


## GASTROENTEROLOGY

**Impacts of the COVID-19 pandemic on functional dyspepsia and irritable bowel syndrome: A population-based survey**Tadayuki Oshima,\*  Kewin Tien Ho Siah,<sup>†,‡</sup> Takanori Yoshimoto,\* Ko Miura,\* Toshihiko Tomita,\* Hirokazu Fukui\* and Hiroto Miwa\* 

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**Key words**

COVID-19, Functional dyspepsia, Functional gastrointestinal disorders, Irritable bowel syndrome, Psychological disease, SARS-CoV-2.

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**Author contribution:** Tadayuki Oshima is responsible for the design of the study, acquisition of the data, analysis, data interpretation, and writing of the paper. Kewin T H Siah is responsible for the conception and design of the study, data interpretation, and writing of the paper. Analysis and data interpretation were performed by Takanori Yoshimoto, Ko Miura, Toshihiko Tomita, and Hirokazu Fukui. Conception and design of the study, and data interpretation were carried out by Hiroto Miwa.

**Introduction**

Functional gastrointestinal disorders (FGIDs) are common gastrointestinal diseases in the community that normally affect 5–20% of the general population.<sup>1</sup> Despite their prevalence, their pathophysiology is poorly understood and likely multifactorial, including genetic predispositions, dietary factors, gut dysbiosis, immune activation, altered intestinal permeability and dysregulation of the gut–brain axis.<sup>2</sup> FGIDs are also well known to be stress-sensitive disorders. Functional dyspepsia (FD) and irritable bowel syndrome (IBS) are two of the most common FGIDs. Negative life events, stress, and anxiety are known to trigger and exacerbate IBS and FD.<sup>3,4</sup>

**Abstract**

**Background and Aim:** Functional gastrointestinal disorders are a group of stress-sensitive gut–brain disorders. The COVID-19 outbreak has caused immense stress and anxiety among the general public. Strict measures to counter COVID-19 emergency, including physical distancing, have also taken a toll on physical and mental health. We investigated the impact of the COVID-19 pandemic on the gastrointestinal and psychological symptoms of functional dyspepsia (FD) and irritable bowel syndrome (IBS).

**Methods:** An online survey was conducted in Japan for a group of randomly assigned panelists from May 26 to 27, 2020. Each respondent answered a questionnaire on stress, physical distancing, and worries about COVID-19. Gastrointestinal symptoms were assessed to diagnose FD and IBS (Rome III), and psychological symptoms were assessed using the Hospital Anxiety and Depression Scale.

**Results:** A total of 5157 subjects were finally enrolled, with FD in 8.5%, IBS in 16.6%, and FD–IBS overlap in 4.0%. For both gastrointestinal and psychological symptoms, respondents with FD–IBS overlap showed the worst scores, followed by IBS-alone, then FD-alone respondents. During the COVID-19 pandemic, 11.9% of respondents reported deterioration and 2.8% reported improvement of gastrointestinal symptoms. FD–IBS overlap, psychological disease comorbidity, and stress at work/school were significantly associated with symptom deterioration. Younger age, commuting by public transport, and work/study from home were associated with symptom improvement.

**Conclusions:** The COVID-19 pandemic negatively affected FD/IBS subjects, with respondents showing FD–IBS overlap syndrome as the most important independent factor associated with deterioration in gastrointestinal symptoms. Physicians need to take extra care of FD/IBS patients in the post-COVID period.

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic represents the most significant epidemiological event in modern human history. This infection and the resulting coronavirus disease 2019 (COVID-19) was first reported in mainland China around December 2019. On January 16, 2020, the first case of COVID-19 was diagnosed in Japan. On March 11, 2020, the World Health Organization officially classified the COVID-19 outbreak as a pandemic.<sup>5</sup> On April 7, 2020, Japan declared a state of emergency because of the worsening coronavirus outbreak in the country. This resulted in many changes to the everyday lives of Japanese people, from going to work to buying groceries.<sup>6</sup> Some methods used to counter the surge in COVID-19 cases include personal hygiene and physical distancing practices.

