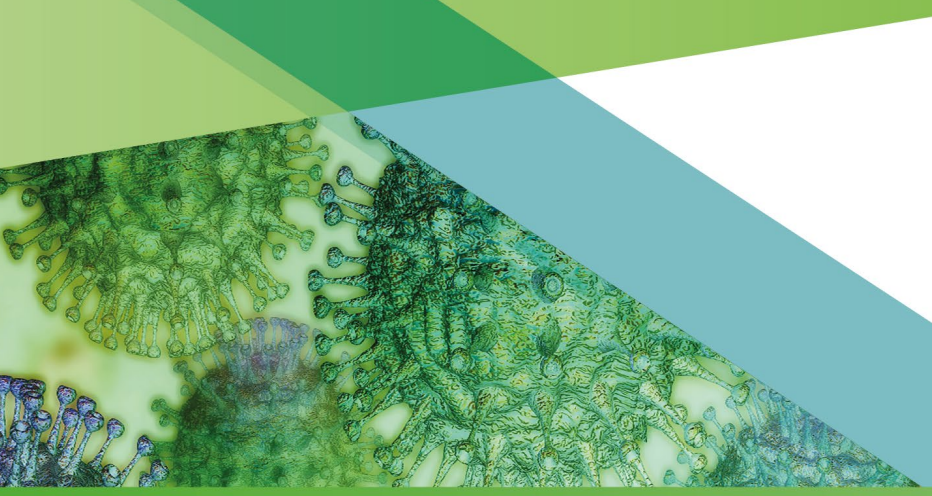

TECHNICAL REPORT

Guidance for discharge and ending of isolation of people with COVID-19

16 October 2020

Scope of this document

This document provides guidance for planning the discharge and ending of isolation of COVID-19 patients.

Target audience

Public health authorities in European Union/European Economic Area (EU/EEA) countries and the United Kingdom (UK).

Background

Since the publication of the first update of ECDC's advice on discharge criteria for and ending of isolation of COVID-19 cases [1], and as of October 2020, all EU/EEA countries and the UK continue to experience varying degrees of community transmission of SARS-CoV-2.

In the context of ongoing community transmission of SARS-CoV-2, increasing testing capacity across EU/EEA countries and the UK, and accumulating evidence on the viral shedding and infectiousness, there is a need to update the guidance for discharge and ending of isolation of people with COVID-19 [1].

The current document reflects the information available at the time of publication and may change if more information on the incubation period of SARS-CoV-2 infection and viral shedding becomes available.

Scientific evidence on SARS-CoV-2 shedding

Incubation period and quarantine of close contacts of cases

Based on the known incubation period of 1–14 days, a duration of 14 days is advised for the quarantine of persons who have had contact with confirmed COVID-19 cases [2-5]. A test at day 10 after the last exposure can be performed, and quarantine can be discontinued if the test is negative, although ending quarantine early has a residual risk. Such residual risk is not acceptable in vulnerable population settings, e.g. long-term care facilities (LTCFs), prisons or migrant and refugee reception and detention centres [6, 7].

Viral shedding

The exact duration of infectivity of COVID-19 patients is not yet known with certainty. Several studies have shown that most transmission happens around the onset of symptoms and that SARS-CoV-2 can initially be detected in upper respiratory samples around two days before the onset of symptoms. In studies of non-severe cases, the virus was successfully isolated for 10 days from the onset of symptoms [8-13]. In an analysis of 72 infector-infected pairs in South Korea, the estimated median transmission onset was 1.31 days (standard deviation (SD) 2.64 days) following the onset of symptoms, with a peak at 0.72 days before the onset of

