

Rapid Review Report

Review Title:	What is the period of communicability of symptomatic SARS CoV-2?
Keyword Title:	
Review ID:	INF042401 RR
Date/Time:	April 27, 2020
Version: [to be used for updated reviews]	1
Revision History:	None
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Cite As:	Williams-Roberts, H; Lee, S; Young, C; Dalidowicz, M; Mueller, M. What is the period of communicability of symptomatic SARS CoV-2? 2020 Apr 27; Document no.: INF042401 RR. In: COVID-19 Rapid Evidence Reviews [Internet]. SK: SK COVID Evidence Support Team, c2020. 24 p. (CEST rapid review report)

Key Findings

- The period of communicability of symptomatic SARS CoV-2 infections remains unclear.
- Viral RNA shedding measured from the onset of illness is a common proxy used to estimate the period of communicability; however, confirmation of the viability of viral remnants in secretions through culture or other methods seldom occurs in practice.
- Several factors including age, male sex and clinical severity influence individual variation in viral shedding and suggest the need for tailored control efforts.
- Temporal patterns in viral shedding across different types of bodily secretions has implications for transmissibility and criteria for discontinuation of control measures during convalescence.

Limitations

- Small samples and marked heterogeneity across studies limit comparisons and broader inferences.
- Overrepresentation of hospitalized patients among samples may have selected for more severe clinical course.

GRADE of Evidence: C - Low

A grade of "C" is assigned when further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate. The review may consist of one or more studies with severe limitations.

For more information about how this rating was determined, visit https://www.essentialevidenceplus.com/product/ebm_loe.cfm?show=grade

Background/Context

In December 2019, a novel coronavirus was first identified in Wuhan, China. The novel pathogen Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2) has since spread causing a global pandemic and prompted studies about its epidemiology and transmission dynamics in order to develop effective control measures. The period of communicability refers to the time during which the virus can be transferred directly or indirectly from an infected person. It represents a critical piece of information that is needed for optimal control of COVID 19 spread and has implications for the period required for isolation.

Purpose

The purpose of the review is to identify the best available evidence and scientific knowledge about the period of communicability or infectiousness of SARS CoV-2 and/ or duration of viral shedding with the goal of determining the minimum period required for isolation. The main method of control remains isolation of infected persons and close contacts. Given the social and economic consequences of these measures, a better understanding of when and how long we should isolate an individual with COVID-19 infection or close contacts is needed to guide mitigation efforts.

Review Question(s)

- What is the period of communicability of symptomatic SARS CoV-2?

Method

A rapid review is a type of knowledge synthesis for which the steps of the systematic review are streamlined or accelerated to produce evidence in a shortened timeframe [1]. In times of crisis, rapid reviews can provide strategic evidence to guide health system response and inform critical decisions. Knowledge about the novel SARS-CoV-2 is evolving and there remain many questions about its transmission dynamics and effective control measures. An expedited review of the literature related to the period of communicability of SARS-CoV-2 was requested to inform local planning efforts. The review was produced in 72 hours.

The search strategy was developed by a team of medical librarians in collaboration with an infectious disease specialist. Peer reviewed literature was searched in PubMed, Medline, CINAHL and EMBASE. The

search was also supplemented with grey literature sources including websites of organizations and agencies that produce guidelines and recommendations such as Centers for Disease Control and Prevention, World Health Organization, European Centres for Disease Control, Health Canada, Public Health Agency of Canada as well as content specific databases such as LitCovid, medRxiv. In addition, Google and Google Scholar engines were searched as well as references and citation lists to ensure relevant articles were not missed in the primary search. The full list of search terms can be found in the Evidence Search Report. Few limits were applied in the review outside of English language and time in selected databases.

Findings

Thirty three studies that were included in the review. Tables 1A & B summarize key characteristics reported in studies or documents. Four technical reports/summaries were identified among eligible records; however, **the period of communicability of SARS CoV-2 was seldom quantified** with any precision. A Canadian technical report did not define the earliest period of communicability but reported that later boundary as 10 days after onset of illness provided symptoms were no longer present [2]. It was recommended that consecutive negative lab tests at least 24 hours apart could objectively signal the end of the communicable period. Another Canadian overview identified the earliest period for communicability as possibly occurring five days before onset and lasting for several weeks after onset of symptoms [3]. Two technical reports reported on viral shedding measured by onset of illness or hospital admission [4, 5]. The EU document translates the information about viral clearance into discharge recommendations for persons with COVID-19 such that clinical resolution is required as well as laboratory evidence of viral clearance with 2-4 consecutive negative RT-PCR tests on respiratory samples at least 24 hours apart [4]. The WHO report acknowledges an early period for communicability as within 3 days before symptom onset but did not provide an end for when someone is no longer capable of infecting another person [5].

The majority of primary studies occurred in China with few other countries including France, Singapore, Italy and United States [13, 16, 19, 28]. There was marked heterogeneity in the number of study participants (ranging from 1 to 410), type of testing, sampling procedures, timing and clinical severity and management. This makes study comparisons challenging. The majority of studies were case series or other retrospective observational studies of adult patients who were treated in hospital settings. There were three studies that pertained only to children [6, 23, 27].

