

The following information resources have been selected by the National Health Library and Knowledge Service Evidence Virtual Team in response to your question. The resources are listed in our estimated order of relevance to practicing healthcare professionals confronted with this scenario in an Irish context. In respect of the evolving global situation and rapidly changing evidence base, it is advised to use hyperlinked sources in this document to ensure that the information you are disseminating to the public or applying in clinical practice is the most current, valid and accurate. For further information on the methodology used in the compilation of this document—including a complete list of sources consulted—please see our National Health Library and Knowledge Service Summary of Evidence Protocol.

### **YOUR OUESTION**

What is the false negative rate for swab tests for COVID-19 and are there more reliable ways of testing? Are rectal swab tests effective in detecting COVID-19 for patients presenting with gastrointestinal problems?

### **IN A NUTSHELL**

The diagnosis of COVID-19 is made by detection of SARS-CoV-2 RNA by reverse-transcription polymerase chain reaction (RT-PCR). RT-PCR is widely seen as the gold standard for clinical detection of SARS-CoV-2<sup>5,8,10,11,15</sup>. The CDC recommends collection of a nasopharyngeal swab specimen to test for SARS-CoV-2<sup>4</sup>. Oropharyngeal, nasal mid-turbinate or nasal swabs of both nares are acceptable alternatives for symptomatic patients if nasopharyngeal swabs are unavailable<sup>5</sup>. In order to reduce the level of false negatives, an optimised droplet digital PCR (ddPCR) test has been developed to detect SARS-CoV-2 which has had romising results<sup>8</sup>. A positive test for SARS-CoV-2 generally confirms the diagnosis of COVID-19, but false negative tests from upper respiratory specimens have been well documented<sup>5</sup>. It is unclear the exact percentage of tests that produce false negatives but evidence from China proposes a rate as high as 30%<sup>14,26,27</sup>. A systematic review of the accuracy of COVID-19 tests reported false negative rates of between 2% and 29%<sup>14</sup>.

One report suggests that inadequate nasopharyngeal sampling performed by untrained operators in the presence of nasal obstruction can be a relevant case of false-negative findings<sup>10</sup>. If initial testing is negative but the suspicion for COVID-19 remains it is suggested to repeat the test which decreases the chances of failing to identify infected individuals<sup>5,15,18</sup>; in such cases, it is recommended to test lower respiratory tract specimens, if possible<sup>2,4,5</sup>.



Clinical judgement should be used in the case of patients returning negative tests if patients are thought likely to be infected. 27.

Chest CT scans have been suggested as a screening modality for SARS-CoV-2 especially if swab tests are negative for patients with a high suspicion of infection 9,14,17,18. Although the sensitivity of chest CTs is high, a negative result does not exclude COVID-19. Blood test analysis has been suggested as an alternative to RT-PCR for identifying COVID-19, especially in poorer countries that have a shortage of specialised laboratories.

Some patients may present with digestive symptoms such as abdominal pain, nausea or vomiting as their chief complaint suggest that rectal swabs have an important part to play in confirming SARS-CoV-2 infection. Prolonged fecal shedding in infected patients even after viral clearance in the respiratory tract indicates that stool testing should be considered in patients with COVID-19 with appropriate transmission precautions for hospitalised patients who remain stool positive. Some patients test positive on rectal swabs in the first days of COVID-19 onset which points towards the usefulness of rectal swabs at the very onset of the disease to confirm or even diagnose COVID-19<sup>20,23</sup>.

Serologic tests—as soon as generally available and adequately evaluated—should be able to identify patients who have either a current or a previous infection but a negative PCR test<sup>5</sup>. In cases where NAAT assays are negative and there is a strong epidemiological link to COVID-19 infection, paired serum samples in the acute and convalescent phase could support diagnosis once validated serology tests are available<sup>3</sup>.



