Adv Ther (2025) 42:1834–1859
https://doi.org/10.1007/s12325-024-03078-3

ORIGINAL RESEARCH

Patient and Health Care Professional Perspectives on the Burden and Daily Life Impact of Ulcerative Colitis and Crohn's Disease: Results from the Japanese CONFIDE Study

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Received: July 21, 2024 / Accepted: November 22, 2024 / Published online: February 28, 2025

ABSTRACT

Introduction: The global Communicating Needs and Features of Inflammatory Bowel Disease Experiences (CONFIDE) study aimed to evaluate the impact of ulcerative colitis (UC)- and Crohn's disease (CD)-related symptoms on patients' lives and elucidate communication gaps between patients and health care professionals (HCPs). We report the findings from the study in patients with UC or CD and HCPs in Japan.

Methods: Online, quantitative, cross-sectional surveys were conducted in Japan for patients with moderate-to-severe UC or CD and HCPs responsible for the care of patients with UC and/or CD. Subgroup analyses based on disease activity were conducted using the Manitoba Inflammatory Bowel Disease Index. Data were described using descriptive statistics.

Results: Surveys were completed by 124 patients with UC, 99 patients with CD, and 100 HCPs in Japan. Differences were noted in the most common patient-reported symptoms experienced in the month prior to survey completion between patients with UC and CD (diarrhea [45.2% UC, 68.7% CD], flatulence [34.7% UC, 32.3% CD], increased stool frequency [32.3% UC, 43.4% CD], bowel urgency [BU; 25.0% UC, 32.3% CD], and fatigue [36.4% CD]). More patients with active disease than inactive disease reported these symptoms. BU and BU-related accidents were among the symptoms ranked as

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Prior Presentation: This manuscript is based on work that was presented in part at the 31st Japan Digestive Disease Week (JDDW 2023), November 2–5, 2023, Kobe, Japan, and at the 32nd Japan Digestive Disease Week (JDDW 2024), October 31 to November 3, 2024, Kobe, Japan.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12325-024-03078-3.

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most impactful by patients with UC and CD. HCP-perceived symptoms with the greatest impact on patients were diarrhea and blood in stool. Findings in the Japanese cohort of CONFIDE were generally consistent with those in the United States (US)/European cohorts. The percentage of patients reporting BU as the symptom with the greatest impact was higher in the US/European cohorts than in the Japanese cohort, potentially as a result of differences in baseline characteristics and social environments such as toilet facilities.

Conclusion: BU is an impactful symptom among Japanese patients with UC and CD and should be considered by HCPs during treatment of these conditions.

Keywords: Bowel urgency; Crohn's disease; Japan; Quality of life; Symptom burden; Ulcerative colitis

Key Summary Points

Why carry out this study?

The prevalence of ulcerative colitis (UC) and Crohn's disease (CD) has steadily increased in recent decades in Japan, with symptoms and related complications having substantial negative impact on health-related quality of life.

We report the findings from the global Communicating Needs and Features of Inflammatory Bowel Disease Experiences (CONFIDE) study in patients with UC or CD and health care professionals (HCPs) in Japan.

What was learned from the study?

Bowel urgency (BU) and BU-related accidents were two of the symptoms ranked as having the greatest impact by Japanese patients with UC and CD, and a substantial proportion reported ever wearing a diaper/pad/protection because of fear/anticipation of BU-related accidents.

BU and BU-related accidents were not a high priority for HCPs during routine clinical appointments, highlighting a potential gap in communication between Japanese patients and HCPs.

HCPs in Japan should consider BU when making treatment decisions.

INTRODUCTION

Ulcerative colitis (UC) and Crohn's disease (CD) are two main types of inflammatory bowel disease (IBD) characterized by chronic remitting/relapsing inflammation in the gastrointestinal tract. UC affects the submucosal and mucosal layers of the colon and rectum [1], whereas CD can affect any region of the gastrointestinal tract and may extend throughout the bowel wall [2, 3]. A nationwide survey revealed a steady rise in the prevalence of both UC and CD in recent decades in Japan, with an almost tenfold increase in patients with IBD over the span of 23 years [4]. Studies examining the clinical and economic burden of these conditions in Japan and the potential requirement for modifications to resource allocation are warranted.

Common symptoms of UC and CD are diarrhea, bloody stools, abdominal pain, fever, and bowel urgency (BU) [1, 2]. BU, the sudden or immediate need for a bowel movement, is one of the most common and disruptive symptoms [5]. The underlying mechanisms of BU are multifactorial and are likely to be variable between UC and CD. Patient-reported outcome measures have recently been developed to assess the severity of BU [5, 6]. However, although BU is considered important for patients, it is often not assessed in clinical trials and clinical settings.

Japanese patients report that IBD symptoms and related complications have substantial negative impacts on health-related quality of life (HRQOL) and disrupt daily activities, with patients with CD reporting more severe disturbances than those with UC [7]. In a non-interventional analysis of Japanese patients with UC, BU, bowel incontinence, and rectal bleeding were identified as symptoms significantly affecting daily life [8, 9]. Notably, in Japan, BU has been identified by patients as one of the most disruptive IBD symptoms, with worse HRQOL and real-world clinical outcomes reported for patients with BU than for those without BU [9, 10]. The American College of Gastroenterology guidelines recommend that initial treatment of UC focus on restoration of normal bowel frequency and control of the primary symptoms of bleeding and urgency [1]. However, current Japanese guidelines on the management of IBD do not include recommendations regarding the assessment and management of BU [11], and limited studies on IBD-related BU have been conducted in Japan.

Several studies have revealed discrepancies regarding the burden of IBD symptoms between patients and health care professionals (HCPs), which point to potential issues in patient–HCP communication [12–15]. Gaps in patient–HCP communication may differ globally as a result of cultural differences and country- and ethnic-specific variability in health care. The Communicating Needs and Features of IBD Experiences (CONFIDE) study was conducted in the USA, Europe, and Japan to explore the experience and impact of UC- and CD-related symptoms, including BU, on patients' lives and to elucidate the barriers in communication between HCPs and patients. The results from patients with UC and CD and HCPs managing these conditions in the USA and Europe have previously been published [16, 17]. We report the CONFIDE study results from patients with moderate-to-severe UC or CD and HCPs in Japan.

METHODS

Study Design

The CONFIDE study was a non-interventional observational study conducted via online surveys in Japan, the USA, France, Germany, Italy, Spain, and the UK. This report includes results from patients and HCPs in Japan. The study consisted of two online quantitative, cross-sectional surveys, one for patients with UC or CD and the other for HCPs who manage these conditions. Surveys were designed and conducted by Adelphi Real World in collaboration with Eli Lilly and Company and were developed in consultation with patients with UC or CD and gastroenterologists with clinical expertise in IBD treatment, patient-reported outcomes, and/or IBD surveys, as previously described [16, 17]. Translated surveys were locally reviewed by native speakers to ensure culture relevance and understanding in Japan.

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki, Good Pharmacoepidemiology Practice guidelines, and all local laws and regulations. All participants provided informed consent prior to participation in the study. The protocol and data collection materials were approved by the Western Institutional Review Board.

Study Population

Patients and HCPs were recruited via online patient panels and screened online to ensure eligibility. Patient and HCP cohorts were independent from one another. For the patient cohort, Japanese adults (≥ 18 years old) with self-reported, HCP-diagnosed, moderate-to-severe UC or CD were enrolled in the study. Moderate-to-severe disease was defined by meeting one or more of the following criteria: (1) anti-tumor necrosis factor, anti-integrin, Janus kinase inhibitor, anti-interleukin-12/23, or immunomodulator treatment in the last 12 months; (2) steroid treatment for ≥ 1 month out of the last 12 months; and (3) hospitalization for ≥ 4 consecutive weeks in the last 5 years. Patients who had undergone a colectomy were excluded. No more than 20% of the sample was allowed to have a self-reported HCP diagnosis of concomitant irritable bowel syndrome. HCPs were eligible for study inclusion if they were gastroenterologists or internal medicine practitioners with a gastroenterology focus in Japan. Eligible HCPs were responsible for making prescribing decisions for ≥ 10 patients with CD or UC, with ≥ 5 of these patients having moderate-to-severe

UC and/or CD per month, and spending ≥ 50% of working time actively seeing patients.

Survey Content and Data Collection procedures

Survey content and data collection procedures have previously been published in detail [16, 17]. In brief, participants accessed the survey via email links, and links remained open until the sample target number was met. Surveys were conducted on a secure website. Both patients and HCPs were required to answer all questions for which they were eligible, and only completed surveys were included in the study. All participants were provided a nominal honorarium for completing the survey. No personally identifiable information was directly collected, and all data were anonymized. Additional steps were taken to prevent identification of participants via data linking. For both patients and HCPs, surveys included an initial section on demographic data, followed by sections on the experience, impact, and burden of UC- or CD-related symptoms on patients' lives, the perception of symptoms on patient quality of life, productivity, and psychological and social health and aimed to identify gaps in HCP–patient communication.

Additionally, symptoms experienced by patients in the past month (and ever) were selected from a list of 30 possible symptoms and ranked according to which were most impactful, using a scale of 1 to 5 in which 1 was the most impactful. Patients who reported experiencing BU in the past month rated the severity of urgency over the last 3 days on the Urgency Numeric Rating Scale (NRS) of 0–10, where 0 denotes "no urgency" and 10 denotes the "worst possible urgency" [18]. HCPs ranked the most common and most impactful symptoms reported by patients on a scale of 1–5, where 1 was the most reported or had the greatest impact. Patients rated levels of comfort reporting BU to HCPs on a scale of 1–7 (where 1 indicated "not at all comfortable" and 7 indicated "completely comfortable"), and scores ≤ 4 represent "not feeling comfortable."

Statistical Analysis

As a result of the study's descriptive design, no formal sample size calculations were performed. A sample size of approximately 100 patients with UC, 100 patients with CD, and 100 HCPs from Japan was planned. Data were summarized using descriptive statistics, with categorical variables presented as number, frequency, and percentage, ordinal variables as frequency and percentage, and continuous variables as number and means/medians with standard deviations (SDs).

Subgroup analyses based on disease activity were conducted using the Manitoba IBD Index [19], where a numerical score of ≤ 3 indicates active disease while a score of ≥ 4 represents inactive disease. The Manitoba IBD Index is a validated clinical index that assesses disease activity based on patient self-reports of symptom persistency for the previous 6 months; it is scored on a scale of 1 to 6, where 1 corresponds to "constantly active," "giving me symptoms every day" and 6 corresponds to "I was well in the past 6 months, which I consider a remission or absence of symptom" [19].

