

Novel coronavirus (SARS-CoV-2)

Discharge criteria for confirmed COVID-19 cases – When is it safe to discharge COVID-19 cases from the hospital or end home isolation?

This document has been produced upon request of an EU/EEA Member State. It suggests criteria to be considered when deciding whether a confirmed COVID-19 case can be safely (i.e. without being infectious) discharged from hospital or released from home isolation.

To address this request, the following working questions were developed:

- What is the duration of SARS-CoV-2 virus shedding in bodily fluids of symptomatic patients after remission of symptoms?
- What is the duration of SARS-CoV-2 virus shedding in bodily fluids of asymptomatic patients?
- Which tests are available to document the lack of infectivity in a previously diagnosed infection?
- What is the longest documented transmission from an asymptomatic person?

Below ECDC provides a desk review of existing guidance documents and protocols from national and international organisations and a convenient search of peer-reviewed publications.

What is the duration of SARS-CoV-2 virus shedding in bodily fluids of symptomatic patients after remission of symptoms?

SARS-CoV-2 virus can initially be detected 1–2 days prior to symptom onset in upper respiratory tract samples; the virus can persist for 7–12 days in moderate cases and up to 2 weeks in severe cases (WHO mission to China Report) [1]. In faeces, viral RNA has been detected in up to 30% of patients from day 5 after onset and up to 4 to 5 weeks in moderate cases. The significance of faecal viral shedding for transmission still has to be clarified [1].

Prolonged viral shedding from nasopharyngeal aspirates – up to at least 24 days after symptom onset – was reported among COVID-19 patients in Singapore [2]. Researchers from Germany also reported prolonged viral shedding with high sputum viral load after recovery in a convalescent patient [3]. They acknowledge, however, that viability of SARS-CoV-2 detected by qRT-PCR in this patient has not been proven by viral culture.

Prolonged virus shedding has been observed among convalescent children after mild infections, in respiratory tract samples (22 days) and faeces (between two weeks and more than one month) [4].

A shift from positive oral swab samples during early infection to positive rectal swab samples during late infection was observed on Chinese patients; the authors raised concerns about the fact that COVID-19 patients were discharged from hospital on the basis of negative oral swabs [5].

Researchers from China report that in upper respiratory specimens, the pattern of viral nucleic acid shedding in SARS-CoV-2-infected patients resembles that of patients with influenza; it also appears to be different from the pattern seen in patients infected with SARS-CoV-1 [6].

ECDC comment: Although the oral-faecal route does not appear to be a driver of transmission, its significance remains to be determined. Discharged patients should be advised to strictly follow personal hygiene precautions in order to protect household contacts. This applies to all convalescing patients, but particularly to convalescent children.

What is the duration of SARS-CoV-2 virus shedding in bodily fluids of asymptomatic patients?

The virus has been detected in asymptomatic persons. Pan et al. report on a family cluster where a mother and a child were both asymptomatic but had positive RT-PCR results [7]. Hoehl et al. (2020) also report that two out of 114 Germans who were evacuated from Hubei province on 1 Feb 2020 tested positive in two throat swab specimens by RT-PCR and presented no symptoms [8]. The two persons were isolated in a hospital in Frankfurt where a faint rash and minimal pharyngitis was observed in one of them. Both patients were still well and afebrile 7 days after admission. Potential infectivity was confirmed by virus culture.

Zou et al. 2020 report that the viral load of asymptomatic patients was similar to symptomatic patients, indicating a transmission potential of asymptomatic or pre-symptomatic patients [6]. The study reports that patients with few or no symptoms had modest levels of detectable viral RNA in the oropharynx for at least 5 days [6].

Potential transmission from asymptomatic persons has been reported. Bai et al. 2020 report a familial cluster of five COVID-19 patients hospitalised with fever and respiratory symptoms that had contact before onset of symptoms with an asymptomatic family member, a young 20-year-old woman, after her return from Wuhan. She remained asymptomatic for the entire duration of laboratory and clinical monitoring (19 days) [9].

ECDC comment: Provided that there are sufficient resources, there is a clear benefit in testing asymptomatic patients before they are released from isolation. However, in the context of limited resources for healthcare and laboratories during the COVID-19 epidemic, the testing of symptomatic persons should have priority over the testing of asymptomatic patients before release from isolation.

Which tests are available to document the lack of infectivity in a previously diagnosed infection?

