



Coronavirus COVID-19

BC Centre for Disease Control | BC Ministry of Health



HOW YOU CAN SLOW THE SPREAD OF COVID-19

Take care of others by taking care of yourself.

Wash your hands, don't touch your face, and stay home if you are sick.

Stay at Home and Physically Distance

Stay at home whenever you can. Maintain 2 meters distance from those outside of your household.

Interpreting the results of Nucleic Acid Amplification testing (NAT; or PCR tests) for COVID-19 in the Respiratory Tract

April 30, 2020

1. How does the test work?

The NAT works by detecting RNA specific to the SARS-CoV-2 virus that causes COVID-19 infection, after RNA has been extracted from the specimen and then amplified in the laboratory. NATs are typically performed on nasopharyngeal swabs, but the test can also be done on other sample types such as throat swabs, saliva, sputum, tracheal aspirates, and broncho-alveolar lavage (BAL) specimens.

The NAT has a high analytical sensitivity (i.e., it works well at detecting the virus when the virus is present). The NAT can potentially detect as few as 10-100 copies of viral RNA per mL in a respiratory sample. Note that this is not the same as clinical sensitivity of NAT for detection of COVID-19 *infection*, which is unknown at this time (see #5 below).

2. What do the test results mean?

- **Positive:** Viral RNA is detected by NAT and this means that the patient is confirmed to have COVID-19 infection. A positive NAT does not necessarily mean that a patient is infectious, as viral RNA can be shed in the respiratory tract for weeks but cultivatable (live) virus is typically not detected beyond 8 to 10 days after symptom onset.
- **Negative:** Viral RNA is not detected in the sample. However, a negative test result does not totally rule out COVID-19 infection as there may be reasons beyond test performance that can result in a lack of RNA detection in patients with COVID-19 infection (false negatives; see below).
- **Indeterminate:** The NAT result is outside the validated range of the test (i.e., RNA concentration is below the limit of detection, or a non-specific reaction), or this might occur when the sample collected is of poor quality (i.e., does not contain a sufficient amount of human cells). Indeterminate results do not rule in or rule out infection.

Overall, clinical judgement remains important in determining the implications of NAT test results, and whether a repeat test is indicated for negative or indeterminate results (for example, if the patient's recent exposures or clinical presentation suggest COVID-19 infection is likely, diagnostic tests for other respiratory pathogens remain negative, or there is worsening of symptoms). For clinical guidance including testing and specimen collection, please refer to [COVID-19 testing guidelines for British Columbia](#).



Ministry of Health



BC Centre for Disease Control

If you have fever, a new cough, or are having difficulty breathing, call 8-1-1.

Non-medical inquiries (ex. travel, physical distancing): 1-888-COVID19 (1888-268-4319) or text 604-630-0300



For the latest public health guidance on isolation in relation to symptoms and test results, please refer to [the BCCDC public health guidelines for case management](#).

3. Can a patient with symptoms have a negative NAT test and still have COVID-19 infection (i.e., a false negative result)?

Yes, there are a number of reasons why a NAT test result can be negative in patients who have COVID-19 infection:

- a) The specimen was not collected properly (e.g., too few human respiratory tract cells were sampled).
- b) The specimen was collected at a time when viral shedding levels were too low to enable detection of viral RNA. This could be before the patient develops symptoms or afterwards, when the patient's infection is resolving (see below).
- c) In some cases, COVID-19 infection behaves more like a lower respiratory illness ("viral pneumonia") with viral shedding in the lower respiratory tract and limited shedding in the nasopharynx. A NAT on an upper respiratory tract sample may not detect infection in this scenario.

4. What is the natural history of virus shedding in the respiratory tract during COVID-19 infection?

The levels of virus shed during COVID-19 infection in the respiratory tract vary over time and with illness severity, and also depend on host factors. There is limited information on the optimal timing for sample collection. Overall, the literature suggests that in the upper respiratory tract in symptomatic patients:

- Virus shedding appears to begin during the pre-symptomatic stage, shortly before the onset of symptoms.
- The levels of the virus in the upper respiratory tract appear highest in the first week following infection, then decline.
- After the decline, viral RNA may be detectable at low levels for some time after symptom onset (up to 37 days in some studies).

5. What is the clinical sensitivity of the NAT test?

A statistic commonly quoted is that there is a 30% chance of a false negative result for a NAT test in a patient with COVID-19 infection (i.e., a 70% sensitivity). These and other similar estimates are based on a small number of studies that compared the correlation between CT scan findings suggestive of COVID-19 infection to NAT on upper respiratory tract specimens. In these studies, 20-30% of people with a positive CT scan result had negative NAT results – and as discussed above a number of factors can contribute to false negative results. CT scan is not a gold standard for diagnosis of COVID-19 infection, and CT scan cannot differentiate amongst the many microbiological causes of pneumonia.

Ultimately, for COVID-19 testing, there is currently no gold standard, and the overall clinical sensitivity and specificity of NAT in patients with COVID-19 infection is unknown (i.e., how well NAT results correlate with clinical infection, "true positivity" or "true negativity" rate).

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