RESULTS

Demographics and Characteristics

Among the 486 patients who were contacted, 124 patients with UC and 99 patients with CD in Japan completed surveys from July 1, 2021 to September 9, 2021. Key patient demographics and characteristics are reported in Table 1. The mean age of patients with UC and CD in the study cohort was 48.8 and 43.0 years, respectively (Table 1). In total, 70.2% and 67.7% of patients in the study cohort with UC and CD, respectively, were male. The mean (SD) duration of disease was 12.5 (9.6) and 15.7 (10.2) years for UC and CD, respectively. On the basis

Table 1 Demographics and characteristics of Japanese patients with ulcerative colitis or Crohn's disease

	Patients with ulcerative colitis			Patients with Crohn's disease			HCPs $N = 100$
	All patients $N = 124$	Active disease[a] $N = 33$	Inactive disease[a] $N = 91$	All patients $N = 99$	Active disease[a] $N = 46$	Inactive disease[a] $N = 53$	
Age (years), mean (SD)	48.8 (10.5)	46.5 (10.0)	49.6 (10.5)	43.0 (10.8)	43.4 (9.7)	42.6 (11.7)	–
Sex, *n* (%)							
Male	87 (70.2)	20 (60.6)	67 (73.6)	67 (67.7)	31 (67.4)	36 (67.9)	92 (92.0)
Female	37 (29.8)	13 (39.4)	24 (26.4)	31 (31.3)	14 (30.4)	17 (32.1)	8 (8.0)
Prefer not to say	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)	1 (2.2)	0 (0.0)	0 (0.0)
Time since diagnosis (years), mean (SD)	12.5 (9.6)	10.8 (6.6)	13.1 (10.5)	15.7 (10.2)	15.1 (11.4)	16.3 (9.1)	NA
Current treatments, *n* (%)							
5-ASA	92 (74.2)	27 (81.8)	65 (71.4)	32 (32.3)	18 (39.1)	14 (26.4)	NA
Corticosteroids	33 (26.6)	15 (45.5)	18 (19.8)	18 (18.2)	15 (32.6)	3 (5.7)	NA
Immunomodulator	35 (28.2)	11 (33.3)	24 (26.4)	14 (14.1)	9 (19.6)	5 (9.4)	NA
Advanced therapy[b]	52 (41.9)	16 (48.5)	36 (39.6)	86 (86.9)	41 (89.1)	45 (84.9)	NA
Year of qualification, *n* (%)							
Before 1985	NA	NA	NA	NA	NA	NA	6 (6.0)
1985–2018	NA	NA	NA	NA	NA	NA	88 (88.0)
After 2018	NA	NA	NA	NA	NA	NA	6 (6.0)

5-ASA 5-aminosalicylic acid, *HCPs* health care professionals, *NA* not applicable, *SD* standard deviation

[a] Active and inactive disease was based on the Manitoba Inflammatory Bowel Disease Index [19]

[b] Advanced therapy consisted of adalimumab (including biosimilars), infliximab (including biosimilars), golimumab, certolizumab pegol, vedolizumab, natalizumab, ustekinumab, and tofacitinib

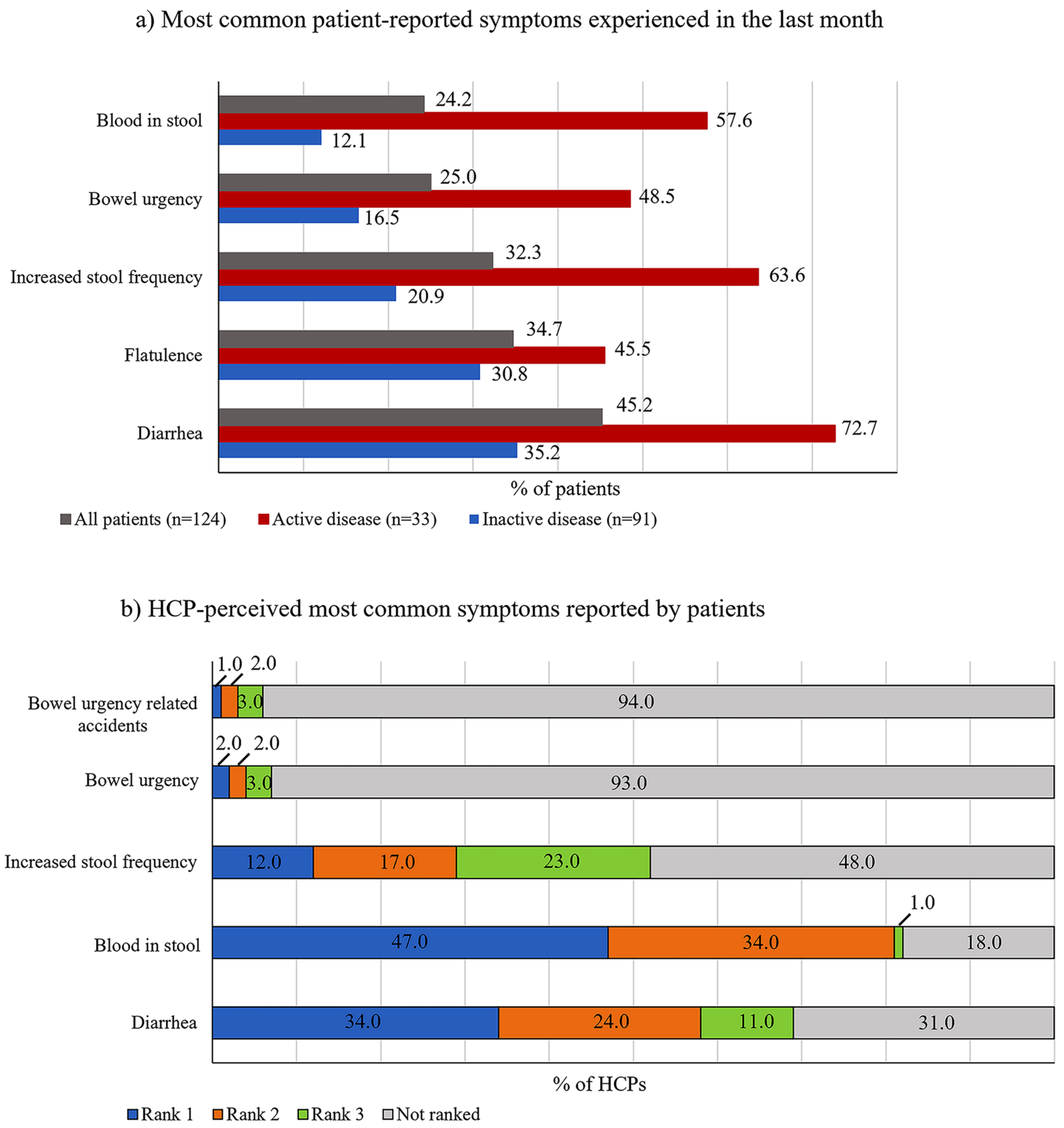


Fig. 1 Patient and HCP perceptions of UC symptoms in Japan. **a** Most common patient-reported symptoms experienced in the last month. Patients were asked which symptoms they currently have (i.e., in the last month). Symptoms were selected from a list of 30 options. **b** HCP-perceived most common symptoms reported by patients. HCPs were asked to rank the top five symptoms most reported by patients. Active and inactive disease was based on the Manitoba Inflammatory Bowel Disease Index [19]. *HCP* health care professional, *UC* ulcerative colitis

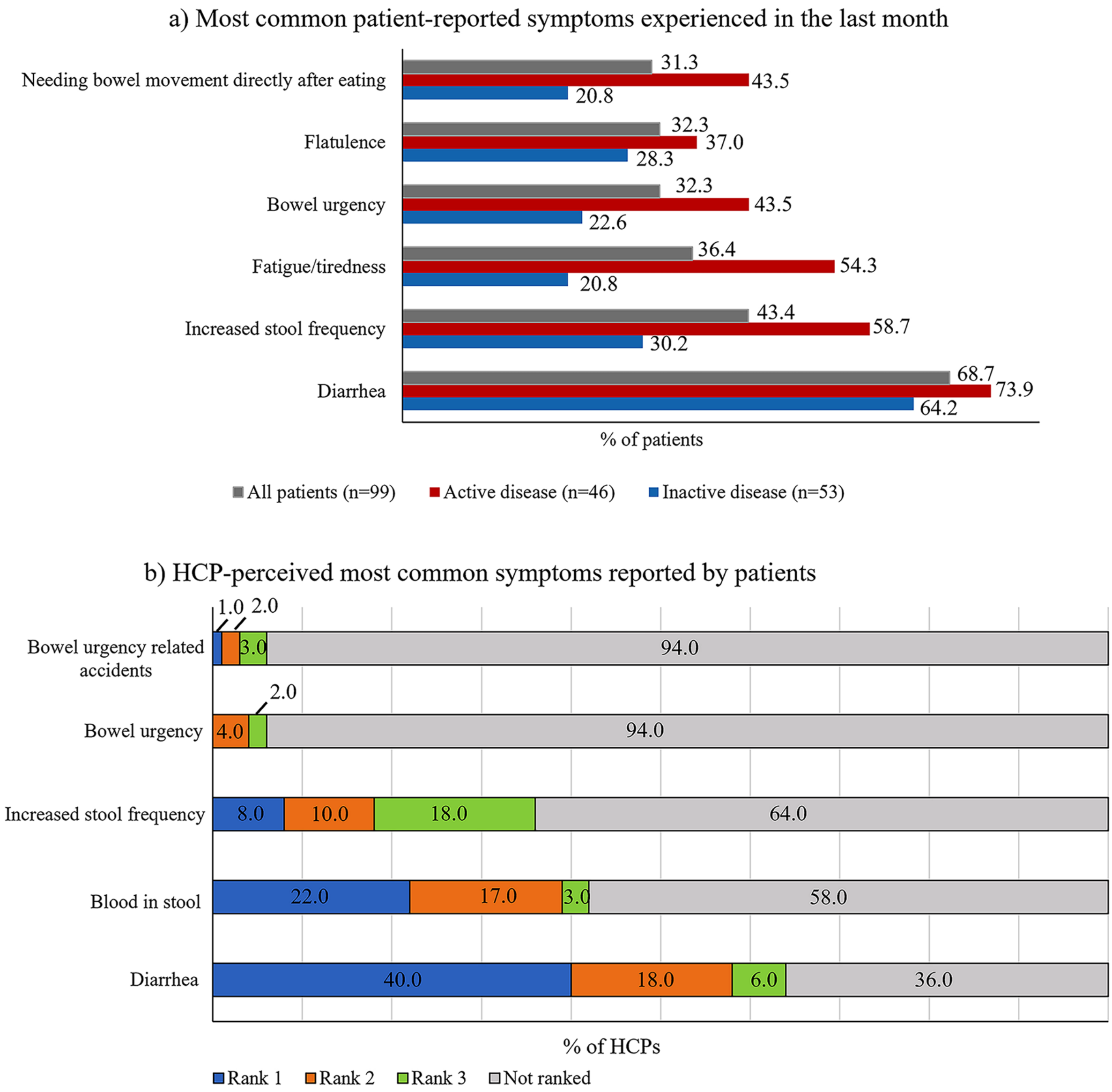
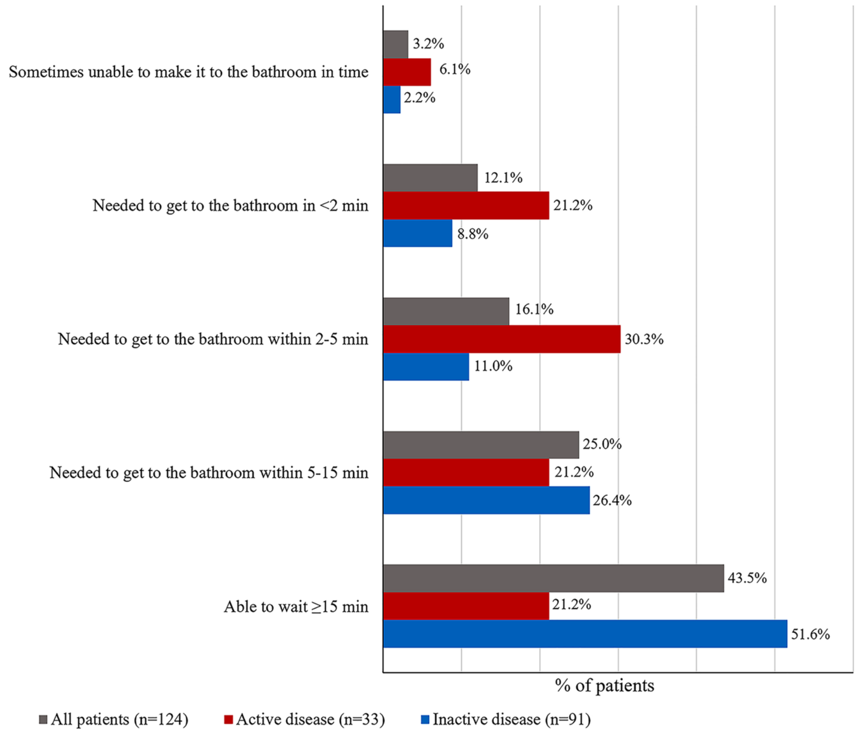
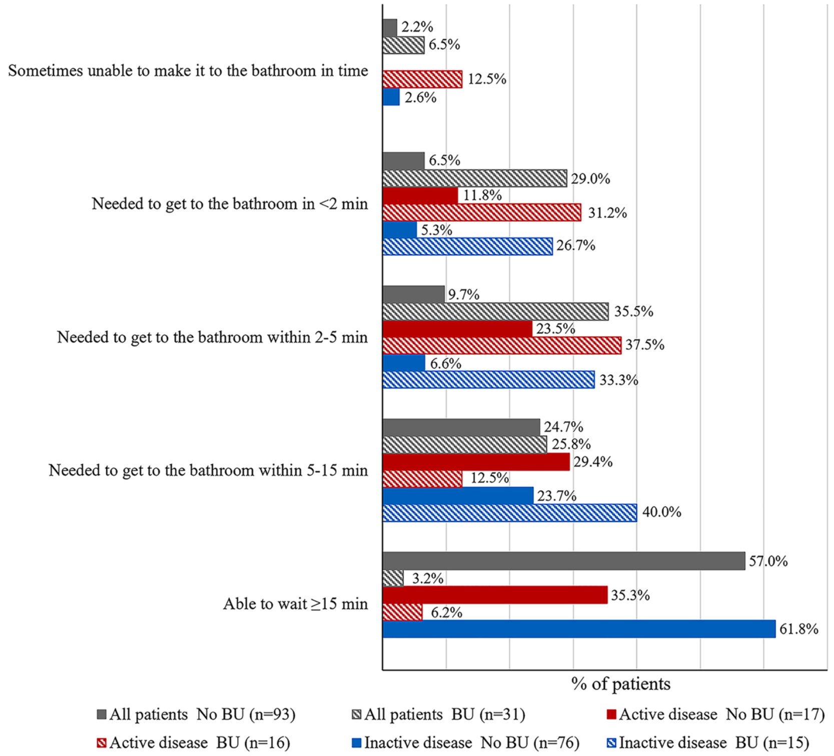


