

Treatment Satisfaction With Current Medications for Chronic Constipation

An Internet Survey of Japanese Patients

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Goals: This survey aims to determine relevant patient characteristics, treatment satisfaction, and bothersome symptoms in Japanese patients with chronic constipation (CC) treated at medical institutions.

Background: Epidemiological surveys of Japanese patients with CC are limited.

Study: This internet survey, conducted in 2017, included 500 adults (selected from 589 respondents to match age composition ratio in Japan) who experienced constipation-like symptoms for ≥ 6 months, were treated at medical institutions for symptoms, and were taking any prescribed medication.

Results: Of 500 patients, 65.6% were female and 62.6% had experienced constipation for > 10 years. Abdominal bloating, infrequent bowel movement, hard consistency of stool, and difficulty of defecation were the most frequently reported and most bothersome symptoms in males and females. Overall, 29% of patients were satisfied with treatment (36% of males, 26% of females); the individual major CC symptom with the highest level of treatment satisfaction was infrequent bowel movement (31% of total, 45% of males, 26% of females). The level of treatment satisfaction for most individual major CC symptoms was lower in females than in males, and overall treatment satisfaction by therapeutic categories ranged from 16% to 46%. Mean overall treatment satisfaction, as well as mean treatment satisfaction for each major symptom, decreased with increasing number of treatments.

Conclusions: The survey results suggest that conventional treatment options were not effective enough to improve bothersome symptoms or treatment satisfaction. Treatment selection that is tailored to individual symptoms and takes patient characteristics into consideration may be key to improving patients' treatment satisfaction.

Key Words: constipation, health care surveys, Japan, patient satisfaction, symptom assessment

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Chronic constipation (CC) is very common throughout the world, with prevalence reported to range from 3% to 28.4% in North America, Europe, Asia, and Japan, depending on definitions of constipation and regions/countries.^{1–6} The prevalence is greater in females than males and increases with age.^{1,7} Clinical symptoms of CC are primarily difficult, infrequent, or incomplete defecation.⁸ However, according to a US population-based survey, two thirds of patients with CC have abdominal symptoms, including abdominal pain, which is characteristic of irritable bowel syndrome, and abdominal bloating.⁹ Because CC and irritable bowel syndrome may be considered to exist on a continuum rather than being individual disorders, some abdominal symptoms may be present in CC, although they are not predominant symptoms.⁸

We previously conducted a survey to investigate prescription patterns and gaps between physicians and patients in their points of view on treating CC.¹⁰ In that survey, we identified important gaps between physicians and patients regarding which constipation symptoms need to be resolved.¹⁰ Physicians considered that objective symptoms including infrequent bowel movement and/or hard consistency of stool were important. However, patients suffered from not only objective symptoms, but also subjective symptoms, including abdominal bloating and excessive straining; patients reported both objective and subjective symptoms as bothersome.^{10–12} In addition, physicians had a positive view of the efficacy of treatments that was inconsistent with patient-reported treatment satisfaction,¹⁰ in part because patients felt that conventional treatment options were not effective enough to treat constipation symptoms compared with their expectations.^{10,12} This likely contributed to lower health-related quality of life in patients with CC compared with matched controls.¹³ However, epidemiological surveys of Japanese patients with CC are limited, and there are no direct data assessing bothersome symptoms and treatment satisfaction in these patients.

The purpose of this survey is to determine relevant patient characteristics, treatment satisfaction, and bothersome symptoms—including those that affect patients' treatment satisfaction—in Japanese patients with CC who were treated at medical institutions.

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For the Astellas criteria on data sharing see: <https://clinicalstudydatarequest.com/Study-Sponsors/Study-Sponsors-Astellas.aspx>.

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MATERIALS AND METHODS

The internet survey was conducted by a Rakuten research panel (Rakuten Insight Inc, Tokyo, Japan), funded by Astellas Pharma Inc.

Patients

The recruitment criteria included males and females who were 20 years and above, who continuously experienced constipation-like symptoms for more than 6 months, who sought treatment at medical institutions for the symptoms, and who were taking any prescribed medication. The definition of “constipation-like symptoms” was an infrequent bowel movement and/or difficulty of defecation, which had persisted for 6 months or more. These criteria were adapted from the definition of functional constipation of the Rome III criteria¹⁴ and were shown on the questionnaire only for respondents’ reference. Patients were self-identified and not verified through medical records and/or diagnosis, and were incentivized to complete the questionnaire.