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symptoms [14]. Among hospitalised/severe COVID-19 patients, isolation of SARS-CoV-2 was possible until day 20 after onset of symptoms, with a median of eight days (interquartile range (IQR) 5-11 days) [13, 15]. The probability of detecting infectious SARS-CoV-2 dropped below 5% after 15.2 days post onset of symptoms (95% confidence interval (CI) 13.4 – 17.2). In this study, the risk of having a positive SARS-CoV-2 culture was three times higher in immunocompromised patients than in other patients, which suggests that immunocompromised patients may shed SARS-CoV-2 for prolonged periods [15]. Older age and a more severe infection have been associated with a higher viral load [16, 17]. However, it was also recently demonstrated that children have viral loads similar to that of adults [18], and asymptomatic patients have viral loads similar to that of symptomatic patients [19]. On the other hand, the infectious dose of SARS-CoV-2 has not yet been determined. Data from contact tracing studies, have shown that exposure of the secondary cases had occurred up to five days after onset of symptoms of the index case [20, 21], but the number of cases for which a sound conclusion for this time period could be made was limited.

Some patients with laboratory-confirmed COVID-19 have had a positive SARS-CoV-2 RT-PCR test result over prolonged periods of time after infection and clinical recovery. Studies in hospitalised COVID-19 cases have found that the RT-PCR test for SARS-CoV-2 could remain positive in respiratory samples up to six weeks from illness onset [22, 23]. Some evidence is emerging that these cases were not linked with secondary transmission [24, 25]. Prolonged shedding of SARS-CoV-2 RNA has been shown even after seroconversion [25, 26]. The identification of SARS-CoV-2 RNA through RT-PCR (i.e. viral RNA shedding) does not equate to the presence of viable, infectious SARS-CoV-2 in a patient. However, in the case of immunocompromised patients, the significance of prolonged viral RNA shedding for transmission remains unclear. In patients with a positive SARS-CoV-2 RT-PCR test result over a prolonged period, virus culture or sub-genomic RNA detection can be used to confirm positivity for viable SARS-CoV-2. If viable SARS-CoV-2 is detected, the patient would need to continue being placed in isolation at a designated facility or at home.

Possibility of transmission during the pre-symptomatic stage of infection
In symptomatic patients, the high viral load close to onset of symptoms suggests that SARS-CoV-2 can be easily transmitted at an early stage of infection [16, 27-30]. Several studies have indicated that secondary transmissions from an index case can occur up to 3 days before the onset of symptoms of the index case [30-33]. One study suggested that viable SARS-CoV-2 was isolated from specimens collected from six days before to up to nine days after the first evidence of typical symptoms of COVID-19 [34]. The proportion of pre-symptomatic transmission from an index case was estimated to be 37% (95% CI 16–52%) [14] and 44% [32].

Possibility of transmission by asymptomatic individuals
Asymptomatic infection at the time of laboratory confirmation has been reported from many settings, with a large proportion of these cases experiencing some symptoms of COVID-19 at a later stage of infection [16]. There are, however, reports of cases remaining asymptomatic throughout the whole duration of laboratory and clinical monitoring, and the proportion of asymptomatic cases has been estimated at 30–40% of all COVID-19 infections [35-37]. SARS-CoV-2 RNA, as well as infectious SARS-CoV-2 has been detected in asymptomatic patients [27, 38, 39]. In a study from South Korea, the viral load and the probability of detecting viable SARS-CoV-2 were similar in symptomatic and asymptomatic persons, indicating that asymptomatic persons represent a source of transmissible SARS-CoV-2 [19].

Immunity
The understanding of immunity against SARS-CoV-2 is still incomplete. Binding and neutralising antibodies against SARS-CoV-2 have been shown to develop in most individuals between day 10 and day 21 after onset of symptoms [16, 40-42]. Reviews of the published literature indicate that >91% patients develop IgG seropositivity and >90% develop neutralising antibodies following primary infection with SARS-CoV-2 [43-45]. More recent studies found that antibody titres peak between 3-4 weeks after onset of symptoms, and remain relatively stable for up to four months [46]. However, correlates of protection against COVID-19 and the meaningful titres of antibodies against SARS-CoV-2 are still to be defined.