Fig. 2 Patient and HCP perceptions of CD symptoms in Japan. **a** Most common patient-reported symptoms experienced in the last month. Patients were asked which symptoms they currently have (i.e., in the last month). Symptoms were selected from a list of 30 options. **b** HCP-perceived most common symptoms reported by patients. HCPs were asked to rank the top five symptoms most reported by patients. Active and inactive disease was based on the Manitoba Inflammatory Bowel Disease Index [19]. *CD* Crohn's disease, *HCP* health care professional

a) Patient’s deferral time over the last 3 days



b) Patient’s deferral time over the last 3 days by BU experience



◀ **Fig. 3** BU experience in patients with UC. **a** Patient-reported deferral time over the last 3 days (how much urgency patients had before bowel movements over the last 3 days). **b** Patients' deferral time over the last 3 days. **c** Patient-reported BU (sudden or immediate need to have a bowel movement) in the last 3 days, rated on the Urgency NRS from 0 ("no urgency") to 10 ("worst possible urgency"). **d** Frequency of BU in the past 3 months. Active and inactive disease was based on the Manitoba Inflammatory Bowel Disease Index [19]. *BU* bowel urgency, *NRS* Numeric Rating Scale, *SD* standard deviation, *UC* ulcerative colitis

of disease activity (as assessed by the Manitoba IBD index), 33 patients (26.6%) with UC and 46 patients (46.5%) with CD had active disease. The most common current treatment in UC was 5-aminosalicylic acid (74.2% for UC and 32.3% for CD) and advanced therapy (biologic therapy, biosimilars, or Janus kinase inhibitor) for CD (41.9% for UC and 86.9% for CD). A total of 840 HCPs in Japan were contacted, and 100 HCPs completed the survey from May 28, 2021 to October 2, 2021. Overall, 92.0% of HCPs in Japan were male, with 88.0% becoming qualified between 1985 and 2018 (Table 1).

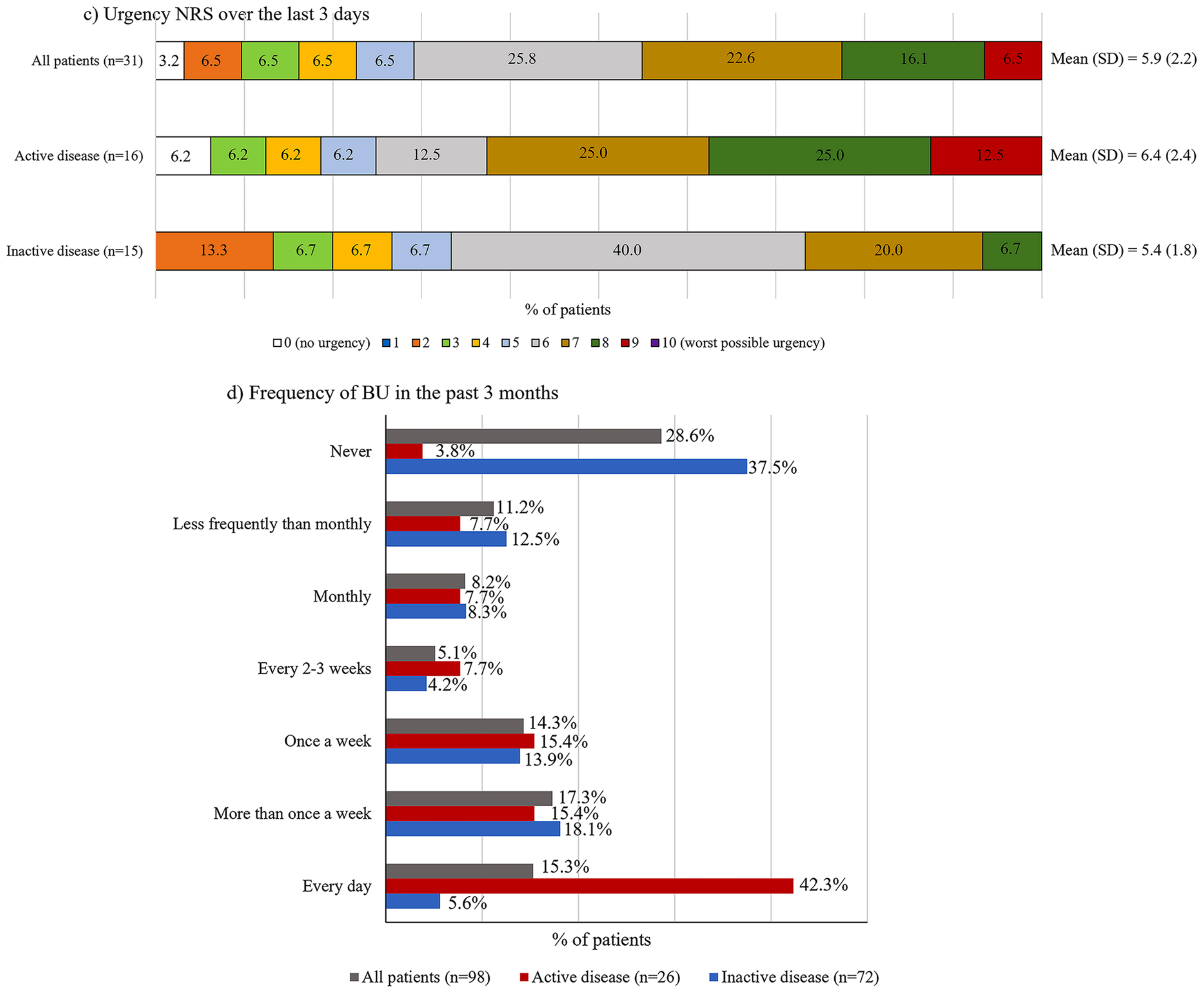
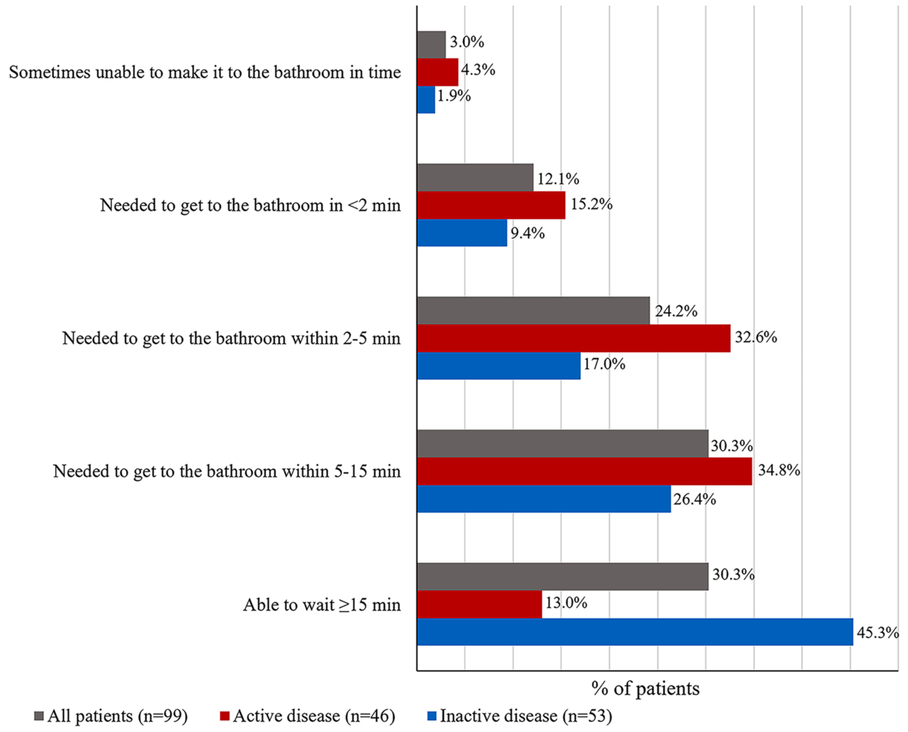
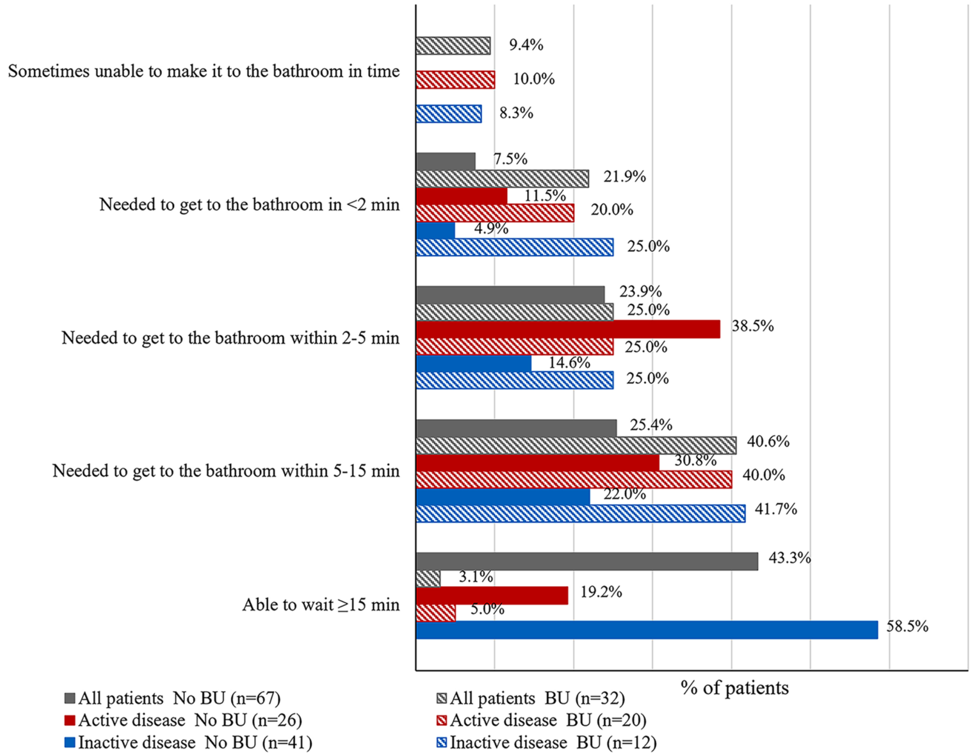


