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Evidence summary for SARS-CoV-2 viral load and infectivity over the course of an infection

9 June 2020

Version history

Version	Date	Specific updates
V1.0	1 April 2020	
V2.0	21 April 2020	Updated search with 26 new studies
V3.0	9 June 2020	Updated search with 60 new studies

Evidence summary for SARS-CoV-2 viral load and infectivity over the course of an infection

Key points

- A total of 113 studies conducted in 17 countries were included in this updated evidence summary.
- In general, SARS-CoV-2 viral ribonucleic acid (RNA) levels peak around symptom onset or a few days after, and become undetectable (from upper respiratory tract samples) about two weeks after symptom onset.
- Some evidence suggests that viral RNA levels from lower respiratory tract samples may be higher, peak later and persist for longer than those from upper respiratory tract samples.
- There is evidence of prolonged viral shedding in stool samples. However, the clinical significance of this finding is uncertain.
- There may be an association between higher viral loads, detection of the virus in blood, longer duration of virus detection and poorer patient outcomes such as increased disease severity. However, these relationships were not consistently found.
- Based on a limited number of studies which have compared findings between children and adults, there appears to be no difference between children and adults in terms of viral load or duration of virus detection.
- The precise duration of infectivity has not yet been established; the presence of viral RNA may not represent transmissible live virus, hence patients may not be infectious for the entire duration of viral RNA detection. However, there are limited reports of live virus isolated up to six days before and up to 13 days (from upper respiratory tract samples) and 18 days (from lower respiratory tract samples) after symptom onset. Limited evidence suggests that infectivity may be related to the viral load.
- Given that the majority of these studies comprised case series and case reports, these findings should be viewed with caution and will require confirmation using larger, more robust study designs.

Evidence summary for SARS-CoV-2 viral load and infectivity over the course of an infection

The Health Information and Quality Authority (HIQA) has developed a series of 'Evidence Summaries' to assist the Clinical Expert Advisory Group (EAG) in supporting the National Public Health Emergency Team (NPHE) in their response to COVID-19. These summaries are based on specific research questions. This evidence summary was developed to address the following research question:

What is the viral load over the course of the infection (including any asymptomatic or pre-symptomatic phase), and the duration of infectivity?

The processes as outlined in HIQA's protocol (available on www.hiqa.ie) were followed. Relevant databases of published literature and pre-print servers were searched. Data published by national agencies are not included. This evidence summary was first published on 1 April 2020. It was updated to include all relevant evidence until 12 May 2020.

Results

Search results

A total of 53 studies were included from the original and updated searches (30 November 2019 to 3 April 2020).⁽¹⁻⁵³⁾ A further 60 studies were included from the updated search conducted to 12 May 2020, resulting in a total of 113 studies (Table 1).⁽⁵⁴⁻¹¹³⁾ Seventy-four studies were conducted in China.^(1-7, 11, 12, 15, 18, 26-30, 32-36, 43-48, 50-53, 55, 57, 60, 62-67, 71, 72, 74, 75, 77, 79, 83, 87, 89-91, 93-113) Five studies each were conducted in Taiwan^(8, 9, 23, 76, 85) and the United States (US).^(17, 21, 61, 70, 73) Four studies each were conducted in Singapore^(14, 19, 41, 49) and Italy,^(59, 68, 86, 92) three studies each were conducted in Germany,^(10, 42, 80) France^(13, 24, 58) and Vietnam,^(22, 37, 81) two studies each were conducted in Hong Kong,^(39, 40) the United Kingdom (UK)^(16, 84) and South Korea,^(20, 25) with one study conducted in each of the following: Bangladesh,⁽⁷⁸⁾ Switzerland,⁽⁸²⁾ Thailand,⁽⁸⁸⁾ Japan,⁽⁶⁹⁾ Australia,⁽³⁸⁾ and Canada.⁽³¹⁾ Of these, 111 studies were observational in nature,^(1-3, 5-12, 14-113) one study was a randomised controlled trial (RCT)⁽⁴⁾ and one was a non-randomised controlled trial (NRCT).⁽¹³⁾ The majority of included observational studies (n=95) were case reports or series.^(1-3, 5-7, 9-12, 14, 16-32, 34-38, 40-51, 53, 54, 56, 60, 61, 63, 64, 66-72, 74-79, 81-89, 91-98, 100-104, 106-113)

Additionally, there were eight cohort studies,^(33, 39, 52, 55, 62, 65, 99, 105) five cross-sectional studies,^(58, 59, 73, 80, 90) two modelling studies^(15, 57) and one prospective case-ascertained study.⁽⁸⁾ Seventy-three studies contained adults exclusively,^(3-6, 9, 10, 12, 14-17, 20, 21, 23-25, 27-29, 31, 34-41, 43, 45, 47-49, 51-55, 60, 61, 63, 65, 67-70, 73, 75-78, 83-86, 88, 89, 92, 94, 97-99, 101-105, 107-110, 112, 113) 12 contained children (18 years or younger) exclusively,^{(2, 11, 19, 22,}

33, 44, 46, 79, 82, 95, 96, 111) 24 contained a combination of children and adults,^(1, 8, 13, 18, 26, 30, 50, 56, 57, 59, 62, 64, 66, 71, 72, 74, 80, 81, 87, 90, 91, 93, 100, 106) and four did not provide demographic information.^(7, 32, 42, 58) The sample size of included studies ranged from one patient (26 studies)^(5, 9, 11, 14, 16, 17, 19, 22, 23, 25, 29, 31, 34, 37, 38, 61, 68-70, 78, 79, 85, 86, 89, 101, 107) to 3,712 patients,⁽⁸⁰⁾ with a median sample size across all studies of 15 patients.

Viral load of SARS-CoV-2

Association between sample type and viral load

Fifty studies reported the viral load of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) over the course of the coronavirus disease (COVID-19) using real-time reverse transcriptase polymerase chain reaction (rRT-PCR) testing.^(4, 7, 10, 13-17, 19-21, 24, 25, 28, 29, 31, 32, 35-40, 42, 44-46, 49, 51, 53, 56, 58, 59, 65, 67, 70, 72, 73, 76, 80-82, 85, 87, 90, 92, 94, 98, 107, 108) In general, the highest viral loads from upper respiratory tract samples were observed at the time of symptom onset and for a few days after, with levels slowly decreasing over the next one to three weeks. However, different patterns of viral kinetics are being described in the literature. A case series study conducted in France described three general patterns of viral kinetics and clinical progression observed in COVID-19 patients:⁽²⁴⁾

- 1) patients with mild symptoms, with high viral loads within the first 24 hours of symptom onset based on upper respiratory tract samples and viral RNA detection in stools (usually for a prolonged period)
- 2) a two-step disease progression in patients presenting initially with mild-to-moderate disease, with a secondary worsening around 10 days after disease onset despite decreasing viral load in upper respiratory tract samples and
- 3) older patients with severe and critical symptoms, with a rapid evolution towards multi-organ failure and a persistently high viral load in lower and upper respiratory tract and systemic virus dissemination and detection in plasma.

Some studies have observed clear differences between the viral loads detected in upper respiratory tract samples compared with stool samples. In general, viral loads from the upper respiratory tract samples were observed to peak earlier and followed a relatively consistent downward trajectory, whereas viral loads from stool samples were found to peak much later in the disease (often when the patient has recovered) and followed a more erratic pattern.^(19, 20, 37, 42, 44, 46, 51, 60, 63-66, 68, 75, 79, 85, 93, 95, 96, 99, 109, 111) However, data on the differences in viral load dynamics between different upper respiratory sample sites is contradictory with some studies reporting higher viral loads in nasal samples (for example, Zou et al.),⁽⁵³⁾ and others reporting higher viral loads in throat samples (for example, Yu et al.).⁽⁷²⁾ Moreover, this latter study by Yu et al. also reported that viral loads from sputum samples were significantly higher than those from either throat or nasal samples. Viral loads from

urine and blood samples were found to be negligible in this study.⁽⁷²⁾ Four studies reported that viral RNA from sputum samples may peak at a later stage than upper respiratory tract samples (after about two weeks from symptom onset),^(65, 70, 85, 99) and another four studies reported that sputum samples may contain higher viral loads than upper respiratory tract samples.^(32, 72, 75, 85)

Association between disease severity and viral load

Nine studies reported an association between higher viral loads and more severe symptoms.^(24, 28, 32, 39, 65, 72, 90, 94, 108) One of these studies (n=76 patients) found that the mean viral load of severe cases was around 60 times higher than that of mild cases, and this relationship was maintained from early to later stages of the infection.⁽²⁸⁾ Although another study (n=23 patients) found numerically higher viral loads in those with severe disease, this relationship was not found to be statistically significant.⁽³⁹⁾

Seven studies observed increases in viral loads prior to clinical deterioration (particularly those based on lower respiratory tract samples), with decreases in viral load then observed prior to improvement of symptoms.^(20, 32, 42, 65, 72, 94, 108) One of these studies analysed sputum samples from 92 patients collected at hospital admission and found a significant positive association between higher sputum viral load at baseline and risk of disease progression.⁽¹⁰⁸⁾ Another study (n=76 patients) reported that samples from patients in the 'early and progressive stages' of COVID-19 had significantly higher viral loads than samples from patients in either the 'recovery' or 'clinical cure' stages.⁽⁷²⁾

Viral load in asymptomatic or pre-symptomatic patients

Seven studies measured viral load in asymptomatic or pre-symptomatic patients.^(10, 13, 19, 59, 73, 81, 98) A study was conducted in the municipality of Vo in Italy, where SARS-CoV-2 testing was undertaken in 85.9% (n=2,812) and 71.5% (n=2,343) of the total population (n=3,275) at two consecutive time points less than two weeks apart.⁽⁵⁹⁾ At the first time point, 73 people (2.6%) tested positive and at the second time point, 29 (1.2%) tested positive. Notably, 43.2% (95% CI 32.2-54.7%) of the confirmed SARS-CoV-2 infections detected across the two time points were asymptomatic. The authors found no statistically significant difference in the viral load (as measured by genome equivalents inferred from cycle threshold (Ct) data) between samples from symptomatic compared with asymptomatic patients.⁽⁵⁹⁾

A similar study by Arons et al. was conducted in a nursing facility in Washington State, US, where residents in the facility were offered SARS-CoV-2 testing on two separate occasions, seven days apart.⁽⁷³⁾ Of the 76 residents tested, 48 (63%) tested positive and 28 (37%) tested negative. Of the 48 test-positive residents, 27 (56%) had no symptoms at the time of testing; 24 of these 27 patients (88%) subsequently developed symptoms (that is, they were pre-symptomatic). The authors found that the viral loads were similar between asymptomatic, pre-symptomatic and symptomatic patients. Symptomatic patients were sub-divided into

those displaying typical symptoms (that is, fever, cough and shortness of breath) and those displaying atypical symptoms (that is, chills, malaise, increased confusion, rhinorrhoea/nasal congestion, myalgia, dizziness, headache, nausea, and diarrhoea). The median Ct values for asymptomatic residents, pre-symptomatic residents, residents with atypical symptoms and residents with typical symptoms, were 25.5, 23.1, 24.2, and 24.8, respectively (note that lower Ct values infer higher viral loads).⁽⁷³⁾ Notably, of the 12 residents who had two consecutive positive rRT-PCR results, four had viral loads peaking prior to symptom onset (up to five days before symptom onset).⁽⁷³⁾

A case report of a child noted no symptoms on admission to hospital, but a relatively high viral load (nasopharyngeal sample targeting ORF1ab-gene, peak viral load Ct value = 13.73). The viral load decreased over the next nine days, although it raised slightly when the child experienced a fever on day two of admission, before falling again once the fever resolved.⁽¹⁹⁾ Corman et al. described two patients who presented with no symptoms and remained asymptomatic for at least two weeks after first testing positive.⁽¹⁰⁾ These patients had peak viral loads (lowest Ct values) of 30.10 and 24.39, respectively.⁽¹⁰⁾ Gautret et al. measured viral loads in six patients who presented without any symptoms (median Ct value = 27.5); however, it is unclear whether these patients subsequently developed any symptoms due to the limited follow up of six days.⁽¹³⁾

One individual adult from a case series of 12 hospitalised COVID-19 patients in Vietnam was asymptomatic for at least 14 days and had a peak viral load seven days after first testing positive (median Ct value from three target genes = 28).⁽⁸¹⁾ A case series conducted in China described two patients who remained asymptomatic for at least two weeks and had peak viral loads (Ct values) of 29.96 and 23.32, respectively, on their first day of testing.⁽⁹⁸⁾

Duration of SARS-CoV-2 detection

Association between sample type and duration of virus detection

Eighty-eight studies reported the duration of virus detection, with the end point being the first day of two consecutive negative tests taken 24 hours apart, using rRT-PCR.^(1-3, 5, 6, 9, 11-13, 15, 16, 18, 20-39, 42-44, 46-52, 54-56, 58-66, 68-71, 74-76, 78, 81, 83-89, 91, 92, 94, 96-104, 106, 109-113) Additionally, two recent studies required three consecutive negative tests taken 24 hours apart prior to establishment of virus clearance.^(77, 105) Of these 90 studies, 66 reported the duration of virus detection from onset of symptoms using upper respiratory tract samples,^(1-3, 5, 6, 9, 11-13, 15, 16, 20, 22-24, 26, 29-32, 34-38, 42, 43, 46-49, 51, 52, 59, 61, 63-66, 68, 69, 74, 76, 78, 81, 83-89, 92, 96, 99-104, 110-113) and 10 reported the duration of virus detection from onset of symptoms using lower respiratory tract samples.^(9, 20, 21, 25, 32, 42, 76, 85, 99, 105) The longest duration observed was 83 days in one patient based on upper respiratory tract samples.⁽⁸³⁾ At the aggregate study level, the

median duration of virus detection from symptom onset using upper respiratory tract samples was 14.5 days (median range 1-53.5 days).^(61, 83)

In relation to lower respiratory tract samples, the median duration of virus detection from symptom onset at the aggregate study-level was 15.5 days (median range 10-44 days).^(32, 85) Four studies reported that viral RNA in lower respiratory tract samples (that is, sputum samples) may persist for longer periods than upper respiratory tract samples.^(56, 65, 85, 99) One of these studies reported a case where SARS-CoV-2 continued to be detectable from sputum samples (targeting the E gene) for 62 days since symptom onset in a 50-year-old woman in Taiwan.⁽⁸⁵⁾ However, the duration of virus detection from sputum samples varied for this patient depending on the gene targeted in rRT-PCR testing (for example, 30 days for N gene and 44 days for RdRp gene).

Detection of virus in non-respiratory sample types

In general, studies that tested blood samples in populations with mild to moderate severity disease did not detect viral RNA or reported weakly positive or inconsistent results.^(2, 16, 19, 20, 26, 39, 42, 49, 85, 95, 96) Four studies observed that detection of viral RNA in blood samples was associated with severe disease.^(7, 10, 21, 24) Three of these studies detected viral RNA in the blood of patients with severe or critical disease (and not in the blood of those with milder disease).^(10, 24, 37) Another study observed greater rates of positive tests in blood samples in intensive care unit (ICU) patients (87.5% (seven out of eight)) compared with non-ICU patients (66.7% (16 out of 24)).⁽¹²⁾ In contrast, one case report of a patient with severe pneumonia did not detect viral RNA in the blood.⁽¹⁷⁾

Thirty-two studies, reported detectable levels of viral RNA in stool samples for a prolonged period of time (often greater than three to four weeks after symptom onset),^(1, 3, 9, 11, 17, 19, 21, 24, 26, 30, 37, 42-44, 46, 51, 56, 60, 63-66, 68, 75, 79, 85, 93, 95, 96, 99, 109, 111) and possibly longer in children.^(3, 11, 19, 30, 44, 46, 79, 93, 95, 96, 111) However, there are concerns regarding truncated data for the duration of virus detection in stool samples, as the data appear to reflect the maximum duration of follow-up, rather than the true duration of virus detection.^(9, 11, 21, 24, 26, 30, 37, 42, 43, 51, 56, 60, 64, 65, 75)

Other sample sites such as urine,^(2, 9, 12, 16, 17, 19-21, 24, 26, 32, 37-39, 42, 49, 51, 60, 65, 68, 72, 75, 86, 107) conjunctival fluid^(24, 68) and semen^(68, 86) were used less frequently and gave more inconsistent findings.

