Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Conflicts of interest
The authors disclose no conflicts.

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SARS-CoV-2 RNA Detection in Gastrointestinal Sample Displays Poor Performance

Dear Editors:

We have recently read with interest the recent article titled "Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples from the Hong Kong Cohort and Systematic Review and Meta-analysis"[1] published in *Gastroenterology*. The authors concluded that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA could be detected in stool samples from 48.1% of patients. However, the pragmatic usefulness of SARS-CoV-2 RNA detection in gastrointestinal sample needs to be evaluated. Real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) typically has been used for SARS-CoV-2 detection. To compare the SARS-CoV-2 rRT-PCR of gastrointestinal sample versus respiratory sample for diagnostic performance of the coronavirus disease 2019 (COVID-19), we performed a retrospective analysis of patients from the East Branch of the Renmin Hospital of Wuhan University (a designated hospital for critical care), China between January and March, 2020.

All patients treated by the medical assistance teams from hospitals all over the country and diagnosed as having COVID-19 according to World Health Organization interim guidance, were recruited if they were tested for SARS-CoV-2 RNA of gastrointestinal samples during their hospital stay. The rRT-PCR assay simultaneously amplified and tested two reported target genes of SARS-CoV-2, including open reading frame 1ab (ORF1ab) and nucleocapsid protein (N).[2] The state of SARS-CoV-2 RNA at the detection time was determined by all rRT-PCR results of all samples (including nasopharyngeal swabs, feces, sputum, anal swabs, bronchoalveolar lavage fluid, and urine) in a specific period: if any one was positive, it was defined SARS-CoV-2 RNA (+), otherwise SASR-CoV-2 RNA (-). The specific period was from the day before the detection to hospital discharge. An Informed Consent for Exempt and Minimal Risk Research was approved by the ethics committee of West China Hospital and reported to the National Health Commission.

All rRT-PCR results were collected from 144 confirmed patients (67 male, 77 female; age, 20–87 years), including 853 results of nasopharyngeal swabs, 232 results of sputum samples, 195 results of gastrointestinal samples, and 34 results of other samples (like urine and bronchoalveolar lavage fluid samples). As shown in Supplementary Table 1, the positive detection rates of nasopharyngeal swabs (312/550, 56.7%; 95% confidence interval [CI], 52.6%–60.9%) and sputum samples (74/148, 50.0%; 95% CI, 41.9%–58.1%) were significantly higher than those of fecal samples (17/99, 17.2%; 95% CI, 9.6%–24.7%) and anal swabs (22.6%; 95% CI, 11.0%–34.3%) in the indirect comparisons (all $P < .05$). Each result of fecal sample or anal swab was matched with the corresponding result of nasopharyngeal swab or sputum sample nearest to its time. The simultaneous examinations with various samples were performed for directly comparing the diagnostic value. The positive detection rate of nasopharyngeal swab test was similar to that of sputum sample test ($P = .705$), but was significantly higher than that of anal swab and fecal sample test (all $P < .001$; Supplementary Table 1). Moreover, SARS-CoV-2 (+) was associated with the increased IgM antibody ($P = .004$) and decreased IgG antibodies ($P < .001$) in COVID-19 patients (all $P < .05$). However, no significant difference was observed in the subgroup analysis of specimen type (all $P > .05$).

COVID-19 has a high incidence and rapid infection, and has become a huge threat to global public health. Previous studies have shown that SARS-CoV-2 can infect gastrointestinal cells and remain in feces,[3,4] which creates the potential for fecal–oral viral transmission.[5,6] Also, gastrointestinal symptoms like diarrhea have been frequently reported.[7,8] Our data suggested that rRT-PCR test of gastrointestinal sample had limited value for diagnosis of COVID-19. Finding This illustrated that, as a method to screen and monitor whether the virus exists, gastrointestinal sample testing for SARS-CoV-2 RNA displays poor performance. Although both of them had low positive detection rates, the efficiency of rRT-PCR test of respiratory sample was better than that of gastrointestinal sample. In terms of health economics, nasopharyngeal swab and sputum sample tests are more cost effective than gastrointestinal sample test and should be a main sampling method for diagnosing SARS-CoV-2 infection in the epidemic areas with limited resources. Furthermore, the state of SARS-CoV-2 RNA might depend on the level of IgM/IgG antibody, rather than on the specimen type. Some indistinct trends of association between IgM/IgG antibody level and result of fecal sample test for SARS-CoV-2 RNA were observed ($P = .096$ and $P = .044$), probably because of the low positive detection rate. The patient's benefit for diagnosis from conducting a gastrointestinal sample test for SARS-CoV-2 RNA was far from enough, compared with that of a nasopharyngeal swab or sputum sample test.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2020.05.084.