None of the primary studies directly reported a period of communicability for SARS Cov-2 but appeared to operationalize the definition as the period extending from day of onset of symptoms until the case is no longer infectious [4,5]. The latter was often determined as resolution of clinical symptoms and consecutive negative RT-PCR tests at least 24 hours apart in upper respiratory secretions. Consistent with this framing, most studies measured viral shedding for SARS CoV-2 as presence of viral RNA and duration in relation to onset of symptoms/hospital admission until clearance [6,7,8,9,10.11.12.13.14.17, 20, 28, 29, 30, 31, 32]. Other outcomes reported included serial interval in relation to incubation period and attack rate in specific types of contacts [9, 12, 15, 24]. The presence of viral RNA in secretions do not necessarily correlate with active viral replication. Viability of the virus must be demonstrated by culture or analysis of viral subgenomic replication intermediates. One small study of nine patients has reported that virus could be isolated from some upper respiratory tract infections until the eighth day after the onset of symptoms and then negative until day 13 [25]. Although the earliest period of communicability is uncertain, the short serial interval (median of 4.6 days; 95% CI: 3.5, 5.9) within the

incubation period suggests that the potential exists for transmission prior to the onset of symptoms [15, 24].

Temporal pattern in viral shedding across types of secretions

Studies have also found there is a temporal pattern in viral shedding of SARS CoV-2 from various types of secretions [27, 32]. Zheng and colleagues reported the median duration of virus in stool samples (22 days, interquartile range 17-31 days) was significantly longer than in respiratory (18 days, 13-29 days; $P=0.02$) and serum samples (16 days, 11-21 days; $P<0.001$) [32]. Similarly, clearance of viral RNA was also delayed in stool samples compared to oropharyngeal swabs [21, 23]. This sequence has implication for diagnosis as well as monitoring during convalescence for clearance.

Factors that impact on prolonged viral shedding

A few studies have reported that prolonged duration of SARS CoV-2 viral shedding is associated with old age, male sex, severity of illness, mechanical ventilation and corticosteroid treatment [10, 21, 22, 28]. These factors suggest there is individual variation in viral shedding with potential implications for transmissibility and tailoring criteria for discontinuation of isolation and other control measures.

Conclusions

Despite growing knowledge about SARS CoV-2, the precise period of communicability remains unclear. Current proxy measures of communicability such as viral shedding have practical utility but require additional evaluation of viral activity and infectivity to confirm disease transmission and infection potential. There are several factors including sex, age group and comorbidity that influence viral shedding and have implications for individual variation in infectiousness and consideration of circumstances in tailoring control measures. The temporal sequence in viral RNA shedding that occurs across different body secretions should be considered for diagnosis and monitoring of clinical improvement and guide discharge criteria for discontinuation of control efforts in convalescence.

Glossary

Attack rate: The probability that an infection occurs among susceptible people in a specific group (e.g. household contacts)

Period of communicability: The time during which an infectious agent can be transferred directly or indirectly from an infected person to another person.

Series interval: the time between the start of symptoms in the primary patient (infector) and onset of symptoms in the patient receiving that infection from the infector (the infectee).

Viral shedding: When a virus replicates and is released into the environment.

Table 1A: Summary of grey literature in technical reports

Ref	Country context	Type	Primary outcome measure	Additional findings	Quality of study
2	Canada	Technical summary	<p><u>Period of communicability</u> Mild cases who were not hospitalized are presumed to be no longer communicable 10 days after onset of illness, as long as afebrile and improved clinically. Two consecutively negative lab test results at least 24 hours apart can be used to determine end of communicable period.</p>	<p>Period of communicability not well understood. Assumed that most of transmission occurs from symptomatic individuals although acknowledge the potential for transmission before significant symptoms are apparent.</p>	Unable to determine if peer reviewed or the process for developing the summary
3	Ontario, Canada	Review	<p><u>Period of communicability</u> Transmission is possible as early as 5 days prior to onset of symptoms. Presence of viral RNA has been detected several weeks after symptom onset.</p>	<p>Period of communicability not definitively known. Limited evidence of viable virus in respiratory secretions within 8 days of onset of symptoms despite ongoing presence of viral RNA. One small study viral isolation was confirmed in upper respiratory samples during the first 8 days of onset of symptoms and becoming negative after 13 days. Another study isolated virus from a stool sample 15 days post onset of symptoms.</p>	Unable to determine as process not described
4	EU/EEA Member State	Technical report	<p><u>Viral shedding</u> Viral RNA found in respiratory tract specimens up to 1–2 days before the onset of symptoms. Viral load persists up to eight days after the onset of symptoms in mild cases and peaks in day 11 in more severe cases. Prolonged viral RNA shedding in various secretions such as nasopharyngeal (37 days after onset</p>	<p>Guidance offered that patients who are discharged from hospital to continue to isolate if discharged earlier than 8 days after onset of symptoms in mild cases and 14 days for severe cases if the criteria was not met in hospital. Additional criteria for ending self-isolation include resolution of fever and clinical improvement of other symptoms for three days.</p>	Produced by desk review of of existing guidance documents/ protocols from national and international organisations and a convenient

			in adults) and faeces (from day 5 of onset up until 4 – 5 weeks) has raised concerns about prolonged infectiousness. However, presence does not equate to viable virus demonstrated by viral cultures.		search of peer-reviewed publications.
5	World Health Organization	Technical Report	<u>Viral shedding</u> Viral shedding in the upper respiratory tract is highest early in the course of disease i.e. in the first 3 days of symptom onset . Onset of symptoms can take up to 14 days after exposure and pre-symptomatic persons may be contagious.	No specific mention of period of isolation	