Association between duration of virus detection and severity of disease or old age

There are inconsistent findings for the association between disease severity (and or ICU admission), and the duration of virus detection, with studies reporting either a positive association,^(1, 3, 6, 12, 18, 24, 28, 35, 65, 72, 75, 77, 94) or no association.^{(33, 39, 47, 64, 66,}

¹¹²⁾ There are also inconsistent findings for the association between old age and the duration of virus detection, with studies reporting either a positive^(1, 3, 24, 47, 55, 65, 103) or no association.⁽¹¹²⁾

Duration of virus detection in asymptomatic or pre-symptomatic patients

Eight studies measured the duration of virus detection in asymptomatic or pre-symptomatic patients,^(18, 33, 64, 66, 81, 96, 98, 106) with estimates found to vary widely. One study included 24 cases with asymptomatic and pre-symptomatic COVID-19 infections screened from close contacts.⁽¹⁸⁾ Data were available for 23 of the 24 cases for at least 14 days after suspected exposure. The estimated median duration from the first positive test to the first of two consecutive negative tests was 9.5 days (range 1-21 days), while the estimated median time from suspected exposure to the first of the two consecutive negative tests was 20.5 days (interquartile range, 16-26.25 days, range 12-32 days). The authors reported that the virus was detected for a longer period of time in those who subsequently developed symptoms (pre-symptomatic, n=5 cases) compared with those who remained asymptomatic (n=19 cases) (median, 12 vs 6 days). Of the five pre-symptomatic cases, the earliest positive rRT-PCR test occurred two days before symptom onset in one patient. Two of the five pre-symptomatic cases had previously tested negative seven and eight days prior to first symptoms, respectively (but after suspected exposure).⁽¹⁸⁾

A case series study conducted by Xu et al. investigated the epidemiological and clinical features of 15 asymptomatic hospitalised COVID-19 patients in China.⁽¹⁰⁶⁾ All 15 patients remained asymptomatic for the duration of hospitalisation, which was a median of 11 days. The authors reported a median time of seven days (IQR 4-9 days) from the first positive test to the first of two consecutive negative tests.

In the study by Lo et al. the asymptomatic patient tested positive, and remained asymptomatic, for the duration of their 19 day hospitalisation period.⁽⁶⁶⁾ In the study by Yongchen et al., the five asymptomatic patients had a longer median duration of virus detection (18 days) compared with that of the five patients with severe disease (14 days) and the 11 patients with non-severe, but symptomatic disease (10 days).⁽⁶⁴⁾ Other case series studies reported detection of virus in hospitalised asymptomatic adults ranging from seven to 23 days.^(66, 81, 98)

In terms of paediatric cases, a study involving 36 children, reported 10 cases (28%) who remained asymptomatic for the duration of hospitalisation (ranging from 10 to 20 days) and for a further two weeks of post-discharge quarantine.⁽³³⁾ Though individual rRT-PCR results were not provided for each of these 10 cases, for one of these asymptomatic cases, it took 10 days to become SARS-CoV-2 rRT-PCR-negative.⁽³³⁾ In a case series study by Tan et al. one asymptomatic child had detectable virus for 17 days.⁽⁹⁶⁾

Although several other studies reported patients with asymptomatic infections, it is not clear whether patients in these studies were followed up for long enough to determine whether they were truly asymptomatic or simply pre-symptomatic.^(6, 12, 13, 30, 45, 46, 53)

Re-detection of SARS-CoV-2 in discharged patients

There was evidence of patients retesting positive for SARS-CoV-2 despite previously testing negative with rRT-PCR on at least two consecutive occasions.^(1, 5, 20, 25, 34, 39, 51, 54, 60, 62, 64, 68, 72, 91, 103, 104, 109) One study (n=262 patients) observed that patients who had re-detection of RNA had previously had a relatively fast clearance of the RNA during their initial hospitalisation. The authors of this study also observed that patients who retested positive tended to be younger with milder forms of COVID-19 during their initial hospitalisation.⁽¹⁾ However, another study (n=301 patients) found that older patients were more susceptible to retesting positive; the authors suggested that longer observation periods and more than two consecutively negative rRT-PCR tests prior to discharge may be necessary for patients aged 65 years or older.⁽¹⁰³⁾

Duration of SARS-CoV-2 infectivity

Virus culture studies

Four studies were found that correlated serial rRT-PCR test results with virus culturing.^(42, 58, 73, 85)

Arons et al. conducted virus culturing in 46 of the 48 residents of a nursing facility in the US who tested positive for SARS-CoV-2.⁽⁷³⁾ Positive culture growth was recorded in 31 (67.4%) of these upper respiratory tract samples. Viable virus was isolated from asymptomatic, pre-symptomatic and symptomatic residents. The lowest viral load (Ct value targeting N1 gene) for which there was positive culture growth was 34.3 (and this occurred in a pre-symptomatic resident). The highest viral load (Ct value targeting N1 gene) for which there was positive culture growth was 13.6 (in a resident with typical symptoms). Viable virus was isolated from samples collected between six days before, to nine days after, the first evidence of typical symptoms (that is, fever, cough or shortness of breath). When atypical symptoms (that is, chills, malaise, increased confusion, rhinorrhoea/nasal congestion, myalgia, dizziness, headache, nausea, and diarrhoea) are also considered, viable virus was isolated from samples collected six days before to 13 days after first evidence of any symptoms. However, as samples were only collected from residents up to a maximum of 13 days after symptom onset, it is not known if samples collected at later dates may have resulted in positive culture growth.

Woelfel et al. found that no infectious isolates were obtained from any sample (n=9 patients) taken after day eight (of symptom onset) in spite of ongoing high viral

loads. The authors suggested that early discharge followed by home isolation could be chosen for patients with less than 100,000 viral RNA (ribonucleic acid) copies per millilitre (mL) of sputum who are beyond day 10 of symptom onset.⁽⁴²⁾ The detection of infectious isolates was noted to differ by sample site, being readily isolated from throat and lung-derived samples, but not stool samples. This was despite prolonged detection of SARS-CoV-2 viral RNA in stool samples.⁽⁴²⁾

A study by La Scola et al. conducted serial rRT-PCR testing and virus culturing of 183 nasopharyngeal samples from 155 patients.⁽⁵⁸⁾ They found that the virus could not be isolated from samples collected after day eight of symptom onset, in spite of ongoing high viral loads of approximately 10^5 RNA copies/mL of sample. Additionally, they found that positive culture growth decreased progressively according to the viral load. No culture was obtained from samples with Ct values ≥ 34 targeting the E gene. The authors inferred that patients with Ct values ≥ 34 were no longer contagious and could be considered suitable for discharge.⁽⁵⁸⁾

Liu et al.⁽⁸⁵⁾ reported virus isolation in cell cultures from throat swabs collected upon admission and from all sputum samples collected within 18 days of symptom onset in a 50-year-old woman in Taiwan. SARS-CoV-2 continued to be detectable from sputum samples using rRT-PCR (targeting the E gene) for 62 days from symptom onset. The authors concluded that the contagious period of COVID-19 might last more than one week after 'clinical recovery' in certain cases of prolonged virus shedding.⁽⁸⁵⁾ However, there is very limited information relating to the virus culturing results reported in this letter to the editor; as such, these findings should be interpreted with caution.⁽⁸⁵⁾

Epidemiological and modelling studies

Five studies that used epidemiological or modelling approaches to address the duration of infectivity were found.^(8, 15, 41, 57, 70) A prospective case-ascertained study found that all 22 secondary cases, identified from a total of 2,761 close contacts of 100 index cases (ranging from mild-to-severe disease), had their first day of exposure within five days of the index case's symptom onset, suggesting high transmissibility near, or even before, symptom onset. No contacts were infected when first exposure occurred five days after the index case's symptom onset. The authors suggest the rapid reduction of transmissibility over time implies that prolonged hospitalisation of mild cases might not be necessary in large epidemics.⁽⁸⁾ A study conducted in Singapore evaluating seven clusters of COVID-19 found that pre-symptomatic transmission likely occurred between one-to-three days before symptom onset in the pre-symptomatic source patient in four of these clusters.⁽⁴¹⁾ The authors report that it was not possible to determine the exact timing of transmission in the other clusters because the cases lived together and hence exposure was continuous. An epidemiological investigation of an individual with mild disease in the US, found no onward transmission to 16 close contacts (defined as persons exposed to the case, from one day before diagnosis) including one intimate partner.⁽⁷⁰⁾ However, six of the close contacts did not undergo rRT-PCR testing; they

only had symptom monitoring for 14 days. Hence the possibility of asymptomatic infection in these individuals cannot be excluded.

One modelling study based primarily on epidemiological data estimated that 44% of transmission could occur before first symptoms present (starting from 2.3 days before symptom onset (95% CI, 0.8 – 3.0 days) and reaching its peak at 0.7 days before symptom onset (95% CI, –0.2 – 2.0 days). The authors also estimated that infectivity declines relatively quickly within seven days of illness onset.⁽¹⁵⁾ A study conducted in Guangzhou, China applied a statistical transmission model to contact-tracing data of 349 lab-confirmed COVID-19 cases in that region.⁽⁵⁷⁾ The authors found that a mean incubation period of four days and a maximum infectious period (including the incubation period) of 13 days yielded the smallest difference between observed and model-fitted numbers. The model suggested that COVID-19 cases were at least as infectious during their incubation period as from symptom onset.⁽⁵⁷⁾

Differences between adults and children

Thirty-six studies included children (18 years or younger) either exclusively,^(2, 11, 19, 22, 33, 44, 46, 79, 82, 95, 96, 111) or in combination with adults.^(1, 8, 13, 18, 26, 30, 50, 56, 57, 59, 62, 64, 66, 71, 72, 74, 80, 81, 87, 90, 91, 93, 100, 106) No discernible differences with regards to viral load or duration of virus detection were apparent between adults and children. As discussed above, there are inconsistent findings for the association between old age and the duration of virus detection, with studies reporting either a positive^(1, 3, 24, 47, 55, 65, 103) or no association.⁽¹¹²⁾ However, it is unclear whether these findings are directly applicable to children due to the fact that only two of these studies included children and they only comprised a limited (19/242, 7% under the age of 14 years)⁽¹⁾ or unknown⁽¹¹²⁾ proportion of the total study population.

Two included studies compared viral loads between children and adults, either directly⁽⁸⁰⁾ or indirectly (through reference to published findings).⁽⁸²⁾ One of these studies additionally compared virus culturing results indirectly between children and adults.⁽⁸²⁾ In a Swiss case series study, L’Huillier et al. conducted rRT-PCR testing and virus culturing in 23 symptomatic children (age range, seven days to 15.9 years).⁽⁸²⁾ The median viral load at time of diagnosis was 3×10^6 copies/mL (IQR 6.9×10^3 - 4.4×10^8 copies/mL), which the authors comment, is comparable to peak viral load levels typically reported in adults in the literature. Virus isolation was successful in 52% of the children. The youngest patient that SARS-CoV-2 was successfully isolated from was a seven-day old neonate. The authors concluded that infectious virus isolation success was largely comparable to that of adults, although two samples yielded an isolate at a lower viral load (1.2×10^4 and 1.4×10^5 copies/mL) than is typically reported in adults in the literature.⁽⁸²⁾

Another study by Jones et al. analysed viral loads from 3,712 patients (of all ages) with confirmed COVID-19 identified from routine testing at a large laboratory testing centre in Germany.⁽⁸⁰⁾ The authors found no significant difference in viral load across age groups. These data indicate that viral loads in children may not differ

significantly from those of adults, although the relative sample size of children aged ten years or younger (n=49, 1.3%) was small compared with older age groups and therefore, may not be reflective of the general paediatric population.⁽⁸⁰⁾ There has been criticism of the statistical analysis,⁽¹¹⁴⁾ with a secondary re-analysis of these data suggesting there is moderate, but not overwhelming evidence for increasing viral load with increasing age based on a test for trend. The commentator also points to the unbalanced sample sizes between children and adults and suggests that the study is inconclusive.⁽¹¹⁴⁾ Hence, caution is urged when interpreting the findings by Jones et al.⁽⁸⁰⁾

Association between certain health products and viral load or duration of virus detection

Twelve studies included in this review, observed associations between the administration of certain health products and the impact on the viral load or duration of virus detection.^(4, 13, 25-27, 35, 36, 65, 76, 92, 105, 110) One NRCT (n=36 patients) claimed that administration of hydroxychloroquine was significantly associated with faster viral load reduction and that this effect was reinforced by the addition of azithromycin. However, given certain critical flaws with this study (as discussed below), no such conclusion can logically be deduced from this study.⁽¹³⁾ Two studies (one cohort study [n=96 patients]⁽⁶⁵⁾ and one case series study [n=66 patients]⁽²⁶⁾) found delayed viral clearance in patients given glucocorticoids. However, two other studies (one cohort study [n=113 patients]⁽¹⁰⁵⁾ and one case series study [n=31 patients]⁽¹¹⁰⁾) found no association between delayed viral clearance and glucocorticoid administration.

Studies evaluating the effect of lopinavir-ritonavir also reported contrasting findings. Early reports based on a case report⁽²⁵⁾ and a small case series (n=10 patients)⁽²⁷⁾ of accelerated clearance associated with lopinavir-ritonavir administration were refuted by a larger RCT (n=199 patients) that found that lopinavir-ritonavir did not reduce viral loads or duration of virus detectability compared with standard supportive care alone.⁽⁴⁾ A more recent case series study (n=5 patients) also found no association between lopinavir-ritonavir administration and reduced viral shedding.⁽⁷⁶⁾

Two small case series studies (n=5⁽³⁵⁾ and n=2 patients,⁽³⁶⁾ respectively) reported an association between convalescent plasma administration and accelerated viral clearance, suggesting that this treatment may be beneficial and warranted RCT evaluation. A small case series study (n=4 patients) reported that baricitinib was associated with improved lung function, illness resolution and reductions in viral load, indicating that further large scale RCT evaluations may be warranted.⁽⁹²⁾

Methodological quality

The studies were of low-to-moderate quality for their study design. There are some concerns relating to how cases were selected^(7, 10, 12, 23, 27, 28, 30, 32, 34, 36-38, 40, 42, 48, 51, 53, 54, 58, 69, 75-78, 89, 91-93, 100, 104, 107, 109-113) and the pre-print status of 17 included

studies.^(1, 37, 50, 51, 56, 57, 59, 61, 62, 71, 77, 80, 82, 92, 97, 99, 101) Furthermore, given that the majority of these studies comprised case series and case reports, their findings should be viewed with caution and will require confirmation using larger more robust study designs. Another concern is the truncation of data for the duration of virus detection in stool samples, as the data appear to reflect the maximum duration of follow-up rather than the true duration of virus detection in stool samples.