The current update reflects the above findings. However, more research is needed on the level and duration of SARS-CoV-2 shedding in the various patient groups, and in the context of asymptomatic and pre-symptomatic infections.

In summary, and based on the still limited evidence indicating that infectious SARS-CoV-2 shedding persists up to 10 days after the onset of symptoms in mild/moderate cases and up to 20 days in severe cases, patients should continue self-isolation at home or in a safe place if they are discharged from hospital earlier than 10 days for mild/moderate cases and earlier than 20 days for severe cases.

Discharge and ending of isolation criteria

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

COVID-19 patients may be discharged based on criteria that take into account the following: a) clinical resolution of symptoms; b) time elapsed since onset of symptoms; c) severity of disease; d) immune status; and e) evidence of viral RNA clearance from the upper respiratory tract (Table 1, Figure 1).

Severely ill patients who need to be discharged from hospital before fulfilling the criteria for discharge and without a negative SARS-CoV-2 RT-PCR test result should self-isolate at home or at a safe place for at least 14 and up to 20 days from the onset of symptoms based on an individual case risk assessment. The assessment needs to take into account the presence of immunosuppression and whether the patient will be in contact with people who are vulnerable to severe COVID-19 or are in settings in which there is a risk of large outbreaks (e.g. residents in LTCFs, prisons or migrant/refugee hosting facilities). Patients should seek medical advice if they develop symptoms again.

Asymptomatic people who have had a positive SARS-CoV-2 test should self-isolate for 10 days from the date the sample was taken.

Criteria for discharge and ending of isolation may be adapted for specific groups of patients. Two consecutive negative SARS-CoV-2 RT-PCR test results, ideally in a 24-hour period, are recommended for the discontinuation of isolation for immunocompromised cases. The second test is needed as confirmatory, to exclude the possibility of a false negative result. Similarly, two consecutive negative SARS-CoV-2 RT-PCR tests can be considered for the discontinuation of isolation of severely ill patients, especially if they will be transferred to other units within the hospital or discharged to a LTCF. All patients who are instructed to complete quarantine at home or another safe place should follow infection prevention and control guidance with personal hygiene precautions in order to protect household contacts [47].

Contributing ECDC experts (in alphabetical order)

