

# Gastrointestinal symptoms in coronavirus disease 2019: a cross-sectional study in Wuhan, China

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## Research article

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# Abstract

## Background

To investigate the clinical symptoms of coronavirus disease 2019 (COVID-19), particularly the prevalence, time of symptom onset, and duration of gastrointestinal (GI) symptoms.

## Methods

This was a cross-sectional study using paper questionnaires. COVID-19 patients in a temporary hospital in Wuhan voluntarily completed surveys collecting data on COVID-19 symptoms and investigation results.

## Results

A total of 212 adults were enrolled in this study, of whom 127 (59.9%) were female, mean age was  $48.50 \pm 13.15$  years. Concerning symptoms, 78.8% (167/212) had fever, and 66% (140/212) had cough. Diarrhoea occurred in 43.8% (93/212) of patients. Nausea and vomiting were also common (20.7%). Fever and cough were frequently the initial symptoms of COVID-19, and they lasted for 5.00 [interquartile range (IQR): 3.00–10.00] days and 10.00 (IQR: 5.00–24.00) days, respectively. Most patients developed nausea and vomiting 2.00 (IQR: 0–9.00) days and diarrhoea 5.00 (IQR: 0.25–11.00) days after the onset of initial symptoms, respectively. There was a median duration of 4.00 (IQR: 2.00–8.75) days with diarrhoea, and 6.00 (IQR: 4.00–10.00) days with nausea and vomiting. The patients with diarrhoea were younger [ $45.85 \pm 13.28$  years vs  $50.61 \pm 12.82$  years,  $P=0.009$ ] and were more likely to have an abnormal chest CT (95.7% vs 82.4%,  $P=0.001$ ) than those without diarrhoea.

## Conclusions

In our cohort of patients, GI symptoms were common in COVID-19, occurred mostly during the middle stage of the disease, and lasted for a short duration. GI symptoms may not be associated with COVID-19 related treatment.

## Background

Coronavirus disease 2019 (COVID-19) has recently become a global pandemic[1]. The disease was first identified in the Wuhan City of China in December 2019[2]. At the time of this writing on 11 March 2020, a total of 113,702 confirmed cases and 4,012 deaths have been reported globally[3]. Fever and cough are the most common clinical symptom[4–6]. Gastrointestinal symptoms (GI symptoms) such as nausea, vomiting, and diarrhoea are often seen in coronavirus infections such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) [7–8]. However, early studies reported

low prevalence of typical GI symptoms, with the prevalence of diarrhoea in the range of 1–3.8% [4–6]. On the contrary, with current growing attention to GI symptoms, the latest published studies have shown that GI symptoms are also common in COVID-19, and the prevalence of diarrhoea is between 12.0–29.2% [9–12]. However, the time of symptom onset and duration of GI symptoms have not been commonly investigated in recent studies [9, 12]. We recently worked in a temporary hospital and conducted a detailed cross-sectional study of the clinical symptoms of patients with COVID-19 to further recognize the clinical characteristics of GI symptoms.

## **Methodology**

### **Ethical considerations**

This study was reviewed by the ethics committee of Renmin Hospital of Wuhan University (Ethics Approval No.: WDRY2020-K033) and written informed consent from patients was waived. Only a verbal explanation was required, and verbal informed consent was obtained from patients.