In relation to the included RCT, there are concerns regarding the open label nature of this trial, specifically the lack of blinding of physicians, patients and outcome assessors.⁽⁴⁾ As viral load is an objective measure, this study is at a low risk of bias in this regard, though the findings should still be viewed with caution. In relation to the included NRCT, this study has some critical flaws including bias due to confounding, selection of participants, protocol deviations, missing data, outcome measurements and reporting of outcomes.⁽¹³⁾ The inconsistent and incomplete reporting of the viral load outcome among participants and the very limited follow-up of six days (among other fundamental flaws) indicates that any findings from this study should be interpreted with extreme caution.⁽¹³⁾

The two included modelling studies^(15, 57) are considered to be at a moderate risk of bias as there are some concerns regarding the structure of the model,⁽¹⁵⁾ the underlying source of data,⁽⁵⁷⁾ and the potential lack of internal validation.^(15, 57)

Crucially, the majority of included studies (n=74 studies, 65.5%) were conducted in China.^(1-7, 11, 12, 15, 18, 26-30, 32-36, 43-48, 50-53, 55, 57, 60, 62-67, 71, 72, 74, 75, 77, 79, 83, 87, 89-91, 93-113)

Hence, the findings may not be generalisable to the Irish population given differences in demographics and healthcare practices. Differences in the prevalence of comorbidities could impact the generalisability of these findings; however, it is not known if there is an association between comorbidities and viral load or duration of infectivity as this was not explored. Furthermore, given the volume of Chinese studies published, particularly those comprising single case reports and small case series at the early stages of the pandemic, there is a strong possibility of overlapping data with later publications of larger studies.

Discussion

The evidence to date suggests that the viral load in respiratory tract samples peaks around symptom onset and decreases within one to three weeks. However, different patterns have been observed depending on the sample site, and may describe different clinical evolutions of the disease. Although the duration of detection and the size of the viral load differs between patients, viral RNA generally becomes undetectable (from upper respiratory tract samples) about two weeks after symptom onset. For lower respiratory tract samples, there is conflicting evidence regarding the timing of peak viral loads and duration of virus detection, with some evidence suggesting that the peak occurs later and the duration is longer compared with

upper respiratory tract samples.^(56, 65, 70, 72) Viral shedding in stool samples is prolonged and sometimes erratic.

The clinical significance of virus detection in stool samples is unclear, with no evidence of successful virus isolation from stool samples in any of the 113 studies included in this review. However, a study published after the search was conducted, reported the successful isolation of SARS-CoV-2 virus from stool samples in two of the three patients tested.⁽¹¹⁵⁾ Hence, it is possible that faecal-oral transmission may occur, and so ongoing monitoring is required.

There may be a relationship between higher viral loads or the presence of viral RNA in blood samples and more severe symptoms. There may also be an association between prolonged viral RNA detection and greater severity of disease, ICU admission and or old age. However, these associations were not consistently found. There is also some evidence of prolonged periods of virus detection from upper respiratory tract samples in individuals with mild disease, the reasons for which are not understood.⁽³⁶⁾ In two studies, viral RNA was found to persist longer in asymptomatic patients than in symptomatic patients,^(64, 66) with virus detection exceeding 20 days in some asymptomatic cases.^(18, 64, 66, 98)

The relationship between SARS-CoV-2 detection, viral load and infectivity is not fully understood, and it is known that the presence of viral RNA may not represent transmissible live virus. There is evidence that COVID-19 patients are infectious from one to three days before symptom onset, although viable virus has been successfully isolated from upper respiratory samples up to six days before onset of symptoms, indicating that a pre-symptomatic patient could be infectious for longer than previously thought.⁽⁷³⁾ Two separate epidemiological investigations concluded that there was high transmissibility near, and even before, symptom onset.^(8, 41) The evidence regarding pre-symptomatic and asymptomatic transmission has been reported separately by HIQA.⁽¹¹⁶⁾ Based on the totality of the evidence, it was concluded that pre-symptomatic transmission is possible. Evidence of transmission in asymptomatic (never symptomatic) patients is more limited (perhaps due to difficulties in identifying truly asymptomatic cases) and, while plausible, may not be a driver of overall transmission. Important questions remain regarding the duration of infectivity in asymptomatic and pre-symptomatic patients. There is some evidence that the viral loads in these patients are similar to those in symptomatic patients.^(59, 73)

In symptomatic patients, there is evidence of a reduction in infectivity after seven to 10 days of symptoms, despite prolonged viral shedding. Two virus culturing studies obtained no infectious isolates from any sample taken eight days after symptom onset in spite of ongoing high viral loads.^(42, 58) One of these studies found that patients with Ct values (targeting the E gene) ≥ 34 were no longer contagious.⁽⁵⁸⁾

These findings appear to support early epidemiological and modelling studies,^(8, 15, 57) although one study suggested that transmission may be limited to five days after symptom onset.⁽⁸⁾ The duration of infectivity, however, remains uncertain as two recent studies have reported isolation of viable virus from upper and lower respiratory samples 13 days (maximum follow-up)⁽⁷³⁾ and 18 days⁽⁸⁵⁾ respectively after symptom onset.

A number of studies reported cases of recovered patients re-testing positive for SARS-CoV-2.^(1, 5, 20, 25, 34, 39, 51, 54, 60, 62, 64, 68, 72, 91, 103, 104, 109) In a separate evidence summary, HIQA examined the infectiousness of individuals re-detected positive for SARS-CoV-2 and found no evidence of reinfection or of onward transmission in individuals that re-detect positive during their recovery phase.⁽¹¹⁷⁾ It is possible that the confirmation of virus clearance in the initial infection was based on inconsistent viral shedding or a false negative test result. One possible explanation is that the viral dynamics of SARS-CoV-2 across the course of the infection are not fully understood. Hence, false negative test results may occur if samples are tested during the late convalescent phase, when virus levels may be fluctuating.⁽⁵³⁾ Molecular diagnostic tests (such as rRT-PCR) detect viral RNA, but do not confirm presence of live virus. Intermittently positive test results may therefore reflect inconsistent shedding of non-viable virus, later in the course of an infection. Testing practices differ with some settings requiring three consecutive negative tests taken 24 hours apart to confirm virus clearance, potentially due to concerns regarding false negative results and the potential infectiousness of patients who re-test positive after discharge.^(77, 105)

A limited number of studies that compared findings between children and adults report no differences in terms of viral load and duration of virus detection.^(80, 82) However, there are concerns regarding the statistical analysis undertaken in the largest of these studies.^(80, 114) Although children may have comparable viral loads to adults,^(80, 82) the relationship between viral load and infectivity is not fully understood as viral load is only a proxy measurement of infectivity and may not translate to transmissibility. HIQA has conducted a separate evidence summary examining the role of children in the transmission of SARS-CoV-2 and concluded that, based on the limited number of studies to date, children do not appear to contribute substantially to the spread of COVID-19.⁽¹¹⁸⁾ Children have generally been under-represented in COVID-19 studies to date; although this may be a function of testing practices which have typically prioritised those with more severe symptoms, healthcare workers and those residing in long-term care settings. Given reports of milder symptoms in children, they would be less likely to be tested and diagnosed.⁽¹¹⁹⁾ Therefore, there is substantial uncertainty as to how children become infected, how the virus manifests in children and how it transmits from children to others.

The early peak of viral load in COVID-19 patients, and the detection of virus in asymptomatic and pre-symptomatic patients, underlines the critical importance of ongoing widespread public health and social measures and the rapid detection, diagnosis, isolation and contact tracing of suspected COVID-19 cases.⁽¹²⁰⁾ In particular, the evidence suggests that due to the potentially high viral load in the early stages of the infection, often prior to symptom onset, contact tracing should include a period of at least 48 hours prior to symptom onset in the index case.^(120, 121) These review findings highlight a key virological difference between the current SARS-CoV-2 virus and the SARS-CoV-1 virus that caused severe acute respiratory syndrome (SARS) in 2002 to 2003. That is, SARS-CoV-1 viral load peaked later in the disease trajectory (usually seven to 10 days after symptom onset);^(122, 123) hence, different public health strategies were more successful in containing this infection. However, recent findings of later viral load peaking and prolonged virus detection from lower respiratory tract samples of SARS-CoV-2, as well as evidence of virus isolation from stool samples, warrants further investigation as these findings may have important public health implications.^(56, 65, 115)

Larger and more robust study designs are needed to validate these findings. Notably, virus culturing studies are inherently fraught with challenges (such as low levels of pathogens, the presence of growth suppressive factors in the samples and the lack of a suitable tissue culture system).⁽¹²⁴⁾ Furthermore, research examining the relationship between viral load and transmissibility, particularly in children, is required.

Conclusion

The updated evidence suggests a somewhat consistent trajectory of the viral load of SARS-CoV-2 over the course of the disease, peaking (from respiratory tract samples) around the time of symptom onset or a few days after. However, some studies report that, for lower respiratory tract samples, this peak may occur at a slightly later stage and that the virus may persist for longer. Viral load in stool samples tends to peak at a later stage and follow a more erratic pattern. There is evidence of prolonged viral shedding in stool samples. However, the clinical significance of this finding is uncertain.

There is some evidence that asymptomatic and pre-symptomatic patients have similar viral loads to those in symptomatic patients. Viral ribonucleic acid (RNA) appears to be detectable for around two weeks from symptom onset in symptomatic patients, with limited evidence suggesting it may be detectable for a longer period in asymptomatic patients.

There is some evidence that patients may not be infectious for the entire duration of viral RNA detection, and that infectivity may be related to the viral load. There is

evidence of high transmissibility near or even before symptom onset. Although there is evidence of a reduction in infectivity after seven to 10 days of symptoms, viable virus has been isolated more than 10 days after symptom onset in a limited number of cases.

Based on a limited number of studies which have compared findings between children and adults, there appears to be no difference between children and adults in terms of viral load or duration of virus detection.

There may be an association between higher viral load, detection of viral RNA in blood, longer duration of virus detection and outcomes such as disease severity; however, these relationships were not consistent throughout the literature.

More research is required to establish the duration of infectivity of COVID-19, which is key to informing public health policy in managing the pandemic.

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Table 1 Characteristics of included studies

Author	Population setting	Primary outcome results				
Country						
Study design						
Study URL						
Studies found in original search (30.12.19 to 20.03.20) (n=27 studies)						
J. Cai⁽²⁾	Population setting: 10 patients admitted to a Children's Hospital.	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
China						
Case series	Demographics: Children <i>Age:</i> 3-131 months (mean: 74 months) <i>Sex:</i> Male 4, female 6.	Test: rRT-PCR	From onset of symptoms to the first of two consecutive negative tests: <i>NP/Throat</i> Median (IQR), 12 (8-15) days Range, 6-22	NR	Not tested	NA
https://doi.org/10.1093/cid/ciaa198	Clinical characteristics: <i>Presentation:</i> Fever, 8 (80%); cough, 6 (60%); sore throat, 4 (40%); stuffy nose, 3 (30%); sneezing and rhinorrhea, 2 (20%).	Thresholds: Ct < 35 = positive				
	COVID-19 Clinical syndromes (WHO definition): Mild, 10 (100%).	Gene Targets: N, ORF	Sample site(s): <i>Faeces</i> Range, 10 to >30 days (and still detected) <i>Urine/serum:</i> ND			

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Q. Cai⁽³⁾</p> <p>China</p> <p>Case series</p> <p>https://pubmed.ncbi.nlm.nih.gov/32239761/</p>	<p>Population setting: 298 confirmed COVID-19 cases admitted to a designated hospital.</p> <p>Demographics: Adults <i>Age:</i> Median, 47 years (IQR, 33-61) <i>Sex:</i> Male, 149 (50%); female, 149 (50%).</p> <p>Clinical characteristics: <i>Presentation:</i> Fever 192 (64%); cough, 54 (18.1%); fatigue, 6 (2.0%); headache, 4 (1.3%); diarrhoea, 6 (2.0%); sore throat, 3 (1.0%); nasal congestion, 2 (0.7%); no symptoms, 30 (10%).</p> <p>COVID-19 Clinical syndromes (American Thoracic Society and Infectious Disease Society of America definitions for pneumonia) : Non-severe, 240 (81%); severe, 58 (19%).</p>	<p>Test parameters</p> <p>Test: rqRT-PCR</p> <p>Thresholds: Not defined</p> <p>Gene Targets: N, ORF1ab</p> <p>Sample site(s): Nasal</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: <i>Nasal</i> Median (IQR), 14 (10-20).</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Old age and severe COVID-19 symptoms independently associated with delayed viral clearance.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>D. Chen⁽⁵⁾</p> <p>China</p> <p>Case report</p> <p>http://www.sciencedirect.com/science/article/pii/S1201971220301223</p>	<p>Population setting: 1 patient admitted to hospital.</p> <p>Demographics: Adult <i>Age:</i> 46 years <i>Sex:</i> Female.</p> <p>Clinical characteristics: <i>Presentation:</i> Fever, sore throat, cough, chest distress.</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: qualitative rRT-PCR</p> <p>Thresholds: Not defined</p> <p>Gene Targets: N, ORF1ab</p> <p>Sample site(s): OP</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: ** <i>OP</i> Day 12</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Patient subsequently tested positive again on day 17. Subsequent tests on days 20, 22 and 32 were negative.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>S. Cheng⁽⁹⁾</p> <p>Taiwan</p> <p>Case report</p> <p>http://www.sciencedirect.com/science/article/pii/S0929664620300449</p>	<p>Population setting: 1 patient admitted to hospital (after being quarantined at the airport).</p> <p>Demographics: Adult Age: 55 years Sex: Female.</p> <p>Clinical characteristics: <i>Presentation:</i> Sore throat, dry cough, fatigue, low-grade fever.</p> <p>COVID-19 Clinical syndromes (WHO definition): Severe pneumonia.</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): OP, sputum, stool and urine.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:: ** <i>OP:</i> Day 21 <i>Sputum:</i> Day 17 <i>Stool/urine:</i> Day 25 (but earlier samples not tested).</p> <p>From hospitalisation to the first of two consecutive negative tests::** <i>OP:</i> Day 12 <i>Sputum:</i> Day 8 <i>Stool/urine:</i> Day 16 (but earlier samples not tested).</p> <p>From first detection to the first of two consecutive negative tests:: <i>OP:</i> 10 days <i>Sputum:</i> 6 days.</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>NA</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>He⁽¹⁵⁾</p> <p>China</p> <p>Epidemiological modelling study</p> <p>https://www.nature.com/articles/s41591-020-0869-5.pdf</p>	<p>Population setting: 94 COVID-19 confirmed patients admitted to hospital.</p> <p>Demographics: Adults <i>Age:</i> Median, 47 years <i>Sex:</i> Male 47 (50%); female 47 (50%).</p> <p>Clinical characteristics: <i>Presentation:</i> Moderate illness (with fever and/or respiratory symptoms and radiographic evidence of pneumonia), 61 (66%).</p> <p>COVID-19 Clinical syndromes: Developed to severe or critical, 20 (21%) (not defined).</p>	<p>Test parameters</p> <p>Test: qRT-PCR</p> <p>Thresholds: Ct < 40 = positive</p> <p>Gene Targets: N</p> <p>Sample site(s): Throat</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: Approximately 21 days after onset of illness (using spline analysis).</p>	<p>Peak viral load</p> <p>Highest viral loads detected soon after illness onset (1st test) (Peak trend value, Ct = 30.73)[†].</p>	<p>Pre-symptomatic viral load</p> <p>Infectiousness in pre-symptomatic phase estimated using modelling approaches.</p>	<p>Other relevant findings</p> <p>No obvious difference in viral loads across sex, age groups and disease severity. Authors estimated that 44% of transmission could occur before first symptoms present. (started from 2.3 days before symptom onset and reached its peak at 0.7 days before symptom onset)^{***}</p> <p>Infectiousness was estimated to decline relatively quickly within 7 days of illness onset.^{***}</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Holshue⁽¹⁷⁾</p> <p>US</p> <p>Case report</p> <p>https://www.nejm.org/doi/pdf/10.1056/NEJMoa2001191?articleTools=true</p>	<p>Population setting: 1 patient initially presenting to an urgent care clinic and subsequently hospitalised.</p> <p>Demographics: Adult Age: 35 years Sex: Male</p> <p>Clinical characteristics: <i>Presentation:</i> 4-day history of cough and subjective fever.</p> <p>COVID-19 Clinical syndromes (WHO definition): Severe pneumonia.</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: N</p> <p>Sample site(s): NP, OP, serum, urine, stool.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: NR</p>	<p>Peak viral load</p> <p><i>Viral load peaked at first test for all sites</i></p> <p><i>NP:</i> Day 4 of illness (Ct, 18-20)***</p> <p><i>OP:</i> Day 4 of illness (Ct, 21-22)</p> <p><i>Stool:</i> Day 7 of illness (Ct, 36-38) (but only 1 test)</p> <p><i>Urine and Serum:</i> All tests negative</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>NA</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Hu⁽¹⁸⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1007/s11427-020-1661-4</p>	<p>Population setting: 24 cases with asymptomatic/pre-symptomatic infection screened from close contacts.</p> <p>Demographics: <i>Mix of adults and children</i> Age: Median (IQR) 32.5 (19.0 - 57.0) 5 (21%) are under the age of 15 Range: 5-95 years Sex: Male, 8 (33%); Female 16 (67%).</p> <p>Clinical characteristics: <i>Presentation:</i> Asymptomatic, 24 (100%).</p> <p>COVID-19 Clinical syndromes: 5 developed mild symptoms after diagnosis (not defined).</p>	<p>Test parameters</p> <p>Test: qRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: ORF1ab, N</p> <p>Sample site(s): Pharyngeal (swab specimens were collected on admission day and every other day thereafter).</p>	<p>Duration of virus detection* (Days)</p> <p>From first day of positive detection to the first of two consecutive negative tests: Median (IQR), 9.5 days (3.5-13.0) Range: 1-21 days.</p> <p>For patients who subsequently developed symptoms: Median (IQR), 12.0 (12.0 - 14.0) days</p> <p>For patients who never developed symptoms: Median (IQR), 6.0 (2.0 - 12.0) days.</p> <p>From suspected exposure time to the first of two consecutive negative tests: Median (IQR): 20.5 days (16-26.25)</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>PCR testing undertaken during pre-symptomatic period but no viral load information provided.</p>	<p>Other relevant findings</p> <p>Found evidence for transmission from an asymptomatic infector to close contacts that led to severe COVID-19 pneumonia.</p> <p>One pre-symptomatic patient tested positive for SARS-CoV-2 (RT-PCR) 2 days before displaying any symptoms.</p> <p>Two pre-symptomatic patients tested negative for SARS-CoV-2 (RT-PCR) 7 and 8 days prior to first symptoms respectively (but after suspected exposure).</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Kam⁽¹⁹⁾</p> <p>Singapore</p> <p>Case report</p> <p>https://doi.org/10.1093/cid/ciaa201</p>	<p>Population setting: 1 child admitted to hospital.</p> <p>Demographics: Child <i>Age:</i> 6-months old <i>Sex:</i> Male.</p> <p>Clinical characteristics: <i>Presentation:</i> Asymptomatic.</p> <p>COVID-19 Clinical syndromes (WHO definition): Mild (developed fever 38.5°C on day 2 of hospitalisation which resolved within 1 hour).</p>	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		<p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: ORF1ab, N</p> <p>Sample site(s): NP, Blood, urine, stool</p>	NR	<p><i>Viral load peaked at first test for all sites (Except stool)</i></p> <p><i>NP (N-gene):</i> 15.57 Ct value <i>NP (ORF1ab-gene):</i> 13.73 Ct value (day 1 of hospitalisation).</p> <p><i>Blood (N-gene):</i> 32.87 Ct value <i>Blood (ORF1ab-gene):</i> 33.90 Ct value (day 2 of hospitalisation).</p> <p><i>Urine:</i> Not detectable at any stage.</p> <p><i>Stool (N-gene):</i> 28.96 Ct value <i>Stool (ORF1ab-gene):</i> 34.80 Ct Value (peaked at day 8, but was not detected on day 2 of hospitalisation).</p>	<p>Patient remained asymptomatic (except for mild fever on day 2 which resolved within 1 hour).</p> <p>Viral load as measured via NP targeting ORF1ab gene increased marginally prior to fever outbreak and then decreased once fever resolved (Ct values: 20.08 to 18.56 (day of fever) to 29.07).</p>	