Table 1B: Summary of primary studies

Ref	Sample/population	Study Design	Primary outcome measure	Additional findings
6	10 children with laboratory confirmed infection in hospital (all admitted to isolation ward within 2 days of illness onset) Age: 3-131 months (mean 74 months) M:F=1:1.5 China	Case series	<u>Viral shedding</u> <u>Nasopharyngeal and throat swabs:</u> Positive for 6 to 22 days from symptom onset (mean 12 days) and undetectable thereafter. <u>Stool:</u> Positive for at least 18 to 30 days from symptom onset in 5 of 5 children with positive stools	Clinical presentation mostly of mild respiratory symptoms. Viral shedding was longer in respiratory secretions and fecal shedding was prolonged. <u>Series interval</u> The interval between symptom onset and exposure to index symptomatic case ranged from 2 to 10 days (mean: 6.5 days)
7	Familial cluster of 6 cases Ages: 36 – 66 years Shenzhen, China	Descriptive study	<u>Viral shedding</u> No evidence of viral shedding in urine and faeces in these six patients.	Higher viral loads detected in lower respiratory secretions suggesting that repeat testing of upper respiratory tract samples or testing of lower respiratory tract samples are warranted in clinically suspected cases with an initially negative result in nasopharyngeal or throat swab.
8	42 lab confirmed cases , 8 had gastrointestinal symptoms Median age=51 (IQR 42.7 -62) years Female:27 China	Retrospective cohort study	<u>Viral shedding</u> The duration of viral shedding from feces after negative conversion in pharyngeal swabs was 7 (6-10) days , regardless of COVID-19 severity. However, presence of viable viral RNA in feces was not confirmed by culture.	Detection of viral RNA in feces in 28 patients and this was not associated with presence of gastrointestinal symptoms or illness severity. Authors suggest that fecal-oral transmission may occur even after viral clearance in respiratory tract.
9	Thirty-two confirmed patients and 12 paired data (index-secondary cases) were identified among the 1,043 contacts	Case series	<u>Attack rate</u> The clinical attack rate was higher among those whose initial exposure to the index case was within five days of symptom onset (2.4%, 95% CI 1.1–4.5%) than those who were exposed later (zero	High transmissibility during early onset of the disease for control measures. For example, the efforts of contacting tracing could focus on the contacts near or even before symptom onset of the index cases when the number of index cases or contacts is too large.

			<p>transmission out of 605 contacts, 95% CI 0–0.61%).</p> <p>There was a trend of increasing secondary clinical attack rate with the age of contacts, ranging from 0% (95% CI 0–5.1%) in those aged less than 20 years to 3.6% (95% CI 0.8–10.3%) in those aged 60 years and above (p for linear trend: <0.001).</p>	
10	<p>32 hospitalized patients Age range: 34-54 years Male:16 8 in ICU</p> <p>Xiangtan, China</p>	Case series	<p><u>Viral shedding</u></p> <p>Average onset of symptoms was 5 days (no interval given)</p> <p>Rate of positivity for viral shedding in different secretions varied. All urine samples were negative.</p> <p>Time for viral shedding in nasal secretions was longer for ICU patients compared to non-ICU (22.25±3.62 days vs 15.67±6.68 days)</p>	<p>In this study, one patient experienced five continuous negative results before admission and then the sixth nasal swab on admission finally supported his diagnosis. This suggests that a combination of tests on various samples might be needed if a high index of suspicion.</p>
11	<p>410 patients discharged from 3 Chinese hospitals Median age =52 years (IQR 38-66) Male=198 (48%)</p> <p>99% of patients received antivirals</p>	Multicentre, Retrospective cohort	<p><u>Viral RNA shedding</u></p> <p>Viral RNA of most patients (89%) turned negative within 26 days after symptom onset, and the median time was 19 days. The median time from the date of normalized temperature to the date of negative SARS-CoV-2 RNA test was 7 days (IQR 4·0-10·0).</p>	<p><u>Factors associated with duration of shedding</u></p> <p>Age (p=0·055), gender (p=0·594), disease severity status (p=0·742), corticosteroid (p=0·656), and antibacterial therapy (p=0·927) were <u>not associated</u> with the duration of viral RNA shedding.</p> <p>The median time of duration from body temperature recovery of a patient to the date of negative nucleic acid test was 7 days, indicating that 1 week after temperature normalized would be an appropriate time for viral RNA test for those patients presented with fever.</p>
12	16 cases of COVID 19 (7 confirmed and 9 probable) in a	Contact Tracing Study	<p><u>Serial interval</u></p> <p>The median interval from last contact with a patient with confirmed or</p>	<p>In this cluster, extended family gatherings (a birthday party, funeral, and church attendance), all of which occurred before major social</p>

