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Understanding Viral Shedding of SARS-CoV-2: Review of Current Literature

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Abstract

**Objective:** Transmission of SARS-CoV-2 has significant implications for hospital infection prevention and control, discharge management, and public health. We reviewed available literature to reach an evidenced-based consensus on the expected duration of viral shedding.

**Design:** We queried four scholarly repositories/search engines for studies reporting SARS-CoV-2 viral shedding dynamics by PCR and/or culture available through September 8, 2020. We calculated the pooled median duration of viral RNA shedding from respiratory and fecal sources.

**Results:** Seventy-seven studies on SARS-CoV-2 were included. All studies reported PCR-based testing and 12 also included viral culture data. The overall pooled median duration of RNA shedding from respiratory sources was 18.4 days (95% CI: 15.5 days - 21.3 days; $I^2=98.87\%$, $p<0.01$) among 28 studies. When stratified by disease severity, the pooled median duration of viral RNA shedding from respiratory sources was 19.8 days (95% CI: 16.2 days – 23.5 days; $I^2=96.42\%$, $p<0.01$) among severely ill patients and 17.2 days (95% CI: 14.0 days - 20.5 days; $I^2=95.64\%$, $p<0.01$) in mild/moderate illness. Viral RNA was detected up to 92 days after symptom onset. Viable virus was isolated by culture from -6 days to 20 days relative to symptom onset.

**Conclusions:** SARS-CoV-2 RNA shedding can be prolonged, yet high heterogeneity exists. Detection of viral RNA may not correlate with infectivity since available viral culture data suggests shorter durations of shedding of viable virus. Additional data is needed to determine the duration of shedding of viable virus and the implications for risk of transmission.
Introduction:

Knowledge of transmission dynamics of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has significant implications for hospital infection prevention and control interventions, timely discharge management, and public health policies. Due to variability in the emerging data, policies on the duration of inpatient and outpatient isolation for people with COVID-19 have been controversial. There is continued uncertainty about the significance of prolonged PCR positivity and the clinical importance of various routes of viral shedding. Understanding the duration and sources of viable viral shedding is critical to inform guidance around transmission-based isolation precautions.

The aim of this paper is to review SARS-CoV-2 viral shedding data to help inform practical decisions related to infection control and public health policies. We reviewed available literature and summarized data on expected duration of viral RNA shedding, longevity of presumed infectivity as detected by viral culture, and factors that may influence shedding duration.

Methods:

Search Method and Data Extraction:

We queried PubMed, LitCoVID, World Health Organization COVID-19 literature repository, and Google Scholar for studies and reports available through September 8th, 2020. Search terms consisted of “SARS shedding,” “COVID and viral shedding,” “COVID RNA and Culture,” and
“COVID culture;” in queries of SARS-CoV-2 specific databases, the words “SARS” and “COVID” were omitted from search terms. Additional studies were identified through review of reference lists from included studies. All authors participated in study identification, screening, and data extraction; all included studies were reviewed by at least two authors. Articles reporting duration of SARS-CoV-2 shedding based upon PCR testing or culture directly from human specimens were included. Day 0 was defined as either the day of the first positive test or the day of symptom onset, per the original study. Studies reporting on exclusively pediatric patients were excluded. For each study, we reviewed the design, objective, population, healthcare system setting, diagnostic testing method, timing of tests, sample source, patient symptoms and severity of illness. Predictors of prolonged shedding were also considered.

**Statistical Analysis:**

We constructed random effects models using the restricted maximum likelihood estimator for $\tau^2$ to calculate pooled median durations of viral RNA shedding.\(^1\) All studies providing sample size and sufficient data on measures of central tendency and spread were included in analysis. We grouped nasopharyngeal (NP), oropharyngeal (OP), saliva, and sputum samples together as “respiratory” samples. Fecal samples included both stool and rectal swabs. We calculated pooled medians among PCR respiratory samples for all available, mild/moderate illness, severe/critical illness and for all fecal samples. Insufficient data were available to warrant calculation of pooled medians for culture data. Analysis was performed using R version 4.0.0.\(^2\) using the metamedian package.\(^3\)
Results:

Included Studies

Seventy-seven studies/reports were eligible for inclusion: prospective case series (N=35), retrospective case series (N=28), case reports (N=11), point prevalence survey (N=2), and position statements (N=1) (Table 1). Fifty-nine of these studies were peer reviewed, 6 were from pre-print servers and 13 were research letters or letters to the editor. Seventy studies described hospitalized patients. All studies reported PCR-based assessments of viral shedding; 12 studies reviewed reported viral culture data.\textsuperscript{4-15} Thirty studies reported PCR testing of non-respiratory specimens.

Duration of Viral RNA Shedding

Seventy-seven reports included data on viral RNA shedding by PCR.\textsuperscript{4-80} Box 1 summarizes the key points of viral shedding duration. The duration of viral RNA shedding ranged from a minimum of 1 day\textsuperscript{4,7,21,33,46} to a maximum of 83 days.\textsuperscript{48} Intermittent PCR positivity did occur through day 92 from symptom onset in one case report; that patient had previously tested negative at day 72 followed by repeat positive PCR.\textsuperscript{57} In a study of 56 serially tested hospitalized patients with mild and moderate disease, 66.1\% of NP/OP swabs were still positive at 3 weeks. Positivity rates then declined weekly and all PCR tests were negative by week 6.\textsuperscript{15} Based on the 28 studies that provided sufficient data (see Appendix Table), the pooled median duration of RNA shedding from respiratory samples was 18.4 days (95\%CI: 15.5 days - 21.3 days). High heterogeneity was observed among these studies ($I^2=98.87\%; p<0.01$).
We reviewed shedding data for patients with mild to moderate illness. Based on parametric regression modeling, Sun et al. concluded that detection of viral RNA in throat swabs beyond 50 days post symptom onset in patients with mild illness would be a low probability event occurring beyond the 95\textsuperscript{th} percentile.\textsuperscript{66} Despite this calculation, there are case reports of patients with viral RNA shedding $\geq 45$ days from symptom onset.\textsuperscript{48,58,67-69,78,80} Among all studies we reviewed, the longest duration of PCR positivity in a patient with mild illness was 92 days after symptom onset from a NP swab.\textsuperscript{57} The pooled median duration of viral RNA shedding from respiratory sources among patients with mild to moderate illness, based upon 10 studies that reported sufficient data (see Appendix Table), was 17.2 (95\% CI: 14.0 days - 20.5 days). Again, there was high heterogeneity among these studies ($I^2=95.64\%$; $p<0.01$).