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### **IRISH AND INTERNATIONAL GUIDANCE**

## What does the Health Protection Surveillance Centre (Ireland) say?

Laboratory Guidance for COVID-19<sup>1</sup>

Sample types accepted for SARS-CoV-2 testing:

- combined swab for oropharyngeal and nasopharyngeal samples [one swab to test both is sufficient] in ambulatory patients; or
- bronchoalveolar lavage or endotracheal aspirate or sputum if produced is preferred in cases of severe illness

## COVID-19 Assessment and testing pathway for use in a hospital setting<sup>2</sup>

If virus is not detected in an upper respiratory tract sample, clinical suspicion for COVID-19 should be maintained in patients with severe respiratory disease that is not readily explained. Testing of lower respiratory tract samples can be considered if available.

### What does the World Health Organization say?

# Laboratory testing for 2019 novel coronavirus (2019-nCoV) in suspected human cases<sup>3</sup>

If a negative result is obtained from a patient with a high index of suspicion for COVID-19 virus infection, particularly when only upper respiratory tract specimens were collected, additional specimens, including from the lower respiratory tract if possible, should be collected and tested.

### Serological Testing

Serological surveys can aid investigation of an ongoing outbreak and retrospective assessment of the attack rate or extent of an outbreak. In cases where NAAT assays are negative and there is a strong epidemiological link to COVID-19 infection, paired serum samples in the acute and convalescent phase could support diagnosis once validated serology tests are available. Serum samples can be stored for these purposes.



## What do the Centers for Disease Control and Prevention (United States) say?

# Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens from Persons for Coronavirus Disease 2019 (COVID-19)<sup>4</sup>

For initial diagnostic testing for SARS-CoV-2, CDC recommends collecting and testing an upper respiratory specimen. CDC also recommends testing lower respiratory tract specimens, if available. Nasopharyngeal specimen is the preferred choice for swab-based SARS-CoV-2 testing. When collection of a nasopharyngeal swab is not possible, the following are acceptable alternatives:

- an oropharyngeal (OP) specimen collected by a healthcare professional; or
- a nasal mid-turbinate (NMT) swab collected by a healthcare professional or by onsite self-collection using a flocked tapered swab; or
- an anterior nares nasal swab (NS) specimen collected by a healthcare professional or by onsite self-collection using a flocked or spun polyester swab; or
- nasopharyngeal wash/aspirate or nasal aspirate (NA) specimen collected by a healthcare professional

#### **POINT-OF-CARE TOOLS**

### What does UpToDate say?

<u>Coronavirus disease 2019 (COVID-19): Epidemiology, virology, clinical</u> features, diagnosis, and prevention<sup>5</sup>

Nucleic acid amplification testing most commonly with a reverse-transcription polymerase chain reaction (RT-PCR) assay to detect SARS-CoV-2 RNA from the upper respiratory tract is the preferred initial diagnostic test for COVID-19. In some settings, antigen testing may be the initial test used, but the sensitivity of antigen tests is lower than that of NAATs, and negative antigen tests should be confirmed with an NAAT test.

Upper respiratory samples are the primary specimens for SARS-CoV-2 NAAT.



The accuracy and predictive values of SARS-CoV-2 NAATs have not been systematically evaluated. They are highly specific tests. Although NAATs have high analytic sensitivity in ideal settings [eg they are able to accurately detect low levels of viral RNA in test samples known to contain viral RNA], clinical performance is more variable.

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#### INTERNATIONAL LITERATURE

### What does the international literature say?

## [Newly Added] <u>Bullis et al (2020) A Cautionary Tale of False-Negative</u> <u>Nasopharyngeal COVID-19 Testing<sup>6</sup></u>

There remains diagnostic uncertainty regarding the sensitivity of reverse transcription polymerase chain reaction in detection of SARS-CoV-2 from nasopharyngeal specimens. We present a case where two nasopharyngeal specimens were negative, followed by a positive sputum sample. Serial testing for COVID-19 is indicated in patients with high pretest probability of disease.