	community cluster of extended family gatherings Ages ranged from 5 to 86 years (three who died were >60 years)		probable COVID-19 to first symptom onset was 4 days . Within 3 weeks after mild respiratory symptoms were noted in the index patient, 15 other persons were likely infected with SARS-CoV-2, including three who died.	distancing policies were implemented, might have facilitated transmission of SARS-CoV-2 beyond household contacts into the broader community.
13	26 studies included Most of the studies originated in China and two were from USA, with remaining from France, Italy and South Korea No of participants in studies ranged from 1 – 206 Ages: 3 months to 87 years	Rapid review	<u>Viral shedding</u> 53.9% (n=291) of those tested for faecal RNA in these studies were positive. Duration of faecal viral shedding ranged from 1 to 33 days after nasopharyngeal swab turned negative with one result remaining positive after 47 days of onset of symptoms. None of the studies were designed to detect live virus in the faeces except for the study by Wang et al . Out of 153 stool specimens tested in this study, 44 were PCR positive and out of 4 specimens cultured, live virus was detected in 2.	The indication for fecal testing was not specified in most studies. Marked heterogeneity of studies in terms of patient characteristics, sample types and timing of samples. All foreign language articles were excluded.
14	206 patients with mild disease in a Chinese hospital Mean age=62 years (27 – 92 years) Sample stratified by the presence of respiratory and gastrointestinal symptoms Female=115	Retrospective cohort	<u>Viral shedding (interval between symptom onset and viral clearance)</u> The mean interval between symptom onset and viral clearance across the study cohort was 38.1 days (SD 8.7; range 15–62). The average hospital stay was 23.7 days while awaiting symptom resolution and objective evidence of viral clearance. Patients with digestive symptoms had a longer period between initial symptom onset and hospital admission than patients with only respiratory symptoms (16.0 ± 7.7 vs 11.6 ± 5.1 days, $P < 0.001$).	The diarrhea lasted from 1 to 14 days, with an average duration of 5.4 ± 3.1 days. The average daily frequency was 4.3 ± 2.2 bowel movements per day. Women were more likely to report diarrhea than men (44/67, 65.7% vs 71/139, 51.1%, $P = 0.048$).

			The study did not confirm whether virus was viable in any of the samples.	
15	94 patients with lab confirmed COVID 19 infection in a Chinese hospital Median age=47 years Male=47 (50%)	Retrospective cohort	<u>Viral shedding</u> High viral loads detected soon after symptom onset , which then gradually decreased towards the detection limit at about day 21. There was no obvious difference in viral loads across sex, age groups and disease severity.	Most cases were isolated after symptom onset, thus preventing some transmission. Study suggests that viral shedding may begin 2 to 3 days before the appearance of the first symptoms . After symptom onset, viral loads decreased monotonically.
	77 transmission pairs based on public sources	Modelling study	Assuming an incubation period distribution of mean 5.2 days, it was we inferred that infectiousness started from 2.3 days (95% CI, 0.8–3.0 days) before symptom onset and peaked at 0.7 days (95% CI, –0.2–2.0 days) before symptom onset . The estimated proportion of presymptomatic transmission (area under the curve) was 44% (95% CI, 25–69%). Infectiousness was estimated to decline quickly within 7 days. Viral load data were not used in the estimation but showed a similar monotonic decreasing pattern	<u>Serial interval</u> Mean of 5.8 days (95% CI, 4.8–6.8 days) and a median of 5.2 days (95% CI, 4.1–6.4 days) based on a fitted gamma distribution, with 7.6% negative serial intervals.
16	35 year old man from Washington (first US case) Recent travel to China	Case report	<u>Oropharyngeal swabs:</u> Positive on days 4, 7, 11 of illness with decreasing viral load; negative on day 12. <u>Nasopharyngeal swabs:</u> Positive on days 4, 7, 11, and 12 of illness with decreasing viral load; no additional tests performed. <u>Stool:</u> Positive on day 7 of illness	An antiviral (Remdesivir) was administered on compassionate grounds.
17	4 patients exposed as medical professionals in a	Case series	<u>Time to recovery/viral clearance</u> Time from symptom onset to recovery	All patients treated with oseltamivir. Study suggests that a proportion of individuals