There were multiple reports of patients with intermittently positive PCR results from respiratory specimens.\textsuperscript{17,21,25,27,28,51,56-58,79,81} Although not consistently defined, cessation of shedding was most often described as 2 consecutive negative PCR results $\geq 24$-48 hours apart.\textsuperscript{21,23,25,38,51,56,58,81} Tests were frequently done in anticipation of discharge from the hospital.\textsuperscript{57,81} One report estimated that 26-49\% of patients were re-positive after a negative test, but in other studies re-positivity varied between 3-35\%.\textsuperscript{17,21,25,27,28,51,56,81} Wang, et al. described a case report of a patient that was discharged 75 days after illness onset following 3 consecutive negative tests. The patient then tested positive on days 82 and 92 followed by negative PCR on days 101 and 105.\textsuperscript{57} Another case report described a woman with mild COVID-
19 who intermittently tested positive by NP PCR swabs for 72 days from disease onset despite developing IgM and IgG antibodies on day 38.\textsuperscript{58}

Wölfel et al. observed the pharyngeal rate of detection was highest in the first 5 days of symptom onset and then declined.\textsuperscript{10} NP swabs may have a higher rate of detection than OP swabs, but they were only compared in two of the studies included in this review.\textsuperscript{63,71} Negative upper tract specimens may not correlate with lower tract specimens, though the significance of these findings is not well understood. In a post-mortem analysis of a patient whose NP sample tested PCR negative, lung tissue was PCR positive and histology revealed coronavirus particles in bronchiolar epithelial cells.\textsuperscript{59}

Some studies included data for presymptomatic or asymptomatic patients and observed that PCR positivity can occur as early as 5 days prior to symptom onset.\textsuperscript{9,10,60,61} Multiple case series reported that the viral load of asymptomatic patients are as high as those with symptoms.\textsuperscript{9,10,62} In one case series, the asymptomatic individual in a family cluster had similar viral RNA loads in nasal and throat swabs to those of symptomatic family members.\textsuperscript{63} The majority of the subjects in this case series converted to a negative PCR by day 18.\textsuperscript{63}

Five studies included saliva samples.\textsuperscript{18,31,48,55,62} In a series of 13 patients with mild disease, viral RNA load was highest in saliva in the first week of illness; 3 of the patients still had detectable viral load in their saliva at day 20 of illness.\textsuperscript{48} In another series, PCR turned negative in the saliva of 13 mildly ill patients before nasal swab PCR – an average of 13.33 +/- 5.27 days and 15.67 +/- 6.68 days, respectively.\textsuperscript{55} In the same study, the average duration of positive PCR in sputum
was shorter in non-ICU patients than ICU patients, who were positive for an average of 16.5 +/- 6.19 days.55

Predictors of extended duration of viral RNA shedding in respiratory samples

The most frequently identified predictor of prolonged viral RNA shedding was disease severity. Patients with severe disease have been observed to shed RNA for longer and have higher viral RNA loads at symptom onset followed by a gradual decline in viral RNA 3 weeks after symptom onset.29,32,50,53,64,65 Based on 10 studies (see Appendix Table), the pooled median duration of viral RNA shedding from respiratory samples in patients with severe illness was 19.8 days (95% CI: 16.2 days - 23.5 days). Again, significant high heterogeneity exists ($I^2=96.42\%$; $p<0.01$). In one cohort of patients, the median duration of positive NP PCRs was 22.25 days +/- 3.62 (SD) days in patients admitted to the ICU, compared to 15.67 days +/- 6.68 (SD) days in non-ICU patients.55 Sun et al. also observed prolonged duration of RNA shedding from NP swabs in those with severe illness compared to those with mild disease, with median durations of 33.5 days and 22.7 days, respectively.66

Predictors of severe disease and duration of shedding ≥ 15 days in hospitalized patients included older age, hypertension, coronary artery disease, and diabetes mellitus.17,27,50,52,53,62 Gender was not consistently identified as a risk factor for severe disease or prolonged shedding but comparisons were limited by small sample sizes.47,49,52,54,62
**Viral RNA shedding in non-respiratory samples**

A subset of studies presented PCR data from both respiratory and fecal samples. Rectal/stool PCR pooled median duration of positivity based on 5 studies was 22.1 days (95% CI: 14.4 days - 29.8 days; $I^2=95.86\%, p<0.01$). Stool PCR positivity has been observed to lag behind both PCR positivity of pharyngeal specimens and symptom improvement and even may become positive after the OP PCR has become negative. RNA replication in the stool was observed $\geq 2$ weeks after symptom onset.

In one study, the number of PCR-positive stool samples increased between the first and third weeks of illness, with a median time to detection in the stool of 19-22 days. Based on the limited data available thus far, illness severity does not seem to impact stool RNA detection, as similar durations of RNA shedding in the stool have been observed in mild and severe illness.

Park et al. detected SARS-CoV-2 RNA in stool 50-55 days after initial diagnosis of asymptomatic or mild SARS-CoV-2 illness; in this study, people with higher viral loads were more likely to have viral RNA in the stool. However, stool shedding was not consistently observed, and some studies showed that virus was detectable in only 35-59% of patients screened.

Data for serum and blood is limited but evolving. Among studies reporting serum/blood testing, viral RNA was detected in 30-87.5% of patients with COVID-19, though one smaller study did not detect viral RNA in any of the 14 patients tested. The ability to detect RNA in blood and serum may be reflective of disease severity. Virus was detected by PCR for longer in blood samples of ICU patients (14.63 +/- 5.88 (SD) days) compared to non-ICU patients (10.17 +/- 6.13 (SD) days).
**Correlation between viral culture and PCR**

Twelve studies also included both PCR and viral culture information. Sequential viral cultures were not performed in all studies, which is a key limitation. Growth of SARS-CoV-2 on viral respiratory culture was reported ranging from 6 days before symptom onset through day 20 after symptom onset. A position statement published in Singapore reported that viable cultured virus was not isolated past day 11. Culture data suggest that duration shedding of viable virus may vary according to illness severity. In a study of patients with moderate to severe illness, Van Kampen et al. found the median duration of shedding viable virus was 8 days (IQR: 5-11 days, range: 0-20 days) with the probability of detecting virus ≤ 5% after 15.2 days. In contrast, four studies of mildly ill patients did not find viable virus past day 8 or 9 of illness, but viral culture was not consistently reattempted. Liu, et al. described a patient with mild disease whose sputum viral culture was positive on day 18, but continued to have viral RNA detection until day 63, 45 days longer than detection of viable virus.

The correlation of SAR-CoV-2 viral loads and PCR cycle thresholds (Ct) values with isolation of viable virus is a topic of interest. The Ct value upper bound cut off that determined a positive PCR was inconsistent among studies reporting this threshold, though the majority reported values of ≤ 35 or ≤ 40. Bullard et al. compared PCR Ct value with culture positivity and found that the ability to isolate virus in culture was reduced when Ct value was > 24; they reported that the odds ratio for infectivity decreased by 32% for every 1 point increase in the Ct value. La Scola et al. report significant correlation between Ct value and culture positivity.
rates; positive cultures occurred in all samples with Ct values 13-17 but culture positivity decreased to 12% at a Ct value of 33.\textsuperscript{8} Isolating virus in culture with positive PCR samples containing viral loads <10\textsuperscript{6} copies per milliliter is less likely to be successful.\textsuperscript{4,10}

Limited data exist regarding SARS-CoV-2 cultures in non-respiratory specimens. Viral culture was attempted in serum samples of PCR positive patients without growth.\textsuperscript{6} Viral stool cultures have yielded mixed results. Wölfel et al. performed viral culture of 13 stool samples from 4 different patients with mild disease on days 6-12 without growth, despite RNA detected in the stool through day 21. Viable virus was detected in the stool of a critically ill patient on day 19 with negative cultures beyond this despite a positive NP/OP PCR through day 28.\textsuperscript{13} Two of seven studies that processed urine samples reported detecting viable virus by culture.\textsuperscript{11,47,50,51,55,62,71} Two studies of patients with positive respiratory PCR samples attempted to culture virus from tears, but yielded no growth.\textsuperscript{55,76}

