that anonymity was an important prerequisite for this study, which is not compatible with repeated testing. Another limitation is the lack of assessment of clinical activity using validated and dedicated clinical scores and objective inflammation using laboratory, morphological and/or endoscopic tools. However, Le Berre *et al* recently showed a good correlation with the overall IBD-disk score and validated clinical scores and C-reactive protein level.[14] It is possible that the daily-life burden VAS

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does not perfectly account for IBD-related disability. However, this limitation is counterbalanced by the use of the VAS in many chronic diseases, including IBD, thus proving its reliability [15–20], and by the fact that none of the alternate scores available to measure IBD-related disability would have been satisfying in this setting.

It should be stressed that the IBD-disk is a communication tool between patients and their healthcare professionals. Our questionnaire was not designed to know if patients found the IBD-disk useful to discuss subjects that would have been otherwise overlooked during appointment time. This would be an interesting approach in future studies regarding patients' experience. Incremental use of the IBD-disk in randomized clinical trials may provide good opportunities in this setting.

The IBD-disk is a visual representation of IBD-related burden. It gives more information than a simple one-dimensional score and it easy to use from the patient and the healthcare professional point of view. The benefit of such tool may be useful for remote monitoring especially at the COVID-19 era.

In conclusion, the IBD-disk questionnaire is a self-administered questionnaire used to evaluate IBD-related disability with a good accuracy and reliability in both UC and CD. We validated this questionnaire and provided evidence of internal consistency in a large multicentre cohort study of 2011 outpatients with IBD. Further studies are needed to highlight the determinants of IBD-related disability and to assess the reliability of the IBD-disk questionnaire in longitudinal follow-up.

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TABLE AND FIGURE LEGENDS

TABLE LEGENDS

Table 1: Demographic, disease and medication characteristics of 2011 patients with inflammatory bowel disease.

Table 2: IBD-disk overall score and subscores in a subset of 1455 patients who completed the 10-item questionnaire according to the patient global assessment of clinical remission

Table 3: Cronbach's alpha coefficients assessing the consistency of the IBD-disk subscores with one-at-a-time deletion of subscores contributing to the overall IBD-disk score

Table 4: Pearson's correlation coefficient R^2 assessing the convergent validity of the overall IBD-disk score with IBD daily-life burden and overall health

Table 5: Multiple logistic regression analysis with IBD-disk subscores as independent variables and daily-life inflammatory bowel disease burden as a dependent variable

FIGURE LEGENDS

Figure 1: Scatter plot (A) and box plot (B) of the distribution of the IBD daily-life burden according to the overall IBD-disk score and predictive accuracy of the overall IBD-score and the simplified shortened IBD-disk score in discriminating patients with high IBD daily-life burden (> 5) summarized using ROC curves analysis (C).

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Table 1: Demographic, disease and medication characteristics of 2011 patients with inflammatory bowel disease.

Characteristic	**Overall population (n = 2011)**
Age at diagnosis, years	40.0 [29.0-52.0]
Male gender, no (%)	47.3%
BMI, kg/m²	24.4 ± 6.5
Duration of IBD, years	10.5 [4.5-18.5]
Age at diagnosis, no (%)	
A1: ≤16 years	14.1%
A2: 17 – 40 years	67.6%
A3: > 40 years	18.3%
Type of inflammatory bowel disease, (%)	
Crohn's disease	67.8%
Ulcerative colitis	32.2%
History of intestinal resection, no (%)	45.6%
Occupational status, %	
Employed	62.1%

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Unemployed	8.5%
Homemaker	8.6%
Student	8.5%
Retired	12.3%
Distance from home, km	46.8 ± 99.6
Current treatment	
None	8.3%
5-ASA	9.2%
Immunomodulator alone	8.6%
Anti-TNF	56.0% (including 14,7% with combination therapy)
Vedolizumab	11.1% (including 0,9% with combination therapy)
Ustekinumab	6.6% (including 1% with combination therapy)

5-ASA: 5-aminosalicylic acid; TNF: tumor-necrosis factor; BMI: body mass index; GI: gastrointestinal; IBD: inflammatory bowel disease.

Variables are presented as n (%), mean ± standard deviation or median (interquartile range).

