

ORIGINAL ARTICLE

Prevalence and risk factor for chronic diarrhea in participants of a Japanese medical checkup

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Abstract

Background and Aim: Although chronic diarrhea is a major digestive disorder, it has not been well studied. The aims of this study were to investigate the prevalence and risk factors of chronic diarrhea in the Japanese population and to assess the relationship between stool type and frequency and symptoms related to chronic diarrhea.

Method: A total of 13 668 adults who underwent a medical checkup at MedCity21 were enrolled, and 9540 who met the inclusion criteria participated in the study. Participants with chronic diarrhea were defined as those who typically had a Bristol Stool Form Scale of type 6 or 7.

Results: The prevalence of chronic diarrhea was 3.0%. The risk factors for chronic diarrhea were younger age (odds ratio [OR] 0.984, 95% confidence interval [CI] 0.972–0.996), male sex (OR = 2.270, CI = 1.730–2.960), alcohol intake on ≥ 5 days per week (OR = 2.390, CI = 1.860–3.060), not getting adequate sleep (OR = 0.712, CI = 0.559–0.907), skipping breakfast ≥ 3 times a week (OR = 1.490, CI = 1.120–1.980), and absence of diabetes mellitus (OR = 0.384, CI = 0.179–0.824). Only 23.5% of the participants in the diarrhea group had ≥ 3 bowel movements per day. Chronic diarrhea was significantly associated with heartburn, nausea, stomach ache, abdominal bloating and distension, and feeling of stress.

Conclusions: Our study shows that chronic diarrhea is common in Japan with a prevalence of 3.0%; unique risk factors related to gender, age, and irregular lifestyle were identified. An understanding of bowel habit in the healthy population is helpful for the assessment of change in bowel habit associated with gastrointestinal disorders.

Introduction

Chronic diarrhea is a common gastrointestinal disorder associated with a reduced quality of life. Previous reports have demonstrated that 3–15% of the population suffers from chronic diarrhea.^{1–4} Compared to chronic constipation, chronic diarrhea has not been well studied, probably because detailed definition of chronic diarrhea varies among research groups.

Most previous studies on diarrhea referred to the forms of stool for the definition of diarrhea. The self-rated Bristol Stool Form Scale (BSFS) is often used to assess stool hardness in both clinical and research situations because of its ease of use; several papers have defined diarrhea by a BSFS rating of type 6 (mushy

consistency with soft edges) or type 7 (liquid consistency with no soft pieces).^{5–7}

In addition to the forms of stool, the frequency of bowel movements is often used to define diarrhea; however, the threshold for the frequency of bowel movements varies among studies. Additionally, most groups do not clearly define diarrhea by the number of bowel movements per day; however, some define it as three or more loose stools per day.⁴ In actual clinical practice, most patients use the term diarrhea to describe stool hardness of BSFS types 6 and 7, regardless of the frequency of bowel movement. Symptoms of frequent bowel movements are considered pseudo-diarrhea, which is distinct from diarrhea. Stool properties are considered to be more important than stool frequency in the assessment of diarrhea because they are thought to reflect the

transit time of the entire colon and not the number of bowel movements.^{8,9}

In Japan, there is a system called voluntary or statutory medical checkup, under which people who do not have obvious diseases under treatment can undergo a medical checkup; this is subsidized by their companies or by the government. Thus, the population that receives this medical checkup is different from hospital patients and volunteers and closely resembles the general Japanese population.

In this study, we defined participants with chronic diarrhea as those who typically had a type 6 (mushy consistency with soft edges) or type 7 (liquid consistency with no soft pieces) BFSF rating. The purpose of this study was to investigate the prevalence and the risk factors associated with chronic diarrhea among the participants of a medical checkup in Japan. Also investigated were the relationship between stool form and frequency and the symptoms related to chronic diarrhea.