**Discussion**

We summarized available data on duration of SARS-CoV-2 viral RNA shedding, isolation of viable virus and the impact of infection severity on shedding duration. The pooled median duration of RNA shedding from respiratory samples of subjects was 18.4 days (95% CI: 15.54 days - 21.3 days.) In general, the highest viral loads occur within 1-2 weeks of illness onset, regardless of symptoms, with a subsequent gradual decline. However, several studies described PCR positivity beyond 2 weeks. Patients with more severe illness shed viral RNA for a longer period of time, with a pooled median duration of 19.8 days (95% CI: 16.2 days – 23.5 days),
compared to 17.2 (95% CI: 14.0 days - 20.5 days) for mild illness. Though these medians should be interpreted with caution given the high heterogeneity of the studies and overlapping confidence intervals, viral culture data appears to support this conclusion. In reviewed studies, viable virus from respiratory cultures was not recovered past day 9 of illness for mildly ill patients but was cultured from severely ill patients through day 20.⁴,⁵,⁹,¹⁰

Interpreting positive PCR samples beyond 2-3 weeks of illness is complex. Potential explanations for these intermittently negative PCR tests include a viral load below the detection limit of the assay, specimen source, quality of specimen collection, timing of specimen collection or reinfection.⁸³,⁸⁴ Although viral culture positivity may also not correlate perfectly with transmissibility, the correlation between culture data and Ct thresholds may help predict infectiousness. Further data is needed to understand the correlation between transmission risk, culture positivity and Ct thresholds. The studies that examined viral culture were limited by small size, inclusion of patients with mostly mild illness, and lack of serial cultures on all patients. Isolation of viable virus in respiratory samples correlates with the timing of peak viral loads which occur within 1-2 weeks of illness onset. Only one study reported culturing viable virus from a respiratory sample beyond the second week of illness. Based on this information, it seems more likely that a positive PCR past 2-3 weeks of illness represents shedding of non-viable virus. Although the pooled median viral RNA shedding duration from patients with mild/moderate and severe disease do not differ greatly, reports of positive viral cultures through day 20 in severely ill patients support the potential for a prolonged infectious period
for sicker patients. In addition, viable virus has been recovered from stool cultures, but further studies are needed to determine the implications for person-to-person spread.

Our review supports the US Centers for Disease Control and Prevention (CDC) interim guidance, which recommends maintaining transmission-based precautions for 10 days after symptom onset in asymptomatic or mildly ill patients and for 20 days in severely ill patients. The decision to extend the duration of transmission-based precautions is complicated given the potentially profound impact on patients and their families, hospital systems, and public health. Prolonged home isolation may lead to longer periods of unemployment, social separation, and feelings of isolation. In the hospital, the supply of personal protective equipment, staff allocation, availability of patient beds, and the health system budget are impacted by the duration of isolation for patients with COVID-19. That said, aggressive infection control measures are required in the setting of an outbreak to control the virus and to avoid overwhelming healthcare systems.

In calculating the pooled median duration of shedding, we identified a significantly high degree of heterogeneity between studies. In a standard meta-analysis, we would not report a pooled measure of association when heterogeneity was high. However, the pooled median is not intended to inform our knowledge of causality or effect size, but rather to best inform the policy decisions that currently must be made on the very limited data available at this time in the SARS-CoV-2 pandemic. Factors contributing heterogeneity may include the variable timing of sample collection for PCR or viral culture, Ct threshold, sample types, SARS-CoV-2 genotype,
and host factors such as pharmacotherapy, comorbidities, and disease severity. We noted broad variability in the definitions of disease severity applied. While initially no formal definitions existed, the National Commission of China developed a classification scheme for mild, moderate, and severe illness that include specific clinical variables.\textsuperscript{70} The National Institutes of Health and World Health Organization have since also developed similar severity scales.\textsuperscript{85,86} Going forward, these definitions will facilitate the conduct of generalizable studies of viral dynamics.

This comprehensive review details the evidence available to date pertaining to SARS-CoV-2 viral dynamics. Although PCR positivity can be prolonged, culture data suggests that virus viability is typically shorter in duration. Continued reporting of viral shedding data via PCR and viral culture with improved standardization in methods and definitions, in coordination with transmission data, will facilitate evidence-based decision making for the infection control and public health measures necessary to control the pandemic.

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References:

1. McGrath S, Zhao X, Qin ZZ, Steele R, Benedetti A. One-sample aggregate data meta-analysis of medians. *Stat Med* 2019;38:969-984.

2. R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria., 2020. [https://www.R-project.org/](https://www.R-project.org/). Accessed 1 June, 2020.

3. McGrath SZ, X.; Steele, R.; Benedetti, A. Metamedian: Meta-Analysis of Medians. R package version 0.1.5., [https://CRAN.R-project.org/package=metamedian](https://CRAN.R-project.org/package=metamedian). Accessed 1 June, 2020.

4. van Kampen JJA, van de Vijver DAMC, Fraaij PLA, et al. Shedding of infectious virus in hospitalized patients with coronavirus disease-2019 (COVID-19): duration and key determinants. *medRxiv* 2020:2020.2006.2008.20125310.

5. Bullard J, Dust K, Funk D, et al. Predicting infectious SARS-CoV-2 from diagnostic samples. *Clin Infect Dis* 2020; Epub ahead of print.

6. Andersson M, Arancibia - Carcamo CV, Auckland K, et al. SARS-CoV-2 RNA detected in blood samples from patients with COVID-19 is not associated with infectious virus. *medRxiv* 2020:2020.2005.2021.20105486.

7. Le TQM, Takemura T, Moi ML, et al. Severe Acute Respiratory Syndrome Coronavirus 2 Shedding by Travelers, Vietnam, 2020. *Emerg Infect Dis* 2020;26:1624-1626.

8. La Scola B, Le Bideau M, Andreani J, 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. *Eur J Clin Microbiol Infect Dis* 2020;39:1059-1061.
9. Arons MM, Hatfield KM, Reddy SC, et al. Presymptomatic SARS-CoV-2 Infections and Transmission in a Skilled Nursing Facility. *N Engl J Med* 2020;382:2081-2090.

10. Wolfel R, Corman VM, Guggemos W, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature* 2020;581:465-469.

11. Team C-I. Clinical and virologic characteristics of the first 12 patients with coronavirus disease 2019 (COVID-19) in the United States. *Nat Med* 2020;26:861-868.

12. Liu WD, Chang SY, Wang JT, et al. Prolonged virus shedding even after seroconversion in a patient with COVID-19. *J Infect* 2020;18:318-356.

13. Xiao F, Sun J, Xu Y, et al. Infectious SARS-CoV-2 in Feces of Patient with Severe COVID-19. *Emerg Infect Dis* 2020;26:1920-1922.

14. Zhang N, Gong Y, Meng F, et al. Comparative study on virus shedding patterns in nasopharyngeal and fecal specimens of COVID-19 patients. *Sci China Life Sci* 2020; Epub ahead of print.