# [Newly Added] Kwee et al (2020) CT Scanning in Suspected Stroke or Head Trauma: Is it Worth to go the Extra Mile and Include the Chest to Screen for COVID-19 Infection?<sup>7</sup>

Chest CT may be used as a tool for rapid COVID-19 detection. Our aim was to investigate the value of additional chest CT for detection of COVID-19 in patients who undergo head CT for suspected stroke or head trauma in an endemic region.

The sensitivity of additional chest CT is fairly high; however, a negative result does not exclude COVID-19. The positive predictive value is poor. Correlation of chest CT results with epidemiologic history and clinical presentation along with real-time reverse transcriptase polymerase chain reaction is needed for confirmation.

## [Newly Added] <u>Suo et al (2020) ddPCR: a more accurate tool for SARS-</u>CoV-2 detection in low viral load specimens<sup>8</sup>

Quantitative real time PCR (RT-PCR) is widely used as the gold standard for clinical detection of SARS-CoV-2. However, due to the low viral load specimens and the limitations of RT-PCR, significant numbers of false



negative reports are inevitable, resulting in failure to timely diagnose, cut off transmission and assess discharge criteria. As an improvement measure, an optimized droplet digital PCR was used for detection of SARS-CoV-2 which showed that the limit of detection of ddPCR is significantly lower than that of RT-PCR. We further explored the feasibility of ddPCR to detect SARS-CoV-2 RNA from 77 patients, and compared with RT-PCR in terms of the diagnostic accuracy based on the results of a follow-up survey. 26 patients of COVID-19 with negative RT-PCR reports were reported as positive by ddPCR. The sensitivity, specificity, PPV, NPV, negative likelihood ratio (NLR) and accuracy were improved from 40% (95% CI: 27-55%), 100% (95% CI: 54-100%), 100%, 16% (95% CI: 13-19%), 0.6 (95% CI: 0.48-0.75) and 47% (95% CI: 33-60%) for RT-PCR to 94% (95% CI: 83-99%), 100% (95% CI: 48-100%), 100%, 63% (95% CI: 36-83%), 0.06 (95% CI: 0.02-0.18), and 95% (95% CI: 84-99%) for ddPCR, respectively. Moreover, 6/14 (42.9%) convalescents were detected as positive by ddPCR at 5-12 days post discharge. Overall, ddPCR shows superiority for clinical diagnosis of SARS-CoV-2 to reduce the false negative reports, which could be a powerful complement to RT-PCR.

# [Newly Added] <u>He et al (2020) Diagnostic performance between CT and initial real-time RT-PCR for clinically suspected 2019 coronavirus disease</u> (COVID-19) patients outside Wuhan, China<sup>9</sup>

Chest CT is thought to be sensitive but less specific in diagnosing COVID-19. The diagnostic value of CT is unclear. We aimed to compare the performance of CT and initial RT-PCR for clinically suspected COVID-19 patients outside the epicentre in Wuhan, China.

Initial RT-PCR and chest CT had comparable diagnostic performance in identification of suspected COVID-19 patients outside the epidemic center. To compensate potential risk of false-negative PCR, chest CT should be applied for clinically suspected patients with negative initial RT-PCR.

# [Newly Added] <u>Piras et al (2020) Inappropriate Nasopharyngeal</u> <u>Sampling for SARS-CoV-2 Detection Is a Relevant Cause of False-Negative Reports<sup>10</sup></u>

Reverse transcriptase polymerase chain reaction (RT-PCR) detection of SARS-CoV-2 mRNA on nasopharyngeal swab is the standard for diagnosing active COVID-19 disease in asymptomatic cases and in symptomatic patients without the typical radiologic findings. For the present COVID-19 outbreak in Italy, we describe 4 symptomatic patients with negative RT-PCR results at the first nasopharyngeal swab which became positive when collected a few



hours later by an otolaryngologist. All the patients showed nasal obstruction. The present report suggests that inadequate nasopharyngeal sampling performed by untrained operators in the presence of nasal obstruction can be a relevant case of false-negative findings at RT-PCR with a clear negative impact on the efforts to contain the current outbreak.