Methods

Study cohort. This single-center, cross-sectional study was conducted at MedCity21, a health checkup facility affiliated with the Osaka City University. Adults aged 20 years and older who underwent a physical examination at MedCity21 between April 2018 and March 2019 were included in this study. The exclusion criteria were as follows: declining to participate in the study, missing questionnaire data, use of laxatives, or a history of

inflammatory bowel disease (IBD) or gastrointestinal surgical resection.

Bowel health questionnaire. A self-reported, paper-based questionnaire survey regarding stool condition and bowel movement was designed and administered to the participants to identify the presence of chronic diarrhea. Stool condition was assessed using the following written question based on the BFSF scale: “Please look at this picture and select the number of the picture which represents your usual or most common stool type” (Figure S1, Supporting information). In accordance with previous reports, participants with chronic diarrhea were defined as those who reported having BFSF type 6 or 7 as the most common stool consistency.⁵

Stool frequency was assessed with the written question “How often do you have a bowel movement?”

Participant data collection. Participant data obtained from the medical checkup were evaluated in relation to chronic diarrhea. The data included information that is typically collected during a health checkup: age, sex, body mass index (BMI), alcohol intake, smoking habits, exercise habits, sleep duration, eating habits, and medical history. Alcohol consumption, converted to ethanol amount, was divided into three categories: <20 g, ≥20 g but <40 g, and ≥40 g. Sleep duration was divided into two categories: more than 6 h and less than 6 h.

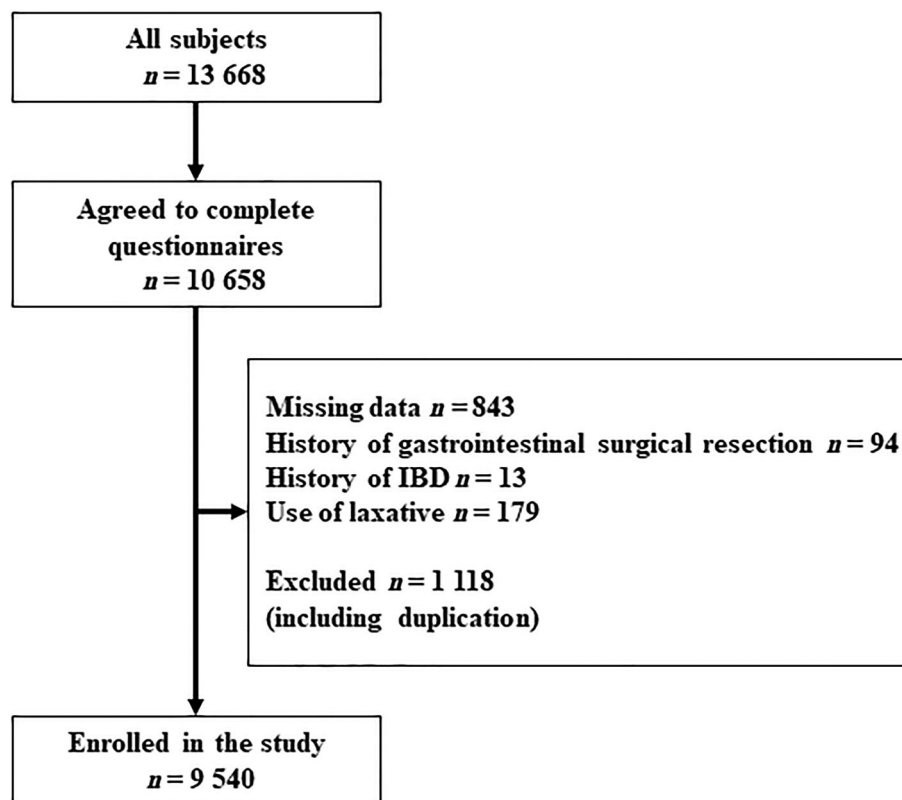


Figure 1 Flowchart of subject enrollment in this study. IBD, inflammatory bowel disease.