15. CATHERINE ONG WEI MIN (2020-05-23). Position Statement from the National Centre for Infectious Diseases and the Chapter of Infectious Disease Physicians AoM, Singapore: Period of Infectivity to Inform Strategies for De-isolation for COVID-19 Patients.. Position Statement from the National Centre for Infectious Diseases and the Chapter of Infectious Disease Physicians, Academy of Medicine, Singapore: Period of Infectivity to Inform Strategies for De-isolation for COVID-19 Patients. Published 2020. Accessed May 23, 2020 from

   https://scholarbank.nus.edu.sg/handle/10635/168938.

16. Chen Y, Chen L, Deng Q, et al. The presence of SARS-CoV-2 RNA in the feces of COVID-19 patients. *J Med Virol* 2020;92:833-840.
17. Sakurai A, Sasaki T, Kato S, et al. Natural History of Asymptomatic SARS-CoV-2 Infection. *N Engl J Med* 2020;383:885-886.

18. Chau NVV, Thanh Lam V, Thanh Dung N, et al. The natural history and transmission potential of asymptomatic SARS-CoV-2 infection. *Clin Infect Dis* 2020.

19. Pongpirul WA, Mott JA, Woodring JV, et al. Clinical Characteristics of Patients Hospitalized with Coronavirus Disease, Thailand. *Emerg Infect Dis* 2020;26:1580-1585.

20. Wu Y, Guo C, Tang L, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. *Lancet Gastroenterol Hepatol* 2020;5:434-435.

21. Di Tian LW, Xiankun Wang et al. Clinical research and factors associated with prolonged duration of viral shedding in patients with COVID-19, 01 June 2020, PREPRINT (Version 1) available at Research Square. *Epub ahead of print*.

22. Kim ES, Chin BS, Kang CK, et al. Clinical Course and Outcomes of Patients with Severe Acute Respiratory Syndrome Coronavirus 2 Infection: a Preliminary Report of the First 28 Patients from the Korean Cohort Study on COVID-19. *J Korean Med Sci* 2020;35:e142.

23. Talmy T, Tsur A, Shabtay O. Duration of Viral Clearance in IDF Soldiers with Mild COVID-19. *medRxiv* 2020:2020.2005.2028.20116145.

24. Fu S, Fu X, Song Y, et al. Virologic and clinical characteristics for prognosis of severe COVID-19: a retrospective observational study in Wuhan, China. *medRxiv* 2020:2020.2004.2003.20051763.

25. Huang J, Mao T, Li S, et al. Long period dynamics of viral load and antibodies for SARS-CoV-2 infection: an observational cohort study. *medRxiv* 2020:2020.2004.2022.20071258.
26. Corsini Campioli C, Cano Cevallos E, Assi M, Patel R, Binnicker MJ, O’Horo JC. Clinical predictors and timing of cessation of viral RNA shedding in patients with COVID-19. *J Clin Virol* 2020;130:104577.

27. Fu Y, Han P, Zhu R, et al. Risk factors for viral RNA shedding in COVID-19 patients. *Eur Respir J* 2020;56.

28. Wang K, Zhang X, Sun J, et al. Differences of Severe Acute Respiratory Syndrome Coronavirus 2 Shedding Duration in Sputum and Nasopharyngeal Swab Specimens Among Adult Inpatients With Coronavirus Disease 2019. *Chest* 2020; *Epub ahead of print*.

29. Huang JT, Ran RX, Lv ZH, et al. Chronological Changes of Viral Shedding in Adult Inpatients with COVID-19 in Wuhan, China. *Clin Infect Dis* 2020; *Epub ahead of print*.

30. Han J, Shi LX, Xie Y, et al. Analysis of factors affecting the prognosis of COVID-19 patients and viral shedding duration. *Epidemiol Infect* 2020;148:e125.

31. Park SY, Yun SG, Shin JW, et al. Persistent severe acute respiratory syndrome coronavirus 2 detection after resolution of coronavirus disease 2019-associated symptoms/signs. *Korean J Intern Med* 2020;35:793-796.

32. Danzetta ML, Amato L, Cito F, et al. SARS-CoV-2 RNA Persistence in Naso-Pharyngeal Swabs. *Microorganisms* 2020;8.

33. Young BE, Ong SWX, Kalimuddin S, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *JAMA* 2020;323:1488-1494.

34. Lin A, He ZB, Zhang S, Zhang JG, Zhang X, Yan WH. Early risk factors for the duration of SARS-CoV-2 viral positivity in COVID-19 patients. *Clin Infect Dis* 2020; *Epub ahead of print*.
35. Noh JY, Yoon JG, Seong H, et al. Asymptomatic infection and atypical manifestations of COVID-19: Comparison of viral shedding duration. *J Infect* 2020; *Epub ahead of print*.

36. Zhao F, Yang Y, Wang Z, Li L, Liu L, Liu Y. The Time Sequences of Oral and Fecal Viral Shedding in Patients With Coronavirus Disease 2019. *Gastroenterology* 2020;159:1158-1160.

37. Li W, Su YY, Zhi SS, et al. Virus shedding dynamics in asymptomatic and mildly symptomatic patients infected with SARS-CoV-2. *Clin Microbiol Infect* 2020; *Epub ahead of print*.

38. Long QX, Tang XJ, Shi QL, et al. Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections. *Nat Med* 2020;26:1200-1204.

39. Gombar S, Chang M, Hogan CA, et al. Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19. *J Clin Virol* 2020;129:104477.

40. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054-1062.

41. Hung IF, Cheng VC, Li X, et al. SARS-CoV-2 shedding and seroconversion among passengers quarantined after disembarking a cruise ship: a case series. *Lancet Infect Dis* 2020;20:1051-1060.

42. Ridgway JP, Shah NS, Robicsek AA. Prolonged shedding of severe acute respiratory coronavirus virus 2 (SARS-CoV-2) RNA among patients with coronavirus disease 2019 (COVID-19). *Infect Control Hosp Epidemiol* 2020:1-2.

43. Lee S, Kim T, Lee E, 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 Intern Med* 2020; *Epub ahead of print*. 

Downloaded from https://www.cambridge.org/core. 22 Oct 2020 at 06:22:37, subject to the Cambridge Core terms of use.
44. Ikegami S, Benirschke R, Flanagan T, et al. Persistence of SARS-CoV-2 nasopharyngeal swab PCR positivity in COVID-19 convalescent plasma donors. Transfusion 2020;Epub ahead of print.

45. Qian GQ, Chen XQ, Lv DF, et al. Duration of SARS-CoV-2 viral shedding during COVID-19 infection. Infect Dis (Lond) 2020;52:511-512.

46. Chang, Mo G, Yuan X, et al. Time Kinetics of Viral Clearance and Resolution of Symptoms in Novel Coronavirus Infection. Am J Respir Crit Care Med 2020;201:1150-1152.

47. Ling Y, Xu SB, Lin YX, et al. Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients. Chin Med J (Engl) 2020;133:1039-1043.

48. Li N, Wang X, Lv T. Prolonged SARS-CoV-2 RNA shedding: Not a rare phenomenon. J Med Virol 2020;92:2286-2287.

49. Zhou B, She J, Wang Y, Ma X. The duration of viral shedding of discharged patients with severe COVID-19. Clin Infect Dis 2020; Epub ahead of print.

