



COVID-19: Infectivity of Patients Who Have Recovered From Disease

A Rapid Guidance Summary from the
Penn Medicine Center for Evidence-based Practice



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This Rapid Guidance Summary is a description of existing guidance and evidence reviews from a variety of sources that was in effect at the time of publication. It should not be used or interpreted as a clinical practice guideline, but instead can be used in development of local recommendations and policies.

Key Questions Answered in This Summary

- At what point after recovery are special precautions no longer necessary for health care providers treating patients with a history of COVID-19 disease?

Procedures for patients who are still symptomatic or otherwise ill with COVID-19 disease are outside the scope of this report. Procedures for patients whose COVID-19 status is "suspected" or uncertain are outside the scope of this report.

Summary of Major Recommendations

- We found no specific guidance from public health agencies or professional societies regarding medical procedures for patients who have recovered from COVID-19
- There is considerable uncertainty about how long a patient remains infectious after onset of COVID-19 disease or the end of the symptoms. Detection of viral RNA via a PCR test does not necessarily mean that infectious virus is present.
- Medical centers use both time-based and test-based strategies for determining when a patient who has had COVID-19 disease no longer requires special precautions during care.
- Most medical centers specify a test-based strategy for hospitalized patients. Two tests should be completed at least 24 hours apart. For patients who are intubated, one of those tests should be done on a tracheal or bronchoalveolar sample.
- Time-based strategies are necessary for asymptomatic patients, but there is considerable variation in how medical centers implement them.

Public Health Agency and Professional Society Guidelines on Medical Procedures

Source	Recommendations
UK Surgery May 13	No recommendations for management of patients with prior COVID-19 disease. If patient scheduled for surgery has a positive throat swab, surgery should be postponed by at least 14 days and a repeat test should be done within 72 hours of rescheduled surgery.

UK Surgery—intercollegiate guidelines for elective cancer surgery jointly issued by 8 UK surgery societies

Public Health Agency and Professional Society Guidelines on Lifting Isolation and Other Precautions (Not Specific to Medical Care Settings)

S o u r c e	Recommendations

<p>P HE M a y 20</p>	<p>Infection prevention and control (IPC) measures should continue for COVID-19 patients until 14 days have elapsed since their first positive SARS-CoV-2 test. This is due to uncertainties about the duration of infectiousness for patients with more severe illness or underlying immune problems that may delay them clearing the virus. Once the 14 days since the test have elapsed IPC measures for hospitalized patients can be stopped if there is:</p> <ul style="list-style-type: none"> • Clinical improvement with at least some respiratory recovery • Absence of fever (> 37.8°C) for 48 hours without the use of medication • No underlying severe immunosuppression <p>If SARS-CoV-2 testing has not been done, then isolation periods for hospitalized patients with presumed COVID-19 should be measured from the day of admission.</p>
<p>C DC A p ril 30</p>	<p>Symptomatic patients with COVID-19 should remain in Transmission-Based Precautions until either: <u>Symptom-based strategy</u></p> <p>At least 3 days (72 hours) have passed since recovery defined as resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath); and at least 10 days have passed since symptoms first appeared.</p> <p><u>Test-based strategy</u></p> <p>Resolution of fever without the use of fever-reducing medications and improvement in respiratory symptoms (e.g., cough, shortness of breath), and Negative results of an FDA Emergency Use Authorized COVID-19 molecular assay for detection of SARS-CoV-2 RNA from at least two consecutive respiratory specimens collected 24 hours apart (total of two negative specimens) [1]. See Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for 2019 Novel Coronavirus (2019-nCoV). Of note, there have been reports of prolonged detection of RNA without direct correlation to viral culture.</p> <p>Patients with laboratory-confirmed COVID-19 who have not had any symptoms should remain in transmission-based precautions until either:</p> <p><u>Time-based strategy</u></p> <p>10 days have passed since the date of their first positive COVID-19 diagnostic test, assuming they have not subsequently developed symptoms since their positive test. Note, because symptoms cannot be used to gauge where these individuals are in the course of their illness, it is possible that the duration of viral shedding could be longer or shorter than 10 days after their first positive test.</p> <p><u>Test-based strategy</u></p> <p>Negative results of an FDA Emergency Use Authorized COVID-19 molecular assay for detection of SARS-CoV-2 RNA from at least two consecutive respiratory specimens collected 24 hours apart (total of two negative specimens). Note, because of the absence of symptoms, it is not possible to gauge where these individuals are in the course of their illness. There have been reports of prolonged detection of RNA without direct correlation to viral culture.</p> <p><u>Note that detecting viral RNA via PCR does not necessarily mean that infectious virus is present.</u></p> <p>Consider consulting with local infectious disease experts when making decisions about discontinuing Transmission- Based Precautions for patients who might remain infectious longer than 10 days (e.g., severely immunocompromised).</p>
<p>E C DC A p ril 8</p>	<p>If testing and hospitalization capacity allows, for a clinically recovered patient, two negative RT-PCR tests from respiratory specimens at 24 hours interval at least eight days after onset of symptoms.</p> <p>If limited/no testing capacity, the discharged patient should self-isolate at home or in a safe place until resolution of fever for at least three days and clinical improvement of other symptoms AND until eight days after the onset of symptoms for mild cases or for 14 days (severe cases) if these criteria have not been fulfilled in hospital.</p>