### **Study participants**

From February 18 to March 2, 2020, patients with confirmed COVID-19 according to WHO interim guidelines [13], and who were  $\geq 16$  years of age, were recruited from Wuchang mobile cabin hospital. Wuchang mobile cabin hospital was a temporary hospital facility designed specifically for the care of patients with confirmed COVID-19. Our exclusion criteria were (i) incomplete data, (ii) cases with GI symptoms resulted from new medication and (iii) individuals below the stipulated age limit. A total of 240 patients were invited, and 222 responses were received (response rate 92.5%). Among the patients, 10 responses met the exclusion criteria (6 cases with GI symptoms resulted from new medication and 4 cases below the stipulated age limit) and these were not included in the data analysis. The patients themselves completed a form that collected general demographic information, current medical history, past medical history, date of first positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid test results, chest computed tomography (CT) results, and COVID-19 contact history. COVID-19-related clinical symptoms were listed with tick boxes in the form. The study participants were asked to check the boxes of their recent abnormal symptoms and write down the specific date of symptom onset and duration of each symptom. On handing over the questionnaire (supplementary material pp1-2), we checked the data completion. If there were incomplete data, we required the patients to fill in the blank. So, there was no missing data. All patients in this temporary mobile hospital were long-time residents of Wuhan and tested positive for SARS-CoV-2 nucleic acid by reverse transcription polymerase chain reaction (RT-PCR) from a nasopharyngeal swab before admission. After patients completed the hardcopy forms, photographs were taken, and the data were uploaded onto the network. Before the temporary mobile hospital was closed, the hardcopy forms were destroyed as medical waste.

### **Patient and Public Involvement**

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

## Statistical analyses

Symptom duration was defined as the interval from the onset of the symptom to resolution or investigation. Time of symptom onset refers to the duration from onset of the initial symptom of COVID-19. High fever was defined as a temperature  $\geq 39^{\circ}\text{C}$ . The definition of diarrhoea was the passing of loose stools  $\geq 3$  times per day, and the two types of abnormal loose stools included mushy stool (type 6) and watery stool (type 7) according to Bristol stool chart. A history of chronic disease was defined as other diseases that persisted for three months before COVID-19, such as hypertension, diabetes mellitus, liver disease, and respiratory disease. The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. Normally distributed variables were expressed as the mean and standard deviation, while non-normally distributed variables were expressed as the median and interquartile range (IQR). Categorical variables were summarized as the counts and percentages in each category. We grouped patients into diarrhoea and non-diarrhoea groups. Wilcoxon rank-sum tests were applied to non-normally continuous variables, t tests were applied to normally distributed variables, and chi-square tests were used for categorical variables as appropriate. Fisher's chi-square tests were applied when the expected values in any of the cells of a contingency table were below 5. A two-sided P of  $< 0.05$  was considered statistically significant. SPSS (V.26.0) was used for all analyses.

## Results

A total of 212 adults were enrolled in the study, of whom 127 (59.9%) were female, and the mean age was  $48.50 \pm 13.15$  (range: 17–79) years. The average time from symptom onset to hospital admission was  $16.00 \pm 9.87$  (range: -2–60) days. The mean duration from symptom onset (for patients with symptoms) or positive SARS-CoV-2 test results (for asymptomatic patients) to resolution or the time of investigation was  $26.78 \pm 9.16$  (range: 3–60) days. Of the patients, 5.7% (12/212) had no clinical symptoms related to COVID-19. Results of chest CT scan of most patients (88.2%, 187/212) in this study were suggestive of viral pneumonia, of whom four patients had no clinical symptom. Approximately 44.3% (94/212) of the patients claimed to have a clear contact history with other individuals with COVID-19. There were 23.1% (49/212) patients with chronic medical illnesses, including hypertension in 26, chronic respiratory disease in 7, diabetes mellitus in 3, chronic stomach illness in 3, chronic thyroid disease in 3, anemia in 3, chronic liver disease in 3, cardiovascular disease in 1, and chronic renal disease in 1. Prior to admission, 94.3% (200/212) of patients were receiving antiviral treatment (e.g., arbidol hydrochloride capsule and Lianhuaqingwen capsule, the latter of which is a traditional Chinese medication), while 40.1% (85/212) were on antibiotics. After hospitalization, all patients received antiviral treatment, and 69.8% (148/212) took antibiotics. Additionally, 14 patients with persistently positive SARS-CoV-2 nucleic acid test results, 4 patients with worsening pneumonia and 1 patient with severe liver impairment, were transferred to a formal hospital. The other 193 patients were discharged and no patients died. Among the discharged patients, the mean in-hospital stay was  $18.47.4 \pm 8.07$  (range: 2–33) days.