Fig. 3 continued

a) Patient’s deferral time over the last 3 days



b) Patient’s deferral time over the last 3 days by BU experience



◂ **Fig. 4** BU experience in patients with CD. **a** Patient-reported deferral time over the last 3 days (how much urgency patients had before bowel movements over the last 3 days). **b** Patients' deferral time over the last 3 days. **c** Patient-reported BU (sudden or immediate need to have a bowel movement) in the last 3 days, rated on the Urgency NRS from 0 ("no urgency") to 10 ("worst possible urgency"). **d** Frequency of BU in the past 3 months. Active and inactive disease was based on the Manitoba Inflammatory Bowel Disease Index [19]. *BU* bowel urgency, *CD* Crohn's disease, *NRS* Numeric Rating Scale, *SD* standard deviation

Patient and HCP Perceptions of UC and CD Symptoms

Overall, the most common patient-reported UC symptoms experienced in the month prior to survey completion were diarrhea (45.2%), flatulence (34.7%), increased stool frequency (32.3%), BU (25.0%), and blood in stool (24.2%), with a greater proportion of patients with active disease reporting each of these symptoms than those with inactive disease (Fig. 1a). The most common UC symptoms perceived by HCPs were blood in stool (47.0%), diarrhea (34.0%), and increased stool

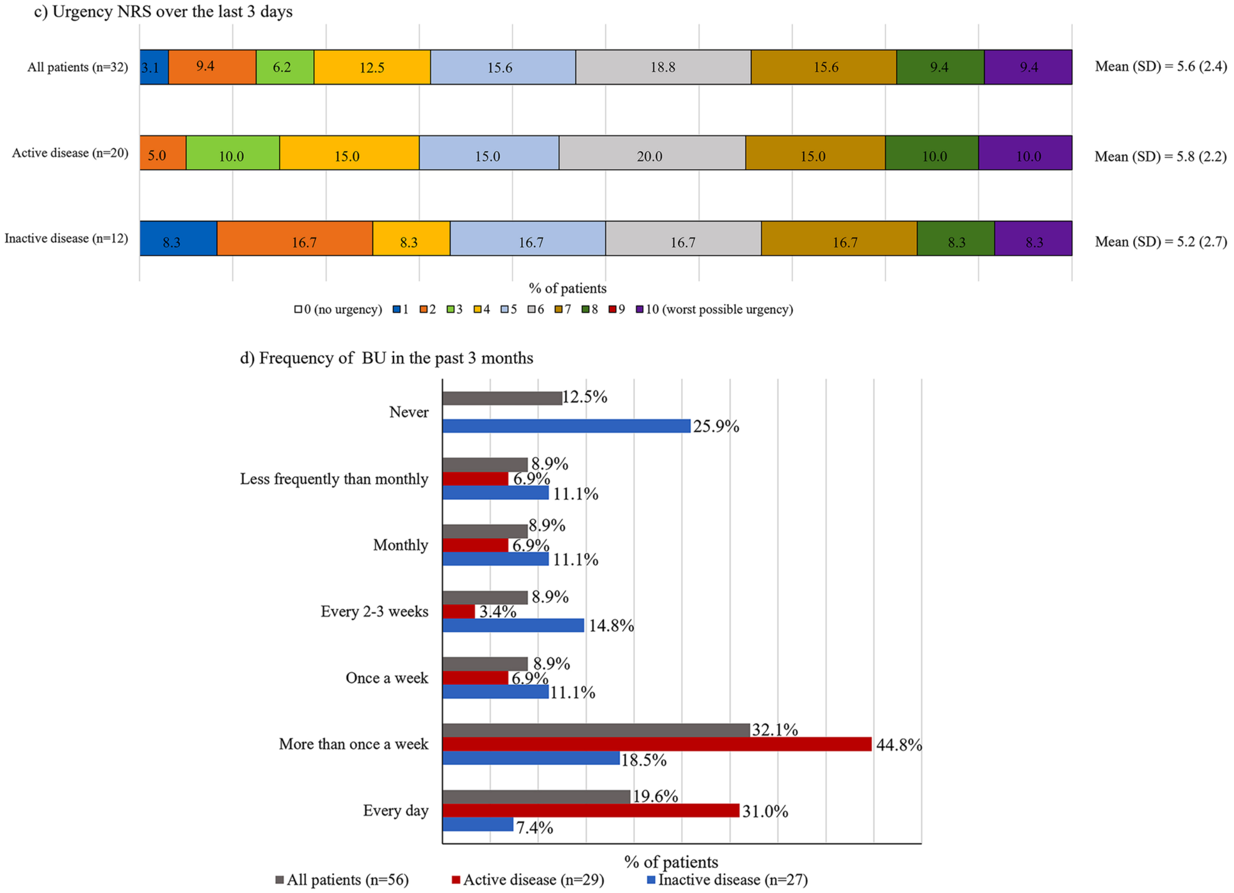
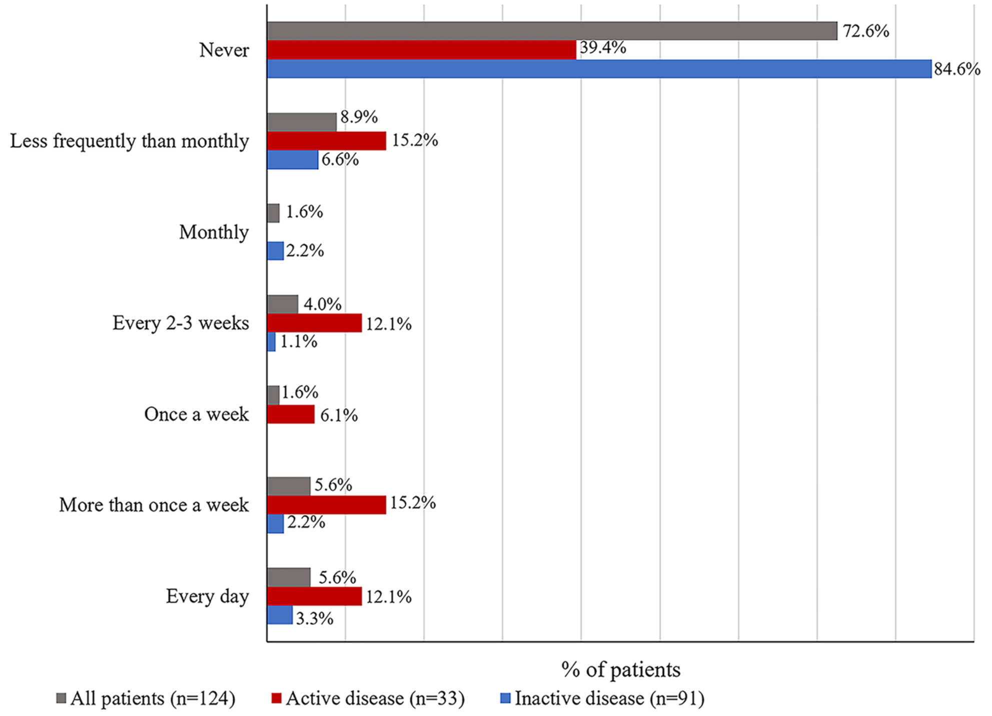
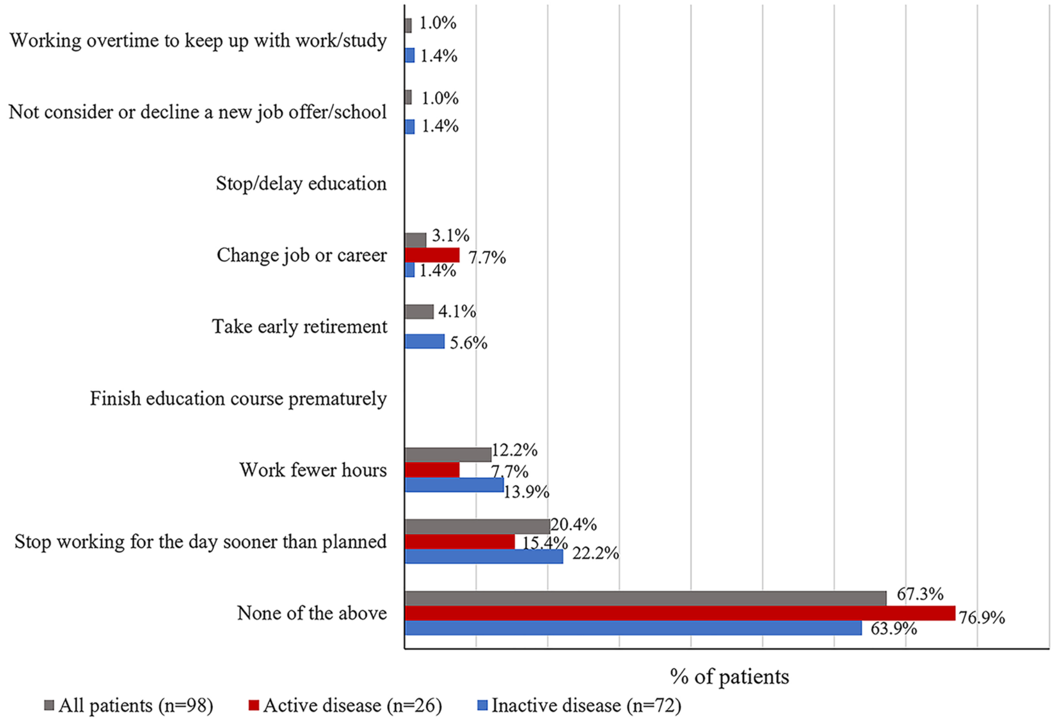


Fig. 4 continued

a) Frequency of diaper/pad/other protection use due to fear/anticipation of BU related accidents in the past 3 months



b) Consequences of BU on work/school in the past 3 months



◀ **Fig. 5** Impacts of BU on the daily lives of patients with UC and HCP–patient communication. **a** Frequency of diaper/pad/other protection use due to fear/anticipation of fecal urge incontinence over the past 3 months. **b** Impact of BU on work or school over the past 3 months among patients who ever experienced BU. **c** Percentages of patients not comfortable discussing BU with their HCP, based on patients rating how comfortable they are at reporting BU to their HCP on a scale of 1 ("not at all comfortable") to 7 ("completely comfortable"); patients with scores ≤ 4 are shown. **d** Reasons for patients feeling uncomfortable reporting BU to HCPs. **e** Among patients who do not discuss BU at every appointment, percentage who would like to discuss BU more frequently with their HCP. **f** HCP-reported symptoms proactively discussed at a routine appointment. **g** Reasons for HCPs not proactively discussing BU in routine appointments. **h** HCP-perceived most impactful symptoms on treatment decisions. HCPs were asked to choose from a list of possible symptoms, the top three most impactful on treatment decisions. Active and inactive disease was based on the Manitoba Inflammatory Bowel Disease Index [19]. *BU* bowel urgency, *HCP* health care professional, *UC* ulcerative colitis

frequency (12.0%; Fig. 1b). Overall, UC symptoms with the greatest impact among those reported as ever experienced (i.e., ranked 1 or 2) were ranked by patients as blood in stool, diarrhea, BU-related accidents, increased stool frequency, and BU (Supplementary Material, Fig. S1). Among these symptoms, BU-related accidents and blood in stool were ranked as having the most impact by patients with inactive and active UC, respectively. The UC symptoms with the most impact as rated by HCPs were blood in stool and diarrhea (Supplementary Material, Fig. S2).