Responses for gastrointestinal and psychiatric symptoms were obtained using a standard Japanese questionnaire for specific health examinations.

The gastrointestinal questionnaire included questions on typical gastrointestinal symptoms such as heartburn, nausea, stomach ache, and abdominal bloating/distention. The mental health questionnaire included questions on stress, getting annoyed, lack of motivation, fatigue upon waking, depression, and lack of interest (Figure S2). The data collected from the two questionnaires were used for the analysis.

Outcome measurement. The primary outcome of this study was the evaluation of the prevalence of chronic diarrhea in participants of a Japanese medical health screening and the risk factors associated with it. The secondary outcome was the relationship between the stool type and frequency. We also investigated the symptoms related to chronic diarrhea.

Ethics. The research protocol complied with the principles of the Declaration of Helsinki. This study was approved by the Ethical Committee of the Osaka City University (approval number: 2021-094). Written informed consent from the participants was obtained at the time of administering the stool characteristics questionnaire, and a web-based opt-out was also organized.

Statistical analyses. Data are expressed as medians and interquartile ranges for continuous variables and as numbers for categorical variables. Continuous variables were compared using the Mann–Whitney *U* test, and categorical variables using the Pearson χ^2 test. Clinical factors associated with chronic diarrhea were investigated using logistic regression analyses, and the odds ratios (ORs) and 95% confidence intervals (CIs) were estimated for each factor. Statistical calculations and analyses were performed using IBM SPSS statistics version 26 (IBM Corporation, Armonk, NY, USA) or R software, version 3.4.4 (The R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $P < 0.05$.

Results

A total of 13 668 subjects underwent a medical checkup at MedCity21 between April 2018 and March 2019; 10 658 agreed to complete questionnaires and reported their most common stool consistency using the BSFS. Among them, 1118 participants were excluded (843 for missing data, 94 for history of gastrointestinal surgical resection, 13 for history of IBD, and 179 for the use of laxatives, including some duplicates). The remaining 9540 participants, including 4533 men and 5007 women, were finally enrolled in the study (Fig. 1). Among them, 289 participants (3.0%) reported BSFS types 6 or 7 as their most common stool

Table 1 Baseline characteristics of subjects

Variables	All subjects	Diarrhea	Non-diarrhea	<i>P</i> -value (diarrhea vs non-diarrhea)
Number of cases	9540	289 (3.0%)	9251 (97.0%)	
Age (years, median [IQR])	51.0 [43.0–59.0]	49.5 [43.0–55.0]	51.4 [43.0–59.0]	0.003
Male sex	4533 (47.5%)	203 (70.2%)	4330 (46.8%)	<0.001
BMI > 25 (kg/m ²)	2194 (22.3%)	68 (23.5%)	2126 (23.0%)	0.831
Alcohol intake (≥5 days a week)	2473 (25.9%)	139 (48.1%)	2334 (25.2%)	<0.001
Daily drinking quantity				
<20 g	6014 (63.0%)	169 (58.1%)	5845 (63.2%)	0.161
≥20 g and <40 g	1584 (16.6%)	59 (20.4%)	1525 (16.5%)	
≥40 g	1942 (20.4%)	61 (21.1%)	1881 (20.3%)	
Smoking habit (current smoker)	1420 (14.9%)	40 (13.8%)	1380 (14.9%)	0.675
Exercise for ≥30 min at least twice a week	2378 (24.9%)	56 (19.4%)	2322 (25.1%)	0.027
for ≥1 year				
Walking (or exercise equal to it)	3958 (41.5%)	104 (36.0%)	3854 (41.7%)	0.060
for ≥1 h a day				
Walking faster than other people of the same age and sex	4986 (52.2%)	168 (58.1%)	4815 (52.0%)	0.042
Sleeping for ≥6 h a day	6361 (66.7%)	195 (67.5%)	6166 (66.7%)	0.800
Getting adequate sleep	5600 (58.7%)	147 (50.9)	5453 (58.9%)	<0.001
Skipping breakfast ≥3 times a week	1380 (14.5%)	73 (25.3%)	1307 (14.1%)	<0.001
Eating ≤2 h before going to bed ≥3 times a week	2682 (28.1%)	119 (41.2%)	2563 (27.7%)	<0.001
Eating faster than other people	3719 (39.0%)	118 (40.8%)	3601 (38.9%)	0.540
History of stroke	147 (1.5%)	7 (2.4%)	140 (1.5%)	0.218
History of heart disease	291 (3.1%)	7 (2.4%)	284 (3.1%)	0.727
Presence of renal failure	50 (0.5%)	1 (0.3%)	49 (0.5%)	1.000
Presence of liver cirrhosis	9 (0.1%)	0 (0.0%)	9 (0.1%)	1.000
Presence of hypertension	1537 (16.1%)	47 (16.3%)	1490 (16.1%)	0.935
Presence of hyperlipidemia	2882 (30.2%)	80 (27.7%)	2802 (30.3%)	0.363
Presence of diabetes mellitus	571 (6.0%)	7 (2.4%)	564 (6.1%)	0.008

