# Criteria for releasing COVID-19 patients from isolation

## Scientific Brief

17 June 2020

## Background

On 27 May 2020, WHO published updated interim guidance on the clinical management of COVID-19,[1,2] and provided updated recommendations on the criteria for discharging patients from isolation. The updated criteria reflect recent findings that patients whose symptoms have resolved may still test positive for the COVID-19 virus (SARS-CoV-2) by RT-PCR for many weeks. Despite this positive test result, these patients are not likely to be infectious and therefore are unlikely to be able to transmit the virus to another person.

This scientific brief provides the rationale for the changes made to the clinical management of COVID-19 guidance, based on recent scientific evidence.  WHO will update these criteria as more information becomes available. For more information about clinical care of COVID-19 patients, see WHO's full guidance.[1]

## Previous recommendation

## Initial recommendation (published on 12 January 2020)

WHO's first technical package of guidance for the clinical management of the novel coronavirus, now known as COVID-19, was published in early January 2020, shortly after a cluster of atypical pneumonia cases was first reported in Wuhan, People's Republic of China,[3] and included recommendations on when a patient with COVID-19 is no longer considered infectious.

The initial recommendation to confirm clearance of the virus, and thus allow discharge from isolation, required a patient to be clinically recovered and to have two negative RT-PCR results on sequential samples taken at least 24 hours apart.[4] This recommendation was based on our knowledge and experience with similar coronaviruses, including those that cause SARS and MERS.[5]

## Updated recommendation

# New recommendation (published on 27 May 2020 as part of more comprehensive clinical care guidance1)

Within the Clinical Management of COVID-19 interim guidance published on 27 May 2020,[1] WHO updated the criteria for discharge from isolation as part of the clinical care pathway of a COVID-19 patient. These criteria apply to all COVID-19 cases regardless of isolation location or disease severity.

Criteria for discharging patients from isolation (i.e., discontinuing transmission-based precautions) without requiring retesting[1]:

- **For symptomatic patients: 10 days after symptom onset, plus at least 3 additional days without symptoms (including without fever [2] and without respiratory symptoms)[3]**
- **For asymptomatic cases[4]: 10 days after positive test for SARS-CoV-2**

*For example, if a patient had symptoms for two days, then the patient could be released from isolation after 10 days + 3 = 13 days from date of symptom onset; for a patient with symptoms for 14 days, the patient can be discharged (14 days + 3 days =) 17 days after date of symptom onset; for a patient with symptoms for 30 days, the patient can be discharged (30+3=) 33 days after symptom onset).*

**Countries may choose to continue to use testing as part of the release criteria. If so, the initial recommendation of two negative PCR tests at least 24 hours apart can be used.*

## What is the reason for the change?

In consultations with global expert networks and Member States, WHO has received feedback that applying the initial recommendation of two negative RT-PCR tests at least 24 hours apart, in light of limited laboratory supplies, equipment, and personnel in areas with intense transmission, has been extremely difficult, especially outside hospital settings.

With widespread community transmission, these initial criteria for SARS-CoV-2 posed several challenges:

- **Long periods of isolation for individuals with prolonged viral RNA detection after resolution of symptoms, affecting individual well-being, society ,and access to healthcare.[13]**
- **Insufficient testing capacity to comply with initial discharge criteria in many parts of the world.**
- **Prolonged viral shedding around the limit of detection, having negative results followed by positive results, which unnecessarily challenges trust in the laboratory system.[23-28]**

These challenges and newly available data on the risk of viral transmission over the course of the COVID-19 illness provided the framework for updating WHO's position on the timing of discharging recovered patients from isolation in and outside health care facilities. WHO continuously reviews scientific literature on COVID-19 through its Science Division and its COVID-19 technical teams. All aspects of clinical management of COVID-19 patients and laboratory testing strategies are discussed within WHO and with Member States and WHO's global expert networks of public health professionals, clinicians, and academics around the world. These expert networks and the Strategic and Technical Advisory Group for Infectious Hazards (STAG-IH)[7] considered the challenges and reviewed the available data in the decision process to change the initial recommendation.

The updated criteria for discharge from isolation balances risks and benefits; however, no criteria that can be practically implemented are without risk. There is a minimal residual risk that transmission could occur with these non–test-based criteria. There can be situations in which a minimal residual risk is unacceptable, for example, in individuals at high risk of transmitting the virus to vulnerable groups or those in high-risk situations or environments. In these situations, and in patients who are symptomatic for prolonged periods of time, a laboratory-based approach can still be useful.

WHO encourages the scientific community to compile additional evidence to further improve isolation discharge criteria and establish the conditions under which isolation can be abbreviated or where the possible risks of the current discharge criteria require further adaptation. Better understanding of transmission risk among individuals with different clinical presentations or comorbidities and in different settings will aid further refinement of these criteria. For situations that might still require a laboratory-based approach, we encourage the further optimization of such a laboratory algorithm. WHO encourages countries to continue testing patients, if they have the capacity to do so, for systematic data collection that will enhance understanding and better guide decisions about infection prevention and control measures, especially among patients with prolonged illness or those who are immunocompromised.