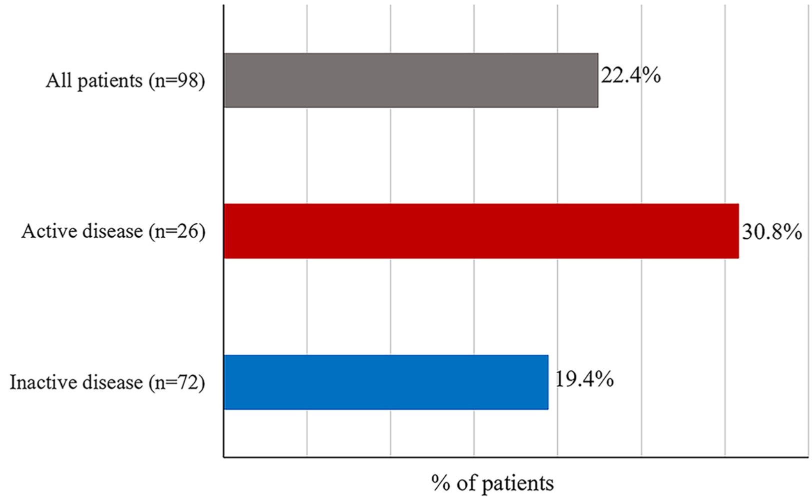
The most common patient-reported CD symptoms experienced in the month prior to survey completion were diarrhea (68.7%), increased stool frequency (43.4%), fatigue/tiredness (36.4%), BU (32.3%), flatulence (32.3%), and needing a bowel movement directly after eating (31.3%). A greater proportion of patients with active disease reported each of these symptoms than those with inactive disease (Fig. 2a). The most common CD symptoms perceived by HCPs were diarrhea (40.0%), blood in stool (22.0%), and increased stool frequency (8.0%; Fig. 2b).

Overall, CD symptoms with the greatest impact ever experienced (i.e., ranked 1 or 2) were ranked by patients as diarrhea, blood in stool, increased stool frequency, BU, and BU-related accidents (Supplementary Material, Fig. S2). Among these symptoms, diarrhea was ranked as the most impactful by patients with inactive CD, and diarrhea and BU were ranked as having the most impact by patients with active CD. The CD symptoms with the most impact as rated by HCPs were diarrhea and blood in stool (Supplementary Material, Fig. S2).

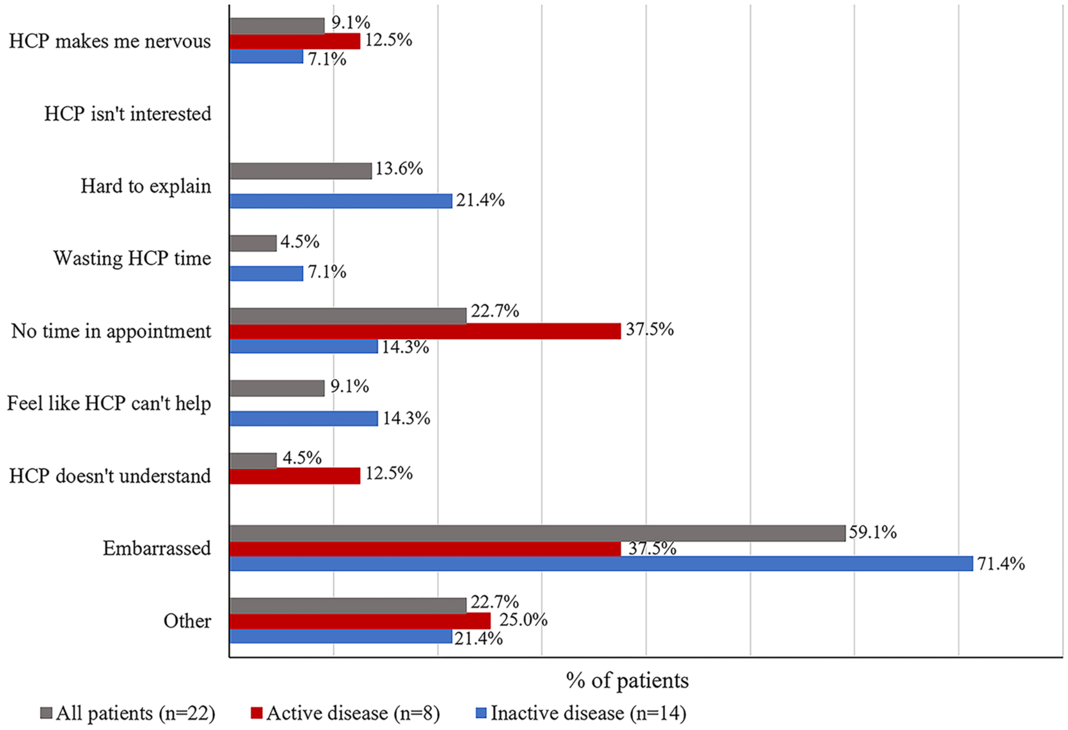
BU Experience in Patients with UC and CD

When asked about deferral time (the period during which it is possible to defer defecation after the desire to evacuate) in the last 3 days, approximately one-third of all patients with UC and CD reported that they could not defer defecation for more than 5 min (Figs. 3a and 4b). Notably, 3.2% and 3.0% of patients with UC and CD, respectively, reported sometimes not being able to make it to the bathroom in time. For both UC and CD, almost twice the number of patients with active disease than inactive disease experienced shorter deferral time (needed to go to the bathroom within 2–5 min; needed to go to the bathroom in < 2 min; sometimes unable to make it to the bathroom in time; Figs. 3a and 4a). As anticipated, patients with BU experienced shorter deferral time than those without BU (Figs. 3b and 4b).

Mean (SD) ranking on the Urgency NRS was 5.9 (2.2) for all patients with UC (Fig. 3c). Patients with active UC had a higher mean (SD) Urgency NRS score (6.4 [2.4]) than those with inactive UC (5.4 [1.8]; Fig. 3c). Patients



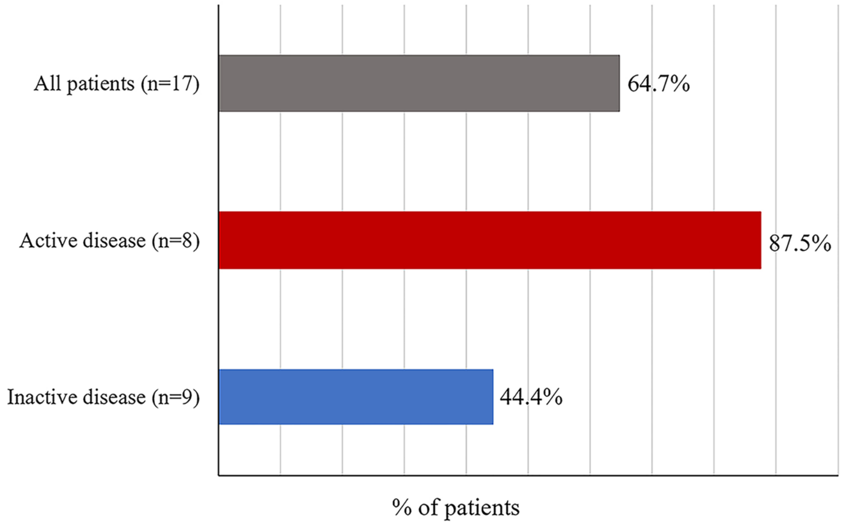
c) Patients not comfortable discussing BU with their HCP



d) Reasons for not feeling comfortable reporting BU

Fig. 5 continued

e) Patients who would like to discuss BU more frequently with their HCP



f) HCP-reported symptoms most commonly discussed at a routine appointment

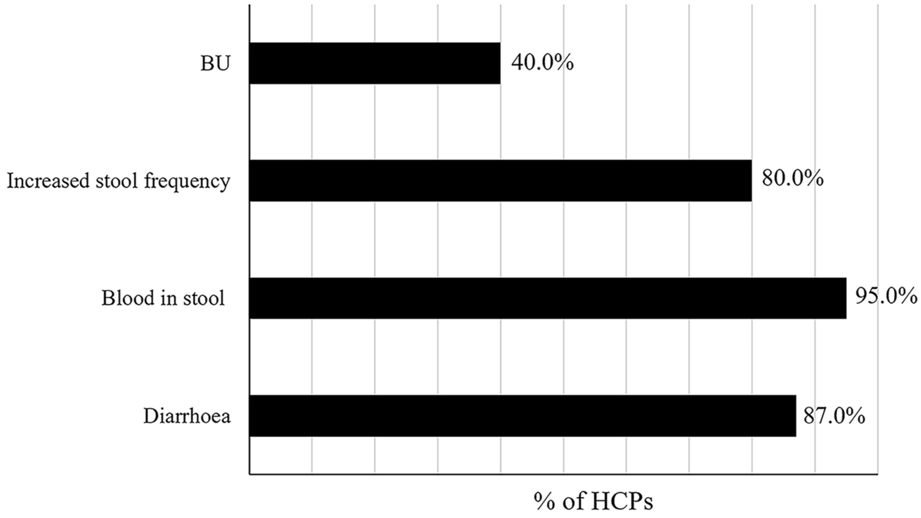
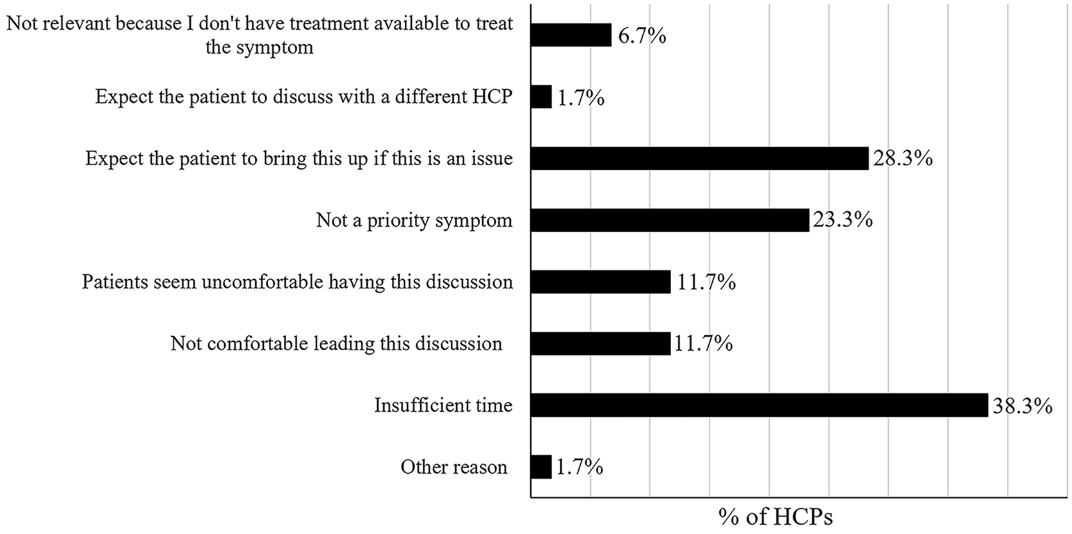


Fig. 5 continued

with CD had a mean (SD) Urgency NRS score of 5.6 (2.4), which was slightly higher in patients with active (5.8 [2.2]) than in those with inactive CD (5.2 [2.7]; Fig. 4c). Mean Urgency NRS scores were generally higher in patients reporting shorter defecation deferral times (Supplementary Material, Fig. S3).