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Table 2: IBD-disk overall score and subscores in a subset of 1455 patients who completed the 10-item questionnaire according to the patient global assessment of clinical remission

	Overall study population (n = 1455)	**Presence of clinical remission (n = 648)***	**Absence of clinical remission (n = 638)***	**Missing values** (%)**	**p**
Joint pain	3.9 ± 3.3	3.5 ± 3.2	4.2 ± 3.2	16.3%	<0.001
Abdominal pain	4.2 ± 3.1	3.5 ± 2.9	5.1 ± 3.0	15.6%	<0.001
Regulating defecation	3.9 ± 3.4	2.9 ± 3.1	4.8 ± 3.5	15.9%	<0.001
interpersonal interactions	2.4 ± 2.9	1.9 ± 2.7	2.9 ± 3.0	18.2%	<0.001
Education and work	4.0 ± 3.4	3.1 ± 3.2	4.9 ± 3.3	16.1%	<0.001
Sleep	5.0 ± 3.4	4.4 ± 3.3	4.7 ± 3.4	15.1%	<0.001
Energy	5.7 ± 3.2	5.1 ± 3.2	6.5 ± 2.9	14.2%	<0.001
Emotions	4.5 ± 3.2	3.8 ± 3.2	5.3 ± 3.2	15.5%	<0.001
Body image	4.0 ± 3.4	3.5 ± 3.3	4.5 ± 3.4	17.0%	<0.001

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Sexual functions	2.8 ± 3.2	2.3 ± 3.0	3.4 ± 3.3	19.4%	<0.001
Overall IBD-disk score	39.3 ± 23.0	32.9 ± 21.5	46.7 ± 22.2	26.2%	<0.001
IBD daily-life burden scale	5.2 ± 2.9	4.1 ± 2.8	6.2 ± 2.6	4.2%	<0.001
Overall health scale	6.6 ± 2.2	7.5 ± 1.8	5.7 ± 2.1	2.9%	<0.001

IBD: inflammatory bowel disease.

Variables are presented as mean ± standard deviation. Quantitative variables between groups was compared using Mann-Whitney test.

*The patient global assessment of global remission was missing in 169 out of 1455 patients.

**Missing values are given with respect with the overall study population of 2011 patients.

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Table 3: Cronbach's alpha coefficients assessing the consistency of the IBD-disk subscores with one-at-a-time deletion of subscores contributing to the overall IBD-disk score

	Cronbach's alpha coefficient	Corrected item-total correlation	Cronbach's alpha coefficient if item deleted
Joint pain	0.888	0.492	0.888
Abdominal pain	0.877	0.652	0.877
Regulating defecation	0.880	0.605	0.880
interpersonal interactions	0.879	0.627	0.879
Education and work	0.870	0.740	0.870

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Sleep	0.877	0.647	0.877
Energy	0.873	0.709	0.873
Emotions	0.872	0.719	0.872
Body image	0.886	0.525	0.886
Sexual functions	0.883	0.566	0.883

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Table 4: Pearson's correlation coefficient R^2 assessing the convergent validity of the overall IBD-disk score with IBD daily-life burden and overall health

	IBD daily-life burden	Overall health
Joint pain	0.348	-0.319
Abdominal pain	0.499	-0.490
Regulating defecation	0.535	-.0500
interpersonal interactions	0.438	-0.389
Education and work	0.590	-0.532
Sleep	0.463	-0.419
Energy	0.515	-0.505
Emotions	0.491	-0.454
Body image	0.299	-0.246

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Sexual functions	0.371	-0.329
Overall IBD-disk score	0.650	-0.614
New IBD-disk score	0.670	-0.640

P-values for each pearson's correlation coefficient was < 0.001.

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Table 5: Multiple logistic regression analysis with IBD-disk subscores as independent variables and daily-life inflammatory bowel disease burden as a dependent variable

Independent variables	Coefficient	Standardized and rounded coefficient	P
Abdominal pain	4.485	1	< 0.001
Regulating defecation	7.623	2	< 0.001
Education and work	9.491	2	< 0.001
Energy	5.642	1	< 0.001
Emotions	4.041	1	< 0.001

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Figure 1