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Kim⁽²⁰⁾</p> <p>South Korea</p> <p>Case series</p> <p>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7036338/pdf/jkms-35-e86.pdf</p>	<p>Population setting: 2 hospitalised patients</p> <p>Demographics: Adults Patient 1: 35 year old woman Patient 2: 55 year old man</p> <p>Clinical characteristics: <i>Presentation:</i> Patient 1: fever, chills, and myalgia Patient 2: sore throat and intermittent myalgia.</p> <p>COVID-19 Clinical syndromes: Patient 1: Moderate Patient 2: Mild (not defined).</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: Ct > 37 = negative</p> <p>Gene Targets: RdRp, E</p> <p>Sample site(s): URT, LRT, serum, plasma, urine, stool</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:**</p> <p>Patient 1: <i>URT(RdRp):</i> Day 14 <i>URT:(E):</i> Day 14 <i>LRT(RdRp):</i> Day 13 <i>LRT(E):</i> Day 11 <i>Stool(E):</i> Day 10 <i>Serum, Urine, Stool(RdRp):</i> <i>ND on multiple initial tests but fluctuated from positive to negative at several times</i> <i>Plasma:</i> ND at any stage.</p> <p>Patient 2: <i>URT (RdRp):</i> Day 17 <i>URT: (E):</i> Day 17 (both turned positive again on day 25) <i>LRT: (E)</i> Day 14 (turned positive again on day 26) <i>Plasma(RdRp), Stool(RdRp), Serum and urine:</i> ND at any stage <i>LRT(RdRp),Plasma(E), Stool (E):</i> Only 1 positive test each despite near daily testing.</p>	<p>Peak viral load</p> <p>Viral load was highest during the early phase of the illness.</p> <p>Patient 1: Days 3-5</p> <p>Patient 2: Days 14-17 (but only presented on day 14) Initial viral loads from Patient 2 (mild disease) substantially lower than those from Patient 1 (moderate disease).</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Increase and decrease in viral loads may signal worsening and improvement of clinical symptoms respectively.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Kujawski⁽²¹⁾</p> <p>US</p> <p>Case series</p> <p>https://www.nature.com/articles/s41591-020-0877-5</p>	<p>Population setting: 12 patients with COVID-19 (7 were hospitalised)</p> <p>Demographics: Adults Age: Median: 53 Range 21-68 Sex: Male 8 (67%), Female 3 (33%)</p> <p>Clinical characteristics: <i>Presentation:</i> cough (n=8), fever (n=7), diarrhoea (n=1) and sore throat (n=1)</p> <p>COVID-19 Clinical syndromes: Mild to moderate, 12 (100%) (not defined)</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): NP, OP, sputum, serum, urine, stool</p>	<p>Duration of virus detection* (Days)</p> <p>Maximum length of virus detection from onset of symptoms to the first of two consecutive negative tests:** NP: Day 26 OP: Day 26 Sputum: Day 29 Stool: Day 25</p>	<p>Peak viral load</p> <p>Ct values were lower in the first week of illness than the second in most patients. However 1 patient had positive sputum sample > 2 weeks after symptom resolution.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Among 98 pairs of simultaneous NP and OP specimens, only 58 (59%) had concordant results.</p> <p>The only patient with detected RNA in serum experienced the most severe clinical deterioration during the second week of illness.</p> <p>SARSCoV-2 RNA was detected after reported symptom resolution in 7/11 patients, including in NP (n=6), OP (n=2), sputum (n=1), and stool (n=3) specimens.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
Lee⁽²³⁾ Taiwan Case report http://www.sciencedirect.com/science/article/pii/S1684118220300608	Population setting: 1 patient presenting to emergency department Demographics: <i>Adult</i> 46 year old woman Clinical characteristics: <i>Presentation:</i> fever, dyspnoea and cough. COVID-19 Clinical syndromes (WHO definition): Pneumonia	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		Test: qRT-PCR, SARS-CoV-2 (ALLTEST 2019-nCoV IgG/IgM Rapid TestCassette) Thresholds: NR Gene Targets: E/RdRp1/RdRp2/N Sample site(s): NP, OP, serum	From onset of symptoms to the first of two consecutive negative tests:** NP: Day 20 of illness (Day 16 of hospitalisation). OP: Only 1 negative sample detected on day 25 of illness.	NR	Not tested	SARS-CoV-2 IgG antibody was detected in five serum samples since Day 11 of illness, but was not detected at Days 6 or 7.
Lim⁽²⁵⁾ South Korea Case report https://www.ncbi.nlm.nih.gov/pubmed/32056407	Population setting: 1 patient admitted to hospital Demographics: <i>Adult:</i> 54 year old man Clinical characteristics: <i>Presentation:</i> Chills and muscle pains. COVID-19 Clinical syndromes (WHO definition): Pneumonia	Test: qRT-PCR Thresholds: NR Gene Targets: RdRp, E Sample site(s): Sputum	From onset of symptoms to the first of two consecutive negative tests:** Sputum (both E and RdRp): Day 11 of illness (Day 9 of hospitalisation). <i>However virus became detectable again on days 13 to 16 of illness (Days 11-14 of hospitalisation)</i>	Day 9 of illness for both gene targets (first day of testing) E: Ct 28.50 RdRp: Ct 30.71	Not tested	Authors claim that administration of lopinavir/ritonavir was associated with a reduction in viral clearance, however this hypothesis remains to be tested in RCTs.

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Ling⁽²⁶⁾</p> <p>China</p> <p>Case series</p> <p>https://journals.lww.com/cmj/Fulltext/publishahead/Persistence_and_clearance_of_viral_RNA_in_2019.99362.aspx</p>	<p>Population setting: 66 COVID-19 patients admitted to hospital who have recovered.</p> <p>Demographics: <i>Mix of adults and children (predominantly adults)</i> Age: Median (IQR) 44.0 (34.0-62.0) Range: 16-78 <i>Sex:</i> Females, 28 (42.4%); males 38 (57.6%).</p> <p>Clinical characteristics: <i>Presentation:</i> NR</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): OP, stool, urine, and serum</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:</p> <p>OP: Median (IQR) 9.5 (6.0-11.0) days. Range 2-22 days</p> <p>Faecal (n=55): Median (IQR): 11 (9.0-16.0) days.</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>The authors report that administration of corticosteroids was associated with delayed clearance of viral RNA in both OP and stool samples.</p> <p>78.2% (43/55) cases had longer duration for stool specimens detected negative for viral RNA than throat swabs, with median delay of 2.0 (1.0-4.0) days.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>F. Liu⁽²⁷⁾</p> <p>China</p> <p>Case series</p> <p>http://www.sciencedirect.com/science/article/pii/S1201971220301326</p>	<p>Population setting: 10 patients admitted to hospital</p> <p>Demographics: <i>Adults</i> Age: Median (IQR) 42 (34–50). Sex: Females, 6 (60%), males 4 (40%)</p> <p>Clinical characteristics: <i>Presentation:</i> Cough, 8 (80%), phlegm, 4 (40%), headache, 3 (30%), nausea, 3 (30%), sore throat, 4 (40%), chest congestion, 1 (10%), fever, 7 (70%), anxiety, 1 (10%).</p> <p>COVID-19 Clinical syndromes: Mild, 5 (50%), moderate, 3 (30%), severe, 2 (20%) (not defined).</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: Ct value ≤ 35 = positive</p> <p>Gene Targets: E, N, RdRp</p> <p>Sample site(s): Nasal, throat</p>	<p>Duration of virus detection* (Days)</p> <p>From first day of hospitalisation to the first of two consecutive negative tests:** Median (IQR): Day 11 (10-13) Range: Days 7 - 18</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Authors claim that administration of lopinavir/ritonavir was associated with an increase in viral clearance; however, this hypothesis remains to be tested in RCTs.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
Marchand-Senecal⁽³¹⁾ Canada Case report https://doi.org/10.1093/cid/ciaa227	Population setting: 1 patient admitted to hospital Demographics: <i>Adult</i> 56 year old male Clinical characteristics: <i>Presentation:</i> new onset fever and non-productive cough. COVID-19 Clinical syndromes (WHO definition): Pneumonia	Test parameters Test: RT-PCR Thresholds: Ct value <40 = positive Gene Targets: RdRp, E, N, ORF3a Sample site(s): NP, mid-turbinate, throat.	Duration of virus detection* (Days) From onset of symptoms to the first of two consecutive negative tests: Throat: 7 days NP: 23 days Mid-turbinate: Positive in all tests. Only conducted 5 tests in the initial phase of illness.	Peak viral load <i>Viral load increased slightly on day 2 of testing for both throat and NP and then fell. Highest viral load for mid-turbinate detected on first test.</i> Throat: Ct =28.09 (3 days after symptom onset) NP: Ct = 28.09 (6 days after symptom onset) Mid-turbinate: Ct = 28.55 (1 day after symptom onset) [†]	Pre-symptomatic viral load Not tested	Other relevant findings NA

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<p>Pan⁽³²⁾</p> <p>China</p> <p>Case series</p> <p>http://www.sciencedirect.com/science/article/pii/S1473309920301134</p>	<p>Population setting: 2 patients admitted to hospital (plus samples from 80 patients at different stages of COVID-19).</p> <p>Demographics: NR</p> <p>Clinical characteristics: NR</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: N</p> <p>Sample site(s): Nasal, Throat, sputum, urine and stool.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:</p> <p>Patient 1: Sputum: 8 days Throat: 9 days Urine/stool: ND</p> <p>Patient 2: Sputum: 12 days Throat: 9 Days Urine/stool: ND</p>	<p>Peak viral load</p> <p>The viral loads in throat swab and sputum samples peaked at around 5–6 days after symptom onset, ranging from around 10⁴ to 10⁷ copies per mL during this time.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Sputum samples generally showed higher viral loads than throat swab samples. Two individuals (from the sample of 80) showed positive results on RT-PCR a day before symptom onset, suggesting that infected individuals can be infectious before they become symptomatic.</p> <p>An individual who subsequently died had very high viral load 8 days after symptom onset.</p> <p>Lower viral loads in stool samples than from other sites.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
Qu⁽³⁴⁾ China Case report http://www.sciencedirect.com/science/article/pii/S1477893920300879	Population setting: 1 patient admitted to hospital Demographics: <i>Adult</i> 49 year old man Clinical characteristics: <i>Presentation:</i> Fever COVID-19 Clinical syndromes: NR	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		Test: RT-PCR Thresholds: NR Gene Targets: N Sample site(s): Throat and Sputum.	From onset of symptoms to the first of two consecutive negative tests: Throat: 22 days (however sputum sample tested 4 days later was positive).	NR	Not tested	NA
L.V. Tan⁽³⁷⁾ Vietnam Case report https://www.medrxiv.org/content/medrxiv/early/2020/03/16/2020.03.07.20032052.full.pdf	Population setting: 1 patient hospitalised Demographics: <i>Adult</i> 73 year old man Clinical characteristics: <i>Presentation:</i> Dry cough and breathing difficulties. COVID-19 Clinical syndromes (WHO definition): Severe pneumonia	Test: RT-PCR Thresholds: Ct value < 40 = positive Gene Targets: ORF-1 Sample site(s): Throat, rectal, plasma, urine.	From onset of illness to the first of two consecutive negative tests:** Throat: Day 16 (Day 11 of hospitalisation) Rectal: Day 23 (Day 18 of hospitalisation) Urine and Plasma: Only detected on one occasion each (days 11 and 7 respectively).	Throat: Ct = 28.15 (Day 6 of illness onset) Rectal: Ct=29.62 (Day 21 of illness) Plasma: Ct = 39.68 (Day 7 of illness) Urine: Ct = 44.91 (Day 11 of illness)†	Not tested	Rectal samples remained positive upon patient discharge.