Physical distancing involves a set of interventions intended to prevent the spread of COVID-19 by maintaining distance between people and reducing the number of contacts between people. Key measures include avoiding physical contact, stay-at-home orders, and working from home, as well as canceling mass gatherings. However, concerns have been raised that physical distancing is likely to take a toll on mental health.<sup>7,8</sup> A study from the UK showed that physical distancing is leading to increased anxiety and depression among the general public.<sup>9</sup> People are fearful they

will experience negative health and occupational effects from the COVID-19 pandemic.<sup>10,11</sup> Parker *et al.* reported that IBS patients perceived more adulthood life events as negative and had a higher negative life event impact score, associated with more severe IBS symptoms.<sup>12</sup>

To date, no published literature has been available on how FD and IBS patients have coped during the COVID-19 pandemic. Accordingly, we performed a cross-sectional online survey to investigate the impact of the COVID-19 pandemic on FD and IBS symptoms.

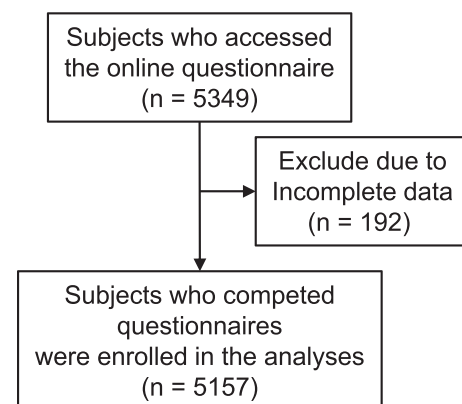
**Table 1** Respondents' demographic and occupational characteristics and thoughts on COVID-19

	Respondents (n = 5157)
Mean age, years (SD)	50.0 (15.8)
20–29 (Male/Female)	347/333
30–39	433/424
40–49	509/501
50–59	423/425
60–69	484/510
70–79	350/418
Sex	
Male	2546 (49.4%)
Female	2611 (50.6%)
Marital status	
Single (including divorced/separated/widowed)	1755 (34.0%)
Married	3402 (66.0%)
Household income (Japanese yen/year) <sup>†</sup>	
<6 000 000	3144 (61.0%)
≥6 000 000	2013 (39.0%)
What was the most applicable living environment under the COVID-19 emergency?	
Used car as usual	1037 (20.1%)
Used public transport as usual	601 (11.7%)
Flexible work/school	277 (5.4%)
Work/study from home	969 (18.8%)
Housewife/Househusband	830 (16.1%)
Lost job	161 (3.1%)
Unemployed	813 (15.8%)
Others	469 (9.1%)
Do you take physical distance at more than 2 m?	
No	2904 (56.3%)
Yes	2253 (43.7%)
What do you think your probability of getting COVID-19?	
<20%	3943 (76.5%)
≥20%	1214 (23.5%)
Do you feel stress in daily work/school?	
No	3514 (68.1%)
Yes	1643 (31.9%)
Do you go to medical institutes for more than 3 months by following diseases?	
Functional dyspepsia/irritable bowel syndrome	168 (3.3%)
Psychological diseases (anxiety, neurosis, autonomic imbalance etc.)	420 (8.1%)
Chronic disease (hypertension, diabetes mellitus, dyslipidemia etc.)	1032 (20.0%)

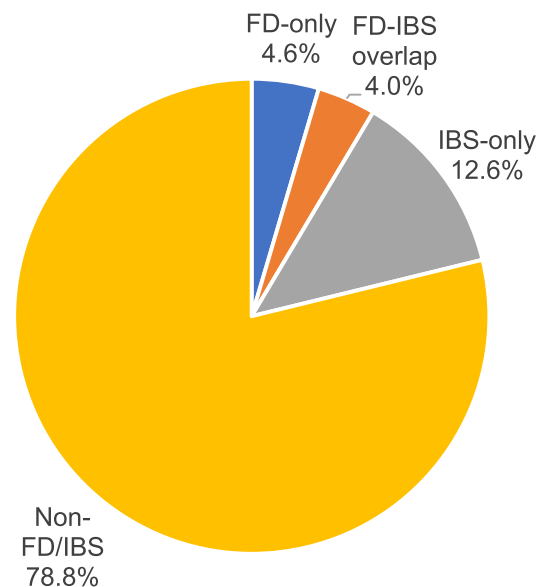
<sup>†</sup>As of May 26, 2020, 1 Japanese yen = \$0.0093 US. SD, standard deviation; COVID-19, coronavirus disease 2019.