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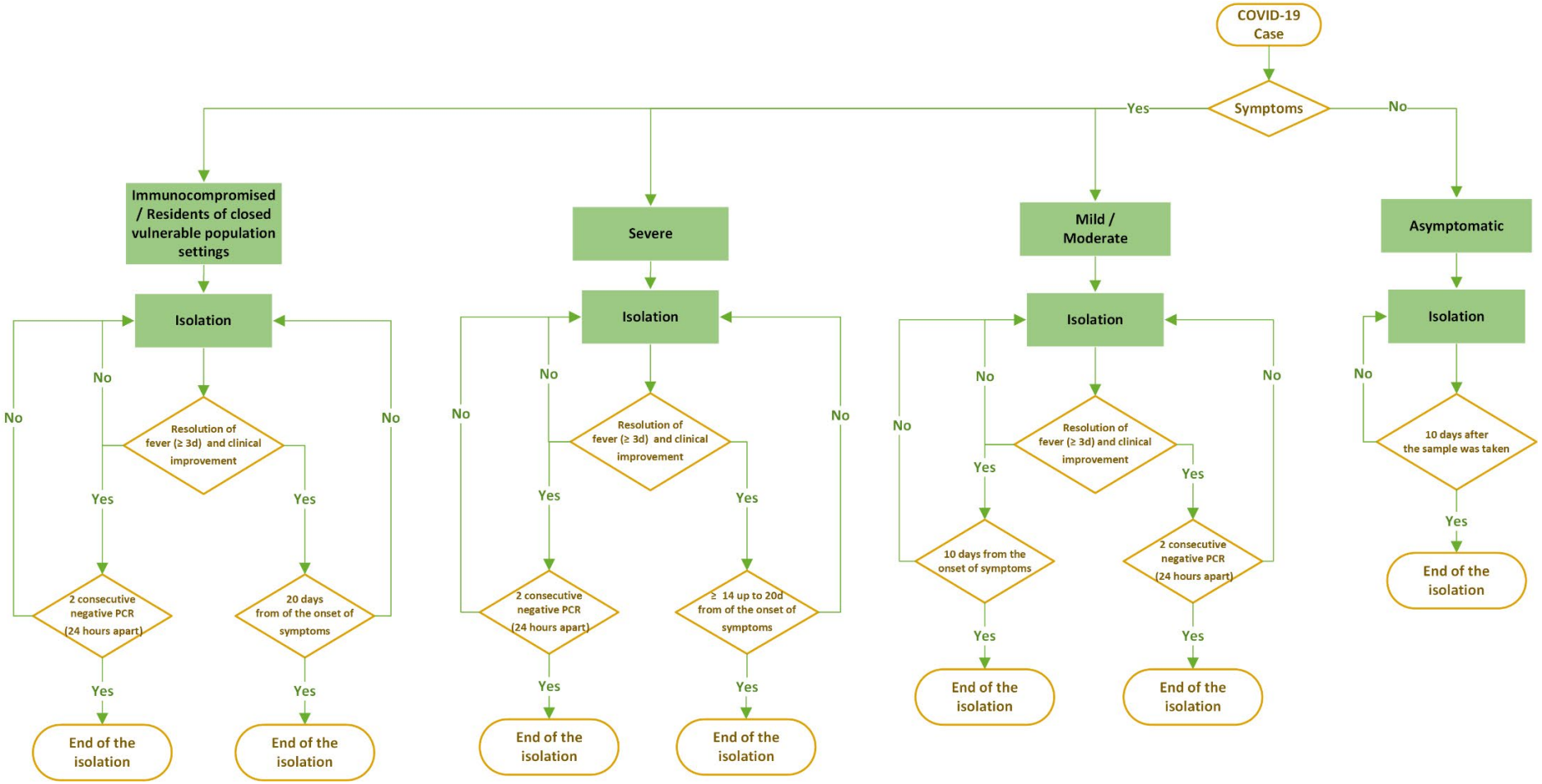
Table 1. Guidance on discharge and ending isolation of people with COVID-19

Description	Guidance
Mild/moderate COVID-19 Probable or confirmed COVID-19 case that is neither immunocompromised nor a resident in a closed vulnerable population setting	The patient can be released from isolation when the following criteria are fulfilled: • Resolution of fever for at least three days and clinical improvement of symptoms other than fever **AND** – 10 days after the onset of symptoms **OR** – two consecutive negative SARS-CoV-2 RT-PCR tests in a 24-hour interval from respiratory specimens. Hospitalised patients who are discharged early based on clinical criteria per evaluation of the treating physician should be instructed to self-isolate at home or in a safe place until the above criteria are fulfilled.
Severe COVID-19 Probable or confirmed COVID-19 case that is neither immunocompromised nor a resident in a closed vulnerable population setting	The patient can be released from isolation when the following criteria are fulfilled: • Resolution of fever for at least three days and clinical improvement of symptoms other than fever **AND** – minimum 14 and up to 20 days after the onset of symptoms **OR** – two consecutive negative SARS-CoV-2 RT-PCR tests in a 24-hour interval from respiratory specimens. Hospitalised patients who are discharged early based on clinical criteria per evaluation of the treating physician should be instructed to self-isolate at home or in a safe place until the above criteria are fulfilled.