Among patients who ever experienced BU (UC, $n = 98$; CD, $n = 56$), 46.9% of those with UC and 60.6% of those with CD reported


g) Reasons HCPs do not proactively discuss BU

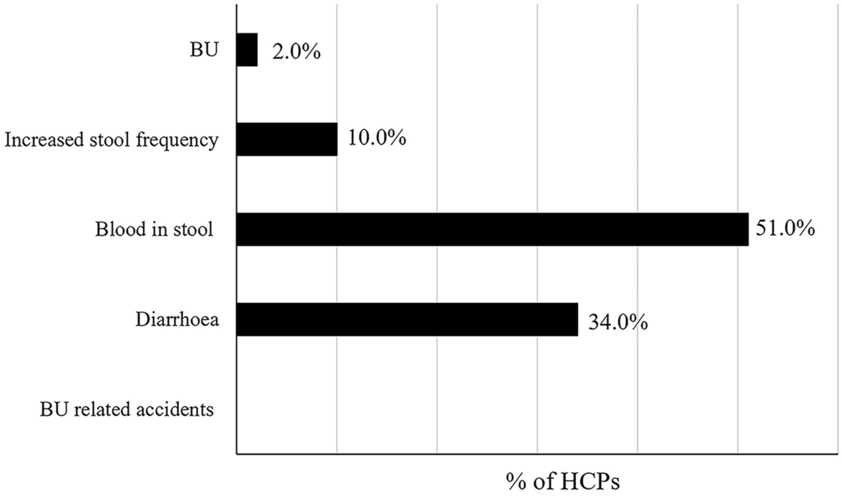

h) HCP-perceived most impactful symptoms on treatment decisions

Fig. 5 continued

experiencing BU at least once a week over the past 3 months. Percentages increased to 73.1% and 82.7% for patients with active UC or CD, respectively (Figs. 3d and 4d).

Impact of BU on the Daily Lives of Patients and HCP–Patient Communication

A total of 27.4% of patients with UC and 39.4% with CD reported ever wearing a diaper/pad/

protection because of fear/anticipation of BU-related accidents, and 12.8% and 16.2% of all patients with UC and CD, respectively, reported wearing protection for this reason at least once a week in the past 3 months. The proportions reported wearing protection for this reason at least once a week rose to 33.4% and 32.6% among patients with active UC and active CD, respectively (Figs. 5a and 6a).

Patients were asked whether they declined participation in activities over the past 3 months, with a selection of multiple reasons possible. The most common reasons for patients with UC to decline participation in work or school-related activities were BU (8.9%) and fear of BU-related accidents (8.9%; Table 2). A higher proportion of patients with active UC declined participation in activities (all reasons, 9.1–30.3%) than those with inactive UC (all reasons, 0–3.3%; Table 2). The most common reasons for patients with CD to decline participation in work/school-related activities was BU (14.1%), tiredness/fatigue (12.1%), fear of BU-related accidents (10.1%), and abdominal pain before defecation (10.1%). A higher proportion of patients with active CD declined participation in activities (all reasons, 4.3–23.9%) than those with inactive CD (all reasons, 0–9.4%; Table 2). The most common consequence of BU in patients with both UC and CD was "stopped working for the day sooner than planned" (20.4% and 28.6%, respectively; Figs. 5b and 6b).

The proportion of patients not completely comfortable discussing BU with HCPs was 22.4% for UC and 23.2% for CD. For UC, a higher proportion of patients with active disease were not completely comfortable discussing BU with HCPs (30.8%) than those with inactive disease (19.4%; Figs. 5c and 6c). The most common reason for not being completely comfortable discussing BU with HCPs was embarrassment (Figs. 5d and 6d).

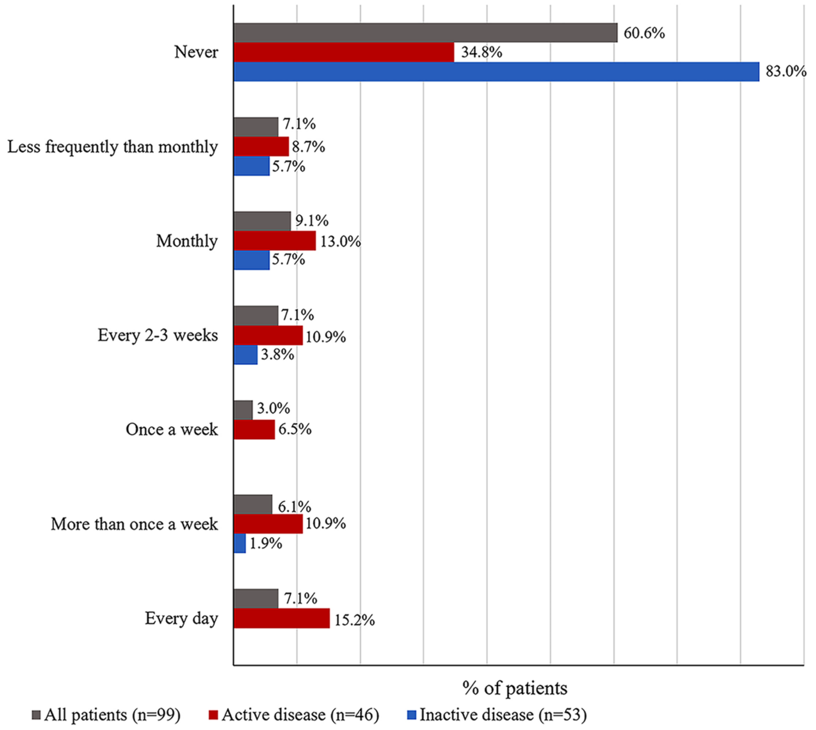
The proportion of patients who discuss BU with HCPs at every appointment was 45.2% for UC and 18.8% for CD. Patients with active disease were more likely than those with inactive disease to discuss BU at every appointment (Supplementary Material, Fig. S4). The proportion of patients who would like to discuss BU more frequently with HCPs was 64.7% for UC and 50.0% for CD. Patients with active disease reported wanting to discuss BU more often than those with inactive disease (Figs. 5e and 6e).

HCP-reported symptoms most commonly discussed at routine appointments were blood in stool, diarrhea, increased stool frequency, and BU (Figs. 5f and 6f). The reasons for HCPs not proactively discussing BU with patients were insufficient time, the expectation for patients to initiate the discussion, and BU not being a priority issue (Figs. 5g and 6g). The HCP-perceived symptoms with the most impact on treatment decisions were blood in stool, diarrhea, and increased stool frequency, with very few HCPs (2.0% for UC and 0.0% for CD) reporting BU as the most impactful symptom on treatment decisions (Figs. 5h and 6h).

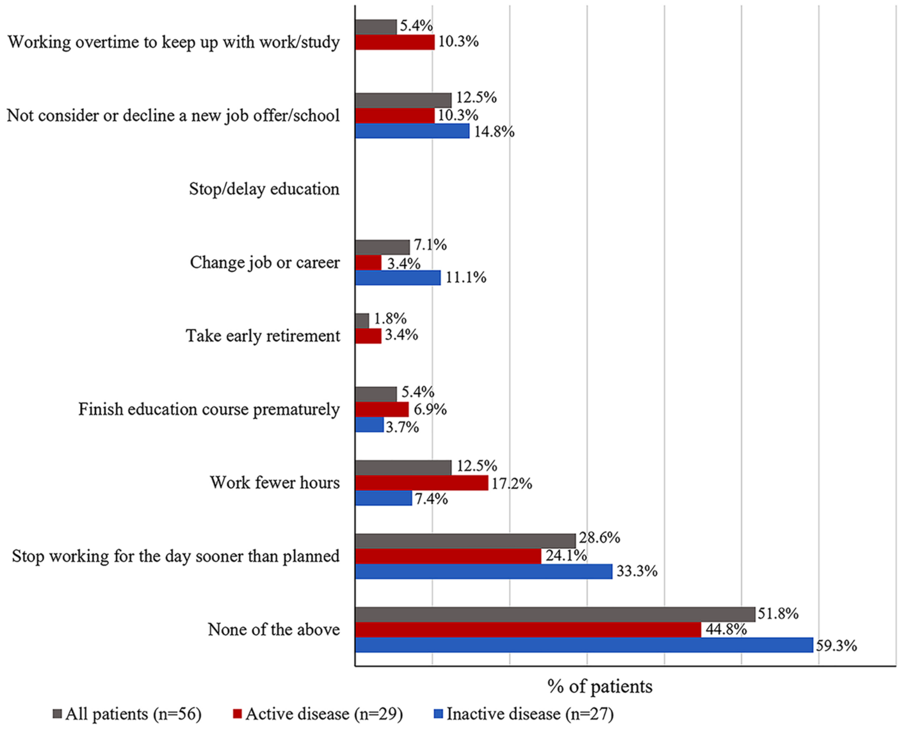
DISCUSSION

Despite the availability of multiple therapies for IBD, many patients still experience symptoms that significantly affect their quality of life. The CONFIDE study provided "real-world" perspectives on the burden of BU in patients with UC or CD. Our findings in Japanese patients from the CONFIDE study suggest that BU impacts the daily lives of those with UC and CD and is a symptom that HCPs should consider during medical treatment of these conditions. This study also highlights a potential communication gap between patients with IBD and HCPs in Japan, with discrepancies between their perceptions on the most impactful symptoms.