## Material and methods

**Internet-based questionnaire survey.** An internet-based questionnaire survey was administered from May 26 to 27, 2020, targeting the general Japanese population aged



**Figure 1** Flow chart of the study.



**Figure 2** Prevalence of functional dyspepsia (FD), irritable bowel syndrome (IBS), and FD-IBS overlap.

between 20 and 79 years, with the cooperation of an internet research company. Male and female subjects in the age groups 20 to <30 years (20s), 30 to <40 years (30s), 40 to <50 years (40s), 50 to <60 years (50s), 60 to <70 years (60s), and 70 to <80 years (70s) were randomly selected from the registered

panelists based on Japanese demographics (Table 1). Respondents in this study were assigned to groups on the internet in reference to the population ratio in Japan by generation and sex according to the national census conducted by the Ministry of Internal Affairs and Communications Statistics Bureau (2017). It was planned to

**Table 2** Factors associated with FD and IBS symptoms during the COVID-19 pandemic

	Much improved	Slightly improve	No change	Slightly worse	Much worse	<i>P</i>
Young (<50 years) ( <i>n</i> = 602)	9 (1.5)	27 (4.5)	371 (61.6)	177 (29.4)	18 (3.0)	NS
Old (≥50 years) ( <i>n</i> = 490)	2 (0.4)	8 (1.6)	317 (64.7)	152 (31.0)	11 (2.2)	—
Male ( <i>n</i> = 462)	6 (1.3)	14 (3.0)	295 (63.9)	135 (29.2)	12 (2.6)	NS
Female ( <i>n</i> = 630)	5 (0.8)	21 (3.3)	393 (62.4)	194 (30.8)	17 (2.7)	—
Single ( <i>n</i> = 399)	5 (1.3)	22 (5.5)	239 (59.9)	119 (29.8)	14 (3.5)	<0.001
Married ( <i>n</i> = 693)	6 (0.9)	13 (1.9)	449 (64.8)	210 (30.3)	15 (2.2)	—
Living environment						
Used car as usual ( <i>n</i> = 212)	0 (0.0)	3 (1.4)	150 (70.8)	56 (26.4)	3 (1.4)	<0.01
Used public transport as usual ( <i>n</i> = 130)	3 (2.3)	6 (4.6)	74 (56.9)	46 (35.4)	1 (0.8)	—
Flexible work/school ( <i>n</i> = 55)	0 (0.0)	5 (9.1)	32(58.2)	17 (30.9)	1 (1.8)	—
Work/study from home ( <i>n</i> = 233)	6 (2.6)	13 (5.6)	127 (54.5)	76 (32.6)	11 (4.7)	—
Housewife/Househusband ( <i>n</i> = 162)	0 (0.0)	2 (1.2)	106 (65.4)	50 (30.9)	4 (2.5)	—
Lost job ( <i>n</i> = 49)	0 (0.0)	2 (4.1)	30 (61.2)	16 (32.7)	1 (2.0)	—
Unemployed ( <i>n</i> = 151)	2 (1.3)	2 (1.3)	103 (68.2)	39 (25.8)	5 (3.3)	—
Others <sup>†</sup> ( <i>n</i> = 100)	0 (0.0)	2 (2.0)	66 (66.0)	29 (29.0)	3 (3.0)	—
Income low ( <i>n</i> = 662)	7 (1.1)	22 (3.3)	430 (65.0)	189 (28.5)	14 (2.1)	NS
Income high ( <i>n</i> = 430)	4 (0.9)	13 (3.0)	258 (60.0)	140 (32.6)	15 (3.5)	—
Physical distancing <2 m ( <i>n</i> = 611)	6 (1.0)	16 (2.6)	402 (65.8)	174 (28.5)	13 (2.1)	NS
Physical distancing ≥2 m ( <i>n</i> = 481)	5 (1.0)	19 (4.0)	286 (59.5)	155 (32.2)	16 (3.3)	—
Fear of COVID-19 <20% ( <i>n</i> = 744)	5 (0.7)	24 (3.2)	472 (63.4)	224 (30.1)	19 (2.6)	NS
Fear of COVID-19 ≥20% ( <i>n</i> = 348)	6 (1.7)	11 (3.2)	216 (62.1)	105 (30.2)	10 (2.9)	—
FD or IBS-only ( <i>n</i> = 887)	9 (1.0)	29 (3.3)	595 (67.1)	240 (27.1)	14 (1.6)	<0.0001
FD-IBS overlap ( <i>n</i> = 205)	2 (1.0)	6 (2.9)	93 (45.4)	89 (43.4)	15 (7.3)	—
Stress at work/school – ( <i>n</i> = 643)	8 (1.2)	21 (3.3)	431 (67.0)	164 (25.5)	19 (3.0)	<0.01
Stress at work/school + ( <i>n</i> = 449)	3 (0.7)	14 (3.1)	257 (57.2)	165 (36.7)	10 (2.2)	—
Psychological diseases – ( <i>n</i> = 934)	8 (0.9)	25 (2.7)	610 (65.3)	270 (28.9)	21 (2.2)	<0.001
Psychological diseases + ( <i>n</i> = 158)	3 (1.9)	10 (6.3)	78 (49.4)	59 (37.3)	8 (5.1)	—
HADS anxiety – ( <i>n</i> = 799)	7 (0.9)	28 (3.5)	539 (67.5)	210 (26.3)	15 (1.9)	<0.0001
HADS anxiety + ( <i>n</i> = 293)	4 (1.4)	7 (2.4)	149 (50.9)	119 (40.6)	14 (4.8)	—
HADS depression – ( <i>n</i> = 692)	7 (1.0)	18 (3.0)	473 (68.5)	182 (25.7)	12 (1.8)	<0.0001
HADS depression + ( <i>n</i> = 400)	4 (1.0)	17 (3.7)	215 (52.8)	147 (38.3)	17 (4.2)	—
MHC-SF – ( <i>n</i> = 923)	10 (1.1)	32 (3.5)	567 (61.4)	289 (31.3)	25 (2.7)	NS
MHC-SF + ( <i>n</i> = 169)	1 (0.6)	3 (1.8)	121 (71.6)	40 (23.7)	4 (2.4)	—
Nonconsulter ( <i>n</i> = 1013)	10 (1.0)	30 (3.0)	641 (63.3)	306 (30.2)	26 (2.6)	NS
Consulter ( <i>n</i> = 79)	1 (1.3)	5 (6.3)	47 (59.5)	23 (29.1)	3 (3.8)	—