Fever and cough were the most common clinical symptoms (Fig. 1), as 78.8% (167/212) of patients had fever, 66% (140/212) of patients had cough, and patients with high-grade fever accounted for 14.2% (30/212). Profuse sweating occurred in 114 patients, of which 89.5% (102/114) had night sweats. Additionally, 66.3% (140/212) patients had GI symptoms, including anorexia in 88, diarrhoea in 93, and nausea and vomiting in 44. When anorexia was excluded from the analysis (since it is less specific), there were 111 total cases (52.3%) in which patients presented with a specific GI symptom. Furthermore, 3.3% (7/212) of the patients developed conjunctival congestion. In the patients with diarrhoea, 86.0% (80/93) had mushy stools and 14% (13/93) had watery stools. There were 42.3% (90/212) patients who developed all types of the three common COVID-19 symptoms such as, flu-like symptoms, pneumonia and GI symptoms.

Nasal congestion, myalgia, headache, chills, fever, fatigue, dry mouth, sore throat, and coughing were common initial symptoms, whereas GI symptoms were rare initial symptoms. In our study, 10.4% (22/212) of patients had an initial symptom of diarrhoea, which was accompanied by fever, cough, or other symptoms on the first day of COVID-19. Additionally, 3.8% (8/212) of patients developed diarrhoea before developing pneumonia symptoms, and 79.6% (74/93) of patients experienced diarrhoea before admission. Diarrhoea disappeared at the time of investigation in 81.7% (75/93) of patients. Most patients developed anorexia 2.00 (IQR: 0–6.00) days after the onset of initial symptoms, nausea and vomiting 2.00 (IQR: 0–9.00) days after symptom onset, and diarrhoea 5.00 (IQR: 0.25–11.00) days after initial symptom onset (Fig. 2).

Cough was the most persistent symptom, whereas conjunctival congestion had the shortest duration. Patients experienced a median duration of 4.00 (IQR: 2.00–8.75) days with diarrhoea, 5.00 (IQR: 3.00–10.00) days with anorexia, and 6.00 (IQR: 4.00–10.00) days with nausea and vomiting, which were shorter than the durations of fever and pneumonia symptoms (Fig. 3).

The patients with diarrhoea were younger ( $45.85 \pm 13.28$  years vs  $50.61 \pm 12.82$  years, OR 0.964, 95%CI (0.942–0.987),  $P = 0.009$ ) and were more likely to have abnormal chest CT results (95.7% vs 82.4%, OR 8.729, 95%CI (2.376–32.064),  $P = 0.001$ ). There was no significant difference in in-hospital stay, duration from onset to hospitalization and antibiotic use between patients with and without diarrhoea. The patients with diarrhoea had a higher percentage to have the symptoms of fever, cough, sputum, shortness of breath, headache, myalgia, fatigue, bitter taste in mouth, dry mouth, excessive sweating, and nausea or vomiting than those without diarrhoea ( $P < 0.05$ ) (Table 1).

Table 1

The associations between patient demographics and symptoms compared with the symptoms of diarrhoea

Factors	Diarrhoea, n (%)		P value
	Yes (93)	No (119)	
Female	55(59.1)	38(40.9)	0.841
Mean age $\pm$ SD(yr)	45.85 $\pm$ 13.28	50.61 $\pm$ 12.82	0.009
Mean in-hospital stay $\pm$ SD(days)	16.24 $\pm$ 8.71	15.82 $\pm$ 10.70	0.449
Mean duration from symptoms onset to admission $\pm$ SD(days)	18.33 $\pm$ 8.16	18.55 $\pm$ 8.07	0.762
Current smoking	13(14.0)	18(15.1)	0.668
Chronic disease	22(23.7)	28(23.5)	0.904
Abnormal chest CT	89(95.7)	98(82.4)	0.001
Antibiotic use before hospitalization	40(41.7)	45(38.8)	0.671
Antibiotic use after hospitalization	63(67.7)	85(71.4)	0.562
Fever	80(86.0)	87(73.1)	0.025
Chill	28(30.1)	35(29.4)	0.913
Cough	70(75.3)	70(58.8)	0.013
Sputum	61(65.6)	50(42.0)	0.001
Shortness of breath	47(50.5)	42(35.3)	0.026
Headache	36(38.7)	24(20.2)	0.003
Sore throat	37(39.8)	35(29.4)	0.115
Conjunctival congestion	6(6.5)	1(0.8)	0.054
Nasal congestion	9(9.7)	8(6.7)	0.434
Myalgia	35(37.6)	23(19.3)	0.003
Fatigue	47(50.5)	31(26.1)	< 0.001
Bitter taste in mouth	42(45.2)	27(22.7)	0.001
Dry mouth	53(57.0)	44(37.0)	0.005
Anorexia	46(49.5)	43(36.1)	0.062
Excessive sweating	61(65.6)	54(45.4)	0.004