On its website, ECDC provides the following [advice](#). The specific tests currently recommended by WHO for the diagnosis and confirmation of SARS-CoV-2 are described on a [dedicated WHO webpage](#). A single positive test should be confirmed by a second RT-PCR assay targeting a different SARS-CoV-2 gene. A single negative SARS-CoV-2 test (especially if from an upper respiratory tract specimen) or a positive test result for another respiratory pathogen result does not exclude SARS-CoV-2 infection.

A high RT-PCR cycle threshold value (e.g. > 35) obtained as a result in E-gene RT-PCR could be due to E-gene positive control contamination of reagents. In countries where the epidemic is not yet widespread, all positive results should therefore be confirmed by a second gene target. In countries with a widespread epidemic, one gene target is considered enough (see WHO's [updated laboratory guidance](#)). However, confirmation of positive test results that have high C_T values should still be considered in all regions and countries.

What is the longest documented transmission from an asymptomatic person?

There is insufficient evidence to provide a qualified answer to this question.

Significance of persistence of viral RNA vs. infectious virus?

Viral RNA can persist over long periods of time in bodily fluids. This does not necessarily mean that the person is still infectious. Isolation of viruses in virus culture is needed to show the infectivity of the virus. Hoehl et al. 2020 reported infectious virus from two asymptomatic cases [8].

An overview of recommendations for the de-isolation of COVID-19 patients from national bodies in countries that have experienced local transmissions of SARS-CoV-2 is presented in the Table below.

- Despite of some differences in practice, a consensus exists to combine a) the evidence for viral RNA clearance from the upper respiratory tract with b) the clinical resolution of symptoms.

- At least two upper respiratory tract samples negative for SARS-CoV-2, collected at \geq 24-hour intervals are recommended to document SARS-CoV-2 clearance.
- For symptomatic patients after the resolution of symptoms, samples should be collected at least seven days after the onset or after $>$ 3 days without fever.
- For asymptomatic SARS-CoV-2-infected persons, the tests to document virus clearance should be taken at a minimum of 14 days after the initial positive test.
- Italy indicates that serology tests to document IgG antibody specific to SARS-CoV-2 will be of value.

Table: Comparison of current guidelines on de-isolation of COVID-19 cases

	Symptomatic cases, hospitalised	Asymptomatic infections, persons isolated at home
Ministero della salute, Consiglio Superiore di Sanità , Italy (28 February 2020)	A COVID-19 patient can be considered cured after the resolution of symptoms and 2 negative tests for SARS-CoV-2 at 24-hour intervals. For patients who clinically recover earlier than 7 days after onset, an interval of 7 days between the first and the final test is advised. Note: Virus clearance is defined as viral RNA disappearance from bodily fluids of symptomatic and asymptomatic persons, accompanied by appearance of specific IgG.	Negative SARS-CoV-2 RNA test at 14 days after the first test (end of the quarantine period).
China CDC Diagnosis and treatment protocol for COVID-19 patients (trial version 7, revised)	Patients meeting the following criteria can be discharged: <ul style="list-style-type: none"> • Afebrile for $>$3 days, • Improved respiratory symptoms, • pulmonary imaging shows obvious absorption of inflammation, and • nucleic acid tests negative for respiratory tract pathogen twice consecutively (sampling interval \geq 24 hours). After discharge, patients are recommended to continue 14 days of isolation management and health monitoring, wear a mask, live in a single room with good ventilation, reduce close contact with family members, eat separately, keep hands clean and avoid outdoor activities. It is recommended that discharged patients should have follow-up visits after 2 and 4 weeks.	
National Centre for Infectious Diseases (NCID) Singapore De-isolation of COVID-19 suspect cases: link	Discharge patient with advisory and clinic follow-up if indicated and with daily wellness calls until day 14 after last possible exposure, under the following conditions: <ul style="list-style-type: none"> • Afebrile \geq 24 hours, • 2 respiratory samples tested negative for SARS-CoV-2 by PCR in \geq 24 hours, • Day of illness from onset \geq 6 days • OR • Alternative aetiology found (e.g. influenza, bacteraemia) • OR • Not a close contact of a COVID-19 case • Does not require in-patient care for other reasons. 	
CDC USA Interim guidance for discontinuation of transmission-based precautions and disposition of hospitalized patients with COVID-19: link	Negative rRT-PCR results from at least 2 consecutive sets of nasopharyngeal and throat swabs collected \geq 24 hours apart from a patient with COVID-19 (a total of four negative specimens) AND resolution of fever, without use of antipyretic medication, improvement in illness signs and symptoms. Note: decision to be taken on a case-by-case basis in consultation with clinicians and public health officials	