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Reply. We thank Xing et al[1] for their findings on the comparison of detection rates of different samples (nasopharyngeal swabs, sputum samples, gastrointestinal samples, and others like urine and bronchoalveolar lavage) for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in response to our recent study.[2] In their cohort of 144 patients with coronavirus disease-2019 (COVID-19), the positive rate of nasopharyngeal swab (56.7%) was similar to that of sputum (50.0%), but was higher than stool samples (17.2%) and anal swab (22.6%). Therefore, they concluded that the performance of gastrointestinal samples for SARS-CoV-2 RNA was poor.

Their findings were in fact in line with our findings[2] and the summary by the American Gastroenterological Association Institute.[3] In the Hong Kong cohort, 15.3% had stool tested positive for viral RNA on presentation.[2] Those who had diarrhea had a higher frequency of stool viral RNA positivity than those who did not (38.5% vs 8.7%). As in our meta-analysis, 48.1% were tested positive for stool viral RNA at various time points from the day of onset of illness but none of the 12 studies (Figure 5 in the original article) tested stool viral RNA on the day of hospitalization. Hence, the important temporal patterns of stool viral RNA positivity were inadequate in our pooled analysis and missing in the current study by Xing et al, which could account for the discrepancies in stool viral RNA positive rates. Of their 144 patients with COVID-19, 195 gastrointestinal samples were taken, which means that the majority of patients were only tested for gastrointestinal samples once at unspecified time points.

Although viral RNA could be detected in stool, it is imperative to emphasize that the testing of upper respiratory specimens should remain the initial test for COVID-19.[4,5] Stool viral RNA seemed to be positive during the later phase of infection and was often positive 2–5 days after the respiratory samples were tested positive.[6] Stool viral RNA could also be detected during the late phase of illness[7] and for $\leq$33 days from symptom onset in our meta-analysis.[2] Among the 124 patients who had serial positive test results in both respiratory and stool specimens in our meta-analysis, 70.3% had persistent positive stool viral RNA despite negative respiratory samples (Figure 6 in the article). Taken together, all these data suggest a temporal difference in the detection rates of viral RNA in respiratory and gastrointestinal samples.

In conclusion, we agree that gastrointestinal sample should not be used as the only test for diagnosis of COVID-19, but it may be useful in patients with delayed presentation or those with gastrointestinal symptoms. Nonetheless, the temporal patterns of viral shedding in different types of specimens as well as the potential fecal–oral transmission risk of SARS-CoV-2 should be the main focus of these findings, rather than overemphasizing the relatively low diagnostic yield of stool viral RNA.

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Supplementary Table 1. Positive Detection Rates of SARS-CoV-2 rRT-PCR Results of Gastrointestinal Samples and Respiratory Samples

	rRT-PCR +	SARS-CoV-2 RNA +	Positive detection rate (95% CI)	*P* value
Nasopharyngeal swab				
Nucleocapsid protein	258	550	46.9% (42.7% to 51.1%)	
Open reading frame 1ab	234	550	42.5% (38.4% to 46.7%)	
Combination	312	550	56.7% (52.6% to 60.9%)	
Sputum sample				
Nucleocapsid protein	58	148	39.2% (31.2% to 47.1%)	
Open reading frame 1ab	53	148	35.8% (28.0% to 43.6%)	
Combination	74	148	50.0% (41.9% to 58.1%)	
Fecal sample				
Nucleocapsid protein	13	99	13.1% (6.4% to 19.9%)	
Open reading frame 1ab	14	99	14.1% (7.2% to 21.1%)	
Combination	17	99	17.2% (9.6% to 24.7%)	
Anal swab				
Nucleocapsid protein	9	53	17.0% (6.5% to 27.4%)	
Open reading frame 1ab	3	53	5.7% (–0.8% to 12.1%)	
Combination	12	53	22.6% (11.0% to 34.3%)	
Nasopharyngeal swab vs sputum sample[a]				
Nasopharyngeal swab	56	127	44.1% (35.3% to 52.8%)	.705
Sputum sample	59	127	46.5% (37.7% to 55.2%)	
Nasopharyngeal swab vs. fecal sample[a]				
Nasopharyngeal swab	47	91	51.6% (41.2% to 62.1%)	<.001
Fecal sample	15	91	16.5% (8.7% to 24.3%)	
Nasopharyngeal swab vs. anal swab[a]				
Nasopharyngeal swab	28	49	57.1% (42.8% to 71.5%)	<.001
Anal swab	11	49	22.4% (10.3% to 34.6%)	
Sputum sample vs. fecal sample[a]				
Sputum sample	21	46	45.7% (30.7% to 60.6%)	<.001
Fecal sample	5	46	10.9% (1.5% to 20.2%)	
Sputum sample vs. anal swab[a]				
Sputum sample	7	12	58.3% (25.6% to 91.1%)	.219
Anal swab	4	12	33.3% (2.0% to 64.6%)	
Fecal sample vs. anal swab[a]				
Fecal sample	0	8	–	.068
Anal swab	4	8	50.0% (5.3% to 94.7%)	

CI, confidence interval; RNA, ribose nucleic acid; rRT-PCR, real-time reverse transcription-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Each pair of 2 tests was matched according to the closest time.