Immunocompromised patient (e.g. transplant recipient, patient receiving prolonged corticosteroid treatment or another immune-modulating medicine or cancer chemotherapy, patient with HIV and a low CD4 count, patient with an immune deficiency)	The patient can be released from isolation when the following criteria are fulfilled: • Resolution of fever for at least three days and clinical improvement of symptoms other than fever **AND** – 20 days after the onset of symptoms **OR** – two consecutive negative SARS-CoV-2 RT-PCR tests in a 24-hour interval from respiratory specimens.
Resident or staff of closed vulnerable population settings (long-term care facility, prison, migrant/refugee hosting facility)	The patient can be released from isolation and return to the vulnerable population setting when the following criteria are fulfilled: • Resolution of fever for at least three days and clinical improvement of symptoms other than fever **AND** – 20 days after the onset of symptoms **OR** – two consecutive negative SARS-CoV-2 RT-PCR tests in a 24-hour interval from respiratory specimens. Residents of closed vulnerable population settings who are discharged earlier based on clinical criteria per evaluation of the treating physician should be isolated at the facility in a single room until the above criteria are fulfilled.
Asymptomatic COVID-19 case Person without symptoms who tested positive for SARS-CoV-2 but did not develop symptoms during follow-up	This patient can end isolation 10 days after the sample was taken.