	Symptomatic cases, hospitalised	Asymptomatic infections, persons isolated at home
CDC USA Interim guidance for discontinuation of in-home isolation for patients with COVID-19: link		At least 2 consecutive sets of nasopharyngeal and throat swabs collected \geq 24 hours apart from a patient with COVID-19 (a total of four negative specimens) AND resolution of fever, without use of antipyretic medication, improvement in illness signs and symptoms. Note: decision to be taken on a case-by-case basis in consultation with clinicians and public health officials

Conclusions

When deciding on criteria for hospital discharge of COVID-19 patients, health authorities should take into account several factors such as the existing capacity of the healthcare system, laboratory diagnostic resources, and the current epidemiological situation.

In the early stages of SARS-CoV-2 spread (limited number of cases and no apparent sustained transmission: scenarios 1 and 2 in ECDC's [Rapid Risk Assessment – fifth update](#)) and with no pressure on healthcare facilities and optimal laboratory testing capacity, COVID-19 patients may be discharged from hospital and moved to home care (or other types of non-hospital care and isolation) based on:

- clinical criteria (e.g. no fever for > 3 days, improved respiratory symptoms, pulmonary imaging showing obvious absorption of inflammation, no hospital care needed for other pathology, clinician assessment)
- laboratory evidence of SARS-CoV-2 clearance in respiratory samples; 2 to 4 negative RT-PCR tests for respiratory tract samples (nasopharynx and throat swabs with sampling interval \geq 24 hours). Testing at a minimum of 7 days after the first positive RT-PCR test is recommended for patients that clinically improve earlier.
- Serology: appearance of specific IgG when an appropriate serological test is available.

In the context of sustained widespread transmission (scenario 3 and 4 in ECDC's [Rapid Risk Assessment – fifth update](#)) with increasing pressure on healthcare systems or when healthcare facilities are already overwhelmed and laboratory capacity is restrained, alternative algorithms for hospital discharge of COVID-19 patients are warranted.

The discharge from hospital of mild cases – if clinically appropriate – may be considered, provided that they are placed into home care or another type of community care. After discharge, 14 days of further isolation with regular health monitoring (e.g. follow-up visits, phone calls) can be considered, provided the patient's home is equipped for patient isolation and the patients takes all necessary precautions (e.g. single room with good ventilation, face-mask wear, reduced close contact with family members, separate meals, good hand sanitation, no outdoor activities) in order to protect family members and the community from infection and further spread of SARS-CoV-2.

Due to increasing evidence of virus shedding through faeces by convalescent patients, particularly children, recommendations for careful personal hygiene precautions after de-isolation are warranted.

References

1. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Geneva: WHO; 2020. Available from: <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>.
2. Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, et al. Epidemiologic features and clinical course of patients infected with SARS-CoV-2 in Singapore. *JAMA*. 2020.
3. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV Infection from an asymptomatic contact in Germany. *New England Journal of Medicine*. 2020;382(10):970-1.
4. Cai J, Xu J, Lin D, Yang z, Xu L, Qu Z, et al. A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clinical Infectious Diseases*. 2020.
5. Zhang W, Du R-H, Li B, Zheng X-S, Yang X-L, Hu B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerging Microbes & Infections*. 2020 2020/01/01;9(1):386-9.
6. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, et al. SARS-CoV-2 Viral load in upper respiratory specimens of infected patients. *New England Journal of Medicine*. 2020.
7. Pan X, Chen D, Xia Y, Wu X, Li T, Ou X, et al. Asymptomatic cases in a family cluster with SARS-CoV-2 infection. *The Lancet Infectious Diseases*. 2020 2020/02/19/.
8. Hoehl S, Rabenau H, Berger A, Kortenbusch M, Cinatl J, Bojkova D, et al. Evidence of SARS-CoV-2 infection in returning travelers from Wuhan, China. *New England Journal of Medicine*. 2020.
9. Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, et al. Presumed Asymptomatic carrier transmission of COVID-19. *JAMA*. 2020.