<sup>†</sup>Walking to work, bicycle commuting, temporary closure, etc.

COVID-19, coronavirus disease 2019; FD, functional dyspepsia; HADS, the Hospital Anxiety and Depression Scale; IBS, irritable bowel syndrome; MHC-SF, the Mental Health Continuum-Short Form; NS, not significant.

collect data from approximately 5000 subjects in 13 prefectures designated as “special alert prefectures”, where it was necessary to promote efforts to prevent the spread of SARS-CoV-2 infections in Japan. A 95% confidence level was set, and a confidence interval was 1.38 in 100 000 000 adult Japanese population. Respondents who failed to completely answer all questions were excluded from the analysis. Demographic data for respondents were anonymously obtained as background data for the panelists.

**Questionnaire.** The questionnaire comprised items regarding commuting style, stress, physical distancing, worries about COVID-19, gastrointestinal symptoms, anxiety, depression, and social well-being. The original questionnaire is given in the Supporting information (Fig. S1). Stress at work/school was defined as present when the respondent described feeling this way three or more times per week. Gastrointestinal symptoms were assessed by the validated questionnaire to diagnose FD and IBS in accordance with the Rome III criteria (Japanese version).<sup>13</sup> Good physical health was defined as feeling healthy every day or almost every day. Psychological symptoms (anxiety and depression) were assessed by the validated Japanese version of the Hospital Anxiety and Depression Scale (HADS).<sup>14–17</sup> The HADS consists of seven anxiety-related questions and seven depression-related questions. Each total was calculated, and a score of  $\geq 11$  on either the HADS anxiety or the depression scale was considered as a major abnormal case. We also asked about well-being using the validated Japanese version of the Mental Health Continuum-Short Form (MHC-SF) questionnaire.<sup>18</sup> The MHC-SF is a brief scale measuring positive human functioning.<sup>19</sup>