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Thevarajan⁽³⁸⁾</p> <p>Australia</p> <p>Case report</p> <p>https://www.nature.com/articles/s41591-020-0819-2.pdf</p>	<p>Population setting: 1 patient hospitalised</p> <p>Demographics: <i>Adult</i> 47 year old female</p> <p>Clinical characteristics: <i>Presentation:</i> lethargy, sore throat, dry cough, pleuritic chest pain, mild dyspnoea and subjective fevers.</p> <p>COVID-19 Clinical syndromes: Mild-to-moderate (not defined).</p>	<p>Test parameters</p> <p>Test: RT-PCR, Anti IgM, Anti IgG</p> <p>Thresholds: Ct value < 45 = positive</p> <p>Gene Targets: E</p> <p>Sample site(s): NP, Faecal, sputum, rectal, urine, throat</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of illness to the first of two consecutive negative tests:** Throat: Day 7 Faecal and Sputum: Day 6 (but only a single test performed) Urine and Rectal: ND</p>	<p>Peak viral load</p> <p><i>Viral load highest on first testing</i></p> <p>NP: Ct = 33.03 (Day 4 of illness)</p> <p>Sputum: Ct = 31.87 (Day 6 of illness)</p> <p>Faeces: Ct = 40.11 (Day 6 of illness)[†]</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Anti-IgM antibodies first detected at day 7 of illness. Anti-IgG antibodies first detected at day 9 of illness.</p>
<p>K. To (a)⁽⁴⁰⁾</p> <p>Hong Kong</p> <p>Case series</p> <p>https://doi.org/10.1093/cid/ciaa149</p>	<p>Population setting: 12 hospitalised patients</p> <p>Demographics: <i>Adults</i> Age: Median, 62.5 Range, 37-75 Sex: female, 5 (42%); males, 7 (58%)</p> <p>Clinical characteristics: <i>Presentation:</i> NR</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: qRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: S</p> <p>Sample site(s): Saliva</p>	<p>From onset of illness to the first of two consecutive negative tests: NR</p>	<p><i>Viral load highest on first testing (median of 2 days hospitalised) for all patients (except one where the viral load was slightly higher on second testing)</i></p> <p>Viral load on first test: median, 3.3×10^6 copies/mL (range, 9.9×10^2 - 1.2×10^8 copies/mL)</p>	<p>Not tested</p>	<p>RNA detected in 11/12 saliva samples that were otherwise confirmed to have COVID-19.</p> <p>Authors suggest that saliva testing could be a viable alternative to NP or OP testing.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Woelfel⁽⁴²⁾</p> <p>Germany</p> <p>Case series</p> <p>https://pubmed.ncbi.nlm.nih.gov/32235945/</p>	<p>Population setting: 9 cases (samples taken from inpatients)</p> <p>Demographics: “young- to middle-aged professionals”.</p> <p>Clinical characteristics: <i>Presentation:</i> NR</p> <p>COVID-19 Clinical syndromes: Mild to moderate (not defined).</p>	<p>Test parameters</p> <p>Test: qRT-PCR IgG/IgM immunofluorescence</p> <p>Thresholds: 10² copies/ml</p> <p>Gene Targets: E- and RdRp</p> <p>Sample site(s): OP, NP, sputum urine, serum, stool.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of illness to the first of two consecutive negative tests:</p> <p>Sputum: median 11.5 days</p> <p>OP/NP Swab: median 9.5 days</p> <p>Stool: persistently positive.</p>	<p>Peak viral load</p> <p>OP/NP: The average viral RNA load was 6.76x10⁵ copies per whole swab until day 5 of illness (maximum, 7.11x10⁸ copies/swab). Swab samples taken after day 5 had an average viral load of 3.44x10⁵ copies per swab.</p> <p>In the two patients with pneumonia, sputum viral loads peaked around day 10/11. In all other patients with milder disease viral loads were consistently declining.</p> <p>Urine and serum: ND</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Infectious virus was readily isolated from throat- and lung-derived samples, but not from stool samples in spite of high and prolonged viral RNA concentration.</p> <p>No infectious isolates were obtained from any sample taken after day 8 in spite of ongoing high viral loads.</p> <p>Seroconversion occurred after 6-12 days, but was not followed by a rapid decline of viral loads.</p> <p>The authors suggest that early discharge with ensuing home isolation could be chosen for patients who are beyond day 10 of symptoms with less than 100,000 viral RNA copies per ml of sputum.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Xing⁽⁴⁴⁾</p> <p>China</p> <p>Case series</p> <p>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7141453/pdf/main.pdf</p>	<p>Population setting: 3 hospitalised children</p> <p>Demographics: <i>Children</i> <i>Case 1:</i> 18 month old male <i>Case 2:</i> 5 year old male <i>Case 3:</i> 6 year old female</p> <p>Clinical characteristics: <i>Presentation:</i> Fever, 3 (100%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition): Mild to moderate, 3 (100%)</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat and faecal</p>	<p>Duration of virus detection* (Days)</p> <p>From day of hospitalisation to the first of two consecutive negative tests:** Throat: median Day 14 Faeces: median Day 31</p>	<p>Peak viral load</p> <p>Measured in Case 1 only. Throat: peaked on day of admission, (which was first test), Ct value = 18.17</p> <p>Faecal: peaked on Day 4 of hospitalisation (which was second test), Ct value = 12.31</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Viral clearance in respiratory tract occurred within two weeks after abatement of fever, whereas viral RNA remained positive in stools of paediatric patients for longer than 4 weeks.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>T. Xu⁽⁴⁵⁾</p> <p>China</p> <p>Case series</p> <p>http://www.sciencedirect.com/science/article/pii/S1201971220301417</p>	<p>Population setting: 51 laboratory-confirmed patients admitted to hospital Imported (visited/ originated from Wuhan): 15 Secondary (close contacted with imported patients): 17 Tertiary (acquired through contact with the secondary cases):19</p> <p>Demographics: <i>Adults</i> <i>Age:</i> median (IQR) Imported – 35 (29-51) Secondary – 37.0 (24.0-47.5) Tertiary – 53 (35-65)</p> <p><i>Sex:</i> Male 25 (49%); female 26 (51%)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever (34); cough (23); myalgia (8); diarrhoea (5); dyspnoea (4); pharyngalgia (2); asymptomatic (6).</p> <p>COVID-19 Clinical syndromes (WHO definition): No patients developed severe pneumonia or ARDS, or required mechanical ventilation.</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: Ct value <40 was considered positive.</p> <p>Gene Targets: Orf1ab; N</p> <p>Sample site(s): Throat swabs, anal swab, bronchoalveolar lavage fluid.</p>	<p>Duration of virus detection* (Days)</p> <p>From hospital admission to the first of two consecutive negative tests: NR</p>	<p>Peak viral load</p> <p>The viral load tended to be the highest in the first test and then gradually decreased</p> <p>Ct values (throat) at the time of admission, median (IQR) <i>Imported</i> Orf1ab: 28.0 (26.0-30.0) N: 30.0 (26.0-32.0) <i>Secondary</i> Orf1ab: 30.0 (8.0-31.5) N: 30.0 (27.5-32.0) <i>Tertiary</i> Orf1ab: 30.0 (22.0-34.0) N: 32.0 (26.0-34.0)</p> <p>By Day 7 of hospitalisation: viral load undetectable for 52.63% of tertiary group</p> <p>By Day 14 of hospitalisation: virus detectable for 1/3rd of the imported and secondary patients. Viral load undetectable for all tertiary group cases.</p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>NA</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Young⁽⁴⁹⁾</p> <p>Singapore</p> <p>Case series</p> <p>https://doi.org/10.1001/jama.2020.3204</p>	<p>Population setting: 18 hospitalised patients</p> <p>Demographics: <i>Adults</i> Age: median 47 years Range, 31-73 Sex: Male 9 (50%); female 9 (50%)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever 13 (72%); cough 15 (83%); sore throat 11 (61%); diarrhoea 3 (17%); SOB 2 (11%); Rhinorrhea 1 (6%).</p> <p>COVID-19 Clinical syndromes: Uncomplicated 12 (67%); required supplemental oxygen 6 (33%) (not defined).</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: Ct > 38 = negative</p> <p>Gene Targets: N, S, and Orf1b</p> <p>Sample site(s): Nasopharyngeal swabs, stool, urine, blood.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:** NP: Median: Day 12.5</p> <p>From first to last positive nasopharyngeal swab: Median (range): 12 days (1-24)</p> <p>15 patients (83%) had viral shedding from the nasopharynx detected for ≥7 days.</p>	<p>Peak viral load</p> <p>Peak viral threshold value tends to be positively skewed, peaking around Days 3-5 of illness onset</p> <p><i>The highest detected viral load of all 18 patients was reported on Day 4 of illness (Ct = 20.0). †</i></p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>Virus was detected by PCR in stool (4/8 [50%]) and in whole blood (1/12 [8%]); virus was not detected in urine (0/10 samples).</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Yuan⁽⁵⁰⁾</p> <p>China</p> <p>Case series</p> <p>https://www.medrxiv.org/content/medrxiv/early/2020/03/10/2020.03.06.20031377.full.pdf</p>	<p>Population setting: 25 patients re-hospitalised due to re-detection of SARS-CoV-2 viral RNA.</p> <p>Demographics: <i>Mix of children and adults</i> Age: Median 28 (16.25-42). 6 were under 12. Sex: males 8 (32%); female 17 (68%).</p> <p>Clinical characteristics: <i>Initial presentation:</i> fever 17 (68%); cough 14 (56%) <i>Re-admission due to re-detection of viral RNA:</i> Asymptomatic 25 (100%)</p> <p>COVID-19 Clinical syndromes: <i>Initial:</i> non-severe 24 (96%). <i>Re-admission:</i> No symptoms 25 (100%) (not defined).</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Cloacal swab, nasal swabs, or oropharynx swab</p>	<p>Duration of virus detection* (Days)</p> <p>Time from last negative result to turning positive (Days):</p> <p>Median (IQR), 6 (4-10) days</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>Authors implied that the imperfect antiviral therapy probably was responsible for the re-detection of COVID-19 virus.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Zhou⁽⁵²⁾</p> <p>China</p> <p>Retrospective cohort study</p> <p>http://www.sciencedirect.com/science/article/pii/S0140673620305663</p>	<p>Population setting: 191 adult (≥18 years old) inpatients in two hospitals (Wuhan)</p> <p>Demographics: <i>Adults</i> Age: Median (IQR) 56.0 (46.0 - 67.0) Sex: Male 119 (62%); female 72 (38%)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever 180 (94%); cough 151 (79%); sputum 44 (23%); myalgia 29 (15%); fatigue 44 (23%); diarrhoea 9 (5%); chest distress 1(0.5%); nausea 7(4%).</p> <p><i>Outcome:</i> Died 54 (28.3%); discharged 137 (71.7%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition): General: 72 (38%) Severe: 66 (35%) Critical: 53 (28%)</p>	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		<p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat-swab</p>	<p>From first day of symptoms to the first of two consecutive negative tests: All (n=191) Median (IQR) 20.0 days (16.0 – 23.0)</p> <p>Survivors (n=137) Median (IQR) 20.0 days (17.0–24.0)</p> <p>Non-survivors (n=54) Median (IQR) 18.5 days (15.0–22.0) Shedding continued until death.</p>	NR	NR	The shortest observed duration of viral shedding among survivors was 8 days, whereas the longest was 37 days.

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Zou⁽⁵³⁾</p> <p>China</p> <p>Case series</p> <p>https://www.nejm.org/doi/full/10.1056/NEJMc2001737</p>	<p>Population setting: 18 patients</p> <p>Demographics: <i>Adults</i> Age: median (range) 59 (26 to 76) Sex: Male 9 (50%); female 9 (50%)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever (10), cough (9), SOB (3), weakness (3), chest distress (1), myalgia (2), haemoptysis (2), headache (2), diarrhoea (1), nausea (1), palpation (1), poor appetite (1), asymptomatic (1).</p> <p>COVID-19 Clinical syndromes: 13 with evidence of pneumonia CT. Mild-to-moderate illness with 3 ICU admissions(not defined).</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: Negative = Ct value > 40</p> <p>Gene Targets: N and Orf1b</p> <p>Sample site(s): 72 nasal swabs (sampled from the mid-turbinate and nasopharynx); 72 throat swabs. 1 - 9 sequential samples obtained from each patient.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: NR</p>	<p>Peak viral load</p> <p>When data from all 18 patients (Ct values) are aggregated viral loads peaked in the early stage of the illness.</p> <p>Throat: Day 1 of illness onset (Ct = 25.98.</p> <p>Nasal: Day 3 of illness onset (Ct = 21.10)†</p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>Higher viral loads were detected in the nose than in the throat.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
Studies found in updated search (up to 27.03.20) (n=12 additional studies)						
<p>Cao⁽⁴⁾</p> <p>China</p> <p>RCT</p> <p>https://www.nejm.org/doi/full/10.1056/NEJMoa2001282</p>	<p>Population setting: 199 patients with severe COVID-19 (Sao₂ ≤ 94% while breathing ambient air or a ratio of Pao₂ to Fio₂ < 300 mm Hg).</p> <p>Demographics: <i>Adults</i> <i>Age:</i> Median (IQR), 58 (49–68) <i>Sex:</i> Male, 120 (60.3%) Female (all non-pregnant), 79 (39.7%)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever 182 (91.5%), Respiratory rate >24/min, 37 (18.8%)</p> <p>COVID-19 Clinical syndromes (Chinese CDC definition): Severe, 199 (100%)</p>	<p>Test parameters</p> <p>Test: qRT-PCR</p> <p>Thresholds: Results less than the lower limit of quantification of PCR assay (<10 copies/ul) and greater than the limit of qualitative detection (>1 copy/ul) are imputed with 1 log¹⁰ copies/mL; results of patients with viral negative RNA are imputed with 0 log¹⁰ copies/mL</p> <p>Gene Targets: RdRP, N and E</p> <p>Sample site(s): Throat (n=130)</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: NR</p>	<p>Peak viral load</p> <p>Viral load was highest on Day 1 of randomisation (which took place a median of 13 days (IQR 11–16). after illness onset). The viral load then fell over the next 4 weeks: †**</p> <p><i>Mean ±SD log¹⁰ copies per ml</i></p> <p>Day 1: <i>Total population:</i> 4.0±2.1 <i>Lopinavir–Ritonavir arm:</i> 4.4±2.0 <i>Standard care arm:</i> 3.7±2.1</p> <p>Day 5: <i>Total population:</i> NR <i>Lopinavir–Ritonavir arm:</i> 2.4 <i>Standard care arm:</i> 1.7</p> <p>Day 10: <i>Total population:</i> NR <i>Lopinavir–Ritonavir arm:</i> 1.5 <i>Standard care arm:</i> 1.5</p> <p>Day 14: <i>Total population:</i> NR <i>Lopinavir–Ritonavir arm:</i> 1.3</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Authors found that adding lopinavir–ritonavir treatment did <u>not</u> reduce viral RNA loads or duration of viral RNA detectability as compared with standard supportive care alone.</p> <p>The percentage of patients with detectable viral RNA for SARS-CoV-2 was similar in the lopinavir–ritonavir group and the standard-care group on any sampling day (day 5 (of randomisation), 34.5% vs. 32.9%; day 10, 50.0% vs. 48.6%; day 14, 55.2% vs. 57.1%; day 21, 58.6% vs. 58.6%; and day 28, 60.3% vs. 58.6%).</p>