	Chinese hospital Ages: 30 -36 years Male=2		(defined as resolution of clinical symptoms and two consecutive negative RT-PCR tests) ranged from 12 to 32 days . Repeat RT-PCR tests performed 5 to 13 days post hospital discharge or initial home quarantine were positive despite continued resolution of symptoms.	could continue to be virus carriers despite clinical resolution.
18	20 lab confirmed cases in Chinese hospital in Guandong Mean age (SD):43.2 years (14) Males=10 (50%)	Case series	<u>Time to recovery</u> Viral RNA in nasopharyngeal swabs disappeared at an average of 12 days (maximum, 22 days). SARS-CoV-2 RNA in feces turned negative in 4–16 days. In two cases, the fecal RNA did not turn negative until 5 and 6 days after negative nasopharyngeal swab.	Treatment included antiviral therapy.
19	Five patients at 2 French hospitals Ages: 30 – 80 years Males=3 All with travel-related history One patient died.	Case series	The viral load decreased over time and became negative between illness day 9 and 14 in four patients. In the most severely ill patient, nasopharyngeal virus detection persisted until death.	Three patients admitted to ICU and received antiviral treatment. High viral loads in upper respiratory tract samples are suggestive of potentially high risk of transmissibility during the very first days of symptoms.
20	13 discharged patients with lab confirmed infection at a Chinese hospital Mean age (SD):52.8 (20.2) Male=6 All discharged patients followed for 4 weeks	Case series	<u>Time to recovery</u> The time between initial symptoms and meeting discharge criteria was 18 - 44 days with an average of 25 ± 6 days. <u>Faeces:</u> Two patients still tested positive after meeting discharge criteria. <u>Sputum:</u> Four patients returned positive 5 - 14 days after discharge. The rate of a recurring positive test result in samples from the respiratory system was 31%	Time from onset of symptoms to diagnosis ranged from 1 -19 days. Antiviral therapy provided as one of the treatments. Urine and blood of all patients was negative for viral RNA. Findings suggest that persons may be asymptomatic carriers although it needs to be confirmed whether there is active viral replication.

			(4/13).	
21	66 persons who had recovered from COVID19 infection in a Chinese Public Health Center Median age (IQR):44(34-62) Male: 38	Retrospective cohort	<u>Viral shedding and clearance</u> Median time from symptom onset to first negative RT-PCR results in oropharyngeal swabs was 9.5(6-11) days. Median duration from symptom onset to negative RT-PCR results in fecal samples was 11(9-16) days.	Five persons received glucocorticoids. Duration of viral detection in oropharyngeal swabs was longer in those who received glucocorticosteroids (15 vs 8 days). Duration of viral detection was also longer in fecal samples of those who received glucocorticosteroids (20 vs 11 days). The duration of RNA detection may relate to host cell immunity.
22	76 cases admitted to a Chinese hospital 46 classified as mild Mean age (SD): 43.6 (14.4) years in Mild 55.6 (15.1) years in severe disease Male:48	Case series	<u>Viral shedding</u> Mild cases were found to have an early viral clearance , with 90% of these patients repeatedly testing negative on RT-PCR by day 10 post-onset. By contrast, all severe cases still tested positive at or beyond day 10 post symptom onset	
23	Six children and two adults Ages: 11 months to 9 years; 4 females Adults: 33 and 36 years and female	Case reports	<u>Viral shedding</u> Three children and one adult had viral RNA detection in stool 4 weeks after discharge.	
24	28 pairs of primary and secondary contacts 12 pairs were family clusters	Observational study	<u>Serial interval</u> Accounting for right truncation and analyzing all pairs, the median serial interval at 4.0 days (95%CI: 3.1, 4.9). Limiting data to only the most certain pairs, the median serial interval was estimated at 4.6 days (95% CI: 3.5, 5.9).	The short estimated mean serial interval (shorter than mean incubation period of 5 days) suggest the possibility of transmission prior to onset of symptoms. It is also possible that short serial intervals are the result of case isolation.
25	9 hospitalized cases with mostly mild disease	Case series	<u>Viral shedding</u> <u>Upper respiratory secretions</u>	None of the urine and blood samples tested positive.

	China		<p>Viral load peaked before day 5 and declined over time from symptom onset. Active replication of SARS-CoV-2 confirmed in the throat during the first 5 days after symptoms onset.</p> <p><u>Sputum</u> Viral loads declined more slowly in sputum</p>	<p>Virus was readily isolated during the first week of symptoms from a significant fraction of samples (16.66% in swabs, 83.33% in sputum samples), no isolates were obtained from samples taken after day 8 in spite of ongoing high viral loads. No virus was isolated from feces.</p> <p><u>Antibody response</u> In early sera, taken between day 3 and 6, none of the patients showed detectable antibody. The patients monitored long enough to yield a serum sample after two weeks all showed neutralizing antibodies.</p>
26	<p>Two recovered cases among 62 medical workers in Sichuan province in China</p> <p>Case 1 male in his 40s</p> <p>Case 2: female in her 20s</p>	Case reports	<p><u>Viral shedding and clearance</u></p> <p>Case 1 results of consecutive throat swab tests were negative on day 13 weakly positive on day 14 , 15, and negative on day 16 , weakly positive on day 18 , negative on days 20 and 22. He did not experience any new symptoms.</p> <p>In case 2, detection of viral RNA in consecutive throat swabs was found on day 14, 15 but were negative on 16, 17, 18 only to be detected on day 19 and negative on days 20-22. She did not experience a recurrence of any symptoms.</p>	
27	<p>Three children with lab confirmed infection in Shangdong province, China</p> <p>Ages: 1.5, 5 and 6 years</p> <p>Male: 2</p>	Case reports	<p><u>Viral shedding</u></p> <p>Clearance of SARS-CoV-2 in respiratory tract occurred within two weeks after abatement of fever, whereas viral RNA remained detectable in stools of pediatric patients for longer than 4 weeks. Two children had fecal SARS-CoV-2 undetectable 20 days after throat swabs</p>	<p>All children had mild disease.</p> <p>In the larger cohort, the similar time for viral RNA in respiratory specimens turning negative was observed between pediatric patients and infected adults (these children's family members). At this point, adult patients had negative results for nucleic acid testing in fecal specimens, whereas SARS-CoV-2 RNA remained detectable in stools of</p>