BMI, body mass index; IQR, interquartile range.

Table 2 Multivariate analyses of risk factors associated with chronic diarrhea

Variables	OR (95% CI)	P-value
Age	0.984 (0.972–0.996)	0.008
Male sex	2.270 (1.730–2.960)	<0.001
Alcohol intake (≥ 5 days a week)	2.390 (1.860–3.060)	<0.001
Exercise for ≥ 30 min at least twice a week for ≥ 1 year	0.761 (0.554–1.050)	0.091
Walking (or exercise equal to it) for ≥ 1 h a day	0.818 (0.632–1.060)	0.127
Walking faster than other people of the same age and sex	1.260 (0.986–1.610)	0.065
Getting adequate sleep	0.712 (0.559–0.907)	0.006
Skipping breakfast ≥ 3 times a week	1.490 (1.120–1.980)	0.006
Eating ≤ 2 h before going to bed ≥ 3 times a week	1.210 (0.942–1.560)	0.134
Presence of diabetes mellitus	0.384 (0.179–0.824)	0.014

CI, confidence interval; OR, odds ratio.

consistency and were defined as having chronic diarrhea (Table 1).

Risk factors of chronic diarrhea. On univariate analysis, the prevalence of chronic diarrhea was higher in younger participants ($P = 0.003$), male sex ($P < 0.001$), participants who drank alcohol on more than 5 days per week ($P < 0.001$), those who walked faster than other people of the same age and sex ($P = 0.042$), those who skipped breakfast ≥ 3 times a week ($P < 0.001$), and those who ate ≤ 2 h before bedtime ≥ 3 times a week ($P < 0.001$). On the other hand, exercising for ≥ 30 min at least twice a week for ≥ 1 year ($P = 0.027$), getting adequate sleep ($P < 0.001$), and presence of diabetes mellitus were negatively associated with chronic diarrhea ($P = 0.008$). There was no significant difference in the prevalence of chronic diarrhea based on smoking habits, sleep duration, and other medical histories (Table 1).

Multivariable analysis showed that younger age, male sex, drinking alcohol on more than 5 days per week, not getting adequate sleep, skipping breakfast ≥ 3 times per week, and absence

of diabetes mellitus were risk factors for chronic diarrhea (Table 2).

Stool frequency. In this study, we investigated the relationship between the stool type and stool frequency, which are often used together with stool properties as indicators of diarrhea.

While 6.8% of participants had ≥ 3 bowel movements per day overall, 23.5% of the diarrhea group had ≥ 3 bowel movements per day ($P < 0.001$). Interestingly, 5.5% of the diarrhea group had less than one bowel movement every 3 days (Fig. 2).