				<p><i>Standard care arm: 0.6</i></p> <p>Day 21: <i>Total population: NR</i> <i>Lopinavir–Ritonavir arm: 0.08</i> <i>Standard care arm: 0.06</i></p> <p>Day 28: <i>Total population: NR</i> <i>Lopinavir–Ritonavir arm: 0</i> <i>Standard care arm: 0</i></p>		
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Author Country Study design Study URL	Population setting	Primary outcome results				
<p>J. Chen⁽²⁾</p> <p>China</p> <p>Case series</p> <p>https://www.sciencedirect.com/science/article/pii/S0163445320301195</p>	<p>Population setting: 249 hospitalised patients</p> <p>Demographics: <i>Adults</i> <i>Age:</i> Median 51 (IQR, 36–64 years) <i>Sex:</i> Male, 126 (50.6%), female, 123 (49.7%)</p> <p>Clinical characteristics: <i>Presentation:</i> fever, 217 (87.1%); cough, 91 (36.5%); fatigue, 39 (15.7%), dizziness and headache, 28 (11.2%); shortness of breath, 19 (7.6%); rhinorrhoea, 17 (6.8%); sore throat, 16 (6.4%); diarrhoea, 8 (3.2%); lack of appetite 8 (3.2%); asymptomatic, 7 (2.8%).</p> <p>COVID-19 Clinical syndromes: Authors report that “nearly 10% were severe and critical”. The rest (~90%) were considered mild or asymptomatic.(not defined)</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Upper respiratory tract</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: Median, 11 days (95% CI, 10-12 days)</p> <p>From hospital admission to the first of two consecutive negative tests: <i>Asymptomatic patients (n=7):</i> median 2 days (95% CI, 1-3).</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Median time from initiation of symptoms to viral clearance was significantly longer in ICU patients than in non-ICU patients (HR=3.17, 95% CI, 2.29-4.37).</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>W. Chen⁽⁷⁾</p> <p>China</p> <p>Case series</p> <p>https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1732837</p>	<p>Population setting: 57 hospitalised patients (including 6 patients testing positive for RNA in blood samples)</p> <p>Demographics: NR</p> <p>Clinical characteristics: <i>Presentation:</i> NR</p> <p>COVID-19 Clinical syndromes (Chinese CDC definition):</p> <p>Mild, 39 (68.4%) Severe, 18 (31.6%).</p> <p>Patients with at least one of the following symptoms were classified as severe cases, 1) distress of respiratory with respiratory rate \geq 30/min; 2) Oxygen saturation \leq 93% in the rest state, and 3) PaO₂ / FIO₂ of less than 300 mm Hg.</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: ORF1ab, N</p> <p>Sample site(s): Pharyngeal, blood, anal.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:</p> <p>NR</p>	<p>Peak viral load</p> <p>Patient 1: Pharyngeal sample peaked day 11 of illness while in ICU (ORF1ab, Ct = 15) (4th day of testing) N target: Ct = 25 both on 1st and 4th day of testing (day 5 and 11 of illness) Blood: Peaked day 9 of illness for ORF1ab target (Ct = 36) and day 6 for N target (Ct = 39) Anal: Single positive Peaked day 13 (ORF1ab, Ct = 23; N, Ct = 27).</p> <p>Patient 2: Pharyngeal sample peaked day 10 of illness while in ICU (ORF1ab, Ct = 23; N, Ct = 24) (2nd day of testing) Blood sample peaked on day 7 and 10 for ORF1ab target (Ct = 34) and day 7 for N target (Ct = 36) Anal: Single positive peaked day 10 (ORF1ab, Ct = 24; N, Ct = 39).</p> <p>Patient 3: Pharyngeal sample peaked day 12 of illness while in ICU</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Authors report that the presence of viral RNA in the blood and anal swab is positively correlated with severity of disease.</p>

				<p>(ORF1ab, Ct = 30; N, Ct = 30) (1st day of testing). Single positive blood test on day 12 (ORF1ab, Ct = 37; N, Ct = 39) Anal: ND.</p> <p>Patient 4: No pharyngeal test conducted. Blood test positive on day 8 (ORF1ab, Ct = 32; N, Ct = 37) Anal: Not tested.</p> <p>Patient 5: All 3 pharyngeal tests negative. Blood test positive for ORF1ab on day 6 (Ct = 38). Negative for N target. Anal: not tested.</p> <p>Patient 6: Single positive pharyngeal test on day 13 (ORF1ab, Ct = 25; N, Ct = 27). Single positive blood test on day 9 (ORF1ab, Ct = 37; N, Ct = 37) Anal: ND.</p>		
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Author Country Study design Study URL	Population setting	Primary outcome results				
<p>H. Cheng⁽⁸⁾</p> <p>Taiwan</p> <p>Prospective case-ascertained study</p> <p>https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/276564 <u>1</u></p>	<p>Population setting: 100 confirmed cases and 22 paired cases (index-secondary cases) identified from 2,761 close contacts</p> <p>Demographics of n=100 confirmed cases: <i>Mixture of Adults and Children:</i> <i>Age</i> Median, 44 years (range, 11-88 years) <i>Sex</i> Male, 56 (56%) Female, 44 (44%)</p> <p>Clinical characteristics: <i>Presentation:</i> NR</p> <p>COVID-19 Clinical syndromes (WHO definition): <i>Index cases (n=22)</i> Asymptomatic, 0 (0%) Mild, 4 (18.2%) Mild pneumonia, 5 (22.7%) Severe pneumonia, 7 (31.8%) ARDS, Sepsis, 6 (27.3%)</p> <p>Secondary cases (n=22): NR</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): NR</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: NR</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Authors estimated that the mean incubation period was 4.1 days (95% CrI, 0.4-15.8) and the mean serial interval was 4.1 days (95% CrI, 0.1–27.8).</p> <p>The overall secondary clinical attack rate was 0.7% (95% CI, 0.4%-1.0%)</p> <p>The attack rate was higher among the 1818 contacts whose exposure to index cases started within 5 days of symptom onset (1.0% [95% CI, 0.6%-1.6%]) compared with those who were exposed later (0 cases from 852 contacts; 95%CI, 0%-0.4%). All of the 22 secondary cases had their first exposure before the sixth day of the index case's symptom onset. Hence, suggesting high transmissibility near, or even before symptom onset.</p>

						<p>The 299 contacts with exclusive pre-symptomatic exposures were also at risk (attack rate, 0.7% [95% CI, 0.2%-2.4%]).</p> <p>None of the 9 asymptomatic case patients transmitted a secondary case.</p> <p>The authors suggest that the rapid reduction of transmissibility over time implies that prolonged hospitalisation of mild cases might not be necessary in large epidemics.</p>
Author Country Study design Study URL	Population setting	Primary outcome results				
Fang⁽¹²⁾ China Case series https://www.sciencedirect.com/science/article/pii/S0163445320301390	<p>Population setting: 32 hospitalised adults (8 ICU and 24 non-ICU patients)</p> <p>Demographics: <i>Adults</i> Age: Median, 41 Range: 34-54 Sex: Male, 16 (50%), Female, 16 (50%)</p> <p>Clinical characteristics: <i>Presentation:</i> Cough, 24(75%), fever, 17</p>	<p>Test parameters</p> <p>Test: rT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): nasal, blood, faecal,</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:</p> <p>Conversion time of nasal samples was significantly longer than that of blood or saliva.</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>In ICU patients, the conversion time of blood, nasal and saliva samples all exceeded two weeks.</p>

	<p>(53%), fatigue 5 (15.6%), headache, 6 (18.8%), diarrhoea, 3 (9.4%) sore throat, 7 (21.9%) muscular soreness, 6 (18.8%) and shortness of breath, 10, (31.2%), no symptoms, 4 (12.5%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>urine, saliva and tears</p>	<p>Overall (n=32):‡ <i>Nasal:</i> 17.3±6.6 days <i>Blood:</i> 11.3±6.3 days <i>Saliva:</i> 14.1±5.6 days</p> <p>Non-ICU patients (n=24): <i>Nasal:</i> 15.67±6.68 days <i>Blood:</i> 10.17±6.13 days <i>Saliva:</i> 13.33±5.27 days</p> <p>ICU patients (n=8): <i>Nasal:</i> 22.25±3.62 days <i>Blood:</i> 14.63±5.88 days <i>Saliva:</i> 16.50±6.19 days</p>			
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Author	Population setting	Primary outcome results				
Country						
Study design						
Study URL						
Goh⁽¹⁴⁾	Population setting: 1 hospitalised adult	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
Singapore	Demographics: <i>Adult</i> 64 year old male	Test: rT-PCR	NR	Peak viral load (measured from ETT aspirate) reported on day 10 of illness (Day 4 of hospitalisation) ** (Ct 19.38), which was the first test. Viral load subsequently fell over the next 12 days until the first negative test was reported.	Not tested	N/A
Case report	Clinical characteristics: Fever, dizziness, dyspnoea. Subtle ground glass opacities in the lower zones with minor interstitial changes at the right base and atelectasis in the left lower zone on admission. (On day 3 of hospitalisation, deteriorated rapidly with severe hypoxemic respiratory failure).	Thresholds: Nr				
https://www.ncbi.nlm.nih.gov/pubmed/32200400	COVID-19 Clinical syndromes (WHO definition): ARDS	Gene Targets: NR				
		Sample site(s): Throat, Endotracheal tube aspirate (ETT), stool.				

Author Country Study design Study URL	Population setting	Primary outcome results				
Hill⁽¹⁶⁾ UK (Scotland) Case report https://doi.org/10.1016/j.jinf.2020.03.022	Population setting: 1 person admitted to a High Consequence Infectious Diseases (HCID) unit. Demographics: <i>Adult:</i> 51 year old male Clinical characteristics: Fever, myalgia, malaise and sinusitis, progressing to cough the following day. COVID-19 Clinical syndromes: Mild (not defined)	Test parameters Test: RT-PCR Thresholds: Ct Value > 40 = negative Gene Targets: NR Sample site(s): Nose, throat, (combined nose/throat), urine, faeces, blood.	Duration of virus detection* (Days) From onset of symptoms to the first of two consecutive negative tests: Nasal: 9 days Throat: 6 days Urine, faeces, blood: ND From hospitalisation to the first of two consecutive negative tests: Nasal: 6 days Throat: 3 days	Peak viral load Nose swab Day 1 of hospitalisation (Day3 of symptoms)** Ct 25 Throat (combined with nose) swab** Day 2 of hospitalisation (Day 4 of symptoms) Ct 31.	Pre-symptomatic viral load Not tested	Other relevant findings NR
Le⁽²²⁾ Vietnam Case report https://doi.org/10.1016/S2352-4642(20)30091-2	Population setting: 1 hospitalised infant Demographics: <i>Child:</i> 3 month old female Clinical characteristics: Initial presentation rhinorrhoea and nasal congestion, later developing low-grade fever with an axillary temperature of 37.6°C. COVID-19 Clinical syndromes (WHO definition): Mild	Test: rRT-PCR Thresholds: NR Gene Targets: NR Sample site(s): nasopharyngeal	From onset of symptoms to the first of two consecutive negative tests: 12 days from onset of rhinorrhea and nasal congestion 8 days from onset of fever. From first positive RT-PCR to first negative RT-PCR: 6 days Also reported for the infant's grandmother – from onset of symptoms to first negative RT-PCR: 9 days.	NR	Not tested	NR

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Y. Liu⁽²⁸⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1016/S1473-3099(20)30232-2</p>	<p>Population setting: 76 hospitalised patients</p> <p>Demographics: <i>Adults</i> 48 (63.2%) male 28 (36.8%) female Mean age 48.3 years</p> <p>Clinical characteristics: Fever (82.9%), cough (46.1%), chill (18.4%), fatigue (17.1%), sore throat (13.2%), headache/dizziness (13.2%), dyspnoea (11.8%)</p> <p>COVID-19 Clinical syndromes (author definition): 46 (61%) mild 30 (39%) severe</p> <p>Patients who had any of the following were classified as severe cases: (1) respiratory distress (≥ 30 breaths per min); (2) oxygen saturation at rest $\leq 93\%$; (3) ratio of partial pressure of arterial oxygen to fractional concentration of oxygen inspired air ≤ 300 mm Hg; or (4) severe disease complications (e.g., respiratory failure, requirement of mechanical ventilation, septic shock, or non-respiratory organ failure).</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): nasopharyngeal</p>	<p>Duration of virus detection* (Days)</p> <p>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 onset.</p>	<p>Peak viral load</p> <p>Initial viral load ($C_{t_{sample}} - C_{t_{Ref}}$): Mean (SD) 4.44 (3.99) in mild cases.</p> <p>Mean (SD) -1.42 (3.62) in severe cases.</p> <p>The ΔC_t values of severe cases remained significantly lower for the first 12 days after onset than those of corresponding mild cases.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>The mean viral load of severe cases was around 60 times higher than that of mild cases, suggesting that higher viral loads might be associated with severe clinical outcomes.</p> <p>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 onset.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Qiu⁽³³⁾</p> <p>China</p> <p>Cohort study</p> <p>https://doi.org/10.1016/S1473-3099(20)30198-5</p>	<p>Population setting: 36 hospitalised children</p> <p>Demographics: <i>Children</i> <i>Age:</i> Mean 8.3 years (SD 3.5) Range: 1-16</p> <p><i>Sex:</i> Males, 23 (64%) females, 13 (36%)</p> <p>Clinical characteristics: Fever, 13 (36%), cough, 7 (19%), headache, 3 (8%), sore throat, 2 (6%), vomiting/diarrhoea, 2 (6%) asymptomatic, 10 (28%)</p> <p>COVID-19 Clinical syndromes (paediatrics branch of the Chinese Medical Association definition): Mild (asymptomatic or upper respiratory infection), 17 (47.2%) Moderate (pneumonia), 19 (52.8%)</p>	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		<p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: <i>ORF1ab, N</i></p> <p>Sample site(s): Upper nasopharyngeal</p>	<p>From hospitalisation to the first of two consecutive negative tests: All patients (n=36): mean 10 days (SD 2, range 7-22).</p> <p>For mild cases (n=17), mean 9 days (SD 2, range 7-12) For moderate cases (n=19), mean 11 (SD 2, range 8-22)</p> <p>For children aged 0 to ≤ 5 years (n=10): mean 9 days (SD 2, range 7-14) For children aged >5 to ≤16 years (n=26): mean 11 days (SD 2, range 8-22)</p>	NR	Not tested	The authors noted that the time to achieve a negative PCR result seemed to be unaffected by severity of disease in terms of symptoms and the presence of pneumonia and treatment choices.