## [Newly Added] <u>Ferrari et al (2020) Routine Blood Tests as a Potential</u> Diagnostic Tool for COVID-19<sup>11</sup>

Amplification of viral RNA by rRT-PCR serves as the gold standard for confirmation of infection, but requires a long turnaround time [3-4 hours to generate results] and shows false-negative rates as large as 15%-20%. In addition, the demand on certified laboratories, expensive equipment and trained personnel led many countries to limit rRT-PCR testing to individuals with pronounced respiratory syndrome symptoms. There is a need for alternative, less expensive and more accessible tests.

Combining appropriate cutoffs for certain hematological parameters could help in identifying false-positive/negative rRT-PCR tests. Blood test analysis might be used as an alternative to rRT-PCR for identifying COVID-19-positive patients in those countries which suffer from a large shortage of rRT-PCR reagents and/or specialized laboratories.

# [Newly Added] <u>Kinloch et al (2020) [Preprint Not Yet Peer-Reviewed]</u> <u>Suboptimal biological sampling as a probable cause of false-negative</u> <u>COVID-19 diagnostic test results<sup>12</sup></u>

Improper nasopharyngeal swab collection could contribute to false-negative COVID-19 results. Specimens from confirmed or suspected COVID-19 cases that tested negative or indeterminate [ie suspected false-negatives] contained less human DNA—a stable molecular marker of sampling quality—compared to a representative pool of specimens submitted for testing.

### [Newly Added] Watson et al (2020) Interpreting a COVID-19 Test Result<sup>13</sup>

No test gives a 100% accurate result; tests need to be evaluated to determine their sensitivity and specificity, ideally by comparison with a 'gold standard.' The lack of such a clear-cut gold-standard for COVID-19 testing makes evaluation of test accuracy challenging. A systematic review of the accuracy of COVID-19 tests reported false negative rates of between 2% and 29%, equating to sensitivity of 71%-98%, based on negative RT-PCR tests which were positive on repeat testing. The use of repeat RT-PCR testing as gold standard is likely to underestimate the true rate of false negatives since



not all patients in the included studies received repeat testing and those with clinically diagnosed COVID-19 were not considered as actually having COVID-19.

## Fang et al (2020) Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR<sup>14</sup>

In our series, the sensitivity of chest CT was greater than that of RT-PCR (98% vs 71%, respectively, p<.001). The reasons for the low efficiency of viral nucleic acid detection may include: 1. immature development of nucleic acid detection technology; 2. variation in detection rate from different manufacturers; 3. low patient viral load; or 4 improper clinical sampling. Our results support the use of chest CT for screening for COVD-19 for patients with clinical and epidemiologic features compatible with COVID-19 infection particularly when RT-PCR testing is negative.

# Wikramaratna et al (2020) Estimating false-negative detection rate of SARS-CoV-2 by RT-PCR<sup>15</sup>

Reverse transcription-polymerase chain reaction (RT-PCR) assays are used to test patients and key workers for infection with the causative SARS-CoV-2 virus. RT-PCR tests are highly specific and the probability of false positives is low, but false negatives can occur if the sample contains insufficient quantities of the virus to be successfully amplified and detected. The amount of virus in a swab is likely to vary between patients, sample location—nasal, throat or sputum—and through time as infection progresses. On its own, testing throat and nasal swabs by RT-PCR is not guaranteed to yield a positive result for SARS-CoV-2 infection and this probability decreases with time since the onset of symptoms. In other words, the longer the time from the onset of symptoms until a suspected case is tested, the more likely a false-negative result. Repeat testing of suspected but RT-PCR negative infections drastically decreases the chances of failing to identify infected individuals by this method, but may not always be feasible. In countries that do not currently have mass testing, there are calls for testing to be expanded to the population at large with the aim of determining how many people have, or have recently had, infection. While RT-PCR testing of key workers will be of great importance, particularly those working with vulnerable groups, our results suggest that there may be some benefit to testing indiscriminately; conducting a single test on someone who had symptoms 10 days ago will have a nearly 33% false negative rate using a



nasal swab; 52.89% for a throat swab. As a means of determining population level exposure to SARS-CoV-2, serological tests are far more likely to provide an accurate profile.