50. Zheng S, Fan J, Yu F, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. BMJ 2020;369:m1443.

51. Lo IL, Lio CF, Cheong HH, et al. Evaluation of SARS-CoV-2 RNA shedding in clinical specimens and clinical characteristics of 10 patients with COVID-19 in Macau. Int J Biol Sci 2020;16:1698-1707.

52. Xu K, Chen Y, Yuan J, et al. Factors associated with prolonged viral RNA shedding in patients with COVID-19. Clin Infect Dis 2020;71:799-806.
53. Xiao AT, Tong YX, Zhang S. Profile of RT-PCR for SARS-CoV-2: a preliminary study from 56 COVID-19 patients. Clin Infect Dis 2020; Epub ahead of print.

54. Qi L, Yang Y, Jiang D, et al. Factors associated with duration of viral shedding in adults with COVID-19 outside of Wuhan, China: A retrospective cohort study. Int J Infect Dis 2020;96:531-537.

55. Fang Z, Zhang Y, Hang C, Ai J, Li S, Zhang W. Comparisons of viral shedding time of SARS-CoV-2 of different samples in ICU and non-ICU patients. J Infect 2020;81:147-148.

56. Miyamae Y, Hayashi T, Yonezawa H, et al. Duration of viral shedding in asymptomatic or mild cases of novel coronavirus disease 2019 (COVID-19) from a cruise ship: A single-hospital experience in Tokyo, Japan. Int J Infect Dis 2020;97:293-295.

57. Wang J, Hang X, Wei B, et al. Persistent SARS-COV-2 RNA positivity in a patient for 92 days after disease onset: A case report. Medicine (Baltimore) 2020;99:e21865.

58. Wang C, Xu M, Zhang Z. A case of COVID-19 with long duration of viral shedding. J Microbiol Immunol Infect 2020; Epub ahead of print.

59. Yao XH, He ZC, Li TY, et al. Pathological evidence for residual SARS-CoV-2 in pulmonary tissues of a ready-for-discharge patient. Cell Res 2020;30:541-543.

60. Arashiro T, Furukawa K, Nakamura A. COVID-19 in 2 Persons with Mild Upper Respiratory Tract Symptoms on a Cruise Ship, Japan. Emerg Infect Dis 2020;26:1345-1348.

61. Lan L, Xu D, Ye G, et al. Positive RT-PCR Test Results in Patients Recovered From COVID-19. JAMA 2020;323:1502-1503.
62. To KK, Tsang OT, Leung WS, 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. *Lancet Infect Dis* 2020;20:565-574.

63. Zou L, Ruan F, Huang M, et al. SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *N Engl J Med* 2020;382:1177-1179.

64. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med* 2020;26:672-675.

65. Wang Y, Zhang L, Sang L, et al. Kinetics of viral load and antibody response in relation to COVID-19 severity. *J Clin Invest* 2020.

66. Sun J, Xiao J, Sun R, et al. Prolonged Persistence of SARS-CoV-2 RNA in Body Fluids. *Emerg Infect Dis* 2020;26:1834-1838.

67. Zhang WY, Yu LQ, Huang JA, Zeng DX. Prolonged Viral RNA Shedding Duration in COVID-19. *Am J Ther* 2020; Epub ahead of print.

68. Liu Y, Chen X, Zou X, Luo H. A severe-type COVID-19 case with prolonged virus shedding. *J Formos Med Assoc* 2020;119:155-1557.

69. Zhang L, Li C, Zhou Y, Wang B, Zhang J. Persistent viral shedding lasting over 60 days in a mild COVID-19 patient with ongoing positive SARS-CoV-2. *Quant Imaging Med Surg* 2020;10:1141-1144.

70. Tan W, Lu Y, Zhang J, et al. Viral Kinetics and Antibody Responses in Patients with COVID-19. *medRxiv* 2020:2020.2003.2024.20042382.

71. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in Different Types of Clinical Specimens. *JAMA* 2020;323:1843-1844.
72. Park SK, Lee CW, Park DI, et al. Detection of SARS-CoV-2 in Fecal Samples From Patients With Asymptomatic and Mild COVID-19 in Korea. Clin Gastroenterol Hepatol 2020; Epub ahead of print.

73. Zhang J, Wang S, Xue Y. Fecal specimen diagnosis 2019 novel coronavirus-infected pneumonia. J Med Virol 2020;92:680-682.

74. Jiang X, Luo M, Zou Z, Wang X, Chen C, Qiu J. Asymptomatic SARS-CoV-2 infected case with viral detection positive in stool but negative in nasopharyngeal samples lasts for 42 days. J Med Virol 2020;92:1807-1809.

75. Zhang W, Du RH, Li B, et al. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microbes Infect 2020;9:386-389.

76. Seah IYJ, Anderson DE, Kang AEZ, et al. Assessing Viral Shedding and Infectivity of Tears in Coronavirus Disease 2019 (COVID-19) Patients. Ophthalmology 2020;127:977-979.

77. Zhou R, Li F, Chen F, et al. Viral dynamics in asymptomatic patients with COVID-19. Int J Infect Dis 2020;96:288-290.

78. Zheng X, Chen J, Deng L, et al. Risk factors for the COVID-19 severity and its correlation with viral shedding: a retrospective cohort study. J Med Virol 2020:1-10.

79. Liu F, Cai ZB, Huang JS, et al. Repeated COVID-19 relapse during post-discharge surveillance with viral shedding lasting for 67 days in a recovered patient infected with SARS-CoV-2. J Microbiol Immunol Infect 2020; Epub ahead of print.

80. Li J, Zhang L, Liu B, Song D. Case Report: Viral Shedding for 60 Days in a Woman with COVID-19. Am J Trop Med Hyg 2020;102:1210-1213.
81. Korea Centers for Disease Control and Prevention. Findings from Investigation and Analysis of re-positive cases. Available at: https://www.cdc.go.kr/board/board.es?mid=a30402000000&bid=0030&act=view&list_no=367267&nPage=1. Published 2020. Accessed September 8, 2020.

82. Hogan CA, Stevens BA, Sahoo MK, et al. High Frequency of SARS-CoV-2 RNAemia and Association With Severe Disease. *Clin Infect Dis* 2020; *Epub ahead of print*.

83. Prinzi A. False Negatives and Reinfections: the Challenges of SARS-CoV-2 RT-PCR Testing. Retrieved from. Published April 24th, 2020. https://asm.org/Articles/2020/April/False-Negatives-and-Reinfections-the-Challenges-of. Accessed September 22, 2020.

84. Bullis SSM, Crothers JW, Wayne S, Hale AJ. A cautionary tale of false-negative nasopharyngeal COVID-19 testing. *IDCases* 2020;20:e00791.

85. Center for Disease Control. Discontinuation of Transmission-Based Precautions and Disposition of Patients with COVID-19 in Healthcare Setting (Interim Guidance). Published 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-hospitalized-patients.html. Accessed September 22, 2020.