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>K. To (b)⁽³⁹⁾</p> <p>Hong Kong</p> <p>Cohort study</p> <p>http://www.science.direct.com/science/article/pii/S1473309920301961</p>	<p>Population setting: 23 patients at two hospitals in Hong Kong</p> <p>Demographics: <i>Adults</i> 13 male, 10 female Median age 62 years (range 37–75)</p> <p>Clinical characteristics: Fever, 22 (96%), cough, 5 (22%), chills, 4 (17%), dyspnoea, 4 (17%)</p> <p>COVID-19 Clinical syndromes (author definitions): Severe disease, 10 (43%), Mild disease, 13 (57%).</p> <p>Severe disease defined as the need for supplemental oxygen, admission to ICU, or death.</p>	<p>Test parameters</p> <p>Test: RT-qPCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): posterior oropharyngeal saliva or endotracheal aspirate, blood, urine, rectal.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: NR for most of the sample.</p> <p>Posterior oropharyngeal saliva or other respiratory specimens: Of 21 patients who survived, 7 (33%) had viral RNA detected for 20 days or longer after symptom onset.</p> <p>Urine: ND Blood: Only detected in 5 (22%) patients Rectal: Only detected in 4 (17%) patients.</p> <p>One patient had viral RNA detected for up to 25 days after symptom onset; another patient had undetectable viral load on days 21 and 22 after symptom onset, with rebound of viral load on days 23 and 24, followed by 5 days of undetectable viral load.</p>	<p>Peak viral load</p> <p><i>Salivary viral load was highest during the first week after symptom onset and subsequently declined with time.</i></p> <p>The median viral load at presentation was 5.2 log₁₀ copies per mL (IQR 4.1–7.0).</p> <p>Peak viral load was 6.91 log₁₀ copies per mL (IQR 4.27–7.40) in those with severe disease, and 5.29 log₁₀ copies per mL (IQR 3.91–7.56) in those with mild disease.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Significant positive correlation between age and peak viral load. However, no association was seen between prolonged detection of viral RNA (≥20 days after symptom onset) and severity of illness.</p> <p>An increase was noted in IgG or IgM antibody levels against NP or RBD for most patients at 10 days or later after symptom.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Wu⁽⁴³⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1016/S2468-1253(20)30083-2</p>	<p>Population setting: 74 hospitalised patients</p> <p>Demographics: <i>Adults</i> Female 35 (47.3%) Male 39 (52.7%) Mean age 43.5 years</p> <p>Clinical characteristics: Cough, 37 (50.0%), fever, 45 (60.8%), dyspnoea, 9 (12.2%), snivel, 6 (8.1%), sore throat, 6 (8.1%), diarrhoea/vomit/stomach ache, 23 (31.1%)</p> <p>COVID-19 Clinical syndromes Severe (not defined), 18 24.3%</p>	<p>Test parameters</p>	<p>Duration of virus detection* (Days)</p>	<p>Peak viral load</p>	<p>Pre-symptomatic viral load</p>	<p>Other relevant findings</p>
		<p>Test: Real-time RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: <i>RdRp, N, E</i></p> <p>Sample site(s): Throat, faecal</p>	<p>From onset of symptoms to the first of two consecutive negative tests:</p> <p><i>For all 74 patients: Throat: Mean ± SD, 16.1 ± 6.7 day[#]</i></p> <p>For 33/74 (45%) patients with negative faecal samples, respiratory swabs remained positive for a mean of 15.4 days (SD 6.7) from first symptom onset.</p> <p>Of the 41 (55%) patients with positive faecal samples, respiratory samples remained positive for a mean of 16.7 days (SD 6.7) and faecal samples remained positive for a mean of 27.9 days (10.7) after first symptom onset.</p> <p>For 41 patients who tested positive on both swabs, throat swabs remained positive for a median of 16</p>	<p>NR</p>	<p>Not tested</p>	<p>For over half of patients, their faecal samples remained positive for SARS-CoV-2 RNA for a mean of 11.2 days after respiratory tract samples became negative, implying that the virus is actively replicating in the patient's gastrointestinal tract and that faecal-oral transmission could occur after viral clearance in the respiratory tract.</p>

			days (IQR 12.3, 20.8) from symptom onset. Faecal swabs remained positive for a median of 29 days (IQR 18.3, 36.8).			
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Author	Population setting	Primary outcome results				
Country						
Study design						
Study URL						
Studies found in updated search (up to 03.04.20) (n=14 additional studies)						
An⁽¹⁾	Population setting: 262 discharged COVID-19 patients (38 (14.5%) of whom had tested positive again for SARS-CoV-2 within 14 days)	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
China						
Case series						
https://www.medrxiv.org/content/10.1101/2020.03.26.20044222v1	Demographics: <i>Mix of adults and children</i> Sex: <i>n=242 mild and moderate patients</i> Male, 116 (47.9%) Female, 126 (52.1%) <i>Severe disease:</i> NR Age <i>Mild disease, Median (range)</i> Re-detected patients (n=11), 20 (5-64) Not re-detected (n=19), 23 (2-63). <i>Moderate disease, Median (range)</i> Re-detected patients (n=27), 38 (2-60) Not re-detected (n=185), 48 (1-86). <i>Severe disease:</i> NR	Test: qRT-PCR and Sherlock assay (higher sensitivity) for SARS-CoV-2 RNA detection. ELISA assay for anti-SARS-CoV-2 IgG and IgM antibody. Thresholds: Ct value ≤ 37 = positive Gene Targets: S, ORF1b, N, RF Sample site(s): NP and anal (RNA) Serum (antibodies)	From onset of symptoms to the first of two consecutive negative tests: <i>Mild disease, Median (range)</i> Re-detected patients (n=11), 17 (11-22) Not re-detected (n=19), 15 (8-24) <i>Moderate disease, Median (range)</i> Re-detected patients (n=27), 18 (9-30) Not re-detected (n=185), 20 (5-47) <i>Severe disease:</i> NR	NR	Not tested	Patients who had re-detection of RNA were found to have relatively earlier initial clearance of the RNA. They also tend to be younger with milder forms of COVID-19 during their initial hospitalisation. Disease symptoms did not reoccur despite redetection of RNA. Whereas those that were not re-detected had slower initial clearance of RNA, and were generally older with more severe disease.
	Clinical characteristics:					

	<p><i>Presentation (n=242 mild and moderate patients):</i> Fever, 165 (68.1%) Upper respiratory symptoms, 45 (18.6%) Lower respiratory symptoms, 121 (50%) Digestive tract symptoms, 20 (8.3%)</p> <p>Severe patients: NR</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People’s Republic of China definition): <i>All 262 patients:</i> Mild, 30 (11.4%) Moderate, 212 (81%) Severe, 20 (7.6%)</p> <p><i>38 re-detected patients</i> Mild, 11 (28.9%) Moderate, 27 (71.1%) Severe, 0 (0%)</p>					<p>The hypersensitive Sherlock assay test had higher rates of positive RNA detection than commercial tests.</p> <p>No differences were found between the two groups in terms of levels of IgG and Ig M antibodies in the plasma.</p>
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Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Corman⁽¹⁰⁾</p> <p>Germany</p> <p>Case series</p> <p>https://www.medrxiv.org/content/10.1101/2020.03.29.20039529v1</p>	<p>Population setting: 18 patients (hospital and quarantine settings).</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 12 (66.7%) Female, 6 (33.3%)</p> <p><i>Age:</i> All between 18-65 years</p> <p>Clinical characteristics: <i>Presentation:</i> No symptoms, 3 (16.7%) Flu-like symptoms, 6 (33.3%) Flu-like symptoms plus fever, 5 (27.8%), pneumonia, 2 (11.1%) ARDS, 1 (5.6%)</p> <p>COVID-19 Clinical syndromes (WHO definition): ARDS, 1 (5.6%) Unclear for remainder (but at least 2 developed some level of pneumonia).</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: E, RdRp</p> <p>Sample site(s): OP, sputum, blood</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: NR</p>	<p>Peak viral load</p> <p>Mean (\pm SD) peak viral load of 17/18 patients with detectable OP/Sputum RNA: 27.9 ± 6.4 (days tested unknown).</p>	<p>Pre-symptomatic viral load</p> <p>Three individuals (patients 1-3) were considered asymptomatic on presentation. The 3rd individual had only a mild rash on chest and legs, minimal inflammation on throat examination.</p> <p>Peak Ct values during quarantine/hospitalisation = 30.10, 24.39 and 30.25 respectively.</p>	<p>Other relevant findings</p> <p>The authors report only one positive RNA test from all blood samples (77 in total). This positive sample was in the patient with ARDS.</p> <p>The authors state that based on these limited data, there is no measurable risk for SARS-CoV-2 transmission through blood components in asymptomatic SARS-CoV-2 infected individuals.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Fan⁽¹¹⁾</p> <p>China</p> <p>Case report</p> <p>https://onlinelibrary.wiley.com/doi/10.1002/ped4.12186</p>	<p>Population setting: 1 hospitalised child</p> <p>Demographics: <i>Child</i> 3 month old girl</p> <p>Clinical characteristics: <i>Presentation:</i> Diarrhoea and fever</p> <p>COVID-19 Clinical syndromes (WHO definition): Mild</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): OP, anal</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: OP: 14 days Anal: Still positive at 28 days.</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Authors describe the potential for prolonged faecal-oral transmission in children.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Gautret⁽¹³⁾</p> <p>France</p> <p>Non-randomised controlled trial</p> <p>http://dx.doi.org/10.1016/j.ijantimicag.2020.105949</p>	<p>Population setting: 36 hospitalised patients with i) age >12 years; and ii) PCR documented SARS-CoV-2 carriage in NP sample at admission whatever their clinical status (14 were treated with hydroxychloroquine, 6 were treated with hydroxychloroquine and azithromycin, 16 were treated with neither).</p> <p>Demographics: <i>Mix of adults and children</i> <i>Sex:</i> Male, 15 (41.7%) Female, 21 (58.3%)</p> <p><i>Age:</i> Mean, 45.1 years old. (treatment group substantially older than control group (mean 51.2 years vs. 37.3 years) due to the fact that no child was given the treatment).</p> <p>Clinical characteristics: <i>Presentation:</i> No symptoms, 6 (16.7%) URTI symptoms, 22 (61.1%) LRTI symptoms, 8 (22.2%)</p> <p>COVID-19 Clinical</p>	<p>Test: rRT-PCR</p> <p>Thresholds: Ct value >35 = negative</p> <p>Gene Targets: NR</p> <p>Sample site(s): NP</p>	<p>From first positive test to the first of two consecutive negative tests: For the 15 patients that had consecutive negative tests: median = 3 days (IQR, 2-4) (however follow-up was only for 6 days and 21/36 were still testing positive by the end of this period).</p> <p>From symptom onset to the first of two consecutive negative tests: For the 15 patients that had consecutive negative tests: median = 7 days (IQR, 4.5-9.5) (however follow-up was only for 6 days and 21/36 were still testing positive by the end of this period).</p> <p>For control patients: Only 2/16 tested negative on 2 consecutive tests by the end of 6 day period, however testing was not done every day in all patients.</p>	<p>Where viral loads were reported (n=26 patients) these most commonly peaked on first day of testing (n=15 patients):</p> <p>Median (IQR) viral load (Ct value) of first day of testing from the reporting 26 patients = 26.5 (23.25-29)</p>	<p>The median (IQR) viral load detected in the 6 patients who presented without any symptoms (Ct values) = 27.5 (26-29.75). Not clear whether these patients subsequently developed any symptoms.</p>	<p>The authors conclude that hydroxychloroquine was significantly associated with viral load reduction and this effect was reinforced by addition of azithromycin.</p>

	syndromes: NR		<p>For hydroxychloroquine patients: 7/14 tested negative on 2 consecutive tests by the end of the 6 day period.</p> <p>For hydroxychloroquine + azithromycin patients: All 6 patients tested negative in 2 consecutive tests by the end of the 6 day period.</p>			
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Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Lescure⁽²⁴⁾</p> <p>France</p> <p>Case series</p> <p>https://www.sciencedirect.com/science/article/pii/S1473309920302000?via%3Dihub</p>	<p>Population setting: 5 hospitalised patients</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 3 (60%) Female, 2 (40%)</p> <p><i>Age:</i> Median, 46 Range: 30-80</p> <p>Clinical characteristics: <i>Presentation:</i> Cough, 4 (80%) Fever, 3 (60%) Conjunctivitis, 1 (20%) Diarrhoea, 1 (20%) Shortness of breath, 1 (20%)</p> <p>COVID-19 Clinical syndromes (Chinese CDC): Mild, 2 (40%) Severe, 2 (40%) Critical 1 (20%)</p>	<p>Test parameters</p> <p>Test: Semi-quantitative rRT-PCR</p> <p>Thresholds: Quantification limit = 2 log₁₀ copies per 1000 cells</p> <p>Gene Targets: E, GAPDH, dRp-IP1 and RdRp</p> <p>Sample site(s): Upper respiratory tract, lower respiratory tract (where possible), blood, urine, conjunctival, pleural, stool (or anal swab).</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: NP RdRp target: Patient 1 (severe): 10 days Patient 2 (severe): 11 days Patient 3 (critical): Positive until day of death (24 days) Patient 4 (mild) 9 days Patient 5 (mild) 14 days</p> <p>Median for the 5 patients = 11 days.</p> <p>Urine and conjunctival: ND for all patients.</p>	<p>Peak viral load</p> <p><u>Mild disease patients</u> Patient 4 and 5</p> <p>NP RdRp target: Viral load peaked within the first few days and then declined gradually over next 12 or 16 days respectively. (6.2⁺ log₁₀ copies per 1000 cells for patient 4 on day 4, and 7.4 log₁₀ copies per 1000 cells for patient 5 on day 2 after symptom onset).</p> <p><u>Stool samples:</u> Peaked on day 3 for patient 4 (6.8 log₁₀ copies/g stool) and day 6 for patient 5 (8.1 log₁₀ copies/g stool).</p> <p><u>Severe disease</u></p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Three different clinical evolutions are described by the authors: (1) 2 mildly symptomatic women diagnosed within a day of exhibiting symptoms, with high NP titres of SARS-CoV-2 within the first 24 h of the illness onset and viral RNA detection in stools; (2) a two-step disease progression in 2 young men, with a secondary worsening around 10 days after disease onset despite a decreasing viral load in NP samples; and (3) an 80-year-old man with a rapid evolution towards</p>

				<p><u>patients</u> NP RdRp target: Patient 1 peaked on day 6 (1st day of testing) (7.1 log₁₀ copies/1000 cells). Patient 2 had a detectable but unquantifiable viral load on day 9 (first day of testing also). The secondary evolution to severe disease in these patients (days 10 and 11) was not correlated to any viral load increase. However an uptick in viral load occurs in patient 1 prior to clinical deterioration.</p> <p><u>Critical disease</u> Viral load peaked in patient 3 on day 8 (first day of testing)(6.7 log₁₀ copies/1000 cells) and remained high and stable for the duration of his illness before he died on day 24.</p>	<p>multiple organ failure and a persistently high viral load in lower and upper respiratory tract with systemic virus dissemination and virus detection in plasma (suggesting ability to evade immune system).</p> <p>RNA was only detected in blood and pleural fluids of the critical patient who subsequently died.</p> <p>Remdesivir administered to patients 1-3. Authors report administration was associated with viral load decrease in patient 3, though also caused adverse events in patient 2 and had to be stopped in patient 3 due to dialysis.</p>
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Author Country Study design Study URL	Population setting	Primary outcome results				
Lv ⁽²⁹⁾ China Case report https://www.sciencedirect.com/science/article/pii/S0009898120301340?via%3Dihub	Population setting: 1 hospitalised patient Demographics: <i>Adult</i> 54 year old male Clinical characteristics: <i>Presentation:</i> Fever and cough COVID-19 Clinical syndromes (WHO definition): Pneumonia	Test parameters Test: RT-PCR Thresholds: Ct value <37 = positive Gene Targets: ORF1ab, N (Positive result is determined by 2 positive target genes in the same specimen. Result of single positive gene is assessed as pending (requires retest), and the result of 2 negative genes is assessed as negative). Sample site(s): OP, sputum and anal	Duration of virus detection* (Days) From symptom onset to the first of two consecutive negative tests: OP (N gene): 25 days (Day 19 of hospitalisation) (negative tests on 2 prior occasions, days 3 and 8). OP (ORF1ab): 25 days (Day 19 of hospitalisation) (negative tests on 4 prior occasions, days 3, 8, 9, 10) Sputum and anal: ND	Peak viral load OP (N gene): Ct value = 31.54 (4 th day of testing, 16 days after symptom onset). OP (ORF1ab): Ct value = 33.78, 5 th day of testing, 22 days after symptom onset.	Pre-symptomatic viral load Not tested	Other relevant findings The authors argue that despite successive negative test results in the early phase of infection, if there is any clinical suspicion for COVID-19, then patients should still be treated as such. Authors highlight the importance of clinical signs and symptoms, other laboratory findings, and chest CT images.