Evidence Reviews on Viral Shedding

<p>R e v i e w er</p>	<p>Findings</p>
<p>F L A RE M a y 22</p>	<p>Antibody testing cannot speak to infectivity and contagiousness. Individuals with SARS-CoV-2 seropositivity may nevertheless shed contagious virus and, conversely, seronegativity does not rule out acute infection.</p>

E C DC A p ril 8	<p>Incubation period: The median incubation period is considered to be five to six days for COVID-19, with a range from one to 14 days. According to modelling data it remains prudent to consider a period of at least 14 days as an upper limit of the incubation period.</p> <p>Viral shedding: Over the course of the infection, viral RNA has been identified in respiratory tract specimens up to 1–2 days before the onset of symptoms. Viral load persists up to eight days after the onset of symptoms in mild cases and peaks in day 11 in more severe cases. The current update reflects these findings. However, more research is needed on the level and duration of viral shedding in the various patient groups and in the context of asymptomatic and pre-symptomatic infections. There is no evidence on the duration of viral shedding after resolution of fever.</p> <p>In terms of viral load profile, SARS-CoV-2 is similar to that of influenza, which peaks at around the time of symptom onset, but contrasts with that of SARS-CoV-1 and MERS-CoV, which peak in the second week after symptom onset. Older age and more severe infections have been associated with higher viral loads [5,6]. Viral RNA has been detected in feces from day five after symptom onset and up to four to five weeks in moderate cases, as well as in whole blood, serum, saliva, and urine.</p> <p>Prolonged viral RNA shedding has been reported from nasopharyngeal swabs (up to 37 days after onset of symptoms among adult patients) and in feces (more than one month after infection in pediatric patients)]. The viral load can be a potentially useful marker for assessing disease severity and prognosis: a recent study indicated that viral loads in severe cases were up to 60 times higher than in mild cases. Although there is no specific evidence for COVID-19, immunocompromised patients may shed SARS-CoV-2 virus for prolonged periods similar to other respiratory viruses.</p> <p>Viral RNA shedding of SARS-CoV-2 does not equate with infectivity, unless there is proof that the virus can be isolated and cultured from the particular samples. On the other hand, the infectious dose has not been determined; therefore, it is unclear how much virus is needed to infect humans.</p> <p><i>CEP NOTE: sections on asymptomatic and pre-symptomatic patients are not included here</i></p> <p>Immunity: Based on the currently available data, the IgM and IgG antibodies to SARS-CoV-2 develop between 6- 15 days post-disease onset. However, clinically validated laboratory assays for detection of antibodies are still lacking and therefore these results need to be considered cautiously. In addition, correlates of protection are still to be defined which is necessary to be able to comment on the possibility of re-infection and the duration of immunity. In summary, and based on limited evidence from one study indicating that viral load persists up to eight days after the onset of symptoms in mild cases and longer in more severe cases (peaking in the second week), patients should continue self-isolation at home or in a safe place if they are discharged from hospital before this period. Immunocompromised and patients with severe illness, as well as healthcare workers, should be prioritized for testing to exclude the possibility of prolonged shedding.</p>
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Medical Center Guidance on Procedures for Patients Who Have Had COVID-19