Gastrointestinal and psychological symptoms related to chronic diarrhea. Among digestive symptoms, heartburn ($P = 0.030$), nausea ($P = 0.007$), stomach ache ($P < 0.001$), and abdominal bloating and distension ($P < 0.001$) were significantly associated with chronic diarrhea, whereas only “feeling stressed” was significant among the mental health symptoms ($P = 0.015$) (Table 3).

Discussion

This study demonstrated that chronic diarrhea, as defined by a BSFS type 6 or 7, was prevalent in 3.0% of participants in this Japanese medical checkup. On multivariate analysis, our results indicated that younger age, male sex, habit of drinking alcohol on more than 5 days per week, not getting adequate sleep, skipping breakfast ≥ 3 times a week, and absence of diabetes mellitus were independent risk factors for chronic diarrhea. Among digestive symptoms, heartburn, nausea, stomach ache, abdominal bloating, and distension were positively correlated with chronic diarrhea. Our study focused on participants of a medical checkup who can be considered to represent the general population. This is the first study to characterize chronic diarrhea in a healthy population in Japan.

While there are various definitions of chronic diarrhea, we evaluated it based on stool characteristics alone and not on bowel movement frequency. A few studies have examined the relationship between stool characteristics and stool frequency but no conclusions have been drawn. Singh *et al.* found that stool frequency did not correlate with stool characteristics. However, there are no reports on the relationship between soft stool characteristics and frequent bowel movements.⁵ In our study, only

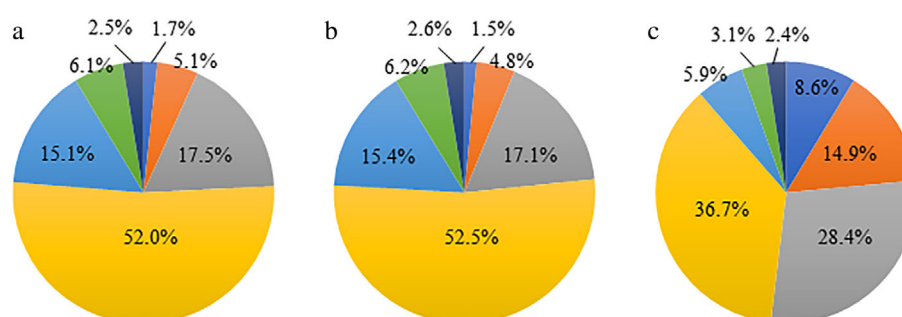


Figure 2 Relationship between stool frequency and characteristics. Stool frequency for (a) all subjects ($n = 9540$), (b) non-diarrhea ($n = 9251$), and (c) diarrhea ($n = 289$). Non-diarrhea was defined as Bristol Stool Forms Scale (BSFS) types 1–5, and diarrhea as BSFS types 6–7. (■), ≥ 4 times a day; (■), 3 times a day; (■), twice a day; (■), once in a day; (■), once in 2 days; (■), once in 3 days; (■), once in more than 4 days.

Table 3 Digestive symptoms and mental health associated with chronic diarrhea

Variables	All subjects	Diarrhea	Non-diarrhea	P-value (diarrhea vs non-diarrhea)
Number of cases	9540	289	9251	
Heartburn	432 (4.5%)	21 (7.3%)	411 (4.4%)	0.030
Nausea	133 (1.4%)	10 (3.5%)	123 (1.3%)	0.007
Stomach ache	570 (6.0%)	35 (12.1%)	535 (5.8%)	<0.001
Abdominal bloating and distension	699 (7.3%)	37 (12.8%)	662 (7.2%)	<0.001
Feeling stressed	2129 (22.3%)	82 (28.4%)	2047 (22.1%)	0.015
Getting annoyed	1073 (11.2%)	37 (12.8%)	1036 (11.2%)	0.395
Lack of motivation	633 (6.6%)	21 (7.3%)	612 (6.6%)	0.631
Fatigue upon waking	1543 (16.2%)	42 (14.5%)	1501 (16.2%)	0.516
Feeling depressed	713 (7.5%)	23 (8.0%)	690 (7.5%)	0.733
Not interested in anything	230 (2.4%)	10 (3.5%)	220 (2.8%)	0.238