86. Wang Y, Zhang L, Sang L, et al. Kinetics of viral load and antibody response in relation to COVID-19 severity. *J Clin Invest* 2020; *Epub ahead of print*.
**Box 1: Brief Summary of Available Literature on SARS-CoV-2 Shedding**

| Duration of Viral Shedding in Respiratory Samples | Duration of Viral Shedding in Stool/Rectal Samples |
|--------------------------------------------------|--------------------------------------------------|
| The pooled median duration of viral RNA shedding in all severities of illness from respiratory isolates is 18.4 days (95%CI: 15.5 days, 21.3 days). Intermittent RNA shedding up to 92 days post symptom onset has been observed. | Viral RNA shedding in stool has not been consistently observed. The pooled median duration of viral RNA shedding is 22.1 days (95%CI: 14.4 days, 29.8 days). Viral RNA shedding up to 55 days after diagnosis has been observed. |
| Viable virus has been isolated via culture from -6 days to 20 days relative to symptom onset. | Viable virus has been isolated via culture of stool on day 19 of illness. |
| Duration of RNA shedding exceeds the duration of viable virus shedding from 13 to 45 days. | Detection of stool RNA may lag behind detection of respiratory RNA by PCR. |
| Study                         | Country            | Design                  | Patient Population                  | No. of Patients | Severity of Illness | Specimen Sources | Testing Methods          |
|------------------------------|--------------------|-------------------------|------------------------------------|-----------------|---------------------|-------------------|--------------------------|
| Andersson M et al.⁶          | United Kingdom     | Prospective case series | Hospitalized, outpatient, recovered | 278             | Not defined         | Serum             | PCR, Viral culture       |
| Arashiro T et al.⁶           | Japan              | Case report             | Hospitalized                       | 2               | Mild                | Not specified      | PCR                     |
| Arons MM et al.⁹             | United States      | Point prevalence       | Skilled nursing facility residents  | 76              | Not defined         | NP, OP            | PCR, Viral culture if PCR + |
| Bullard J et al.⁷            | Canada             | Retrospective cross-sectional | Not specified            | 90              | Not defined         | NP, ET tube       | PCR                     |
| Campioli C et al.²⁶          | United States      | Retrospective case series | Hospitalized, outpatient           | 251             | Not defined         | NP                | PCR                     |
| Chang M et al.⁶              | China              | Prospective case series | Hospitalized                       | 16              | Not defined         | Throat            | PCR                     |
| Chau NVV et al.⁸             | Vietnam            | Prospective case series | Quarantine center                  | 30              | Asymptomatic, mild | Saliva, NP        | PCR                     |
| Chen Y et al.⁶               | China              | Retrospective cohort study | Hospitalized                     | 42              | Uncomplicated, mild, severe | NP, Urine, Stool | PCR                     |
| COVID-19 Investigation Team¹² | United States      | Retrospective case series | Mixed – hospitalized and home isolation | 12              | Not defined         | OP, NP, Serum, Stool, Urine | PCR, Viral culture, Whole genome sequencing |
| Danzetta ML et al.³²         | Italy              | Retrospective case series | Hospitalized and outpatient        | 14,200 tested; 605 positives | Not defined         | NP, OP              | PCR                     |
| Di Tian LW et al.²¹          | China              | Prospective case series | Hospitalized                       | 75              | Mild, moderate, severe, critical | Not specified | PCR                     |
| Study          | Country | Study Design       | Setting | Sample Size | Disease Severity | Sample Site(s) | Method |
|---------------|---------|--------------------|---------|-------------|------------------|----------------|--------|
| Fang Z et al. | China   | Prospective case series | Hospitalized | 32          | ICU or non-ICU   | NP             | PCR    |
| Fu S et al.   | China   | Retrospective case series | Hospitalized | 50          | Severe           | NP             | PCR    |
| Fu Y et al.   | China   | Retrospective case series | Hospitalized | 410         | Not defined      | Throat         | PCR    |
| Gombar S et al. | United States | Retrospective case series | Not specified, but primarily outpatient | 150         | Not defined      | NP             | PCR    |
| Han J et al.  | China   | Retrospective case series | Hospitalized | 185         | Mild, moderate, severe, critical | Respiratory     | PCR    |
| He X et al.   | China   | Prospective case series | Hospitalized | 94          | Moderate         | Throat         | PCR    |
| Huang J et al. | China   | Retrospective case series | Hospitalized | 33          | Moderate and severe | Throat         | PCR    |
| Huang JT et al. | China   | Retrospective case series | Hospitalized | 308         | General, severe, critically ill | Nasal Pharyngeal | PCR    |
| Hung IF et al. | Hong Kong | Prospective case series | Hospitalized | 9           | Symptomatic and asymptomatic | NP Throat      | PCR    |
| Ikegami S et al. | United States | Prospective case series | Outpatient | 272         | Recovered        | NP             | PCR    |
| Jiang X et al. | China   | Case report         | Home isolation | 1           | Asymptomatic     | NP             | PCR    |
| Kim ES et al. | Korea   | Retrospective case series | Hospitalized | 28          | From 1 (no limit of activity) to 8 (death) | NP Sputum | PCR    |
| Study                        | Country | Study Design   | Setting       | n   | Case Definition         | Specimens          | Test Method       |
|------------------------------|---------|----------------|---------------|-----|-------------------------|--------------------|-------------------|
| Lan L et al.                 | China   | Prospective    | Hospitalized  | 4   | Asymptomatic            | Throat             | PCR               |
|                              |         | case series    | Home isolation|     | Symptomatic             |                    |                   |
| La Scola B et al.            | France  | Prospective    | Hospitalized  | 155 | Not defined             | NP                 | PCR               |
|                              |         | case series    |               |     | Sputum                  |                    | Viral culture     |
| Le TQM et al.                | Vietnam | Prospective    | Hospitalized  | 12  | 1 asymptomatic, rest not specified | Throat             | PCR               |
|                              |         | case series    |               |     |                         |                    | Viral culture     |
| Lee S et al.                 | Korea   | Retrospective  | Community     | 303 | Symptomatic and asymptomatic | NP                 | PCR               |
|                              |         | case series    | treatment center|    |                          | OP                 |                   |
| Li N et al.                  | China   | Retrospective  | Hospitalized  | 36  | Mild or severe          | Respiratory        | PCR               |
|                              |         | case series    |               |     |                          | Saliva             |                   |
| Li J et al.                  | China   | Case report    | Hospitalized  | 1   | Mild/moderate           | NP                 | PCR               |
|                              |         |                |               |     |                          | OP                 |                   |
| Li W et al.                  | China   | Retrospective  | Hospitalized  | 18  | Asymptomatic or mild    | NP                 | PCR               |
|                              |         | case series    |               |     |                          | Nasal              |                   |
|                              |         |                |               |     |                          | Sputum             |                   |
|                              |         |                |               |     |                          | Throat             |                   |
|                              |         |                |               |     |                          | Anal               |                   |
| Lin A et al.                 | China   | Prospective    | Hospitalized  | 137 | Mild or severe          | Not specified      | PCR               |
|                              |         | case series    |               |     |                          |                    |                   |
| Ling Y et al.                | China   | Prospective    | Hospitalized  | 66  | Not defined             | OP                 | PCR               |