For Japanese patients with UC or CD, BU was one of the most common and bothersome



a) Frequency of diaper/pad/other protection use due to fear/anticipation of BU related accidents in the past 3 months



b) Consequences of BU on work/school in the past 3 months

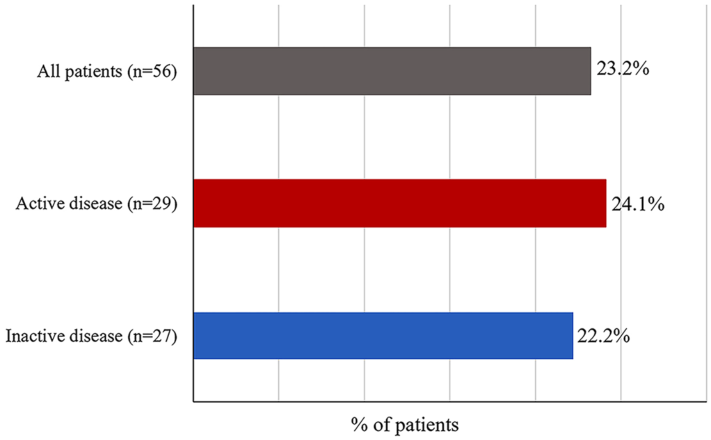
◀ **Fig. 6** Impacts of BU on the daily lives of patients with CD and HCP–patient communication. **a** Frequency of diaper/pad/other protection use in the past 3 months due to fear/anticipation of fecal urge incontinence. **b** Impact of BU on work or school in the past 3 months among patients who ever experienced BU. **c** Percentages of patients not comfortable discussing BU with their HCP, based on patients rating how comfortable they are at reporting BU to their HCP on a scale of 1 ("not at all comfortable") to 7 ("completely comfortable"); patients with scores ≤ 4 are shown. **d** Reasons for patients feeling uncomfortable reporting BU to HCPs. **e** Among patients who do not discuss BU at every appointment, percentage who would like to discuss BU more frequently with their HCP. **f** HCP-reported symptoms proactively discussed at a routine appointment. **g** Reasons for HCPs not proactively discussing BU in routine appointments. **h** HCP-perceived most impactful symptoms on treatment decisions. HCPs were asked to choose from a list of possible symptoms, the top three most impactful on treatment decisions. Active and inactive disease was based on the Manitoba Inflammatory Bowel Disease Index [19]. *BU* bowel urgency, *CD* Crohn's disease, *HCP* health care professional

patient-reported symptoms over the past month, particularly in patients with active disease. Not only was the frequency of BU reported as being high for a substantial proportion of patients but BU and BU-related accidents ranked high as having the greatest impact of symptoms ever experienced. A substantial proportion of patients reported using diapers/pads/other protection every day or more than once a week because of the fear/anticipation of BU-related accidents, particularly for those with active disease. Consequently, BU affected aspects of patients' lives such as work and school, and patients with active disease in particular declined participation in these activities because of the fear of BU-related accidents, BU, and increased stool frequency. Collectively, these findings highlight the burden of BU on the daily lives of Japanese patients with UC and CD.

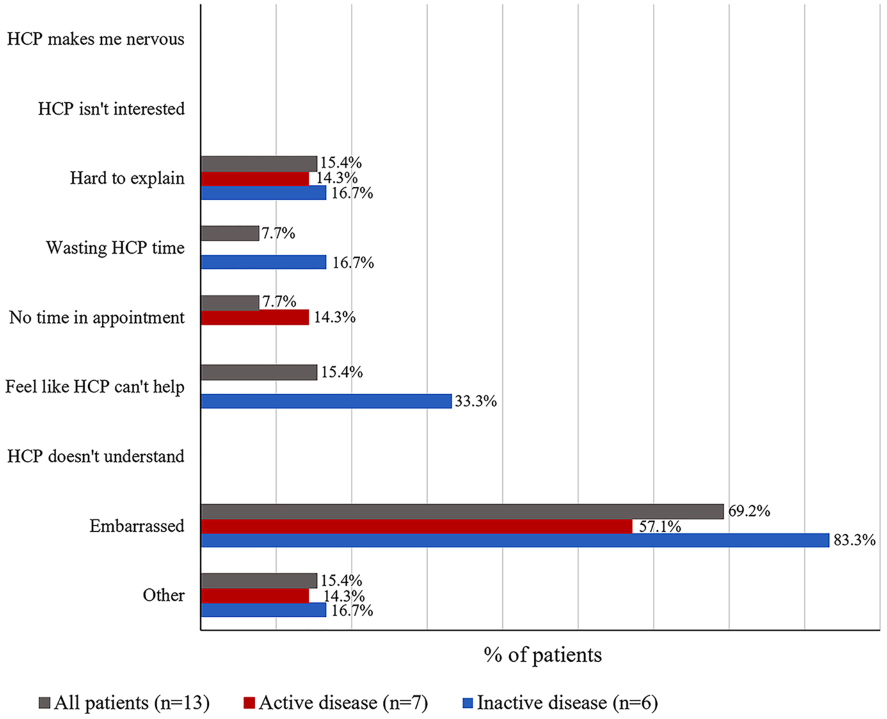
According to HCPs in Japan, the most commonly perceived UC and CD symptoms were diarrhea, blood in stool, and increased stool frequency. BU did not rank as highly as diarrhea, blood in stool, or increased stool frequency in most common HCP-perceived symptoms. HCPs rated blood in stool and diarrhea as having the most impact on patients with UC and CD. HCPs reported BU as the fourth symptom discussed most frequently at routine appointments, with the top three being blood in stool, diarrhea, and increased stool frequency. The reasons for HCPs not proactively discussing BU with patients were insufficient time, the expectation for patients to initiate the discussion, and BU not being a priority issue. Interestingly, HCPs in Japan are less likely to proactively discuss BU than HCPs in other countries [16, 17]. However, according to patient-reported data, a considerable proportion of Japanese patients with UC and CD would like to discuss BU more frequently with their HCP, particularly those with active disease. Taken together, these data suggest that the impact of BU may be overlooked in clinical settings in Japan and highlight a potential gap in communication between Japanese patients and HCPs about the frequency and impact of BU on daily life. Additional studies may help to provide strategies for patients and HCPs to manage the impact of BU.

While abdominal pain is a common symptom in patients with UC and CD, it was not among the most common symptoms reported by Japanese patients in the CONFIDE study. Patient advisors, who assisted in designing the CONFIDE survey questions and response options, recommended distinguishing between "persistent abdominal pain" and "abdominal pain before bowel movement." Consequently, this may have resulted in the two specific terms not appearing among the "top five" symptoms

c) Patients not comfortable discussing BU with their HCP



d) Reasons for not feeling comfortable reporting BU



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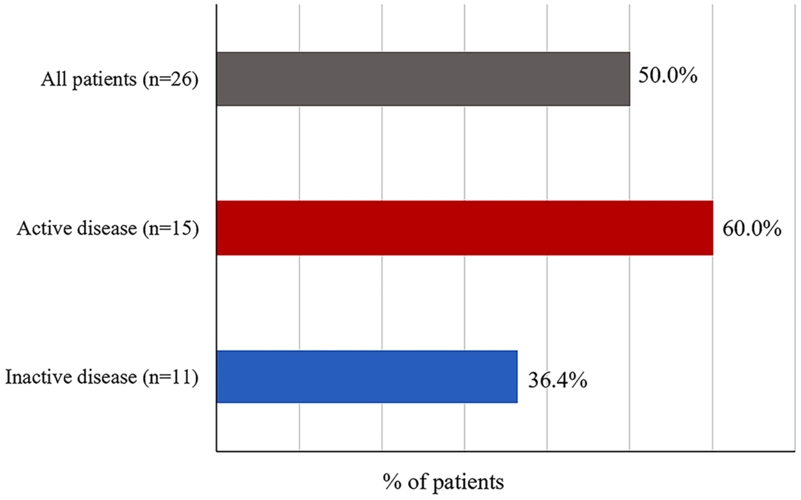
e) Patients who would like to discuss BU more frequently with their HCP



f) HCP-reported symptoms most commonly discussed at a routine appointment

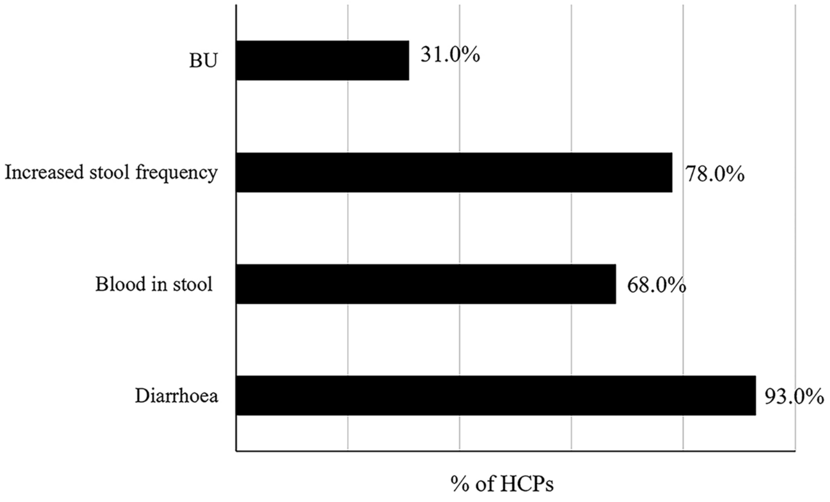
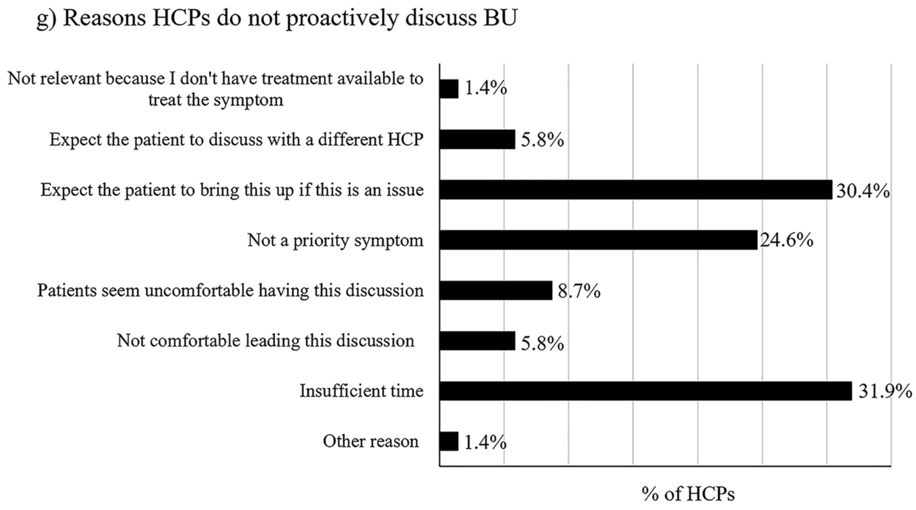


Fig. 6 continued

for Japanese patients with UC and CD. Overall, persistent abdominal pain and abdominal pain before defecation were reported by Japanese patients with UC and CD as one of the most common reasons for declining participation in work/school-related activities in the last 3 months. In general, the findings in the current analysis are generally consistent with those of the US/European cohorts from the CONFIDE study, where it was demonstrated that BU has a substantial impact on patients with UC and CD and is underappreciated by HCPs. For patients in the USA and Europe, 47.0% and 29.7% with UC and 42.3% and 38.0% with CD, respectively,



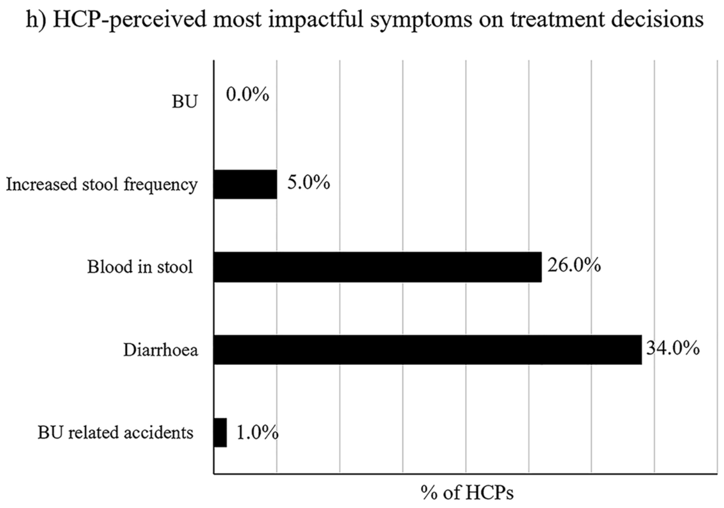


Fig. 6 continued

reported experiencing BU in the previous month [16, 17] compared with 25.0% (UC) and 32.3% (CD) of Japanese patients. In general, the percentage of patients reporting BU as the symptom having the greatest impact was higher in the US and European cohorts than in the Japanese cohort: 24.4% (UC) and 12.7% (CD) for patients in the US cohort, 24.0% (UC) and 24.1% (CD) for the European cohort [16, 17], and 9.2% (UC) and 19.6% (CD) for the Japanese cohort.