In conclusion, we demonstrate how the sensitivity of the RT-PCR assay for detecting SARS-CoV-2 infection depends on the time from the onset of symptoms in symptomatic individuals, and show how nasal swabs appear more sensitive than throat swabs.

### <u>Kucirka et al (2020) Variation in False Negative Rate of RT-PCR Based</u> SARS-CoV-2 Tests by Time Since Exposure<sup>16</sup>

SARS-CoV-2 RT-PCR based tests are being used to rule out infection among high-risk individuals such as exposed inpatients and healthcare workers. It is critical to understand how the predictive value of the test varies with time from exposure and symptom onset in order to avoid being falsely reassured by negative tests.

We used previously published data on RT-PCR sensitivity on samples derived from nasal swabs by day since symptom onset (n=633) and fit a cubic polynomial spline to calculate the false negative rate by day since exposure and symptom onset. Over the four days of infection prior to the typical time of symptom onset (day 5) the probability of a false negative test in an infected individual falls from 100% on day one (95% CI 69-100%) to 61% on day four (95% CI 18-98%), though there is considerable uncertainty in these numbers. On the day of symptom onset, the median false negative rate was 39% (95% CI 16-77%). This decreased to 26% (95% CI 18-34%) on day 8 (3 days after symptom onset), then began to rise again, from 27% (95% CI 20-34%) on day 9 to 61% (95% CI 54-67%) on day 21. Care must be taken when interpreting RT-PCR tests for SARS-CoV-2 infection, particularly if performed early in the course of infection, when using these results as a basis for removing precautions intended to prevent onward transmission. If there is high clinical suspicion, patients should not be ruled out on the basis of RT-PCR alone and the clinical and epidemiologic situation should be carefully considered.

## <u>Li et al (2020) Stability issues of RT- PCR testing of SARS- CoV- 2 for</u> hospitalized patients clinically diagnosed with COVID- 19<sup>17</sup>

In this study, we collected a total of 610 hospitalized patients from Wuhan between February 2, 2020, and February 17, 2020. We reported a potentially high false negative rate of RT-PCR testing for SARS-CoV-2 in the 610 hospitalized patients clinically diagnosed with COVID-19 during the 2019



outbreak. We also found that the RT-PCR results from several tests at different points were variable from the same patients during the course of diagnosis and treatment of these patients. Our results indicate that in addition to the emphasis on RT-PCR testing, clinical indicators such as computed tomography images should also be used not only for diagnosis and treatment but also for isolation, recovery, discharge and transferring for hospitalized patients clinically diagnosed with COVID-19 during the current epidemic. These results suggested the urgent needs for the standard of procedures of sampling from different anatomic sites, sample transportation, optimization of RT-PCR, serology diagnosis/screening for SARS-CoV-2 infection, and distinct diagnosis from other respiratory diseases such as influenza infections.

## Long et al (2020) Diagnosis of the Coronavirus Disease (COVID-19): rRT-PCR or CT?<sup>18</sup>

Purpose: To evaluate the diagnostic value of computed tomography (CT) and real-time reverse-transcriptase-polymerase chain reaction (rRT-PCR) for COVID-19 pneumonia.

Methods: This retrospective study included all patients with COVID-19 pneumonia suspicion who were examined by both CT and rRT-PCR at initial presentation. The sensitivities of both tests were then compared. For patients with a final confirmed diagnosis, clinical and laboratory data in addition to CT imaging findings were evaluated.

Results: A total of 36 patients were finally diagnosed with COVID-19 pneumonia. 35 patients had abnormal CT findings at presentation, whereas 1 patient had a normal CT. Using rRT-PCR, 30 patients were tested positive, with 6 cases initially missed. Amongst these 6 patients, 3 became positive in the second rRT-PCR assay after 2 days, 2 days and 3 days respectively; and the other 3 became positive only in the third round of rRT-PCR tests after 5 days, 6 days and 8 days respectively. At presentation, CT sensitivity was therefore 97.2%, whereas the sensitivity of initial rRT-PCR was only 83.3%. Conclusion: rRT-PCR may produce initial false negative results. We suggest that patients with typical CT findings but negative rRT-PCR results should be isolated, and rRT-PCR should be repeated to avoid misdiagnosis.