Of all 318,776 respondents in the Rakuten research panel’s disease panel, 25,899 patients had constipation; of these, 1890 patients regularly visited medical institutions for treatment of constipation symptoms and were invited by e-mail to participate in this survey.

We expected the response rate of a questionnaire to be 40%; therefore, of the 1890 patients who regularly visited medical institutions, we expected to recruit a maximum of 756 patients. The proportion of patients in the panel who experienced constipation-like symptoms for more than 6 months was unknown; therefore, we targeted 500 patients as the sample size for the survey. Actual responses were obtained from 589 patients [response rate, 31% (589/1890 patients)]; of those, 500 patients were selected for inclusion such that the proportion in each age and sex subgroup matched the age and sex composition ratios of patients in the “2013 Comprehensive Survey of Living Conditions on Prevalence of Constipation”¹⁵ after data were confirmed by the Rakuten research panel. Once a sufficient number of patients in each age and sex subgroup completed the survey, any subsequent respondents in that subgroup were not included in the analysis.

Survey Design

This was an internet survey conducted from January 19 to 27, 2017 in Japan. This project complied with ISO20252: Market, Opinion and Social Research Vocabulary and Service Requirements, including informed consent from survey participants and data protection. The data provided by the market research company were anonymized and could not be linked to individual survey participants. The survey was conducted in Japanese and used an original questionnaire developed by the authors to ask patients about 2 main topics: patient demographics and actual status of constipation symptoms (see Table S1, Supplemental Digital Content 1, <http://links.lww.com/JCG/A641>, which lists the survey questions). Patients were asked about treatments they were currently using or had used before but were not using currently and selected their answers from a predefined list. Treatment satisfaction was assessed by a 5-point response scale (1 = unsatisfied, 2 = somewhat unsatisfied, 3 = neutral, 4 = somewhat satisfied, 5 = satisfied). Medications for CC were selected by therapeutic categories in a multiple choice question. All mandatory fields must have been completed before submitting questionnaire answers.

TABLE 1. Patient Demographics

Variable	Analysis Set (n = 500)
Age (y)	
Mean ± SD	58.3 ± 16.6
<40	101 (20.2)
40-59	115 (23.0)
60-69	120 (24.0)
≥ 70	164 (32.8)
Sex	
Male	172 (34.4)
Female	328 (65.6)
Working/attending school	
Employed or attending school	210 (42.0)
Unemployed or retired	290 (58.0)
Medical institution for constipation treatment	
Hospital	244 (48.8)
Clinic	256 (51.2)
Medical department for constipation treatment	
Gastroenterology	137 (27.4)
General practice	273 (54.6)
Others	90 (18.0)
Timing of constipation onset	
6 mo-1 y ago	20 (4.0)
Male	11 (6.4)*
Female	9 (2.7)*
1-3 y ago	60 (12.0)
Male	48 (27.9)*
Female	12 (3.7)*
3-10 y ago	107 (21.4)
Male	65 (37.8)*
Female	42 (12.8)*
> 10 y ago	313 (62.6)
Male	48 (27.9)*
Female	265 (80.8)*

Values are presented as number of patients (%) unless otherwise noted. *Percentages calculated by sex.

Statistical Analysis

Data were analyzed by Social Survey Research Information Co Ltd (Tokyo, Japan) using BellCurve Hideyoshi Dplus version 2015 and Bellcurve for Excel 2015 version 2 (Social Survey Research Information Co Ltd). All 500 selected patients were included in the analysis. Analyses by subgroups were also conducted depending on the questions. Data are presented as descriptive statistics or summarized according to the predefined answer list.

RESULTS

Patient Demographics

The mean age of patients was 58.3 years, with more than half (56.8%) of patients aged 60 years or older (Table 1). The majority of the patient population was female (65.6%) and had experienced constipation for more than 10 years (62.6% of all patients; 27.9% of male patients; 80.8% of female patients). CC was most often treated in general practice (54.6%), followed by gastroenterology (27.4%) and other (18.0%) departments.