			were negative, while that of another child lagged behind for 8 days.	the two infected children.
28	<p>113 symptomatic patients in 2 hospitals outside of Wuhan Median age:52 years Male: 66 (58.4%)</p> <p>Antiviral treatment as well as corticosteroids were given to patients</p>	Retrospective cohort	<p><u>Viral shedding</u> 74.3% (n=84) patients that had viral RNA clearance within 21 days after illness onset. Median duration in these patients was 15 days (IQR, 11.75–18 days Median time from illness onset to body temperature recovery to normal was 11 days (IQR, 8-14 days). Median duration from illness onset to radiological recovery was 15 days (IQR, 11-18 days).</p>	<p>NB: Less than 10% of swabs were nasopharyngeal or throat swabs as lower respiratory tract specimens were preferred. The median time from illness onset to hospital admission was 5 days (IQR, 3–8 days).</p> <p><u>Risk factors for prolonged viral shedding</u> Male patients, delayed admission to hospital after illness onset, and invasive mechanical ventilation during hospitalization were associated with prolonged SARS CoV-2 RNA shedding. Prolonged RNA shedding was associated with delayed recovery on radiological image (median days, 12 vs. 16, p<0.001).</p>
29	<p>18 patients who travelled to Wuhan but were diagnosed in Singapore Median age=47 years Male: 9</p>	Case series	<p><u>Viral shedding</u> Median duration of viral shedding from first to last positive nasopharyngeal swab collected as part of clinical care was 12 days (range, 1-24), and was prolonged for 7 days or longer among 15 (83%).</p> <p><u>Stool:</u> PCR positive in 4/8 (50%) patients between day 5-9 of illness</p>	Half of patients presented to hospital more than 2 days after symptom onset, thus limiting sampling in earliest stages of disease,
30	<p>Three lab confirmed pediatric cases in Tianjin, China Ages: 3, 6, 8 years Male:3</p>	Case reports	<p><u>Viral shedding</u> Detection of viral RNA in throat swabs of the three patients became negative in 14, 11, and 7 days, and were discharged from hospital after two consecutive negative results on 16, 13, and 9 days, respectively.</p>	<p>All cases considered uncomplicated. One child received antiviral treatment and another received interferon.</p>

			At follow up after discharge: no positive results was found in either of the two times of throat swab nucleic acid tests, but the stool SARS-CoV-2 nucleic acid tests were positive after 10 days. The children were readmitted to hospital and viral RNA detection in stool became negative in 4, 5 and 10 days. There were no symptoms that were reported	
31	20 persons followed post discharge from hospital in Wenzhou, China Age: 23 -57 years Male:14	Case series	<u>Viral clearance</u> Seven days post discharge, three patients had positive detection of viral RNA. For two patients, positive tests occurred by both salivary and faecal samples. Another tested positive only in fecal sample. All patients returned negative tests for viral RNA during the second week of follow up.	Patients received treatment with nebulized interferon
32	96 persons with lab confirmed disease in a university affiliated hospital in China 22 had mild disease Median age (IQR):55 years (44.3-64.8).	Retrospective cohort	<u>Respiratory secretions</u> Rates of viral detection gradually decreased from 95% in the first week of symptom onset to 54% in the fourth week, with subsequent respiratory samples showing negative results. <u>Fecal and serum samples</u> positive rate of viral RNA detection gradually increased from the first week and then decreased from the third week	In addition, the rate of detection in serum samples was higher in patients with severe disease than in patients with mild disease (45% v 27%), but the difference was not significant.
			<u>Viral shedding</u> <u>Feces</u> Median duration of virus in stool samples (22 days, interquartile range 17-31 days) was significantly longer than in	Types and timeliness of antiviral treatments had no overall effect on the duration of the virus and viral load.

			<p>respiratory (18 days, 13-29 days; P=0.02) and serum samples (16 days, 11-21 days; P<0.001).</p> <p><u>Respiratory secretions</u> Median duration of virus in patients with severe disease (21 days, 14-30 days) was significantly longer than in patients with mild disease (14 days, 10-21 days; P=0.04)</p> <p><u>Feces and serum</u> No significant difference was observed in the duration of virus between stool and serum samples among patients with different disease severities.</p>	
33	<p>41 patients with severe disease who were discharged from a Chinese hospital Median age:58.0 (IQR: 48.0-62.0) years, ranging from 17 years to 75 years Male:22</p>	Case series	<p><u>Viral shedding</u> Median duration of viral shedding was 31.0 (IQR: 24.0-40.0) days from illness onset. The shortest observed duration of viral shedding was 18 days, whereas the longest was 48 days. Median total time from illness onset to discharge was 40.0 (IQR: 32.0-46.0) days</p>	
34	<p>18 laboratory confirmed cases 1 case was asymptomatic Median age: 59 (26-76) years Male: 9</p>	Case series	<p>Nasal and throat specimens: Higher viral loads detected soon after symptom onset (peaking around day 3-6), and declining in subsequent days. Viral RNA detected at 21 days at low levels in nasal swab from one patient.</p>	