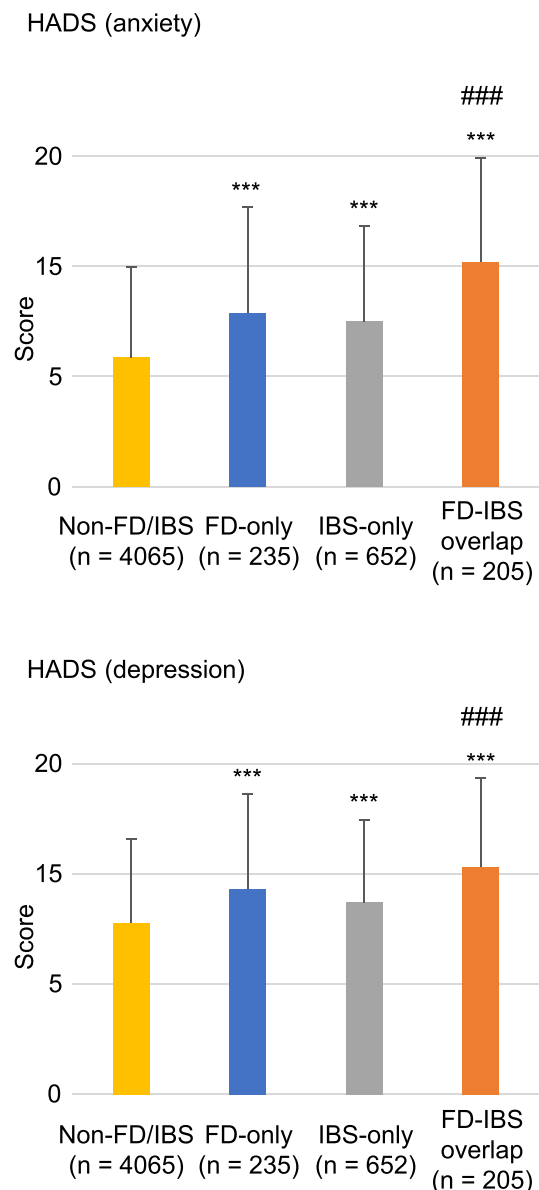
**Statistical analysis.** Continuous variables were presented as mean  $\pm$  standard deviation (SD) and categorical variables as number and proportion. Data were analyzed using the  $\chi^2$  test and one-way ANOVA followed by Tukey’s multiple comparisons, where appropriate. To determine risk factors associated with improvement and deterioration of chronic FD/IBS symptoms, we estimated the odds ratio and 95% confidence interval. A univariate analysis and unrestricted multivariate logistic regression analysis were performed to test the influence of several factors in association with changes in symptoms. All tests were two sided with a significance level of  $P < 0.05$ . All analyses were conducted using SPSS 22.0 (SPSS Inc., Chicago, USA).

## Results

**Response rate and sociodemographic, occupational, and physical health characteristics.** A total of 5349 individuals accessed the online questionnaire, and 5157 subjects (2546 male subjects and 2611 female subjects) who completed the questionnaire were finally enrolled, for participation rate of 96.4% (Fig. 1). The mean age was  $50.0 \pm 15.8$  years, and the male-to-female ratio was 0.98 (2546/2611). Overall, 66.0% (3402/5157) were married, and 34.0% (1755/5157) were single, divorced, separated, or widowed. As family characteristics, 60.8% (3134/5157) of respondents had children. As occupational characteristics, 44.5% (2296/5157) of respondents were workers and technical staff, 6.6% (338/5157) were doing business on their

own, 19.1% (983/5157) were full-time homemakers, 14.1% (726/5157) were part-time workers, 1.7% (87/5157) were students, and 14.1% (727/5157) were in other categories. As physical health status, the majority of respondents reported an absence of chronic medical conditions within the preceding 3 months (69.3%, 3573/5157) or reported good physical health (66.6%, 3432/5157).

**Prevalence of functional dyspepsia, irritable bowel syndrome, and functional dyspepsia-irritable bowel syndrome overlap.** The prevalence of IBS (16.6%, 857/5157) was greater than that of FD (8.5%, 440/5157) (Fig. 2). The 4.0% (205/5157) of subjects with FD-IBS overlap



**Figure 3** Psychological symptoms of functional dyspepsia (FD) and irritable bowel syndrome (IBS). \*\*\* $P < 0.001$  versus non-FD/IBS, ### $P < 0.001$  versus FD- or IBS-only.

comprised 46.6% of FD subjects and 23.9% of IBS subjects. The prevalence of FD and/or IBS was greater in women than in men and decreased with age (Table 2).

**Psychological symptoms.** Mean anxiety and depression scores by HADS were  $6.3 \pm 4.3$  and  $8.1 \pm 3.9$ , respectively, in all respondents under the state of emergency in Japan. The FD-only and IBS-only groups showed significantly higher anxiety ( $7.9 \pm 4.8$  and  $7.5 \pm 4.8$ , respectively) and depression ( $7.5 \pm 4.3$  and  $8.7 \pm 3.7$ , respectively) scores compared with the non-FD or IBS groups ( $5.9 \pm 4.1$  and  $7.6 \pm 3.8$ , respectively) (Fig. 3). Mean scores for anxiety ( $10.2 \pm 4.7$ ) and depression ( $10.3 \pm 4.0$ ) by HADS in the FD–IBS overlap group were significantly higher compared with those in the non-FD or IBS, FD-only, and IBS-only groups. These data indicated that subjects with FD and IBS symptoms experienced more psychological stress under the COVID-19 pandemic.