## Current understanding of transmission risk

Infection with the virus causing COVID-19 (SARS-CoV-2) is confirmed by the presence of viral RNA detected by molecular testing, usually RT-PCR. Detection of viral RNA does not necessarily mean that a person is infectious and able to transmit the virus to another person. Factors that determine transmission risk include whether a virus is still replication-competent, whether the patient has symptoms, such as a cough, which can spread infectious droplets, and the behavior and environmental factors associated with the infected individual. Usually 5-10 days after infection with SARS-CoV-2, the infected individual starts to gradually produce neutralizing antibodies. Binding of these neutralizing antibodies to the virus is expected to reduce the risk of virus transmission.[10,11,29,35]

SARS-CoV-2 RNA has been detected in patients 1-3 days before symptom onset, and viral load in the upper respiratory tract peaks within the first week of infection, followed by a gradual decline over time.[10,12,15,19,21,22,36-39] In the feces and lower respiratory tract, this viral load seems to peak in the second week of illness.[19] Viral RNA has been detected in upper respiratory tract (URT) and lower respiratory tract (LRT) and feces, regardless of severity of disease.[19] There seems to be a trend in longer detection of viral RNA in more severely ill patients.[10,14,15,18,19,41-43] Studies of viral RNA detection in immunocompromised patients are limited, but one study suggested prolonged detection of viral RNA in renal transplant patients.[33] Some studies analyzed the risk of transmission related to symptom of onset, and the estimated risk of transmission was highest at or around the time of symptom onset and in the first 5 days of illness.[13,15]

The ability of the virus to replicate in cultured cells serves as a surrogate marker of infectivity but requires special laboratory capabilities and may not be as sensitive as PCR.[10,20] Animal models can aid understanding of transmission risk. In a study by Sia, et al., hamsters infected with SARS-CoV-2 were housed with healthy hamsters on either day 1 or day 6 after infection. Transmission to healthy hamsters

occurred in the day 1 group, but not in those exposed 6 days after inoculation. In this model, the timing of transmission correlated with the detection of virus using cell culture, but not with detection of viral RNA in donor nasal washes.[31]

Studies using viral culture of patient samples to assess the presence of infectious SARS-CoV-2 are limited.[8-10,21,29,30,34] Viable virus has been isolated from an asymptomatic case.[9] A study of 9 COVID-19 patients with mild to moderate disease found no SARS-CoV-2 virus able to be cultured from respiratory samples after day 8 of symptom onset.[10] Three studies of patients with undisclosed or variable degree of illness showed an inability to culture virus after days 7-9 of symptom onset.[8,29,30] Patients who were RT-PCR positive on retesting after an initial negative RT-PCR on discharge from isolation were also studied, and none of these patients yielded positive viral cultures.[29] One possible outlier is a case report of a patient with mild COVID-19 who remained PCR-positive for 63 days after symptom onset. In this patient, viral cultures were positive from upper respiratory tract specimens only on the day of symptom onset, but were culture-positive from sputum samples until day 18.[22] It is unclear whether this posed a transmission risk as the patient had no respiratory symptoms. In a hospital-based study of 129 patients severely or critically ill with COVID-19, 23 patients yielded at least one positive viral culture. This study included 30 patients who were immunocompromised. The median duration of viral shedding as measured by culture was 8 days post onset, the interquartile range was 5-11, and the range was 0-20 days.[11] The probability of detecting virus in culture dropped below 5% after 15.2 days after of symptoms. In this study, patients testing positive by viral culture were still experiencing symptoms at the time of sample collection.[11] This and other studies have described the correlation between reduced infectivity with the decrease in viral loads[10,11,29,34] and a rise in neutralizing antibodies.[10,11,29] Although viral RNA can be detected by PCR even after the resolution of symptoms, the amount of detected viral RNA is substantially reduced over time and generally below the threshold where replication competent virus can be isolated. Therefore, the combination of time after onset of symptoms and the clearance of symptoms seems to be a generally safe approach based on current data.

## Conclusion

Based on evidence showing the rarity of virus that can be cultured in respiratory samples after 9 days after symptom onset, especially in patients with mild disease, usually accompanied by rising levels of neutralizing antibodies and a resolution of symptoms, it appears safe to release patients from isolation based on clinical criteria that require a minimum time in isolation of 13 days, rather than strictly on repeated PCR results. It is important to note that the clinical criteria require that patients' symptoms have been resolved for at least three days before release from isolation, with a minimum time in isolation of 13 days since symptom onset.

These modifications to the criteria for discharge from isolation (in a health facility or elsewhere) balance the understanding of infectious risk and the practicality of requiring repeated negative PCR testing, especially in settings of intense transmission or limited testing supplies. Although the risk of transmission after symptom resolution is likely to be minimal based on what is currently known, it cannot be completely ruled out. However, there is no zero-risk approach, and strict reliance on PCR confirmation of viral RNA clearance creates other risks (e.g. straining resources and limiting access to health care for new patients with acute disease). In patients with severe disease who are symptomatic for prolonged periods of time, a laboratory-based approach might also aid decision-making on the

need for prolonged isolation. Such a laboratory-based approach can include measuring viral load and neutralizing antibody (or proven equivalent antibody) levels.[10,11,29] More research is needed to further validate such an approach.

WHO will update these criteria as more information becomes available. For more information about clinical care of COVID-19 patients, see WHO's full guidance.[1]

[1] Countries can choose to continue to use a laboratory testing algorithm as part of the release criteria in (a subset of) infected individuals if their risk assessment gives reason to do so.

[2] Without the use of any antipyretics.

[3] Some patients may experience symptoms (such as post viral cough) beyond the period of infectivity. Further research is needed. For more information about clinical care of COVID-19 patients, see our Clinical Management Guidance.[1]

[4] An asymptomatic case is an individual who has a laboratory confirmed positive test and who has no symptoms during the complete course of infection.

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