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Appendix: Evidence Search Details

Search Strategies

CINAHL

Date Run: April 25, 2020 11:05

S14 S7 AND S11 Limiters - English Language 69

S13 S7 AND S11 72

S12 S7 AND S11 72

S11 S8 OR S9 OR S10 56,764

S10 TI ((transmi* or infecti* or communicab* or contagious* or shedding) N2 (period or duration or time or length or days)) OR AB ((transmi* or infecti* or communicab* or contagious* or shedding) N2 (period or duration or time or length or days)) 5,500

S9 TI (transmissibility or infectiousness or infectivity or communicability or "viral shedding" or "viral load" or "viral RNA" or "RNA shedding" or "discharge criteria") OR AB (transmissibility or infectiousness or infectivity or communicability or "viral shedding" or "viral load" or "viral RNA" or "RNA shedding" or "discharge criteria")

7,687

S8 (MM "Disease Transmission+") OR (MM "Viral Load") OR (MM "Polymerase Chain Reaction+") OR (MH "Patient Discharge+") 45,458

S7 S1 OR S2 OR S3 OR S4 OR S5 Limiters - Published Date: 20191201-20201231 1,416

S6 S1 OR S2 OR S3 OR S4 OR S5 4,591

S5 (TI (novel OR new OR nouveau OR "2019") N2 (coronavirus* or corona virus*)) OR (AB (novel OR new OR nouveau OR "2019") N2 (coronavirus* or corona virus*)) 537

S4 ((TI "2019-nCov" OR "COVID-19" OR covid 19 OR "SARS-CoV-2" OR covid19) OR (AB "2019-nCov" OR "COVID-19" OR covid 19 OR "SARS-CoV-2" OR covid19)) OR ((TI (coronavirus* OR corona-virus*) AND (wuhan OR shanghai OR Beijing OR Italy OR south-korea OR china OR chinese)) OR (AB (coronavirus* OR corona-virus*) AND (wuhan OR shanghai OR Beijing OR Italy OR south-korea OR china OR chinese))) 1,386

S3 ((TI "COVID-19" OR "2019-nCoV" OR "SARS-CoV*" OR 2019-nCov OR 2019 coronavirus* OR 2019 corona virus* OR covid19) OR (AB "COVID-19" OR "2019-nCoV" OR "SARS-CoV*" OR 2019-nCov OR 2019 coronavirus* OR 2019 corona virus* OR covid19)) OR MH "Coronavirus+" OR MH "Coronavirus Infections+" OR (TI ((novel or new or nouveau or "2019") N2 (coronavirus* or corona virus* or

pandemi*)) OR AB ((novel or new or nouveau or "2019") N2 (coronavirus* or corona virus* or pandemi*)) 4,305

S2 (TI coronavirus* OR corona-virus OR covid19 OR "covid 19" or SARS-Cov*) OR (((TI (novel OR new OR nouveau OR "2019") N2 (coronavirus* or corona virus*)) OR (AB (novel OR new OR nouveau OR "2019") N2 (coronavirus* or corona virus*)) AND ((MH "China+" OR (TI china OR Chinese) OR (AB china OR chinese) OR MH "Italy" OR (TI Italy OR AB Italy) OR MH "Korea" OR MH "South Korea" OR (TI korea OR AB korea)) OR ((MH "Pneumonia+" OR (TI pneumonia OR AB pneumonia)) AND (TI Wuhan OR AB Wuhan)) 1,120

S1 ((MH "Coronavirus+" OR MH "Coronavirus Infections+") OR (TI coronavirus* OR corona-virus) OR (AB coronavirus* OR corona-virus)) AND ((TI wuhan or beijing or shanghai or Italy or South-Korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV*) OR (AB wuhan or beijing or shanghai or Italy or South-Korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV*)) 1,273

Embase <1974 to 2020 April 23>

Date Run: April 25, 2020 11:15

1 (exp coronavirinae/ or coronavirus*.mp. or corona-virus.mp.) and (wuhan or beijing or shanghai or Italy or South-Korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV*).mp. (7845)

2 (coronavirus* or Corona-virus or covid19 or "covid 19" or SARS-Cov*).ti. or (((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus*).mp. and (exp china/ or china.mp. or Chinese.mp. or exp Italy/ or Italy.mp. or exp south korea/ or south korea.mp.)) or ((pneumonia.mp. or exp pneumonia/) and Wuhan.mp.) (13540)

3 ("COVID-19" or "2019-nCoV" or "SARS-CoV*" or 2019-nCov or 2019 coronavirus* or 2019 corona virus* or covid19).mp. or exp coronavirus Infection/ or ((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus* or Pandemi*2)).mp. (19682)

4 ("2019-nCov" or "COVID-19" or covid 19 or "SARS-CoV-2" or covid19).mp. or ((coronavirus* or corona-virus*) and (wuhan or shanghai or Beijing or Italy or south-korea or china or chinese)).ti,ot,ab. (6840)

5 ((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus*).mp. (3634)

6 1 or 2 or 3 or 4 or 5 (24022)

7 6 and 20191201:20201231.(dc). (7042)

8 exp *disease transmission/ or *virus shedding/ or *viral load/ or exp *polymerase chain reaction/ or hospital discharge/ (232222)