**Gastrointestinal symptoms.** Overall gastrointestinal symptoms became much worse in 0.9% (48/5157) of subjects, slightly worse in 11.0% (567/5157) of subjects, no change or no symptoms in 85.3% (4398/5157) of subjects, slightly improved in 2.1% (107/5157) of subjects, and were much improved in 0.7% (37/5157) of subjects. Among 21.2% (1092/5157) of subjects who had chronic FD or IBS symptoms, respondents with FD-only, IBS-only, or FD–IBS overlap all reported significantly worse symptoms than those in the non-FD/IBS group (Fig. 4). Respondents with FD–IBS overlap experienced the worst symptoms, followed by the IBS-only group and the FD-only group.

**Factors associated with functional dyspepsia and irritable bowel syndrome symptoms during the COVID-19 pandemic.** In subjects with chronic FD and/or IBS symptoms, marital status, living environment, FD–IBS overlap, stress in daily work/school, psychological disease comorbidity, anxiety, and depression were significantly associated with changes in chronic FD and/or IBS symptoms under the COVID-19

pandemic (Table 2). Age, sex, income, maintaining physical distancing, fear of contracting COVID-19, MHC-SF, and consultation with medical institutes were not associated with changes in chronic FD or IBS symptoms (Table 2).

To reveal factors associated with improvement or deterioration of chronic FD or IBS symptoms under the COVID-19 pandemic, univariate and multivariate analyses were performed (Table 3). Deterioration factors included work/study from home, overlap of FD–IBS, comorbid psychological disease, and stress during daily work or school.

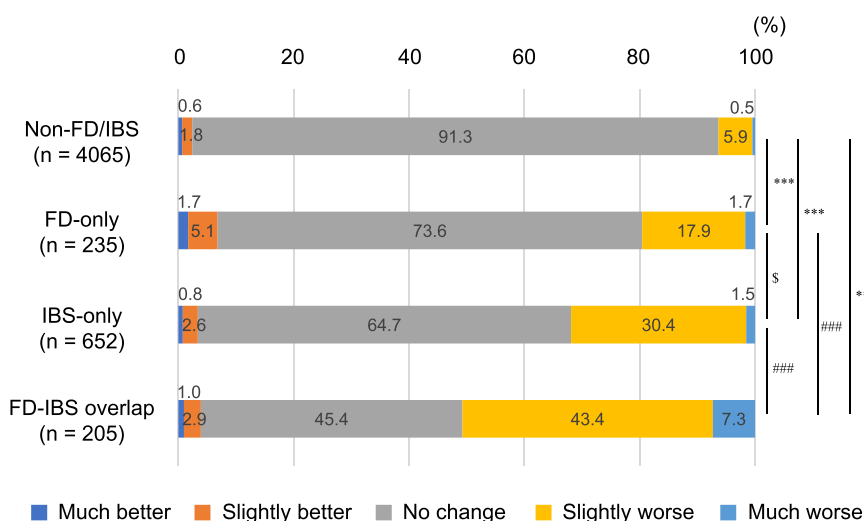
Improvement factors included commuting by public transport, flexible work/school styles, work/study from home, and comorbid psychological disease (Table 3). Older age and stress in daily work/school negatively affected improvements in chronic FD and IBS symptoms.

## Discussion

The results of the present study revealed that more than 20% of respondents with FD or IBS experienced deterioration and a smaller number improved during the COVID-19 pandemic, although most showed no change in symptoms. Respondents with FD–IBS overlap syndrome generally experienced the worst gastrointestinal and psychological outcomes. Interestingly, we found that the key factors determining improvement and deterioration during the COVID-19 pandemic involved both psychological disease comorbidity and occupational issues.

As the prevalences of FD and IBS in the present study were similar to previous data acquired through online surveys in the Japanese general population,<sup>1,20</sup> the present data under the COVID-19 pandemic are considered to represent the condition of FD and/or IBS in the general population in Japan. However, the prevalences of FD and IBS were reported as 2.4% and 2.2% by Rome IV criteria in Japan.<sup>21</sup> As the definitions of FD and IBS by Rome IV are stricter, the outcome might be different by the different definitions.