23.5% of the participants in the diarrhea group had three or more bowel movements per day; the remaining 66.5% of had less than three bowel movements per day. This implies that more than half of the participants did not have excess bowel movements, although they had BSFS types 6 or 7. Additionally, it is known that the frequency of bowel movements increases in dyschezia, as represented by chronic constipation. Therefore, the frequency of bowel movements should be evaluated as a parameter separate from stool characteristics.

Another chronic diarrhea-related disease is irritable bowel syndrome with predominant diarrhea (IBS-D), which is diagnosed based on abdominal pain, stool characteristics, and stool frequency, according to the Rome IV criteria. Although chronic diarrhea is similar to IBS-D in having BSFS types 6 or 7 as the most common stool consistency, unlike chronic diarrhea, IBS-D includes abdominal symptoms in its diagnostic criteria.¹⁰ Therefore, chronic diarrhea is a broader definition, and patients with IBS-D are considered to be included in this group of patients with chronic diarrhea.

There are a few reports on the prevalence of chronic diarrhea. Our study demonstrated a chronic diarrhea prevalence of 3.0%. In the United States, Singh *et al.* reported a prevalence of 6.6% using the same definition as ours.⁵ In two studies from China and Norway, which defined chronic diarrhea as a combination of IBS-D of Rome II and functional diarrhea, the prevalence of chronic diarrhea in the general population was 3.26% and 8.8%, respectively.^{11,12} In Italy, the prevalence of chronic diarrhea in elderly outpatients was found to be 9.1%. The prevalence of chronic diarrhea in our study was slightly lower than those reported in the aforementioned studies. This may be due to racial and lifestyle differences among countries, as well as the fact that this study excluded 179 laxative users during analysis.

Our study revealed that males have an increased risk of chronic diarrhea. This result is consistent with that of previous studies on chronic diarrhea and IBS-D.^{12,13} In contrast, it is well known that females have an increased risk of IBS and constipation.^{13–16} The reason may be that estrogen and progesterone, the female steroid hormones, reportedly decrease gastrointestinal motility by inhibiting colonic smooth-muscle contractility and increase intestinal permeability.^{17,18} Other reports suggest that this sex difference in the prevalence of chronic diarrhea is due to differences in negative GABAergic control of the spinal

defecation center.¹⁹ Thus, although there are several possible mechanisms for the sex difference, being male has been identified as a risk factor for diarrhea in several studies.

The relationship between age and diarrhea is not well established. In our study, younger age was a risk factor for chronic diarrhea. In this context, Callan *et al.* found that diarrhea severity decreases with age in women undergoing menopause transition.²⁰ In contrast, Singh *et al.* found that older age was positively correlated with chronic diarrhea in the United States after adjusting for covariates and that the prevalence of diarrhea increased dramatically with age over 60.⁵ As drug use, and especially polypharmacy, has been associated with an increased prevalence of diarrhea, the possibility of higher incidences of diarrhea in the elderly who take multiple oral medications cannot be ruled out.¹² Because studies are limited and the results are controversial, further research is needed regarding the relationship between age and diarrhea, taking into account the use of medication.

Irregular daily habits, not getting adequate sleep, and skipping breakfast more than thrice a week were related to chronic diarrhea in this study. Since there are no studies that have investigated the relationship between lifestyle irregularities and chronic diarrhea, there is no evidence regarding irregular lifestyles in chronic diarrhea. However, lifestyle irregularity has already been reported to be a risk factor for IBS and other gastrointestinal symptoms.^{21–26} In view of these findings, it can be concluded that lifestyle irregularity negatively impacts bowel movements in general, and the results of this study are valid.