9 (transmissibility or infectiousness or infectivity or communicability or "viral shedding" or "viral load" or "viral RNA" or "RNA shedding" or "discharge criteria").ti,ab. (94219)

10 ((transmi* or infecti* or communicab* or contagious* or shedding) adj2 (period or duration or time or length or days)).ti,ab. (30808)

11 8 or 9 or 10 (344436)

12 7 and 11 (442)

13 limit 12 to english language (421)

14 limit 13 to exclude medline journals (50)

Ovid MEDLINE(R) ALL <1946 to April 24, 2020>

Date Run: April 25, 2020 10:30

1 (exp coronavirus/ or coronavirus*.mp. or corona-virus.mp.) and (wuhan or beijing or shanghai or Italy or South-Korea or China or Chinese or 2019-nCoV or nCoV or COVID-19 or Covid19 or SARS-CoV*).mp. (7252)

2 (coronavirus* or Corona-virus or covid19 or "covid 19" or SARS-Cov*).ti. or (((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus*)).mp. and (exp china/ or china.mp. or Chinese.mp. or exp Italy/ or Italy.mp. or exp Republic of korea/ or south korea.mp.)) or ((pneumonia.mp. or exp pneumonia/) and Wuhan.mp.) (13993)

3 ("COVID-19" or "2019-nCoV" or "SARS-CoV*" or 2019-nCov or 2019 coronavirus* or 2019 corona virus* or covid19).mp. or exp Coronavirus Infections/ or ((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus* or Pandemi*2)).mp. (18912)

4 ("2019-nCov" or "COVID-19" or covid 19 or "SARS-CoV-2" or covid19).mp. or ((coronavirus* or corona-virus*) and (wuhan or shanghai or Beijing or Italy or south-korea or china or chinese)).ti,ot,ab. (7780)

5 ((novel or new or nouveau or "2019") adj2 (coronavirus* or corona virus*)).mp. (3164)

6 1 or 2 or 3 or 4 or 5 (22075)

7 6 and 20191201:20201231.(dt). (7773)

8 exp *Disease Transmission, Infectious/ or *Virus Shedding/ or *Viral Load/ or exp *Polymerase Chain Reaction/ or Patient Discharge/ (127703)

9 (transmissibility or infectiousness or infectivity or communicability or "viral shedding" or "viral load" or "viral RNA" or "RNA shedding" or "discharge criteria").ti,ab. (73862)

10 ((transmi* or infecti* or communicab* or contagious* or shedding) adj2 (period or duration or time or length or days)).ti,ab. (24453)

11 8 or 9 or 10 (216355)

12 7 and 11 (321)

13 limit 12 to english language (298)

PubMed

Date Run: April 25, 2020

(((((coronavirus[MeSH Terms]) OR ((coronavirus* OR corona-virus* or corona virus*)) OR (((coronavirus* OR corona-virus*) and (wuhan OR beijing OR shanghai OR italy OR italian OR south-korea* OR south korea* OR china OR chinese OR 2019-nCoV OR ncov OR COVID-19 OR Covid19 OR SARS-CoV*)))))) OR (((coronavirus*[Title] OR corona-virus*[Title] OR covid19[Title] OR covid-19[Title] OR "covid19"[Title] OR "covid-19"[Title] OR SARS-Cov*[Title]))) OR (((((novel OR new OR nouveau OR "2019") and (coronavirus* OR corona-virus*)) AND (((((china[MeSH Terms]) OR (china OR chinese)) OR italy[MeSH Terms]) OR (italy OR italian)) OR korea, republic of[MeSH Terms]) OR south korea*)) OR (((pneumonias[MeSH Terms]) OR penumonia*)) AND wuhan)))) OR (((("COVID-19" OR "2019-nCoV" OR "SARS-CoV*" OR 2019-nCov OR 2019 coronavirus* OR 2019 corona virus* OR covid19)) OR coronavirus infections[MeSH Terms]) OR ((novel OR new OR nouveau OR 2019)

AND (coronavirus* OR "corona virus*" OR Pandemi*)) OR (((("2019-nCov" OR "COVID-19" OR covid 19 OR "SARS-CoV-2" OR covid19)) OR (((coronavirus*[Title/Abstract] OR corona-virus*[Title/Abstract])) AND (wuhan[Title/Abstract] OR shanghai[Title/Abstract] OR Beijing[Title/Abstract] OR Italy[Title/Abstract] OR south-korea[Title/Abstract] OR china[Title/Abstract] OR chinese[Title/Abstract]))) OR (((novel OR new OR nouveau OR "2019") and (coronavirus* OR corona virus*)))) AND (((disease transmission, communicable[MeSH Terms]) OR disease transmission, infectious[MeSH Terms]) OR ((transmissibility[tiab] OR infectiousness[tiab] OR infectivity[tiab] OR communicability[tiab] OR "viral shedding"[tiab] OR "viral load"[tiab] OR "viral RNA"[tiab] OR "RNA shedding"[tiab] OR "discharge criteria"[tiab]))) Filters: Publication date from 2020/01/01 (Results 325)

Sources

- Grey literature was searched
- Refer to the evidence search report for extensive sources.



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