#### **RECTAL SWABS**

[Newly Added] <u>Kipkorir et al (2020) Prolonged SARS-Cov-2 Detection in Anal/ Rectal Swabs and Stool Specimens in COVID-19 Patients After Negative Conversion in Nasopharyngeal RT-PCR Test<sup>19</sup></u>

Current data available on COVID-19 would suggest that SARS-CoV-2 virus may be shed through the gastrointestinal system via feces. Some reports further indicate that a subset of COVID-19 patients may continue to have positive SARS-CoV-2 anal/rectal swab and stool tests after negative conversion of a nasopharyngeal test. This paper analyses current literature to shed some light on the issue.

## [Newly Added] <u>Zhang B et al (2020) Positive rectal swabs in young</u> patients recovered from coronavirus disease 2019 (COVID-19)<sup>20</sup>

Objectives: To investigate the widely concerned issue about positive real-time RT-PCR test results after discharge in patients recovered from coronavirus disease 2019 (COVID-19). Methods: We identified seven cases of COVID-19 who were readmitted to hospital because of positive RT-PCR after discharge, including three pediatric and four young adult patients. Results: Six patients had positive rectal swabs but negative throat swabs, and one patient had positive throat swabs. All the patients continued to be asymptomatic and had unchanged chest computed tomography from previous images. The time from hospital discharge to positive RT-PCR after recovery was 7-11 days. The time from positive to negative rectal swabs was 5-23 days.

Conclusion: The study might suggest the positive RT-PCR after recovery did not mean disease relapse or virus reinfection. Adding RT-PCR test of rectal swabs to the criteria for discharge or discontinuation of quarantine might be necessary.

## [Newly Added] <u>Yi Xu et al (2020), Characteristics of Pediatric SARS-CoV-2</u> Infection and Potential Evidence for Pesistent Fecal Viral Shedding<sup>21</sup>

We report epidemiological and clinical investigations on ten pediatric SARS-CoV-2 infection cases confirmed by real-time reverse transcription PCR assay of SARS-CoV-2 RNA. Symptoms in these cases were nonspecific and no children required respiratory support or intensive care. Chest X-rays lacked definite signs of pneumonia, a defining feature of the infection in adult cases. Notably, eight children persistently tested positive on rectal swabs



even after nasopharyngeal testing was negative, raising the possibility of fecal-oral transmission.

# [Newly Added] Yu He et al (2020) [Letter] Public Health might be endangered by possible prolonged discharge of SARS-CoV-2 in stool<sup>22</sup>

According to a recent published report by CDC of China, community acquired infections are becoming the predominant route in transmission. Based on these cases and the lessons from SARS, we recommend: 1 attention should be drawn to digestive symptoms and stool or rectal swab tests for patients with suspicion or confirmed SARS-CoV-2 infection; 2 preventive education and publicity on handwashing and bathroom infection; 3 compulsory isolation until swab tests switch to negative; 4 surveillance and adequate disinfection in latrines in areas with severe SARS-CoV-2 infection to avoid fomite transmission.

### Tozzi et al (2020) Rectal Swabs For COVID-19 Diagnosis<sup>23</sup>

Oropharyngeal specimen negativity been described together with anal swab positivity up to 28 days after the onset of symptoms also in in children. These findings suggest that some patients with SARS-CoV-2 infection have viral RNA or live infectious virus in feces well after the negativization of oropharyngeal specimens.