The prevalence of FD–IBS overlap in FD or IBS was consistent with results from previous studies.<sup>1,22</sup> Previously, the severity of gastrointestinal symptoms, but not age or sex, was reported to be



**Figure 4** Influence of the COVID-19 pandemic on gastrointestinal symptoms.

\*\*\* $P < 0.001$  versus non-FD/IBS, ### $P < 0.001$  versus FD or IBS-only,  $^sP < 0.05$  versus FD-only. ■, Much better; ■, Slightly better; ■, No change; ■, Slightly worse; ■, Much worse.

**Table 3** Factors associated with changes in FD and IBS symptoms

	Improvement			Worse			
	Univariate	P	Multivariate	Univariate	P	Multivariate	
Age (per 1 year)	0.96 (0.94–0.98)	<0.0001	0.97 (0.95–0.99)	1.00 (0.99–1.01)	0.87	1.00 (0.99–1.01)	0.398
Male sex (vs female)	1.05 (0.58–1.91)	0.87	0.88 (0.462–1.69)	0.93 (0.71–1.20)	0.56	0.83 (0.62–1.11)	0.83
Marital status (married)	0.39 (0.21–0.71)	<0.01	0.72 (0.36–1.46)	0.96 (0.74–1.25)	0.77	0.93 (0.68–1.26)	0.637
Living environment							
Used car as usual	1.0 (ref)	—	1.0 (ref)	1.0 (ref)	—	1.0 (ref)	—
Used public transport as usual	5.18 (1.38–19.61)	<0.05	5.39 (1.39–20.81)	1.47 (0.92–2.34)	0.107	1.42 (0.88–2.30)	0.154
Flexible work/school	6.97 (1.61–30.13)	<0.01	7.27 (1.63–32.50)	1.26 (0.66–2.39)	0.476	1.19 (0.61–2.29)	0.612
Work/study from home	6.19 (1.80–21.21)	<0.01	4.17 (1.18–14.74)	1.55 (1.04–2.31)	0.033	1.55 (1.01–2.37)	0.045
Housewife/Househusband	0.87 (0.14–5.27)	0.88	0.653 (0.10–4.31)	1.30 (0.83–2.02)	0.251	1.54 (0.91–2.63)	0.109
Lost job	2.97 (0.48–18.24)	0.241	1.74 (0.27–11.23)	1.38 (0.71–2.67)	0.342	1.36 (0.79–2.34)	0.19
Unemployed	1.90 (0.42–8.60)	0.407	1.54 (0.31–7.60)	1.07 (0.67–1.69)	0.785	1.33 (0.79–2.34)	0.269
Others <sup>†</sup>	1.42 (0.23–8.65)	0.7	1.01 (0.16–6.31)	1.22 (0.73–2.05)	0.45	1.33 (0.77–2.30)	0.311
Household income <sup>‡</sup> (>6 000 000 yen/year)	0.90 (0.49–1.66)	0.73	0.83 (0.42–1.62)	1.27 (0.99–1.65)	0.06	1.33 (1.00–1.76)	0.048
Physical distancing (≥2 m)	1.41 (0.78–2.54)	0.26	1.31 (0.70–2.44)	1.25 (0.97–1.61)	0.084	1.22 (0.93–1.59)	0.152
Fear of getting COVID-19 (≥20%)	1.27 (0.69–2.34)	0.45	1.39 (0.73–2.66)	1.02 (0.7801.33)	0.9	0.91 (0.69–1.21)	0.512
Overlap of FD-IBD	0.91 (0.42–1.98)	0.81	0.91 (0.49–2.06)	2.57 (1.88–3.50)	<0.0001	2.37 (1.72–3.26)	<0.0001
Psychological disease (+)	2.45 (1.26–4.76)	<0.01	2.15 (1.05–4.37)	1.63 (1.15–2.30)	<0.01	1.47 (1.02–2.31)	<0.05
Stress at work/school (+)	0.80 (0.60–1.05)	0.09	0.435 (0.21–0.89)	1.61 (1.24–2.07)	<0.0001	1.68 (1.22–2.31)	<0.01

<sup>†</sup>Walking to work, bicycle commuting, temporary closure etc.

<sup>‡</sup>As of May 26, 2020, 1 Japanese yen = \$US0.0093.