Factors	Diarrhoea, n (%)		P value
	Yes (93)	No (119)	
Nausea or vomiting	27(29.0)	17(14.3)	0.010

## Discussion

Coronavirus is a large virus family that can cause various conditions, ranging from the common cold to severe infectious diseases such as SARS and MERS [14]. COVID-19 is a newly discovered coronavirus infection in humans, and is currently a pandemic [1–2]. The most common clinical symptoms associated with coronavirus infection are fever and cough [8, 14]. The results of this study have further supported previous published data that fever and cough are the most common clinical symptoms of COVID-19 [4–6]. Studies have found that GI symptoms are one of the common clinical symptoms in SARS and MERS [7–8, 14]. With growing attention to GI symptoms of COVID-19, the latest studies have found that diarrhoea is also common in COVID-19, with estimates ranging 12–29.2% [9–11]. Pan et al. reported that aside from respiratory symptoms, diarrhoea may be an initial or only symptom of COVID-19 [11]. In this study, we also found that a minority of patients, approximately 10.4%, had an initial symptom of diarrhoea. In contrast to the results of previous studies, this study found that GI symptoms including anorexia, diarrhoea, nausea, and vomiting are more common in COVID-19; especially diarrhoea, with a prevalence of 43.8%. This leads to the following question: why are there major differences between the results of this study and previous clinical investigations? First, the data sources of these studies vary. The reported information in the other studies were obtained from medical records [4–6, 9–11]. whereas the data in this study was provided by the patients themselves. Second, the record time of the data are different. The results of this study found that diarrhoea mostly occurred 5 days after the development of initial symptoms; therefore, patients may not have developed GI symptoms such as diarrhoea, nausea, and vomiting in the other studies. In this study, the average time from symptom onset to admission was  $16.00 \pm 9.87$  days, which far exceeds the duration, 7–8.1 days, in the other studies [11, 15]. In addition, 79.6%(74/93) of patients experienced diarrhoea prior to admission. Diarrhoea disappeared at the time of investigation in 81.7% (75/93) of patients.

Although some studies revealed that GI symptoms, other than respiratory symptoms, may be the initial symptom in a minority of patients with COVID-19[10–11, 16], there were no studies with a large population that showed when GI symptoms occurred. In this study, we found that most patients developed anorexia at 2.00 (IQR: 0–6.00) days, nausea and vomiting at 2.00 (IQR: 0–9.00) days, and diarrhoea at 5.00 (IQR: 0.25–11.00) days after the onset of initial symptoms. The time of symptom onset of diarrhoea in this study was the same as the first US case reported [17]. Furthermore, we found that flu-like symptoms, such as fever, myalgia, headache, and cough were the initial symptoms of COVID-19 in most patients.

Furthermore, we found that, in contrast to the longer median duration of cough and sputum, diarrhoea in COVID-19 patients only lasted for a median duration of 4.00 (IQR: 2.00–8.75) days, which was the same

as the study from Jin et al [12]. Additionally, most diarrhoea occurred as mushy stools instead of watery diarrhoea in SARS [7]. Cholankeril et al [9]. reported that the median duration of GI symptoms was 1 day (IQR: 0–4), which was significantly shorter than the duration of respiratory symptoms. Therefore, diarrhoea may be overlooked by clinicians and patients during COVID-19.