Center	Recommendation
Hopkins June 3	Healthcare settings: the current requirement is 2 sequential negative COVID-19 RT-PCR tests before airborne precautions can be lifted. However, viral RNA may be shed for 2-3 weeks or longer in many patients; unclear if this represents an infectious risk.
Beth Israel May 22	<p>Symptomatic patients: time based strategy (preferred except for hospitalized patients): at least 72 hours since resolution of fever without antipyretic medication, improvement of respiratory symptoms, and at least 14 days since discharge (all criteria must be met).</p> <p>Continue precautions in the healthcare setting for at least 7 days following recovered status if defined using above time-based criteria (negative swab test required in addition for immunocompromised patients).</p> <p>Symptomatic patients: test based strategy (preferred for patients still hospitalized): at least 72 hours since resolution of fever without antipyretic medication, improvement of respiratory symptoms, at least 10 days since initial positive test, and 2 consecutive swab tests at least 24 hours apart (all criteria must be met).</p> <p>Asymptomatic patients: time based strategy: at least 14 days since initial positive test.</p>

<p>Mass Gen eral May 20</p>	<p><u>For inpatients who are intubated</u>: resolution of fever without antipyretic medication, resolution of respiratory status, reduction of supplemental oxygen need, at least 10 days since onset of symptoms, at least one negative swab test (all criteria must be met).</p> <p><u>For inpatients who are not intubated</u>: resolution of fever without antipyretic medication, improvement of respiratory status, at least 10 days since onset of symptoms, at least one negative swab test and at least one negative test of endotracheal aspirate or bronchial lavage (all criteria must be met).</p> <p>For non-hospitalized patients:</p> <p><u>Test-based criteria</u>: resolution of fever without antipyretic medication, resolution of all respiratory symptoms, at least 10 days since first positive tests, and two negative nasal swab tests at least 24 hours apart with the first test at least 10 days since first positive test (all criteria must be met).</p> <p><u>Time-based criteria</u> (discharged inpatient): at least 72 hours since resolution of fever without antipyretic medication and resolution of all respiratory symptoms, and at least 14 days since discharge.</p> <p><u>Time-based criteria</u> (symptomatic case managed as outpatient): at least 72 hours since resolution of fever without antipyretic medication, resolution of all respiratory symptoms, and at least 14 days since symptoms first appeared.</p> <p><u>Time-based criteria</u> (asymptomatic case): at least 72 hours since resolution of fever without antipyretic medication and resolution of all respiratory symptoms, and at least 10 days since first positive test.</p>
<p>Clev eland May 18</p>	<p>For hospitalized patients:</p> <p>At least 10 days since onset of symptoms, at least 72 hours since resolution of fever without antipyretic medication, and at least 72 hours with improvement of respiratory symptoms, two negative swab tests at least 24 hours apart (all criteria must be met).</p> <p><i>CEP Note: guidance for non-hospitalized patients was on restricted web site.</i></p>
<p>Neb raska May 13</p>	<p><u>Persons diagnosed with COVID-19 who are immunologically normal appear to cease shedding transmissible virus around day 10 of illness, but current information is limited and the duration of shedding in immuno-compromised persons may be longer.</u> Based on this information we chose to be conservative with our recommendations:</p> <ul style="list-style-type: none"> • We consider all patients to no longer be infectious 21 days after illness onset and they should be cared for as any other patient • Outpatients who meet the criteria for exiting home isolation can do so before 21 days but should maintain extra caution when entering healthcare settings for the 21 days after symptom onset (see guidance below) <ul style="list-style-type: none"> o Generally, avoid healthcare settings and defer appointments for 21 days after symptom onset if medically possible o Patients who need to attend an appointment or have additional testing (lab, imaging, etc.) or procedures before the 21-day period is complete, must contact the location they will be visiting and discuss beforehand <p>Those who meet the criteria for symptom subsidence above AND are asymptomatic (or returned to baseline for those with chronic symptoms such a cough) can visit without the need for COVID-19 precautions.</p> <p>Current guidance on mask use for non-COVID-19 patients should be followed.</p> <p>Those who do not meet the criteria above (not met criteria for exiting home isolation OR still symptomatic) will be cared for using typical COVID-19 precautions and PPE until they reach 21 days post COVID-19 diagnosis.</p> <ul style="list-style-type: none"> • Outpatient this means entering via a separate entrance and clinic staff utilizing N95 respirators, gowns, gloves, eye protection. • Inpatients will be readmitted to the COVID unit until a negative test is obtained. <p>Patients inside the 21-day period should avoid aerosol generating procedures (bronchoscopy, etc.) if at all possible. If these must be performed, they should be done using COVID precautions unless they can be tested and proven negative.</p> <ul style="list-style-type: none"> o The exception to this rule is those who have had 2 negative tests documenting clearance of viral shedding and that they are non-infectious. Those who have documented viral clearance by testing can visit healthcare setting and should follow current guidance on mask use for non-COVID-19 patients
<p>UC SF May 8</p>	<p><u>Non-hospitalized patients</u>: improvement of symptoms and at least 30 days since onset of symptoms or first positive test. If patient must return for care before 30 days, but at least 14 days after onset of symptoms, do not discontinue precautions unless two consecutive swab tests (at least 24 hours apart) are negative.</p> <p><u>Hospitalized patients</u>: at least 72 hours since resolution of fever without antipyretic medication, improvement of respiratory symptoms, at least 14 days since onset of symptoms or initial positive test, and 2 consecutive swab tests at least 24 hours apart (all criteria must be met).</p> <p><i>CEP Note: Please see full document for guidance on care for patients who have been in close contact with a COVID-19-positive person.</i></p>
<p>Was hing ton May 5</p>	<p>For planning elective aerosol-generating procedures, either two negative tests within 72 hours of the planned procedure or 6 weeks elapse since initial diagnosis.</p> <p>Patients who meet the CDC criteria for release from transmission-based precautions (see above) may be seen in a health-care setting. Patients do not need a test of cure prior to being seen in clinic.</p>