Survey Results

Constipation Management

All patients were currently taking prescribed constipation drugs, as expected for patients under medical care (Fig. 1). More than half (56%) of patients had taken over-the-counter (OTC) drugs in the past and 19% of patients had

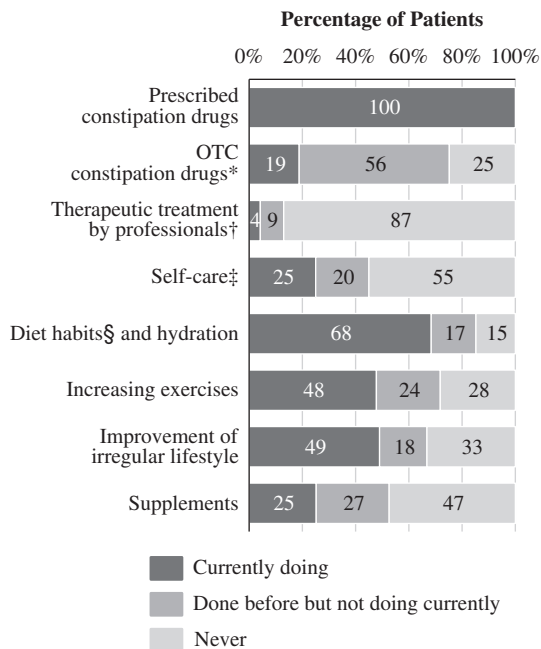


FIGURE 1. Constipation management. Answers to the question, "Please indicate how you manage symptoms considered related to constipation." *Oral, traditional Chinese medicine, and suppository. †Acupuncture, chiropractic treatment, and massage. ‡Massage, etc. §Increased intake of fiber and lactic acid bacterial food (daily probiotic foods). OTC indicates over-the-counter.

continued OTC drugs with prescribed constipation drugs. Most patients had made efforts to treat constipation by improvements in daily life, including diet habits and hydration (currently doing: 68%, done before but not doing currently: 17%, increasing exercises (48%, 24%, respectively), and improvement of irregular lifestyle (49%, 18%, respectively) in parallel with prescribed medications for CC.

Characteristics of CC and Bothersome Symptoms

Figure 2 shows the percentage of patients selecting each symptom as being characteristic of their CC (*x*-axis) and as 1 of their top 3 most bothersome symptoms (*y*-axis). More than half of patients reported infrequent bowel movement (346/500, 69%), hard consistency of stool (340/500, 68%), abdominal bloating (333/500, 67%), difficulty of defecation (297/500, 59%), and incomplete evacuation (267/500, 53%) as characteristic of their CC (Fig. 2). The percentages of males and females reporting these symptoms were about the same except for abdominal bloating (55% in males vs. 73% in females). Infrequent bowel movement, hard consistency of stool, abdominal bloating, and difficulty of defecation, which more than half of patients reported as characteristics of their CC symptoms, were also selected as the most bothersome symptoms in almost half of patients (48%, 48%, 49%, and 42%, respectively) (Fig. 2). Of the 500 patients, 367 patients reported both objective symptoms (infrequent bowel movement and hard consistency of stool) and subjective symptoms (abdominal bloating and difficulty of defecation), indicating an overlap of 73% in objective and subjective symptoms.

The most bothersome symptoms were abdominal bloating (56%), infrequent bowel movement (50%), hard consistency of stool (46%), and difficulty of defecation (41%) in females, and

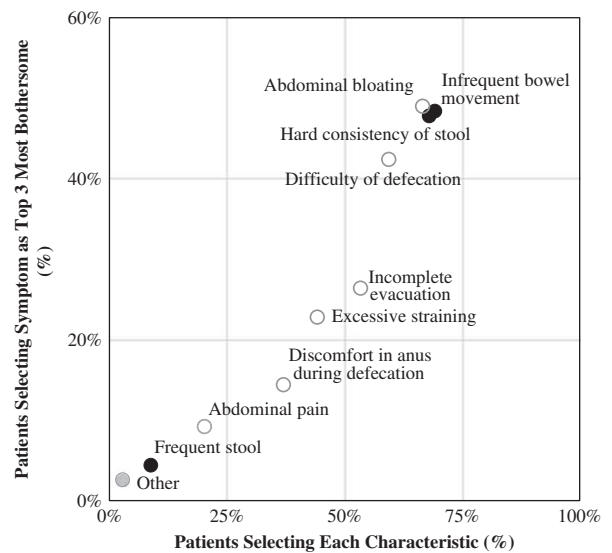


FIGURE 2. Characteristics of chronic constipation and most bothersome symptoms. Answers to the questions, "Which of the following characteristics describe your chronic constipation symptoms?" on the *x*-axis and, "Of the characteristics of your chronic constipation symptoms, what are the top 3 most bothersome symptoms?" on the *y*-axis. White circles (○) represent subjective symptoms and black circles (●) represent objective symptoms.