COVID-19, coronavirus disease 2019; FD, functional dyspepsia; IBS, irritable bowel syndrome.

more related to FD–IBS overlap than to FD or IBS alone.<sup>23</sup> Psychological factors correlated significantly with quality of life in overlap syndrome of FGIDs.<sup>24</sup> The anxiety and depression scores for all respondents in the present study were higher because of the pandemic than those under normal conditions.<sup>22,25</sup> As the FD–IBS overlap group displayed significantly higher anxiety and depression scores than the FD or IBS-only groups, psychological factors and FGID symptoms were closely related. Unfortunately, the direction of causality in the relationship could not be determined, as the present study was cross-sectional in design. Psychological stressors trigger the development of FGIDs, including FD and IBS,<sup>3,4</sup> and antidepressants are effective as a treatment for FD and IBS, although results from individual trials have been variable.<sup>26,27</sup> Psychological factors may thus influence the exacerbation of symptoms, and interactions must be bidirectional to some extent. A previous study identified anxiety as a predictor of FGID diagnosis, but psychological factors did not discriminate between consulters and nonconsulters.<sup>28</sup> The present study showed that consultation behavior was not associated with deterioration of FD/IBS symptoms. These data indicate that consultation behavior is independent of psychological conditions and of changes in gastrointestinal symptoms under tentative, stressful conditions.

Interestingly, the present results revealed that deterioration of symptoms occurred more often among subjects with FD and/or IBS symptoms, and the FD–IBS overlap group showed a higher prevalence than the FD-only or IBS-only groups. Furthermore, overlap of FD–IBS, comorbid psychological diseases and stress in daily work/school were independent risk factors for deterioration of chronic FD/IBS symptoms. These data indicate that subjects with FD–IBS overlap are vulnerable to psychological stress due to the COVID-19 pandemic. Although the combination of stress from COVID-19 and occupational stress would inevitably exacerbate chronic FD/IBS symptoms, the fear of contracting SARS-CoV-2 was surprisingly not associated with deterioration of chronic FD/IBS symptoms.

Among subjects with chronic FD/IBS symptoms, a few showed improved gastrointestinal symptoms under the COVID-19 pandemic. Younger people reportedly may experience stronger stress because of exposure to large amounts of information from social media<sup>29</sup> and may be more likely to experience anxiety, depression, and psychological abnormalities under the COVID-19 pandemic.<sup>10</sup> It is interesting that the present study showed younger age and working from home as independent factors associated with improved chronic symptoms of FD or IBS. As only a few individuals showed improvements in the present study, we should not conclude that circumstances under the COVID-19 pandemic improved gastrointestinal symptoms.

The present study has several strengths and limitations, as the study was an online survey. The study was performed about 100 days after the announcement of COVID-19 as a pandemic by the World Health Organization, at a time when Japan was just lifting the state of emergency. Prolonged emergency status and business closures might have led to social isolation and disruption of lifestyles. Conversely, as no vaccine or effective treatment against COVID-19 has been developed, going outside must also be stressful. Therefore, the impact of COVID-19 on physical and mental health could be fully compared with the initial phase when people tend to panic. A cross-sectional survey was designed with a self-administered online questionnaire to avoid contact between

the interviewer and subject and therefore limit the spread of SARS-CoV-2 infection. Another strength of the study was that data could be obtained throughout the country and were based on the population ratio in Japan. Limitations of the present study include that abuse, smoking, and alcohol intake that may affect the deterioration of FD/IBS were not assessed. The Rome III definition but not the Rome IV definition was used in the present study as the validated Japanese version of the questionnaire to diagnose FD and IBS was only available with the Rome III definition in Japan. The use of self-reported data, which means that organic diseases that may have produced gastrointestinal symptoms could not be excluded from the results. However, identification of an organic explanation is unlikely in the population setting when endoscopy is performed.<sup>30</sup> As subjects with chronic FGID symptoms usually consult doctors soon after symptom onset in Japan,<sup>31</sup> the possibility of organic diseases would be low among subjects with chronic FGID symptoms.<sup>32</sup> Previous reports of online surveys have also produced reasonably important epidemiological data on FGIDs.<sup>33</sup> Furthermore, survey companies have proprietary algorithms and perform surveys only on qualified panels, although the details of the algorithms were not open to the public.

In conclusion, our findings indicate that the COVID-19 pandemic affected FD/IBS subjects negatively, with respondents showing FD–IBS overlap syndrome as the most important independent factor associated with deterioration in gastrointestinal symptoms. The first wave of the pandemic has settled down in Asian countries, including Japan. However, the risk of a second wave of COVID-19 appears very real. Although the psychological and physical stress of a second wave would depend on the size and impact of the wave, the finding that stressful conditions under the COVID-19 pandemic deteriorate FD and IBS symptoms is noteworthy.

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## Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Figure S1.** Questionnaire.