Apart from the inference that patients test positive on rectal swabs even after nasopharyngeal swabs become negative, another deduction can be drawn that is even more important by an operative standpoint. Indeed, the available data suggest that some patients test positive on rectal swabs in the very first days of COVID-19 onset. To take a few examples, in a review article, Tian et al reported fecal PCR positivity 2-5 days after sputum in in 36%-53% of patients, while Xiao et al found that 39/73 hospitalized patients had viral RNA in their feces from 1 to 12 days. Therefore, the occurrence of oro-fecal route points towards the usefulness of rectal swabs at the very onset of the disease to confirm or even diagnose COVID-19.

# Ng and Tilg (2020) COVID-19 and the gastrointestinal tract: more than meets the eye<sup>24</sup>

These studies provide new insights into our understanding of the prevalence, aetiology and potential mechanisms of COVID-19 in the GI tract crucial for defining prevention measures, clinical care and treatment strategies. Unanswered questions and challenges remain, such as the significance of virus detection in the stool/rectal swabs of asymptomatic



subjects, whether ACE2 is a direct mediator for SARS-CoV-2 entry into the GI tract and how the virus could survive passage through extreme pH environment of the digestive system. Currently, prolonged fecal shedding in infected patients even after viral clearance in respiratory tract suggests that stool testing should be considered in patients with COVID-19 with appropriate transmission precautions for hospitalised patients who remain stool positive.

### Hindson (2020) COVID-19: faecal-oral transmission?<sup>25</sup>

The SARS-CoV-2 infection is typically characterized by respiratory symptoms, which indicates droplet transmission. However, several case studies have reported gastrointestinal symptoms and/or evidence that some patients with SARS-CoV-2 infection have viral RNA or live infectious virus present in faeces, which suggests that another possible route might be faecal-oral transmission.

In a clinical characterization of ten paediatric patients with SARS-CoV-2 infection in China, none of whom required respiratory support or intensive care and all of whom lacked signs of pneumonia, eight tested positive on rectal swabs, even after nasopharyngeal testing was negative. The details were published as a Brief Communication in Nature Medicine. The patients, whose ages ranged from 2 months to 15 years, initially tested positive after being screened by nasopharyngeal swab real-time reverse transcription PCR (RT–PCR). Next, the researchers conducted a series of nasopharyngeal and rectal swabs to investigate the pattern of viral excretion. Eight patients had real-time RT–PCR-positive rectal swabs. "The findings suggest that we also need to use rectal swabs to confirm diagnosis of COVID-19," says Kang Zhang, a corresponding author of the study.

There had been earlier reports, particularly in adults, of gastrointestinal symptoms and of the possibility of a faecal–oral route of transmission. In a cohort of 1,099 patients with COVID-19 from 552 hospitals in China, published in the New England Journal of Medicine, 5.0% of patients presented with nausea or vomiting and 3.8% presented with diarrhoea. Also, preliminary findings published in the American Journal of Gastroenterology found that of 204 patients with COVID-19 (mean age 54.9 years) who presented to three hospitals in China, 99 (48.5%) patients presented with digestive symptoms as their chief complaint.



#### **OTHER**

## Watson and Whiting (2020) [Website] Coronavirus: how accurate are coronavirus tests?<sup>26</sup>

There are two main types of COVID-19 tests. SWAB TESTS—which usually take a sample from the throat or nose to detect viral RNA; these determine if you currently have COVID-19. BLOOD TESTS—which detect antibodies; can determine if you have had COVID-19 and are therefore [presumed] immune. No test is 100% accurate. Although tests can perform well in ideal laboratory conditions, in real life lots of other factors affect accuracy including the timing of the test, how the swab was taken and the handling of the specimen.

Early on in the novel coronavirus outbreak, doctors started reporting cases of people who had coronavirus which had been missed by swab tests—also known as false negatives. We don't know for sure how often these false negatives occur in the UK, but evidence from China suggests up to 30 out of every 100 people with coronavirus might test negative. Antibody blood tests are also being developed. These could help us find out who has had coronavirus previously and is therefore presumed to be immune. This could help inform decisions about lifting lockdowns to allow people to go back to work safely.