hard consistency of stool (52%), infrequent bowel movement (46%), difficulty of defecation (45%), and abdominal bloating (35%) in males (Fig. 3). The top 4 symptoms that patients picked as their first, second, and third most bothersome symptoms were abdominal bloating, infrequent bowel movement, hard consistency of stool, and difficulty of defecation, which were the same as the major CC symptoms, in both males and females. However, as noted above, the most bothersome symptom differed between males (hard consistency of stool) and females (abdominal bloating).

Treatment Satisfaction

Overall treatment satisfaction, defined as the total of "satisfied" and "somewhat satisfied," was 29% in all patients, 36% in males, and 26% in females. The individual major CC symptom with the highest level of treatment satisfaction was infrequent bowel movement (31% of all patients) (Fig. 4A). Treatment satisfaction by major CC symptoms was lower in females than in males for all individual symptoms except hard consistency of stool (Fig. 4A). Treatment satisfaction of abdominal bloating, which is the most bothersome symptom in females, was lowest (26%) in the total population and lower in females than in males (24% vs. 33%). Treatment satisfaction for the most bothersome symptom in males, hard consistency of stool, was lower in males than in females (27% vs. 31%). The largest difference in treatment satisfaction between males and females was for infrequent bowel movement (45% in males vs. 26% in females).

Overall treatment satisfaction by therapeutic category ranged from 16% to 46%. The highest treatment satisfaction was for osmotic laxatives (46%), with little difference between males and females (48% vs. 45%, respectively), and for stimulating laxatives (37%), with a difference between males and females (49% vs. 33%, respectively) (Fig. 4B). Mean overall treatment satisfaction, as well as mean treatment satisfaction for each major

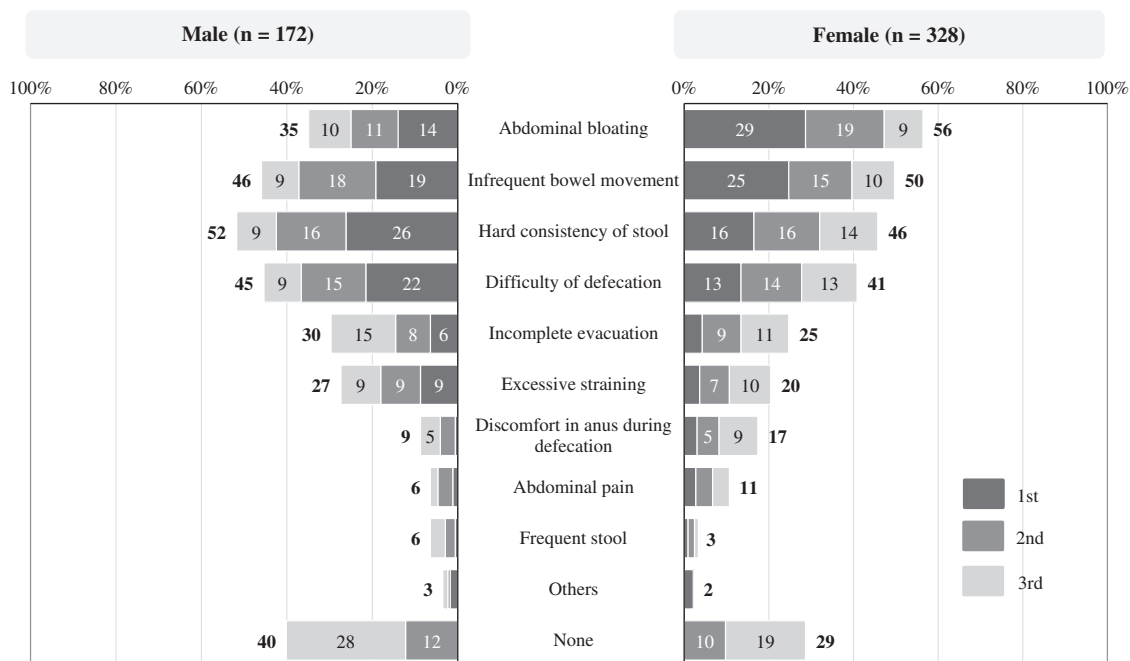


FIGURE 3. Most bothersome symptoms of chronic constipation by sex. Answers to the question, “What are the top 3 bothersome symptoms of your chronic constipation symptoms?” For each symptom, the percentage of patients selecting first, second, and third is shown (except values <5%), as well as the total percentage (all values shown).

symptom, decreased with increasing number of treatments used by patients in the past (Fig. 5).