Figure 1. **Algorithm for ending of isolation of people with COVID-19**



References

1. European Centre for Disease Prevention and Control (ECDC). Guidance for discharge and ending isolation in the context of widespread community transmission of COVID-19 [Internet]. [Updated 8 April 2020]. Available from: https://www.ecdc.europa.eu/en/publications-data/covid-19-guidance-discharge-and-ending-isolation
2. Chinese Center for Disease Control and Prevention (CCDC). Epidemic update and risk assessment of 2019 Novel Coronavirus [Internet]. [updated 28 January 2020]. Available from: http://www.chinacdc.cn/yyrdgz/202001/P020200128523354919292.pdf
3. Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20–28 January 2020. Euro Surveill. 2020;25(5):2000062. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.5.2000062
4. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England Journal of Medicine. 2020;382(13):1199-207.
5. Wei Y, Wei L, Liu Y, Huang L, Shen S, Zhang R, et al. A systematic review and meta-analysis reveals long and dispersive incubation period of COVID-19. medRxiv. 2020. Available from: https://doi.org/10.1101/2020.06.20.20134387
6. Quilty BJ, Clifford S, Flasche S, Kucharski AJ, Edmunds WJ, Group CC-W. Quarantine and testing strategies in contact tracing for SARS-CoV-2. medRxiv. 2020. Available from: https://doi.org/10.1101/2020.08.21.20177808
7. European Centre for Disease Prevention and Control (ECDC). Testing strategies for SARS-CoV-2 [Internet]. [updated 29 September 2020]. Available from: https://www.ecdc.europa.eu/en/covid-19/surveillance/testing-strategies
8. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, et al. Virological assessment of hospitalized patients with COVID-2019. Nature. 2020;581(7809):465-9.
9. Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, et al. Predicting infectious SARS-CoV-2 from diagnostic samples. Clinical Infectious Diseases. 2020. Available from: https://doi.org/10.1093/cid/ciaa638
10. La Scola B, Le Bideau M, Andreani J, Hoang VT, Grimaldier C, Colson P, et al. Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards. European Journal of Clinical Microbiology & Infectious Diseases. 2020;39(6):1059.
11. Weiss A, Jellingsø M, Sommer MOA. Spatial and temporal dynamics of SARS-CoV-2 in COVID-19 patients: A systematic review and meta-analysis. EBioMedicine. 2020;58:102916.
12. Health Information and Quality Authorit (HIQA). Evidence summary for the duration of infectiousness in those that test positive for SARS-CoV-2 RNA [Internet]. [updated 15 September 2020]. Available from: https://www.hiqa.ie/sites/default/files/2020-09/Evidence-summary-for-duration-of-infectiousness-of-SARS-CoV-2.pdf
13. Singanayagam A, Patel M, Charlett A, Bernal JL, Saliba V, Ellis J, et al. Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020. Euro Surveill. 2020;25(32):2001483. Available from: https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.32.2001483
14. Chun JY, Baek G, Kim Y. Transmission onset distribution of COVID-19. International Journal of Infectious Diseases. 2020;99:403-7.
15. van Kampen JJ, van de Vijver DA, Fraaij PL, Haagmans BL, Lamers MM, Okba N, et al. Shedding of infectious virus in hospitalized patients with coronavirus disease-2019 (COVID-19): duration and key determinants. MedRxiv. 2020. https://doi.org/10.1101/2020.06.08.20125310
16. To KK-W, Tsang OT-Y, Leung W-S, Tam AR, Wu T-C, Lung DC, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. The Lancet Infectious Diseases. 2020;20(5):565-74.
17. 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;20(4):410-1.
18. Yonker LM, Neilan AM, Bartsch Y, Patel AB, Regan J, Arya P, et al. Pediatric SARS-CoV-2: clinical presentation, infectivity, and immune responses. The Journal of Pediatrics. 2020. https://doi.org/10.1016/j.jpeds.2020.08.037
19. Lee S, Kim T, Lee E, Lee C, Kim H, Rhee H, et al. Clinical course and molecular viral shedding among asymptomatic and symptomatic patients with SARS-CoV-2 infection in a community treatment center in the Republic of Korea. JAMA internal medicine. 2020. Available from: https://doi.org/10.1001/jamainternmed.2020.3862
20. Cheng H-Y, Jian S-W, Liu D-P, Ng T-C, Huang W-T, Lin H-H. Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset. JAMA internal medicine. 2020;180(9):1156–63.
21. Bernal JL, Panagiotopoulos N, Byers C, Vilaplana TG, Boddington NL, Zhang X, et al. Transmission dynamics of COVID-19 in household and community settings in the United Kingdom. medRxiv. 2020. Available from: https://doi.org/10.1101/2020.08.19.20177188
22. Xiao AT, Tong YX, Zhang S. Profile of RT-PCR for SARS-CoV-2: a preliminary study from 56 COVID-19 patients. Clinical Infectious Diseases. 2020. Available from: https://doi.org/10.1093/cid/ciaa460
23. Zhou B, She J, Wang Y, Ma X. The duration of viral shedding of discharged patients with severe COVID-19. Clinical Infectious Diseases. 2020. Available from: https://doi.org/10.1093/cid/ciaa451
24. Korean Centre for Disease Control (KCDC). Findings from investigation and analysis of re-positive cases [updated 19 May 2020]. Available from: https://www.cdc.go.kr/board/board.es?mid=a30402000000&bid=0030
25. Molina LP, Chow S-K, Nickel A, Love JE. Prolonged Detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) RNA in an Obstetric Patient With Antibody Seroconversion. Obstetrics & Gynecology. 2020;136(4):838-41.
26. Liu W-D, Chang S-Y, Wang J-T, Tsai M-J, Hung C-C, Hsu C-L, et al. Prolonged virus shedding even after seroconversion in a patient with COVID-19. Journal of Infection. 2020;81(2):318-56.
27. Cereda D, Tirani M, Rovida F, Demicheli V, Ajelli M, Poletti P, et al. The early phase of the COVID-19 outbreak in Lombardy, Italy. Arxiv; 2020. arXiv:2003.09320v1
28. Han Y, Yang H. The transmission and diagnosis of 2019 novel coronavirus infection disease (COVID-19): A Chinese perspective. Journal of Medical Virology. 2020;92(6):639-44.
29. 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;382(12):1177-9.