Differences in patient-perceived severity of BU between the Japanese and US and European cohorts may be due to differences in baseline characteristics. Japanese patients who participated in CONFIDE were generally older than those in the US and European cohorts,

Table 2 Most common reasons for declining participation in work/school-related activities in the last 3 months

Reason	Patients who declined participation in work/school (%)					
	Ulcerative colitis			Crohn's disease		
	All patients (*n* = 124)	Active disease[a] (*n* = 33)	Inactive disease[a] (*n* = 91)	All patients (*n* = 99)	Active disease[a] (*n* = 46)	Inactive disease[a] (*n* = 53)
Bowel urgency	8.9	24.2	3.3	14.1	23.9	5.7
Fear of bowel urgency-related accidents	8.9	30.3	1.1	10.1	19.6	1.9
Fear of fecal seepage/unnoticed leakage of stool resulting in stained undergarments/sheets	3.2	12.1	0	5.1	10.9	0
Fear of bowel movement accidents[b]	2.4	9.1	0	3	6.5	0
Increased stool frequency	4	15.2	0	6.1	8.7	3.8
Blood in stool	3.2	12.1	0	3	6.5	0
Abdominal pain before defecation	4	12.1	1.1	10.1	19.6	1.9
Persistent abdominal pain	3.2	9.1	1.1	4	4.3	3.8
Tiredness/fatigue	4.8	15.2	1.1	12.1	15.2	9.4

[a] Active and inactive disease was based on the Manitoba Inflammatory Bowel Disease Index [19]

[b] Bowel movement accidents refer to accidents that occurred without control or any warning as opposed to bowel urgency-related accidents (unable to make it to the bathroom in time)

particularly in the case of UC where Japanese patients were approximately 10 years older than those in the US cohort. In addition, the mean duration of disease was longer in Japanese patients (12.5 years for UC and 15.7 years for CD) than in the US cohort (7.9 years for both UC and CD) and the European cohort (8.7 years for UC and 9.2 years for CD) [16, 17]. The relative older age and longer disease duration in Japanese patients may impact the perception of disease severity, with these patients developing coping mechanisms over time.

BU and the fear of BU-related accidents had substantial effects on daily life. For patients from the US and European cohorts of CONFIDE, 37.0% and 27.2% with UC and 38.6% and 27.6% with CD did not attend work or school because of BU, respectively. This increased to 42.0% and 33.3% with UC and 40.5% and 30.9% with CD in the US and European cohorts, respectively, not attending school or work because of the fear of BU-related accidents [16, 17]. In the Japanese population, the percentage of patients declining work or school was numerically lower than that in the US and European cohorts; 8.9% (UC) and 14.1% (CD) declined because of BU, and 8.9% (UC) and 10.1% (CD) declined because of the fear of BU-related accidents [16, 17]. The differences in work and school attendance rates between the US/European and Japanese cohorts may be attributed to the unique attitude of Japanese people regarding working and completing their required tasks despite having a medical condition or illness (considered "virtue") and an associated feeling of guilt for being absent because of illness, thus leading to low absenteeism. Low absenteeism has been demonstrated in Japanese patients with other diseases such as rheumatoid arthritis [20], and this may indicate that Japanese patients with IBD are likely to continue working even if they have severe symptoms such as BU.

The numerical differences observed between the Japanese and US/European cohorts may be due to the relative low severity of disease in the Japanese population enrolled in CONFIDE. This is supported by the fact that, in general, following stratification using the Manitoba IBD Index, findings in Japanese patients with active disease showed similar trends to those in the US and European cohorts. For example, when Japanese patients were stratified using the Manitoba IBD Index, the percentage of patients with active disease who declined work or school commitments because of BU or fear of BU-related accidents was comparable to that of the US and European cohorts (19.6–30.3%). However, some numerical differences were observed even after stratification. Over a 3-month period, the frequency of diaper/pad/other protection use due to fear of BU-related accidents was reported as “more than once a week” for 6.1% of Japanese patients with CD compared with 24.7% in the US and 15.0% in the European cohorts [17]. Environmental differences such as the high accessibility of public restrooms in Japan may impact this finding.

In a cross-sectional survey of physicians and their patients with UC and CD in Japan, patients with BU exhibited worse clinical outcomes and HRQOL than those without BU [10]. Results of surveys conducted in Japan indicate that UC significantly affects daily life because the symptoms BU and bowel incontinence negatively impact patients’ lives and social activities [8, 9]. These and the current findings highlight an urgent need to address BU in Japanese patients with UC and CD to improve patient outcomes.

The CONFIDE study had several limitations. This study was limited to patients with moderate-to-severe UC or CD, and therefore the results may not be generalizable to the larger UC and CD population. Furthermore, background characteristics such as employment status may impact patient responses. The findings in this study may not be representative of young patients with UC/CD given the mean age was > 40 years. Responses were self-reported and mostly retrospective, which may result in recall bias. Participation was based on willingness to complete the survey, so the included population may not necessarily reflect the general population. A further limitation is the lack of information regarding the availability and accessibility of public bathroom facilities, which may impact patient perceptions of BU and BU-related accidents. Our findings indicate that embarrassment was the primary reason Japanese patients felt uncomfortable discussing BU with HCPs. The feeling of embarrassment may be influenced by a patient’s age and sex; however, as a result of the limited sample size, we did not perform these subgroup analyses. Additional studies or surveys are warranted to better understand how factors of age and sex impact this issue. Furthermore, there were differences in patient characteristics by country, even though the same recruitment criteria were employed for each region. This may be due to the different therapeutic options or treatment prioritizations based on the insurance system or government support for patients’ expenses (i.e., Japanese patients may receive biologics earlier than other patients, as there is no financial burden owing to government support).

CONCLUSIONS

Despite the availability of multiple advanced therapies, BU remains a symptom with significant impact on the daily life of Japanese patients with UC and CD and is one of the symptoms that HCPs should consider when making decisions regarding treatment. BU and BU-related accidents were not a high priority for HCPs during routine appointments, highlighting a gap in communication between Japanese patients and HCPs. Taken together, HCPs should consider proactively discussing BU with their patients.

ACKNOWLEDGEMENTS

The authors thank the survey respondents and the participating institutions.

Medical Writing/Editorial Assistance. Medical writing and editorial assistance were provided by Lisa Cossens and Raena Fernandes of Syneos Health and funded by Mochida Pharmaceutical Co. Ltd and Eli Lilly Japan K.K.

Author Contributions. Alison Potts Bleakman and Theresa Hunter Gibble were involved in study conceptualization and design. Koji Matsuo was involved in data acquisition. Satoshi Osaga and Koji Matsuo were involved in data analysis. Toshifumi Hibi, Taku Kobayashi, Masaru Tanaka, Satoshi Osaga, Alison Potts Bleakman, Theresa Hunter Gibble, Marijana Nedeljkovic Protic, Isabel Redondo, Koji Matsuo, and Tadakazu Hisamatsu were involved in data interpretation and critical revision of the work for important intellectual content. All authors reviewed, revised, and approved the final manuscript for submission. All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article.

Funding. This study, including the Rapid Service Fee and Open Access Fee, was funded by Eli Lilly and Company.

Data Availability. The datasets analyzed during the current study are not publicly available due to proprietary reasons and are intellectual properties of Eli Lilly and Company.

Declarations

Conflict of Interest. Toshifumi Hibi received consultancy fees/grants/research support and/or was a speaker for AbbVie GK, ActivAid, Alfresa Pharma Corporation, Bristol Myers Squibb, Celltrion, EA Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Gilead Sciences, Janssen, JIMRO, JMDC Inc., Kyorin, Mitsubishi Tanabe Pharma Corporation, Mochida Pharmaceutical, Nippon Kayaku Co., Pfizer, Sandoz, Takeda Pharmaceutical, Zeria Pharmaceutical, and MIYARISAN Pharmaceutical. Taku Kobayashi served as an advisory board member, consultant or speaker for AbbVie, Activaid, Alfresa Pharma, Alimentiv, Bristol Myers Squibb, Celltrion, Covidien, EA Pharma, Eli Lilly and Company, Ferring Pharmaceuticals, Galapagos, Gilead Sciences, Janssen Pharmaceuticals, JIMRO, Kissei Pharmaceutical, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Mochida Pharmaceutical, Nippon Kayaku, Pfizer, Takeda, and Zeria Pharmaceutical, and has received research funding from AbbVie, Alfresa Pharma, EA Pharma, Gilead Sciences, Kyorin Pharmaceutical, Mochida Pharmaceutical, Nippon Kayaku, Otsuka Holdings, Pfizer, Sekisui Medical, Takeda, and Zeria Pharmaceutical. Masaru Tanaka and Satoshi Osaga are full time employees of Eli Lilly Japan K.K. and minor stockholders of Eli Lilly and Company. Koji Matsuo was a full-time employee of Eli Lilly Japan K.K at the time this work was completed and is now affiliated with Naramachi Internal Medicine Airi Ladies' Clinic. Alison Potts Bleakman, Theresa Hunter Gibble, Marijana Nedeljkovic Protic, and Isabel Redondo are full time employees of Eli Lilly and Company. Alison Potts Bleakman is a stockholder of Eli Lilly and Company. Tadakazu Hisamatsu received grants from Mitsubishi Tanabe Pharma Corporation, EA Pharma Co. Ltd., AbbVie GK, JIMRO Co. Ltd., Zeria Pharmaceutical Co. Ltd., Kyorin Pharmaceutical Co. Ltd., Nippon Kayaku Co. Ltd., Takeda Pharmaceutical Co. Ltd., Pfizer Inc., Mochida Pharmaceutical Co. Ltd., Boston Scientific Corporation, and Kissei Pharmaceutical Co. Ltd; consulting fees from Mitsubishi Tanabe Pharma Corporation, EA Pharma Co. Ltd., AbbVie GK, Janssen Pharmaceutical K.K., Pfizer Inc., Nichi-Iko Pharmaceutical Co. Ltd., Eli Lilly and Company, Gilead Sciences, and Bristol Myers Squibb; and lecture fees from Mitsubishi Tanabe Pharma Corporation, AbbVie GK, EA Pharma Co. Ltd., Kyorin Pharmaceutical Co. Ltd., JIMRO Co., Janssen Pharmaceutical K.K., Mochida Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co. Ltd., Pfizer Inc., and Kissei Pharmaceutical Co. Ltd.

Ethical Approval. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki, Good Pharmacoepidemiology Practice guidelines, and all local laws and regulations. All participants provided informed consent prior to participating in the study. The protocol and data collection materials were approved by the Western Institutional Review Board.

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