Of the 494 patients who had taken at least 1 treatment in the past, 37% responded that they were “unsatisfied” or “somewhat unsatisfied” with treatment. The most common reason for dissatisfaction was that the treatments were “not as effective as expected” in each of the therapeutic categories (234 of 308 patients in total, 76%). Patients who responded that the treatments were “not as effective as expected” reported that they were unsatisfied with conventional treatments for the major CC symptoms.

DISCUSSION

To date, information about the symptoms experienced by Japanese patients with CC, as well as patients’ satisfaction with treatment for these symptoms, has been limited. To gain insight into these issues, we developed and conducted an internet survey that identified the most frequent and most bothersome symptoms affecting treatment satisfaction in Japanese patients with CC who sought treatment at medical institutions. The most frequently reported symptoms were infrequent bowel movement, hard consistency of stool, abdominal bloating, and difficulty of defecation. These symptoms were also indicated as bothersome symptoms and were the symptoms that most affected treatment satisfaction. Less than half of patients were satisfied with their treatment, with the exception of suppository/enema clysters in male patients, primarily because treatments did not meet the expectations of patients with CC. Because the symptoms varied depending on the patient, with major differences between males and females, these findings suggest that it is important to select treatments that address each patient’s most bothersome symptoms.

In this survey, patients were treated not only by gastroenterology specialists, but also by nonspecialists in

general practice and other departments. This reflects the fact that CC is a very common disease.¹ Among this group of patients who were seeking treatment at medical institutions, most had experienced constipation for more than 10 years and 56% had used OTC treatments in the past, suggesting that their symptoms were not adequately improved by nonprescribed treatments.

Abdominal bloating, infrequent bowel movement, hard consistency of stool, and difficulty of defecation were the most frequently reported and most bothersome symptoms in this survey. In a previous internet survey, these symptoms were commonly reported as constipation symptoms experienced by more than half of respondents and as bothersome symptoms by more than 80% of respondents in a US population who experienced CC symptoms, as defined by Rome II criteria, and who sought medical care within 1 year.¹² However, difficulty of defecation was not included in the US survey, and the order of bothersome symptoms in the US survey was different from this survey. Similarly, a systematic review of Asian adults (excluding Japan) with constipation defined by Rome II or III criteria also reported infrequent defecations and lumpy and hard stool as commonly experienced symptoms.¹¹ The difference between the results of this survey and those of previous studies may be due to differences in the research settings, the definitions of CC (eg, Rome II or III as inclusion criteria), the definitions of symptoms, and the countries involved.

The survey results showed that most patients with CC were not satisfied with past or present treatment options, and only 29% of patients were satisfied or somewhat satisfied with the overall effect of treatment on symptoms. Approximately 30% of patients were satisfied or somewhat satisfied with the effect of treatment on each major CC symptom. These results are very similar to a previous survey in which 28% of participants with CC in Europe were

