

## In brief

### De-isolation and risk of transmission

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### Background

- The [risk of transmission](#) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) depends on a range of factors including the disease status (pre-symptomatic, asymptomatic or symptomatic), time since the symptom onset, viral load, virus variant, and presence of replication-competent virus (infectious virus).<sup>1</sup>
- Decisions about [discontinuation](#) of transmission-based infection control precautions, including de-isolation, may be determined by test-based or non-test-based approaches.<sup>2</sup>

### Summary

- The likelihood of detecting replication-competent virus after 10 days following symptom onset is very low in COVID-19 patients with mild to moderate disease. For people with severe disease, the majority do not [shed infectious virus](#) beyond 10 days (88%, 95% after 15 days).<sup>3</sup> There are however, reports of prolonged infectious virus detection in severely immunocompromised patients, for up to four months following diagnosis.
- The World Health Organization and the United States Centers for Disease Control and Prevention support using non-test-based strategies in determining discontinuation of transmission-based precautions.<sup>1,4</sup> Generally, 10 days passed since symptoms or date of first positive viral test is the timeframe used for discontinuation of transmission-based precautions, including isolation and release of patients from the care pathway. However, the [Communicable Diseases Network Australia](#) uses at least 14 days have passed as the criteria.<sup>5</sup>
- [Extended duration of isolation](#) and precautions for up to 20 days after symptom onset maybe warranted for some people with severe or critical illness.<sup>1</sup> Additional testing and consultation with infectious disease specialist in determining the duration of isolation for severely immunosuppressed patients may be warranted.<sup>1</sup>

### Detection and transmission of SARS-CoV-2 from people with moderate-to-severe disease

- One [systematic review](#) and meta-analysis, including studies published until June 2020, found that no study detected live virus beyond day nine of illness.<sup>6</sup> Centers for Disease Control and Prevention guidance states that the likelihood of recovering replication-competent virus is very low after 10 days following symptom onset, especially in patients with mild to moderate COVID-19.<sup>1</sup> The UpToDate evidence update concludes that it is unlikely for transmission to occur after 10 days of illness, especially among immunocompetent patients without severe symptoms.<sup>2</sup>
- The likelihood of detection of replication-competent virus after 10 days following symptom onset remains low in severely ill COVID-19 patients.<sup>3</sup> There have, however, been reports of prolonged detection of infectious virus beyond 10 days, and beyond 20 days in immunocompromised patients.<sup>1</sup>

- In one study of 129 hospitalised patients with severe or critical COVID-19, the median duration of shedding of infectious virus was eight days (interquartile range 5-11, range 0-20) post onset of symptoms. At 15.2 days post onset of symptoms, infectious virus was detected in less than 5% of the specimens.<sup>3</sup>
- In one single-facility study involving 17 [nursing home residents](#) with COVID-19 (median age 82, range 58 to 97, five with severe illness, four hospitalised, three died), nine patients had any culture-positive specimen. Of these nine patients, eight (89%) were culture-positive (indication of presence of infectious virus) for less than eight days since diagnosis. One patient who were severely immunocompromised had infectious virus for up to 19 days from diagnosis.<sup>7</sup>
- In one [single-centre, retrospective study](#) involving 179 hospitalised patients, the median time to viral clearance (no detection of SARS-CoV-2 ribonucleic acid on nasopharyngeal swab) was 14 days. Age, albumin, tocilizumab and corticosteroid treatment were independently associated with a prolonged SARS-CoV-2 ribonucleic acid shedding. However, detection of viral ribonucleic acid using reverse transcription PCR test in the absence of viral cultures does not provide evidence for presence of infectious virus.<sup>8</sup>
- In one study of 20 [immunocompromised patients](#) who had COVID-19, five had infectious virus detected 8, 17, 25, 26, and 61 days after the onset of symptoms. Three patients who yielded infectious virus beyond 20 days had profound immunosuppression after undergoing hematopoietic stem-cell transplantation or receiving cellular therapies.<sup>9</sup>
- Several case studies report prolonged infectious viral shedding in immunocompromised patients, ranging from [70 days](#) to [four months](#) post symptom onset.<sup>10-12</sup>

### Guidelines and recommendations

[Communicable Diseases Network Australia](#) recommends that cases can be released from isolation if they meet the appropriate criteria.<sup>5</sup>

- Confirmed cases who have remained asymptomatic: the case can be released from isolation if at least 14 days have passed since the first respiratory specimen positive for SARS-CoV-2 by PCR was taken and no symptoms have developed during this period.
- Confirmed cases with resolution of fever and acute respiratory symptoms: the case can be released from isolation if they meet all of the following criteria:
  - at least 14 days have passed since the onset of symptoms
  - there has been resolution of fever and substantial improvement of respiratory symptoms of the acute illness for the previous 72 hours.
- Confirmed cases without complete resolution of fever and acute respiratory symptoms: the case can be released from isolation if they meet both of the following criteria:
  - at least 20 days have passed since the onset of symptoms
  - the case is not significantly immunocompromised.

OR

The case can also be released from isolation if they meet all the following criteria:

- at least 14 days have passed since the onset of symptoms
- there has been resolution of fever for the previous 72 hours

- there has been substantial improvement in respiratory symptoms of the acute illness
- the case has had two consecutive respiratory specimens negative for SARS-CoV-2 by PCR taken at least 24 hours apart after day 10 from symptom onset.
- Significantly immunocompromised persons: they can be released from isolation when they meet the following additional criterion:
  - PCR negative on at least two consecutive respiratory specimens collected at least 24 hours apart after day seven from symptom onset.

### [Centers for Disease Control and Prevention guidance](#)<sup>13</sup>

- Patients with mild to moderate illness who are not severely immunocompromised: isolation for 10 days since symptom onset and 24 hours since fever and symptoms have improved.
- Patients who are asymptomatic throughout their infection and are not severely immunocompromised: 10 days since the date of their first positive viral diagnostic test.
- Patients with severe to critical illness or who are severely immunocompromised: at least 10 days (but up to 20 days) since symptoms and 24 hours since fever and symptoms have improved.
- A test-based strategy can be considered in consultation with infectious disease experts.<sup>1</sup>
- Some people with severe illness, for example those requiring hospitalisation, intensive care, or ventilation support, may shed replication-competent virus beyond 10 days and warrant extending the duration of isolation and precautions for up to 20 days after symptom onset.<sup>1</sup>
- Severely immunocompromised patients may produce replication-competent virus beyond 20 days and require additional testing and consultation with infectious disease specialist to determine the appropriate duration of isolation and precautions.<sup>1</sup>

### [BMJ best practice COVID-19 guidelines](#)<sup>14</sup>

- Discontinue transmission-based precautions (including isolation) and release patients from the care pathway 10 days after symptom onset plus at least 3 days without fever and respiratory symptoms.

### [World Health Organization](#) recommendations<sup>4</sup>

- For symptomatic patients: 10 days after symptom onset, plus at least 3 additional days without symptoms (including without fever and without respiratory symptoms).
- For asymptomatic cases: 10 days after positive test for SARS-CoV-2.

### [UpToDate](#)

- For most patients, a non-test-based approach is preferred. The decision to use a test-based strategy should be determined on a case-by-case basis, depending severity of disease or immunocompromised status.<sup>2</sup>

## Method

To inform this brief, PubMed and Google searches were conducted using terms related to de-isolation, release from isolation, viral shedding, infectious virus and SARS-CoV-2 on 30 September 2021.

## References

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