Pan et al [11]. reported that the patients with GI symptoms had a longer time from symptom onset to hospitalization compared to those without GI symptoms. However, our study did not find this difference, which was probably related to the fact that disease severity of recruited patients was mild in this study. In addition, we found that the patients with diarrhoea were more likely to have flu-like symptoms, pneumonia, and other GI symptoms, and there were 42.3%(90/212) patients who developed all types of the three common COVID-19 symptoms such as, flu-like symptoms, pneumonia and GI symptoms in this study, which further supported developing knowledge that flu-like symptoms, pneumonia, and GI symptoms are common symptoms of COVID-19. Pan et al [11] also found 45% patients with COVID-19 developed both pneumonia and GI symptoms. As for why the patients with diarrhoea were younger, it was not clear. It is possible that there were unknown confounding factors that influenced the recent results.

Why is it important to pay attention to GI symptoms such as diarrhoea, nausea, and vomiting? First, vomiting and diarrhoea affect nutrient absorption in patients and therefore may affect disease outcomes. Our study found that diarrhoea is significantly correlated with fatigue( $P < 0.001$ ), suggesting that diarrhoea may decrease patients' quality of life. Some studies have stated the patients with GI symptoms had a more critical type than those without GI symptoms [10–11, 18]. In addition, two studies isolated viable SARS-CoV-2 virus from stool samples of COVID-19 patients and detected SARS-CoV-2 RNA in the stomach, duodenum, and rectum specimens [10, 19]. Xiao et al. [19] also observed that viral host receptor angiotensin-converting enzyme receptor 2 (ACE2) stained positive primarily in the cytoplasm of gastrointestinal epithelial cells, which highly supports the possibility that SARS-CoV-2 can enter host cells in the digestive tract. Gu et al. [20] and Ng et al. [21] proposed that the GI tract may be one of the target organs of SARS-CoV-2, and fecal–oral transmission may occur in COVID-19. Our study showed that GI symptoms such as diarrhoea, nausea, and vomiting are rather common in COVID-19, suggesting that the possibility of fecal–oral transmission is high. Finally, understanding that GI symptoms typically occur in the early and middle phase of COVID-19 infection, and that they are self-limiting and short-lived, may reduce unnecessary invasive investigations such as diagnostic endoscopy and decrease the infection risk of health providers.

There are several limitations in this study. First, as the subjects of this study were patients with mild cases in a temporary hospital, we were unable to determine whether the same GI characteristics are present in severe COVID-19 patients. Second, there could have been selection bias because this was a voluntary survey. Third, because most patients in this study took medications before diarrhoea in the study, we cannot exclude the influence of medications on GI symptoms. However, we think the possibility that medications caused GI symptoms is small. This is because more patients took medications, in particular antibiotic, during hospitalization than before hospitalization, yet the prevalence of diarrhoea didn't markedly increase after hospitalization. At the same time, Wan Y et al. [18] stated they didn't



observe a correlation between diarrhoea and use of antibiotics or antiviral medicine. Forth, limited by the lack of medical facilities in the temporary hospital, there were no laboratory data to reveal the detailed clinical characteristics of COVID-19, and we also failed to exclude the possibility that diarrhoea resulted from other germs. Besides the above, among the patients with diarrhoea, we failed to test positive SARS-CoV-2 RNA in stool, so the cause of diarrhoea in COVID-19 is probable multifactorial [22].

## **Conclusions**

In summary, fever and cough are the most common initial symptoms of COVID-19, but GI symptoms are also common, primarily occur during the middle stage of the disease, and lasts for a short period of time. GI symptoms may not be associated with COVID-19 related treatment.

## **Declarations**

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### **Funding**

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### **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### **Authors' contribution**

YZ conceived and designed the study. BW, JXC and YGM performed the experiments and performed the literature survey. YZ and ZNL contributed to the writing and checking of the letter.