<p>Penn Med icine May 4</p>	<p><u>Critical care with tracheostomy or mechanically ventilated</u>: at least 21 days since admission, at least 72 hours since resolution of fever, respiratory status improving, negative test on tracheal aspirate, negative swab test at least 24 hours later (all criteria must be met).</p> <p><u>Critical care without tracheostomy or mechanical ventilation</u>: at least 21 days since admission, at least 72 hours since resolution of fever, respiratory status improving, two negative swab tests at least 24 hours apart (all criteria must be met).</p> <p><u>Other inpatients</u> (including those transferred from critical care to regular inpatient unit): at least 10 days since admission, at least 7 days since symptom onset, at least 72 hours since resolution of fever, respiratory symptoms improved, two negative swab tests at least 24 hours apart (all criteria must be met).</p> <p>Criteria for non-hospitalized patients not reported.</p>
<p>Rush May 2</p>	<p><u>Test-based criteria</u> (apply to patients in inpatient care units, patients who have been on mechanical ventilation or ECMO, patients needing immunocompromising treatment, women who have given birth while ill with COVID- 19, and patients requiring a test before being transferred to a long-term care facility): at least 72 hours since resolution of fever without antipyretic medication, improvement or stabilization of respiratory symptoms, and two negative PCR tests at least 24 hours apart (all criteria must be met).</p> <p><u>Time-based criteria</u> (apply to most other patients): at least 72 hours since resolution of fever without antipyretic medication, resolution of respiratory symptoms, and at least 10 days since onset of symptoms or first positive test (all criteria must be met).</p> <p><u>Detecting viral RNA via PCR does not necessarily mean that live virus is present. In observational studies of hospitalized and nursing home COVID-19 infected patients, live virus has not been detected after 9 days of symptoms despite prolonged RNA fragment shedding.</u></p>
<p>Yale May 1</p>	<p>No symptoms currently present, at least 14 days since onset of symptoms, at least 72 hours since resolution of fever without antipyretic medication, and at least 72 hours with improvement of respiratory symptoms (all criteria must be met).</p>

Guidance Sources

ECDC–European Centres for Disease Control and Prevention
FLARE–Massachusetts General Hospital: Fast Literature Analysis and Review
PHE–Public Health England

Update History (Key Additions and Changes Only)

June 8: Initial report.

About this Report

A Rapid Guidance Summary is a focused synopsis of recommendations from selected guideline issuers and health care systems, intended to provide guidance to Penn Medicine providers and administrators during times when latest guidance is urgently needed. It is not based on a complete systematic review of the evidence. Please see the CEP web site (<http://www.uphs.upenn.edu/cep>) for further details on the methods for developing these reports.

Lead analyst: Matthew D. Mitchell, PhD (CEP) Evidence team leader: Emilia J. Flores, PhD, RN (CEP) Reviewers: Nikhil K. Mull, MD (CEP),

Judith G. McKenzie, MD, MPH (Occupational Med.),

Naasha Talati, MD, MSCR (Medicine)

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