30. Wei WE, Li Z, Chiew CJ, Yong SE, Toh MP, Lee VJ. Presymptomatic Transmission of SARS-CoV-2—Singapore, January 23–March 16, 2020. Morbidity and Mortality Weekly Report. 2020;69(14):411.
31. Pan Y, Zhang D, Yang P, Poon LL, Wang Q. Viral load of SARS-CoV-2 in clinical samples. The Lancet Infectious Diseases. 2020;20(4):411-2.
32. He X, Lau EH, Wu P, Deng X, Wang J, Hao X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nature medicine. 2020;26(5):672-5.
33. Kucirka LM, Lauer SA, Laeyendecker O, Boon D, Lessler J. Variation in false-negative rate of reverse transcriptase polymerase chain reaction–based SARS-CoV-2 tests by time since exposure. Annals of Internal Medicine. 2020;173(4):262-7.
34. Arons MM, Hatfield KM, Reddy SC, Kimball A, James A, Jacobs JR, et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. New England Journal of Medicine. 2020;382(22):2081-90.
35. Lavezzo E, Franchin E, Ciavarella C, Cuomo-Dannenburg G, Barzon L, Del Vecchio C, et al. Suppression of a SARS-CoV-2 outbreak in the Italian municipality of Vo'. Nature. 2020;584(7821):425-9.
36. Oran DP, Topol EJ. Prevalence of Asymptomatic SARS-CoV-2 Infection: A Narrative Review. Annals of Internal Medicine. 2020;173(5):362-7.
37. Tao J, Zhang X, Zhang X, Zhao S, Yang L, He D, et al. The time serial distribution and influencing factors of asymptomatic COVID-19 cases in Hong Kong. One Health. 2020. Available from: https://doi.org/10.1016/j.onehlt.2020.100166
38. 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;382(13):1278-80.
39. Luo S-H, Liu W, Liu Z-J, Zheng X-Y, Hong C-X, Liu Z-R, et al. A confirmed asymptomatic carrier of 2019 novel coronavirus. Chinese Medical Journal. 2020;133(9):1123-5.
40. To KK-W, Chan W-M, Ip JD, Chu AW-H, Tam AR, Liu R, et al. Unique Clusters of Severe Acute Respiratory Syndrome Coronavirus 2 Causing a Large Coronavirus Disease 2019 Outbreak in Hong Kong. Clinical Infectious Diseases. 2020. Available from: https://doi.org/10.1093/cid/ciaa1119
41. Seydoux E, Homad LJ, MacCamy AJ, Parks KR, Hurlburt NK, Jennewein MF, et al. Analysis of a SARS-CoV-2-Infected Individual Reveals Development of Potent Neutralizing Antibodies with Limited Somatic Mutation. Immunity. 2020 Jul 14;53(1):98-105.e5.
42. Ni L, Ye F, Cheng M-L, Feng Y, Deng Y-Q, Zhao H, et al. Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals. Immunity. 2020;52(6):971-7.
43. Grifoni A, Weiskopf D, Ramirez SI, Mateus J, Dan JM, Moderbacher CR, et al. Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. Cell. 2020 Jun 25;181(7):1489-501.e15.
44. Weiskopf D, Schmitz KS, Raadsen MP, Grifoni A, Okba NM, Endeman H, et al. Phenotype and kinetics of SARS-CoV-2–specific T cells in COVID-19 patients with acute respiratory distress syndrome. Science Immunology. 2020. 5(48) eabd2071. Available from: https://doi.org/10.1126/sciimmunol.abd2071
45. Braun J, Loyal L, Frentsch M, Wendisch D, Georg P, Kurth F, et al. Presence of SARS-CoV-2 reactive T cells in COVID-19 patients and healthy donors. medRxiv. 2020. Available from: https://doi.org/10.1101/2020.04.17.20061440
46. Gudbjartsson DF, Norddahl GL, Melsted P, Gunnarsdottir K, Holm H, Eythorsson E, et al. Humoral Immune Response to SARS-CoV-2 in Iceland. The New England Journal of Medicine. 2020 Sep 1. Available from: https://doi.org/10.1056/NEJMoa2026116
47. European Centre for Disease Prevention and Control (ECDC). Infection prevention and control in the household management of people with suspected or confirmed coronavirus disease (COVID-19) [Updated 31 March 2020]. Available from: https://www.ecdc.europa.eu/en/publications-data/infection-prevention-control-household-management-covid-19