|                              |         | case series    |               |     |                          | Blood              |                   |
|                              |         |                |               |     |                          | Urine              |                   |
|                              |         |                |               |     |                          | Stool              |                   |
| Liu WD et al.                | Taiwan  | Case report    | Hospitalized  | 1   | Not defined             | Sputum             | PCR               |
|                              |         |                |               |     |                          | Throat             |                   |
|                              |         |                |               |     |                          | Stool              |                   |
| Liu Y et al.                 | China   | Case report    | Hospitalized  | 1   | Severe                  | OP                 | PCR               |
|                              |         |                |               |     |                          |                    |                   |
| Liu F et al.                 | China   | Case report    | Hospitalized  | 1   | Moderate                | NP                 | PCR               |
| Lo IL et al.                 | China   | Prospective    | Hospitalized  | 10  | Mild, moderate, or severe | NP                 | PCR               |
|                              |         | case series    |               |     |                          | Urine              |                   |
|                              |         |                |               |     |                          | Stool              |                   |
| Study                  | Country | Study Design               | Setting            | Sample Size | Symptoms                          | Specimen          | Test   |
|------------------------|---------|---------------------------|--------------------|-------------|-----------------------------------|-------------------|--------|
| Long QX et al. 18       | China   | Point prevalence         | Hospitalized      | 178         | Asymptomatic, mild                | NP                | PCR    |
| Min C et al. 15         | Singapore | Retrospective case series and position statement | Not specified | 766         | Not specified                      | NP                | PCR    |
| Miyamae Y et al. 16     | Japan   | Prospective case series   | Hospitalized      | 23          | Asymptomatic, mild                | NP, OP            | PCR    |
| Noh JY et al. 17        | Korea   | Retrospective case series | Residential treatment center | 199         | Asymptomatic or atypical symptoms | Not defined       | PCR    |
| Park SY et al. 15       | Korea   | Prospective case series   | Hospitalized      | 6           | Not defined                        | NP, OP            | PCR    |
| Park SK et al. 17       | Korea   | Prospective case series   | Outpatient        | 46          | Asymptomatic and mild             | Respiratory, Stool | PCR    |
| Pongpirul WA et al. 19  | Thailand| Prospective case series   | Hospitalized      | 11          | Asymptomatic, mild, moderate      | Upper respiratory | PCR    |
| Qi L et al. 24          | China   | Retrospective case series | Hospitalized      | 147         | Mild, moderate, or severe         | Respiratory       | PCR    |
| Qian GQ et al. 25       | China   | Retrospective case series | Hospitalized      | 24          | Not defined                        | Throat, Rectal    | PCR    |
| Ridgway JP et al. 27    | United States | Retrospective case series | Hospitalized and outpatient | 555         | Not defined                        | NP                | PCR    |
| Sakurai A et al. 17     | Japan   | Retrospective case series | Cruise ship       | 90          | Asymptomatic                       | NP                | PCR    |
| Seah IYJ et al. 26      | Singapore | Prospective case series   | Hospitalized Discharged | 17          | Not defined                        | Tears             | PCR    |
| Sun J et al. 28         | China   | Prospective case series   | Hospitalized      | 49          | Mild or severe                     | NP, Throat, Stool | PCR    |
| Author(s)          | Country | Study Type          | Setting       | Number | Severity | Sample Sites | Diagnostic Methods |
|-------------------|---------|---------------------|---------------|--------|----------|--------------|-------------------|
| Talmy T et al.    | Israel  | Retrospective case  | Hospitalized  | 219    | Mild     | NP, OP       | PCR              |
| Tan W et al.      | China   | Prospective case    | Hospitalized  | 67     | Mild, moderate, severe | NP, Sputum, Blood, Urine, Stool | PCR |
| To KK et al.      | Hong Kong | Prospective case    | Hospitalized  | 23     | Mild or severe | OP, Saliva     | PCR |
| Van Kampen JJA et al. | Netherlands | Prospective case | Hospitalized | 129    | Mechanically ventilated, ICU with oxygen therapy, ward with oxygen therapy, ward without oxygen therapy | NP, Sputum | PCR, Viral culture |
| Wang W et al.     | China   | Prospective case    | Hospitalized  | 205    | Severe, Non-severe | Nasal, Blood, Sputum, Stool, Urine | PCR |
| Wang J et al.     | China   | Case report         | Hospitalized  | 1      | Mild     | NP           | PCR              |
| Wang K et al.     | China   | Prospective case    | Hospitalized  | 68     | CURB-65 scores 1-3 | NP, Sputum | PCR |
| Wang C et al.     | China   | Case report         | Hospitalized  | 1      | Mild     | NP, OP       | PCR              |
| Wang Y et al.     | China   | Prospective case    | Hospitalized  | 23     | Mild and severe | NP, Sputum, Throat, Fecal | PCR |
| Authors       | Country | Study Design            | Clinical Condition         | Hospitalized | Specimens                  | Method          |
|--------------|---------|-------------------------|-----------------------------|--------------|----------------------------|-----------------|
| Wölfl R et al. | Germany | Prospective case series | Hospitalized                | 9            | Mild                       | Sputum, NP, Throat, Stool, PCR, Viral culture, Whole genome sequencing |
| Wu Y et al.  | China   | Prospective case series | Hospitalized                | 98           | Not defined                | Throat, Stool, PCR |
| Xiao F et al. | China   | Prospective case series | Hospitalized                | 28           | Not defined                | NP, OP, Stool, PCR, Viral culture |
| Xiao AT et al. | China   | Prospective case series | Hospitalized                | 56           | Mild to moderate           | NP, Throat, PCR  |
| Xu K et al.  | China   | Retrospective case series | Hospitalized                | 113          | Mild, pneumonia, severe pneumonia, ARDS, septic shock | Sputum, NP, Throat, BAL, PCR |
| Young BE et al. | Singapore | Prospective case series | Hospitalized                | 18           | Not defined                | NP, Urine, Stool, Blood, PCR |
| Zhang L et al. | China   | Case report              | Hospitalized                | 1            | Mild                       | Throat, PCR     |
| Zhang J et al. | China   | Retrospective case series | Hospitalized                | 14           | Not defined                | OP, Stool, PCR  |
| Zhang WY et al. | China   | Case report              | Hospitalized                | 1            | Mild                       | Pharyngeal, PCR |
| Zhang W et al. | China   | Prospective case series | Hospitalized                | 39           | Severe, Non-severe, Clinical condition unknown | Oral, Rectal, PCR |
| Zhang N et al. | China   | Prospective case series | Hospitalized                | 23           | Mild, moderate, critical   | Upper respiratory, Urine, Stool, PCR, Viral Culture |
| Authors          | Country | Study Design          | Treatment | Sample Size | Symptoms | Site(s) Tested | Method(s) |
|------------------|---------|-----------------------|-----------|-------------|----------|----------------|------------|
| Zhao F et al.     | China   | Retrospective case series | Hospitalized | 401         | Mild, moderate, severe | Respiratory, Fecal | PCR        |
| Zheng S et al.    | China   | Retrospective case series | Hospitalized | 96          | Mild, severe | Respiratory, Blood, Urine, Stool | PCR        |
| Zheng X et al.    | China   | Retrospective case series | Hospitalized | 80          | Common, severe | Throat | PCR        |
| Zhou B et al.     | China   | Prospective case series | Hospitalized | 41          | Severe | Throat | PCR        |
| Zhou F et al.     | China   | Retrospective case series | Hospitalized | 191         | Mild, moderate, severe, critical | Respiratory | PCR        |
| Zhou R et al.     | China   | Retrospective case series | Hospitalized | 31          | Asymptomatic | NP | PCR        |
| Yao XH et al.     | China   | Case report            | Hospitalized | 1           | Severe | NP, Lung, Liver, Heart, Intestine, Skin | PCR        |
| Zou L et al.      | China   | Prospective case series | Hospitalized | 18          | Asymptomatic, mild-to-moderate, severe | NP | PCR        |