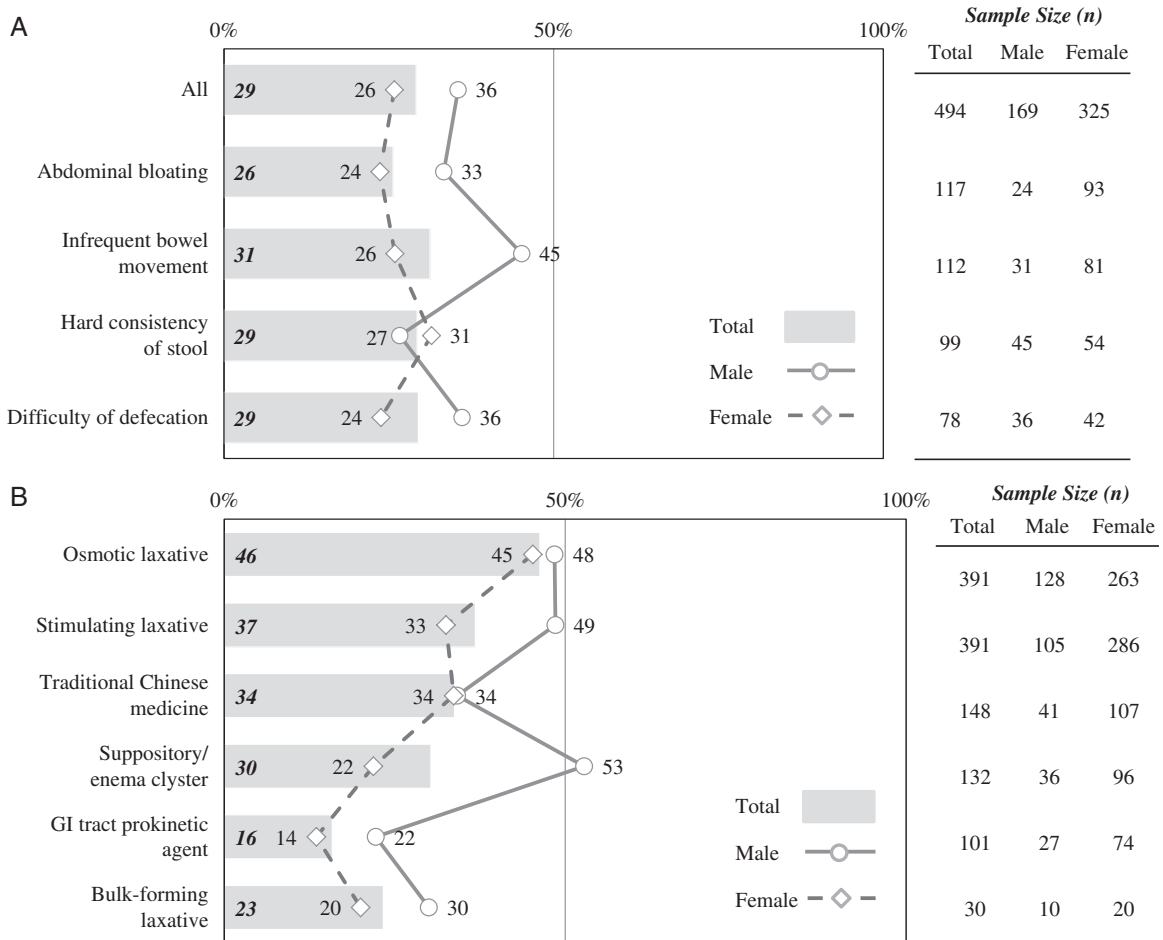


FIGURE 4. Treatment satisfaction. Answers to the question, “How satisfied are you with each treatment you have taken?” The percentages of patients answering “satisfied” or “somewhat satisfied” are shown. A, Treatment satisfaction by symptoms. B, Treatment satisfaction by treatments. GI indicates gastrointestinal.

satisfied with their treatment, although the treatment options were not exactly the same as those listed in this survey.¹⁶

Treatment satisfaction for all major CC symptoms was low, and it was lower in females than in males. The major CC symptoms with the lowest level of treatment satisfaction