In agreement with the present results, alcohol intake has been reported as a well-known risk factor for diarrhea.²⁷ This is because alcohol intake increases permeability of the intestinal mucosa, resulting in decrease absorption of various nutrients, including water and sodium. Therefore, there is no doubt that excessive alcohol consumption is considered a typical risk factor for diarrhea.^{27,28}

Interestingly, the risks for chronic diarrhea and constipation were not completely opposed. While female sex and old age are risk factors for chronic constipation, male sex and young age are risk factors for chronic diarrhea; the opposite risk factors apply in some categories. However, some elements, such as lifestyle irregularity and stress, have been found to be common risk

factors for both chronic diarrhea and constipation.^{23,29,30} Therefore, chronic constipation and diarrhea are not two sides of the same coin.

Our results, as well as those of previous researchers, demonstrate that chronic diarrhea is highly associated with various lower and upper gastrointestinal symptoms, as well as with other gastrointestinal disorders such as chronic constipation and functional dyspepsia. A previous report showed the prevalence of diarrhea and other gastrointestinal symptoms in combination to be as follows: 8.4% with diarrhea/reflux, 4.5% with diarrhea/dyspepsia, and 3.7% with diarrhea/reflux/dyspepsia.³¹ In another report, the prevalence was 9.2% with diarrhea/heartburn, 4.4% with diarrhea/nausea, 10.0% with diarrhea/abdominal pain, and 7.5% with diarrhea/bloating.³² According to these studies, and ours, both upper and lower gastrointestinal symptoms frequently overlap in chronic diarrhea. Also, since chronic diarrhea affects the entire gastrointestinal tract, with detrimental impact to the patient and on other gastrointestinal diseases, it needs to be diagnosed appropriately and studied in further detail.

This study has some limitations. First, the study was conducted at a single medical checkup facility in Japan. Therefore, it did not include patients requiring treatment and thus the participants were mainly healthy Japanese individuals. However, this did not pose a problem, as the study aimed to determine the characteristics of chronic diarrhea in the general Japanese population.

Second, not all participants underwent gastrointestinal endoscopy, so other gastrointestinal diseases, such as cancer, microscopic colitis, IBD, and eosinophilic gastroenteritis, could not be completely ruled out. Moreover, systemic conditions such as collagen or endocrine diseases were not also ruled out. It would be desirable to exclude such diseases, but a detailed examination is not possible in the Japanese medical checkup system. Therefore, as in other studies on constipation, we evaluated only stool characteristics in this study.

Finally, the questionnaire used in this study was based on self-reported measures, so recall bias might have existed. However, this self-assessment questionnaire is a well-established tool that was used in most other studies on constipation and diarrhea; conducting research based on this questionnaire is therefore acceptable.

In conclusion, chronic diarrhea is common among the general Japanese population with a prevalence of 3.0%, and individuals with chronic diarrhea often experience symptoms such as heartburn, nausea, stomach ache, abdominal bloating and distension, and feeling stressed. Our study revealed that male sex, drinking alcohol on more than 5 days per week, not getting adequate sleep, skipping breakfast more than three times a week, and absence of diabetes mellitus were risk factors for chronic diarrhea. However, compared to constipation, which is also an abnormality of bowel movement, chronic diarrhea has not been sufficiently studied. In this context, there may be patients with chronic diarrhea who cannot be diagnosed based on a narrow definition such as IBS; studies that define chronic diarrhea in a broad sense, such as the present one, are therefore needed to better understand the reality of this gastrointestinal disorder. This will help patients suffering from diarrhea, which is currently underdiagnosed.

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Supporting information

Additional supporting information may be found in the online version of this article at the publisher's website:

Figure S1. Bowel Health Questionnaire.

Figure S2. Questionnaire about digestive symptoms and mental health.