Legend: NP, nasopharyngeal; OP, oropharyngeal; PCR, polymerase chain reaction; ET, endotracheal
### Appendix Table. Studies contributing to calculations of pooled median duration of viral shedding of SARS-CoV-2

| Study          | Disease Severity | Sample type | Days of Viral RNA Shedding | Inclusion in Pooled Median Analysis |
|----------------|------------------|-------------|-----------------------------|------------------------------------|
|                |                  |             | Mean | SD | Min | Q1   | Median | Q3   | Max | N   | Respiratory Sample Data | Fecal/Rectal Sample Data |
|                |                  |             |      |   |     |      |        |      |     |     | All severity of illness | Severe Illness | Mild/Moderate Illness |
| Chang M et al. | ND               | Throat      | --   | -- | --  | 4    | 5.5    | 8    | --  | 16  | ✓                  |              |
| Chen Y et al.  | All              | Stool       | --   | -- | --  | 7    | 11     | 13   | --  | 28  | ✓                  | ✓                |
|                | Mild             | NP          | --   | -- | --  | 6    | 8      | 10.5 | --  | 29  | ✓                  | ✓                |
|                | Severe           | NP          | --   | -- | --  | 11   | 13     | 15   | --  | 11  | ✓                  | ✓                |
| Dinzetta ML et al. | All         | OP/NP      | --   | -- | 14  | --   | 30     | --   | 63  | 108 | ✓                  |              |
| Di Tian LW et al. | Moderate      | US          | --   | -- | 1   | 9.5  | 25     | 42   | 63  | 45  | ✓                  | ✓                |
|                | Severe           | US          | --   | -- | 2   | 9.21 | 14     | 21.25| 62  | 20  | ✓                  | ✓                |
| Fang Z et al.  | Mild/Moderate    | Nasal       | 15.67| 6.68| --  | --   | --     | --   | --  | 24  | ✓                  | ✓                |
|                | Severe           | Nasal       | 22.25| 3.62| --  | --   | --     | --   | --  | 8   | ✓                  | ✓                |
| Fu Y et al.    | All              | Throat      | --   | -- | 3   | 16   | 19     | 23   | 44  | 410 | ✓                  |              |
| Han J et al.   | Mild/moderate    | NP/sputum   | --   | -- | 4   | --   | 16     | --   | 51  | 155 | ✓                  |            |
|                | Severe           | NP/sputum   | --   | -- | 4   | --   | 18     | --   | 51  | 30  | ✓                  | ✓                |
| Huang J et al. | Moderate/severe  | Stool       | --   | -- | 11.5| 17   | 32     | --   | 33  | ✓   |              |              |

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| Severity            | Sample Type | Li N et al. | Lin A et al. | Ling Y et al. | Lo IL et al. | Long QX et al. | Miyamae Y et al. | Pongpirul WA et al. | Qi L et al. | Qian GQ et al. | Sakaurai A et al. | Talmy T et al. | Tan W et al. | Wang K et al. |
|---------------------|-------------|-------------|--------------|---------------|--------------|----------------|-------------------|---------------------|-------------|---------------|-------------------|----------------|-------------|---------------|
| Moderate/severe     | Sputum      |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
|                     | --          | --          | -- 18.5      | 22            | 27.5         | -- 33          | ✓                 |                     |             |               |                   |                |             |               |
| Saliva              |             |             | -- 47.75     | 53.5          | 60.5         | -- 36          | ✓                 |                     |             |               |                   |                |             |               |
| US                  |             | All         |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild                | US          |             | 5            | 15            | 38           | 114            | ✓                 |                     |             |               |                   |                |             |               |
| Severe/Critical     | US          |             |              |               |              |                |                   |                     |             |               |                   |                |             | ✓             |
| ND                  | OP          |             | 2            | 6             | 9.5          | 11             | 22                | 66                  | ✓             |               |                   |                |             |               |
| All                 | NP          |              | 18.2         | 4.6           | --           | --             | --                | 10                  | ✓             |               |                   |                |             |               |
| Asymptomatic        | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild                | NP          |             | 6            | 15            | 19           | 26             | 45                | 37                  | ✓             |               |                   |                |             |               |
| Mild/asymptomatic   | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild/moderate       | OP/NP       |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| OP/OP              |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| OP/NP              |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Throat           |              |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| ND                  | Throat      |             | 4            | 9             | 12           | 14             | 34                | 24                  | ✓             |               |                   |                |             |               |
| Asymptomatic        | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild                | NP          |             | 6            | 19            | 37           | --             | 23                | ✓                   |               |               |                   |                |             |               |
| Mild/moderate       | OP/NP       |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| OP/OP              |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| OP/NP              |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Throat           |              |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Asymptomatic        | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild                | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild/moderate       | NP/Sputum   |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Sputum           |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Sputum           |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Throat           |              |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Asymptomatic        | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild                | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild/moderate       | NP/Sputum   |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Sputum           |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Sputum           |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Throat           |              |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Asymptomatic        | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild                | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild/moderate       | OP/NP       |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| OP/OP              |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| OP/NP              |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Throat           |              |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Asymptomatic        | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild                | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild/moderate       | NP/Sputum   |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Sputum           |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Sputum           |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Throat           |              |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Asymptomatic        | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild                | NP          |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Mild/moderate       | NP/Sputum   |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Sputum           |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Sputum           |             |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| NP/Throat           |              |             |              |               |              |                |                   |                     |             |               |                   |                |             |               |
| Study          | Source                     | Severity       | Respiratory Source | Minimum | Q1  | Median | Q3     | Maximum |
|---------------|----------------------------|----------------|--------------------|---------|-----|--------|--------|---------|
| Wu Y et al.   | ND                         | Feces          | 27.9               | 10.7    | --  | --     | --     | 74      |
| Xiao AT et al.| Mild/Moderate              | NP/Throat      | --                 | --      | 18  | 24     | 31     | 56      |
| Xu K et al.   | All                        | Sputum/NP/Throat/BAL | --         | --      | 13  | 17     | 32     | 113     |
| Young BE et al.| All                       | NP             | --                 | --      | 1   | 12     | 24     | 18      |
| Zhang N et al.| All                        | NP/throat      | --                 | --      | 8   | 10     | 17     | 11      |
|               | All                        | Feces          | --                 | --      | 15.5| 22     | 23.5   | 11      |
| Zhao F et al. | All                        | Rectal         | --                 | --      | 23  | 33     | 52     | 80      |
| Zheng X et al.| Severe                     | Throat         | --                 | --      | 14  | 21     | 30     | 74      |
| Zhou B et al. | Severe                     | Throat         | --                 | --      | 18  | 24     | 31     | 48      |
| Zhou F et al. | All                        | US             | --                 | --      | 16  | 20     | 23     | 191     |
|               | Critical                   | US             | --                 | --      | 22  | 24     | 30     | 53      |
|               | Severe                     | US             | --                 | --      | 17  | 19     | 22     | 66      |

ND: Not defined
Min: Minimum
Q1: Quartile 1
Q3: Quartile 3
Max: Maximum
BAL: bronchoalveolar lavage
US: Unspecified respiratory source