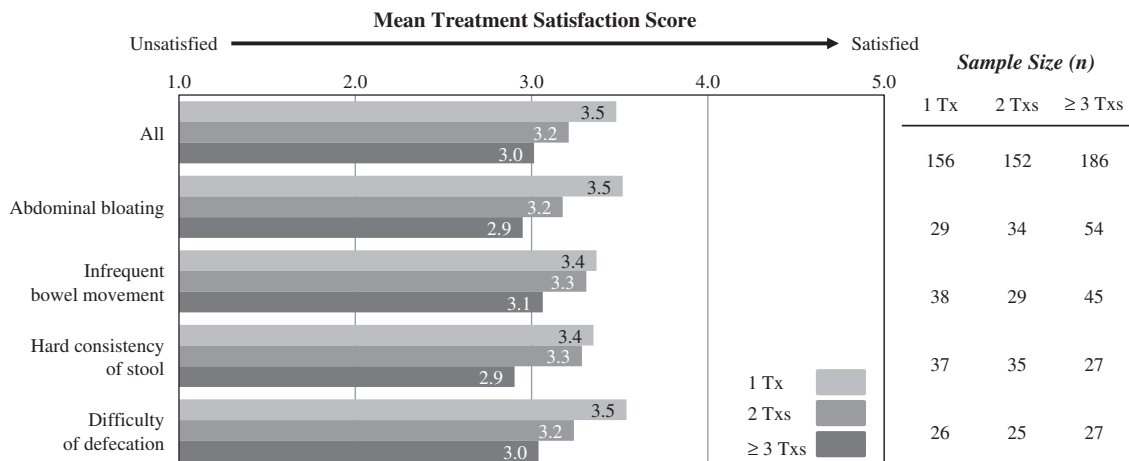


FIGURE 5. Treatment (Tx) satisfaction by number of Tx used by patients. Answers to the question, “How satisfied are you with each treatment you have taken?” Mean scores of Tx satisfaction are shown by most bothersome symptom and by the number of Tx taken.

were hard consistency of stool for males and abdominal bloating for females, which were also the most bothersome symptoms for each sex. This suggests that the level of treatment satisfaction reflected how the most bothersome symptoms were or were not alleviated by treatments. Treatment satisfaction for infrequent bowel movement showed the largest difference between males and females. Patient assessments of constipation symptoms are reported to be associated with health-related quality of life and treatment satisfaction.¹⁷ Therefore, patient demographics, including sex, are key factors to consider when selecting treatments to relieve individual constipation symptoms, including the most bothersome symptoms.

The level of treatment satisfaction with stimulating laxatives and suppository/enema clisters differed between males and females. More than 80% of female patients in this survey had experienced CC for more than 10 years, which was a much higher percentage than in the male patients (27.9%). Because females are likely to have taken some treatments for a longer time, stimulating laxative treatments may become less effective.

Overall treatment satisfaction, as well as treatment satisfaction for each major CC symptom, decreased with the number of previous treatments, suggesting that changing treatments did not improve symptoms. Basilisco and colleagues reported that more severe constipation was associated with lower treatment satisfaction.¹⁸ Lower treatment satisfaction in patients who received multiple treatments may possibly have resulted from more severe symptoms in the patients. The most common reason for low overall treatment satisfaction was that conventional treatment options were not as effective as expected. A previous survey using the same patient panel identified important gaps between patients' needs and physicians' practice regarding CC treatments.¹⁰ Physicians usually focused on resolving objective symptoms, including infrequent bowel movement and hard consistency of stool. In contrast, patients were most concerned with subjective symptoms, including abdominal bloating and difficulty of defecation. These gaps may contribute to the patient feeling unsatisfied with CC treatment. These observations suggest that current treatments are not tailored to individual bothersome symptoms, especially subjective symptoms, or that appropriate treatments are not available. New treatment options with novel modes of action, particularly the ileal bile acid transporter inhibitor elobixibat and the guanylate cyclase activator linaclotide, have been launched in Japan since this survey was conducted.^{19,20} These new options are expected to increase patients' treatment satisfaction.

Several limitations of this survey need to be considered. First, the questionnaire in the survey was originally developed by the authors and was not validated. The definition of CC was developed specifically for this survey, and the scope was wider than the Rome IV diagnostic criteria of functional constipation.⁸ In addition, because the survey was targeted at non-health care professionals, detailed criteria were not included. Therefore, patients with irritable bowel syndrome with constipation (IBS-C) may have been included in the survey. However, it has been suggested that symptoms exist on a continuum between IBS-C and CC.⁸ We understood that patients with CC may have IBS-C and/or functional constipation, but CC and IBS-C are not strictly distinguished in the clinical setting in Japan. Therefore, patients with IBS-C were not excluded from the survey. Second, the predefined answers in the questionnaire were provided for therapeutic categories, not individual laxatives. If the questionnaire

assessed individual laxatives, the findings may vary. Third, severity of constipation symptoms, number of previous therapeutic categories tried, and the order of treatments were not confirmed in the survey but may affect the findings, including treatment satisfaction. Fourth, as concomitant medication was not assessed in the survey, some patients with drug-induced constipation may have been included. Fifth, the patients were selected from the panel by internet questionnaire; therefore, the survey was limited to individuals with access to the internet. Sixth, this was a selected sample of patients who required medical management of their CC. Finally, the questionnaire consisted of multiple choice questions, which is subject to position bias. In addition, patients may have selected their answers from the list even if the choices did not exactly correspond to their answers.

In conclusion, the survey findings suggest that treatment selection that is aligned with individual symptoms and takes into consideration patient characteristics may be key to improving patients' treatment satisfaction.

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