### **Patient approval and consent to participate**

Written informed consent was obtained from all participating patients. The study was approved by the Ethics Committee of Renmin Hospital of Wuhan University (Ethics Approval No.: WDRY2020-K033).

### **Consent for publication**

Not applicable.

### **Competing interests**

No competing interests.

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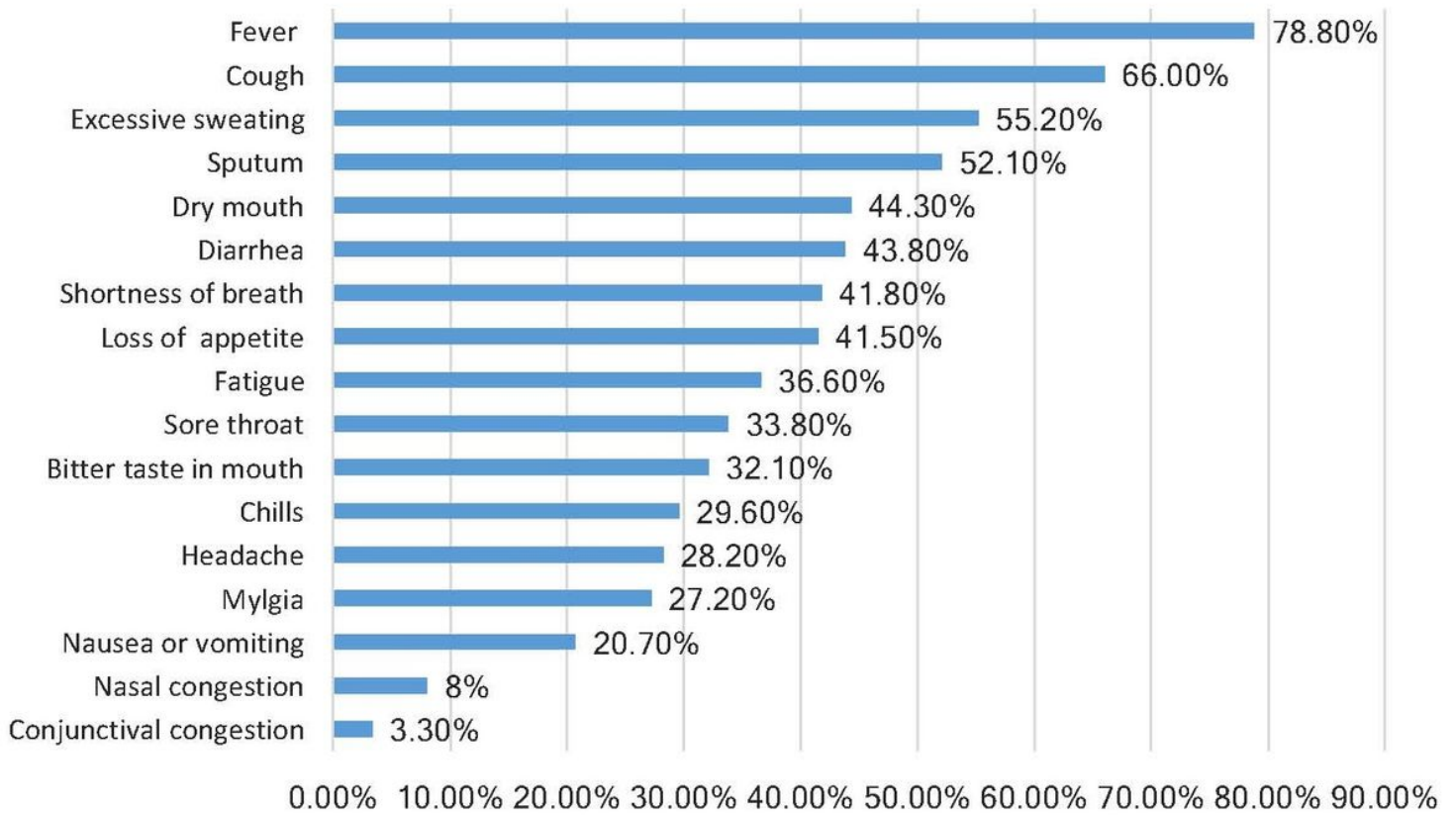
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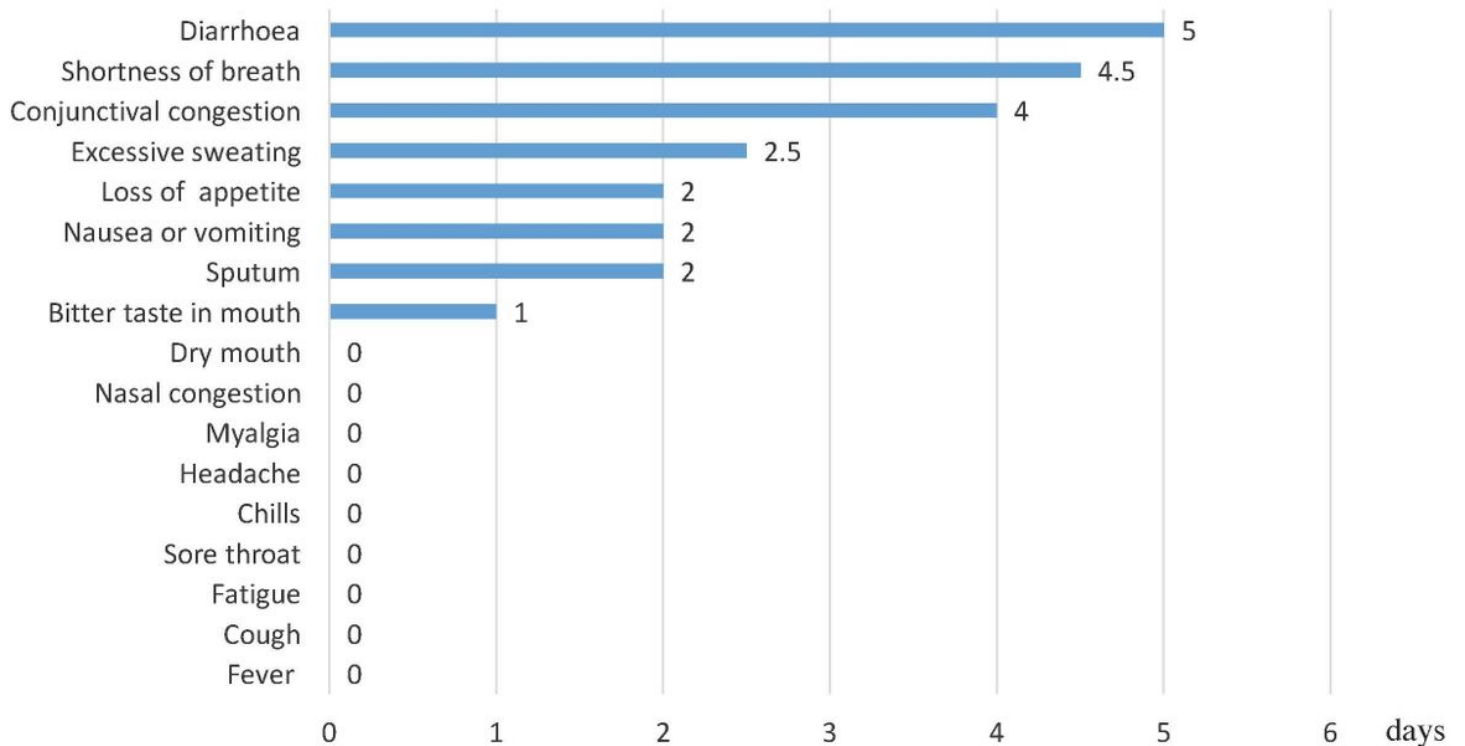
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## Figures