But before these are rolled out, we need to know how accurate they are. This time we need to be confident that the antibody test doesn't falsely reassure people that they are immune, as this could worsen the spread of infection. At the moment we don't have enough information on these tests to be able to answer these questions. The very limited data available suggests they have fewer false negative results than swab tests, but more false positive results. This means there is a possibility that you could test positive without being immune and so these tests may not be as helpful as people are hoping.

# <u>Krumholz, (2020) If You Have Coronavirus Symptoms, Assume You Have the Illness, Even if You Test Negative<sup>27</sup></u>

False-negative test results—tests that indicate you are not infected, when you are—seem to be uncomfortably common. Increasingly, and disturbingly, I hear a growing number of anecdotal stories from my fellow doctors of patients testing negative for coronavirus and then testing positive or people who are almost certainly infected who are testing negative. Unfortunately, we have very little public data on the false-negative rate for these tests in clinical practice. Research coming out of China indicates that





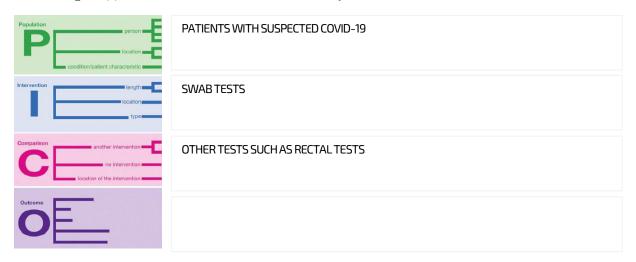
the false-negative rate may be around 30 percent. Some of my colleagues, experts in laboratory medicine express concerns the false-negative rate in this country could be even higher. Even as better tests emerge, we should always put the test result in the context of the other information we have. It's a lesson that endures throughout medicine: look at the big picture, not a single piece of data. Triangulate on the truth, using all the sources of information you have, no matter how good a single test. And don't be shy about questioning a conclusion that doesn't fully fit the facts.



National Health Library and Knowledge Service | Evidence Team Summary of Evidence: COVID-19 CURRENT AS AT JUNE 19 2020 VERSION 2.0

Produced by the members of the National Health Library and Knowledge Service Evidence Team<sup>†</sup>. Current as at 19 June 2020. This evidence summary collates the best available evidence at the time of writing and **does not replace clinical judgement or guidance**. Emerging literature or subsequent developments in respect of COVID-19 may require amendment to the information or sources listed in the document. Although all reasonable care has been taken in the compilation of content, the National Health Library and Knowledge Service Evidence Team makes no representations or warranties expressed or implied as to the accuracy or suitability of the information or sources listed in the document. This evidence summary is the property of the National Health Library and Knowledge Service and subsequent re-use or distribution in whole or in part should include acknowledgement of the service.

The following PICO(T) was used as a basis for the evidence summary:



The following search strategy was used:

FALSE NEGATIVE RESULT\* OR FALSE NEGATIVE RATE\* OR FALSE NEGATIVE OR FALSE NEGATIVE RESULT\* OR FALSE NEGATIVE TEST\* OR SPECIFICITY OR NEGATIVE PREDICTIVE VALUE\* AND COVID-19 OR CORONAVIRUS OR "CORONA VIRUS" OR WUHAN NEAR/3 VIRUS OR (("2019-NCOV" OR "2019 NCOV")) OR "SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2" OR "2019 NOVEL CORONAVIRUS" OR "2019 NEW CORONAVIRUS"

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National Health Library and Knowledge Service | Evidence Team









<sup>&</sup>lt;sup>1</sup> Health Protection Surveillance Centre. Laboratory Guidance for COVID-19. <a href="https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/laboratoryguidance/">https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/laboratoryguidance/</a> [Accessed 22 April 2020].

- <sup>6</sup> Bullis SSM, Crothers JW, Wayne S, Hale AJ. A Cautionary Tale of False-Negative Nasopharyngeal COVID-19 Testing [published online ahead of print, 2020 May 5]. *IDCases*. 2020;20:e00791. doi:10.1016/j.idcr.2020.e00791
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