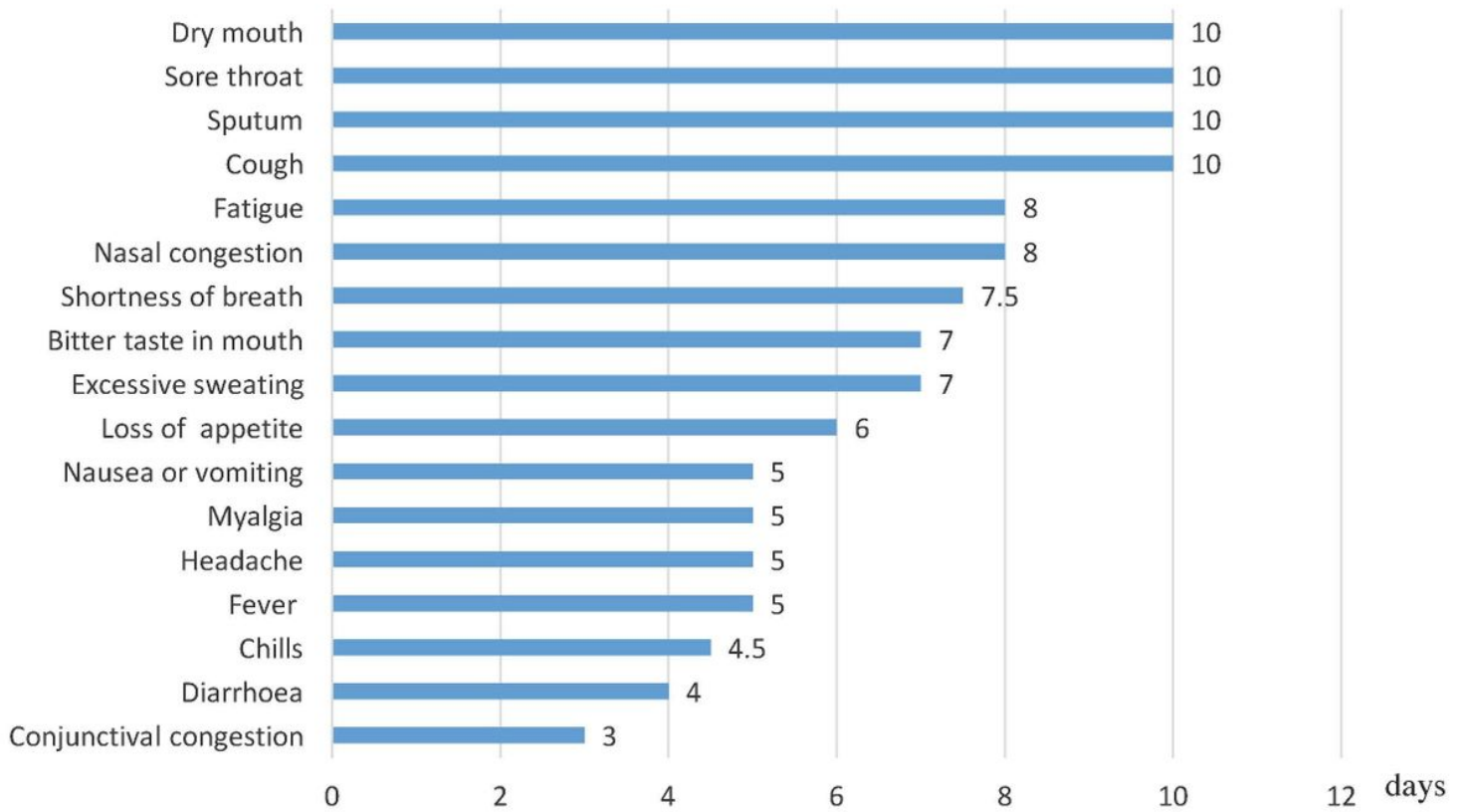
**Figure 1**

Prevalence of clinical symptoms among COVID-19 patients



**Figure 2**

Time of clinical symptom onset among COVID-19 patients Notes: the data above is median.



**Figure 3**

Duration of clinical symptoms among COVID-19 patients Notes: the data above is median.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [covid19questionnaire0810.pdf](#)