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Ma⁽³⁰⁾</p> <p>China</p> <p>Case series</p> <p>http://dx.doi.org/10.1016/j.jmii.2020.03.010</p>	<p>Population setting: 8 patients in a hospital and post-discharge setting</p> <p>Demographics: <i>Mix of Adults (n=2) and Children (n=6)</i></p> <p><i>Sex:</i> Females, 6 (75%) Males, 2 (25%)</p> <p><i>Age:</i> Median (IQR): 70 months old (40.5 -180 months) Range (11 months – 39 years)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever, 3 (37.5%) No symptoms, 5 (62.5%)</p> <p>COVID-19 Clinical syndromes (not defined): Mild to moderate, 8 (100%)</p>	<p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: ORF1ab and N</p> <p>Sample site(s): Stool, Nasal, Throat.</p>	<p>From onset of symptoms to the first of two consecutive negative tests: Nasal: week 2-3 Throat: week 2-3</p> <p>Stool: Turned positive in weeks 3-5 and remained positive until end of follow up (at the end of 5 weeks post symptom onset) in 7 of 8 patients.</p>	NR	Not tested	<p>Authors note the prolonged shedding of virus from stool samples (even when throat and nasal samples are negative) in both adults and children.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Shen⁽³⁵⁾</p> <p>China</p> <p>Case series</p> <p>http://dx.doi.org/10.1001/jama.2020.4783</p>	<p>Population setting: 5 hospitalised patients</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Females, 2 (40%) Males, 3 (60%) <i>Age:</i> Range, 36-65 years</p> <p>Clinical characteristics: <i>Presentation:</i> NR</p> <p>COVID-19 Clinical syndromes (author definition): Critical, 5 (100%)</p> <p>Any of the following were considered critical patients: (1) respiratory failure requiring mechanical ventilation, (2) shock, identified by the use of vasopressor therapy and elevated lactate levels (>2 mmol/L) despite adequate fluid resuscitation, or (3) failure of other organs requiring admission to the intensive care unit (ICU).</p>	<p>Test parameters</p> <p>Test: qRT-PCR</p> <p>Thresholds: Ct value ≤ 37 = positive</p> <p>Gene Targets: NR</p> <p>Sample site(s): NP</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests: For the 3 patients that received 2 consecutive negative tests within the 12 day post-transfusion follow up period: 24-25 days.</p> <p>From day of transfusion to the first of two consecutive negative tests: Of the 5 patients, 3 received 2 consecutive negative tests within the 12 day post-transfusion follow up period. These occurred on days 1 and 3 post transfusion for 1 and 2 patients respectively.</p>	<p>Peak viral load</p> <p>Two patients experienced their highest viral load on admission to hospital (4 and 2 days since symptom onset respectively) (Ct values, 19.7 and 18.9).</p> <p>Two patients experienced their highest viral load at some time (undefined) between hospital admission and prior to transfusion (Ct values, 19.2 and 26.5).</p> <p>One patient experienced their highest viral day just prior to transfusion (21 days since symptom onset) (Ct value, 26.6).</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Patients received transfusion with convalescent plasma with a SARS-CoV-2-specific antibody (IgG) binding titre greater than 1:1000 and a neutralisation titre greater than 40 that had been obtained from 5 patients who recovered from COVID-19.</p> <p>After the transfusion of convalescent plasma, the titres of IgG and IgM in the sera of these patients increased in a time-dependent manner.</p> <p>The authors observed improvement in patients' clinical</p>

						status and viral load post transfusion, but state that RCTs are required to determine efficacy.
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Author Country Study design Study URL	Population setting	Primary outcome results				
<p>L. Tan⁽³⁶⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1101/2020.03.22.20040071</p>	<p>Population setting: 2 hospitalised patients</p> <p>Demographics: <i>Adults</i> Age: Case 1, 40-50 years; Case 2, 70-80 years Sex: Case 1, Male; Case 2, Female</p> <p>Clinical characteristics: <i>Presentation:</i> Case 1: Asymptomatic; history of intermittent fever for one week. Case 2: Intermittent fever and dry cough 10 days prior to presentation.</p> <p>COVID-19 Clinical syndromes (National Health Commission of China definitions): Case 1: moderate Case 2: moderate</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>nucleic acid amplification test (NAPT)</p> <p>Thresholds: Ct > 40 = negative</p> <p>Gene Targets: NR</p> <p>Sample site(s): OP</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: Case 1: 52 days Case 2: 24 days</p>	<p>Peak viral load</p> <p>Peak viral load (Case 1): Day 27 (Ct value = 21.03) †</p> <p>Case 2: NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Authors describe how treatment with convalescent plasma was associated with faster clearance of the virus. This treatment requires testing in RCTs.</p> <p>A relatively mild case had excessive virus shedding (52 days). Authors speculate it could be due to a particular subtype of the virus that has low toxicity and transmissibility but is slow to be cleared from the body.</p> <p>IgG detectable from Case 1, 27 days after symptom onset</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Wei⁽⁴¹⁾</p> <p>Singapore</p> <p>Case series</p> <p>https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm?s_cid=mm6914e1_w</p>	<p>Population setting: 7 clusters of COVID-19 cases in which pre-symptomatic transmission was likely (n=18 patients)</p> <p>Demographics: <i>Adults</i> Sex: Female, 11 (61.1%); Male, 7 (38.9%) Age: Median 52.5 years (range 26 to 63)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever 9 (50.0%), cough 7 (38.9%), sore throat 5 (27.8%), blocked or runny nose 3 (16.7%), myalgia 3 (16.7%), headache 2 (11.1%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): NR</p>	<p>From onset of symptoms to the first of two consecutive negative tests: NR</p>	<p>NR</p>	<p>Not tested</p>	<p>In the 4 clusters for which the date of exposure could be determined, presymptomatic transmission occurred 1–3 days before symptom onset in the presymptomatic source patient. For the remaining 3 clusters (C, D, and E), the exact timing of transmission exposure could not be ascertained because the persons lived together, and exposure was continual.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Y. Xu⁽⁴⁶⁾</p> <p>China</p> <p>Case series</p> <p>https://www.nature.com/articles/s41591-020-0817-4.pdf</p>	<p>Population setting: 10 paediatric cases admitted to hospital</p> <p>Demographics: Children <i>Sex:</i> Male, 6; Female, 4 <i>Age:</i> Range 2 months to 15 years</p> <p>Clinical characteristics: Fever, 7 (70%), cough, 5 (50%), sore throat, 4 (40%), diarrhoea, 3 (30%), nasal congestion and rhinorrhoea, 2 (20%). Asymptomatic, 1 (10%).</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: Ct ≥40 = negative</p> <p>Gene Targets: Orf1ab, N</p> <p>Sample site(s): Nasopharyngeal, rectal</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: Nasopharyngeal swab: Median 5 days (IQR 3.5-13.0)</p> <p>Rectal: Median 22 days (IQR 7-23) [could be longer as 7 positive at study end]</p>	<p>Peak viral load</p> <p>NP: Viral load generally peaked in all cases on the 1st day of testing (Average Ct value = 33.60 on Day 0 since admission) †</p> <p>Rectal: Viral loads from rectal swabs dynamics followed a more heterogeneous patterns and peaked on Day 18 since hospital admission (average Ct value = 27.86) †</p>	<p>Pre-symptomatic viral load* †</p> <p>2 patients tested positive 1 day prior to symptom onset. (Both approx. Ct value ~ 33 on day of no symptoms from rectal swab, and from NP swabs, 1 was ~33 and the other ~39) †</p> <p>1 patient remained asymptomatic for 9 days (Peak NP Ct value = 35 on Day 0 since admission, however subsequently becomes negative) Peak rectal Ct value = 29.98 on Day 2) †</p>	<p>Other relevant findings</p> <p>8/10 patients demonstrated persistently positive real-time RT-PCR tests of rectal swabs after their nasopharyngeal testing had become negative.</p> <p>Authors suggest the potential for faecal-oral transmission but acknowledge that cell culturing is required to confirm.</p> <p>Tends to be more consistent viral kinetics with NP samples than with rectal swabs.</p> <p>Virus detectable in both pre-symptomatic and asymptomatic individuals.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Yan⁽⁴⁷⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1101/2020.03.22.20040832</p>	<p>Population setting: 120 laboratory confirmed patients admitted to isolation wards of a hospital in Hubei</p> <p>Demographics: <i>Adult</i> Age: Median 52 years Sex: Male, 54 (45%); Female 66 (55%)</p> <p>Clinical characteristics: NR</p> <p>COVID-19 Clinical syndromes (Chinese management guideline for COVID-19 version 6.0 definition): General, 89 (74%); Severe, 30 (25%); Critical, 1 (0.8%)</p>	<p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat</p>	<p>From onset of symptoms to the first of two consecutive negative tests: Median 23 days (IQR 18-32 days)</p> <p>For patients treated with Lopinavir/Ritonavir (n=78), median 22 days (IQR 18-29)</p> <p>For those not treated with LPV/r (n=42) median 28.5 days (IQR 19.5-38)</p>	<p>NR</p>	<p>Not tested</p>	<p>The median duration of SARS-CoV-2 shedding did not differ significantly among groups (general 23 days vs. severe 26 days vs. critical 28 days, p=0.51).</p> <p>5 (4.2%) patients had undetectable SARS-CoV-2 RNA within 10 days, 46 (38.3%) tested negative within 20 days, and 85 (70.8%) tested negative within 30 days from symptom onset. 10 patients had detectable SARS-CoV-2 RNA up to 40 days after symptom onset.</p> <p>Authors report that old age and lack of antiviral therapy was</p>

						associated with delayed virus clearance, however this requires evidence from more robust study trials.
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Author Country Study design Study URL	Population setting	Primary outcome results				
Yang ⁽⁴⁸⁾ China Case series https://doi.org/10.1016/j.rmed.2020.105935	<p>Population setting: 82 COVID-19 patients</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 31 (37.8%); Female, 51 (62,2%) <i>Age:</i> Median 56 years (IQR 35–65) for patients with respiratory symptoms; median 51 years (IQR 36–64) for group without respiratory symptoms.</p> <p>Clinical characteristics: Respiratory symptoms, 26 (31.7%); non-respiratory symptoms 56 (68.3%)</p> <p>COVID-19 Clinical syndromes (WHO definition): NR</p>	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		<p>Test: NR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Nasopharyngeal</p>	<p>From onset of symptoms to the first of two consecutive negative tests: For patients with cough: Median duration 17 days (IQR 12-23)</p> <p>For patients without respiratory symptoms: Median 13 days (IQR 6 to 20)</p>	NR	Not tested	<p>Patients who presented with cough had more stable results of COVID-19 testing by nasopharyngeal swab 24 [92.3%] vs 38 [67.9%] for those without respiratory symptoms.</p> <p>The authors found that those with respiratory symptoms had longer duration of positive testing.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Zhang⁽⁵¹⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1101/2020.03.28.20043059</p>	<p>Population setting: 23 patients treated in hospital in Beijing</p> <p>Demographics: Adults <i>Age:</i> 48 years (IQR 40 to 62) <i>Sex:</i> Male, 12 (52.2%); Female, 11 (47.8%)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever 20 (87.0%), cough 13 (56.5%), weakness 9 (39.1%), myalgia 5 (21.7%), pharyngalgia 5 (21.7%), headache 3 (13.0%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition): Severe, 2 (8.7%) Mild-to-moderate, 21 (91.3%)</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: Ct value > 43 = negative</p> <p>Gene Targets: Orf1ab, N, S</p> <p>Sample site(s): Upper respiratory (nasal-throat mixed), faeces, urine, plasma.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: Median duration of viral shedding Nasal-throat mixed swab: 10.0 days (IQR 8.0 to 17.0)</p> <p>Faeces: 22.0 days (IQR 15.5 to 23.5)</p> <p>At 26 days after discharge, 1 case was detected positive again in faeces samples, but appeared healthy and negative for respiratory swabs.</p>	<p>Peak viral load</p> <p>Nasal-throat swabs peaked at 6-9 days after symptom onset (which was generally the 1st or 2nd day of testing), Peak viral load 10^{6.3} copies/ml, mean 2,535 copies/ml</p> <p>Faecal sample peaked at 14-18 days after symptom onset, peak viral load 10^{5.8} copies/ml, mean 5,623 copies/ml</p> <p>Faecal samples contained higher viral titres than nasal-throat swabs</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Plasma and urine samples were all negative, except for urine samples from two severe cases at the latest available detection point (16 or 21 days after symptom onset).</p> <p>All samples from one severe patient were negative until 21 days, when faeces samples were positive.</p>

Author	Population setting	Primary outcome results				
Country						
Study design						
Study URL						
Studies found in updated scoping search (up to 05.05.20) (n=19 additional studies)						
Lo⁽⁶⁶⁾	Population setting: 10 hospitalised patients	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
China (Macau)	Demographics: <i>Mix of adults and children</i>	Test: qRT-PCR	RNA conversion time: NP: mean ± SD, 18.2 ± 4.6 days Stool: mean ± SD, 19.3 ± 3.4 days	NR	Not tested	1 patient who remained asymptomatic for the duration of hospitalisation (19 days), tested positive in NP and stool samples until discharge, except on 2 non-consecutive occasions for NP samples and a single occasion for stool samples.
Case series	Sex: Male, 3 (30%) Female, 7 (70%)	Thresholds: Ct value ≤ 35 = positive; Ct value > 38 = negative; Ct value 36-38 = inconclusive (requires retesting)	From first positive test to the first of two consecutive negative tests: NP: mean ± SD, 10.3 ± 1.2 days Stool: mean ± SD, 9.8 ± 4.1 days			1 patient had 5 consecutive negative or inconclusive tests from NP samples (up to day 6 after symptom onset), despite a positive test from stool and sputum samples. Authors suggest the potential for false negatives
https://www.ijbs.com/v16p1698.htm	Age: Median (IQR), 54 (27-64) <18 years, 1 (10%) 18 to 59 years old, 6 (60%) ≥60 years, 3 (30%)	Gene Targets: ORF1ab and N	Urine: ND in any patient			
	Clinical characteristics: <i>Presentation</i> Body Temperature ≥ 37.5°C, 8 (80%) Diarrhea (≥3 times/day), 8 (80%) Cough, 5 (50%) Dyspnoea, 5 (50%) Sore throat, 5 (50%) Nausea, 5 (50%) Myalgia, 3 (30%) Rhinorrhoea, 2 (20%) Nasal congestion, 2 (20%) Dizziness, 2 (20%) Abdominal pain, 2 (20%)	Sample site(s): NP, sputum, urine and stool				
	COVID-19 Clinical syndromes (National Health Commission of the					

	People's Republic of China definition): Mild, 2 (20%) Moderate, 4 (40%) Severe, 4 (40%) Critical, 0 (0%)				and a potential lag time with NP samples. All patients received lopinavir-ritonavir and 3 received methyl-prednisolone.
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Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Meng⁽⁶⁷⁾</p> <p>China</p> <p>Case series</p> <p>https://www.tandfonline.com/doi/full/10.1080/221751.2020.1746200</p>	<p>Population setting: 42 hospitalised COVID-19 patients with hypertension (17 on ACEi/ARBs and 25 on non-ACEi/ARBs anti-hypertensives)</p> <p>Demographics: <i>Adults</i> Sex: Male, 24 (57.1%) female, 18 (42.9%)</p> <p><i>Age:</i> Median (IQR), 64.5 55.8-69</p> <p>Clinical characteristics: <i>Presentation:</i> Fever, 31 (73.8%) fatigue, 5 (11.9%) dry cough, 20 (47.6%) expectorant cough, 11 (26.2%) anorexia, 1 (2.4%) myalgia, 6 (14.3%) sore throat, 6 (14.3%) bellyache, 3 (7.1%) diarrhoea, 3 (7.1%) nausea, 2 (4.8%) headache, 1(2.4%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition): Moderate, 26 (61.9%) Severe, 16 (38.1%)</p>	<p>Test: RT-PCR</p> <p>Thresholds: Ct value < 37 = positive; Ct value > 40 = negative; Ct value 37-40 = requires retesting</p> <p>Gene Targets: NR</p> <p>Sample site(s): NR</p>	<p>From onset of symptoms to the first of two consecutive negative tests: NR</p>	<p><i>Patients on non-ACEi/ARBs anti-hypertensives (n=25):</i> Median (IQR) Ct values, 24.0 (21.2-28.1) (Unknown day) †</p> <p><i>Patients on ACEi/ARBs anti-hypertensives (n=17):</i> Median (IQR) Ct values, 28.8 (26.2-31.3) (Unknown day) †</p> <p>Authors calculated a statistically significant difference between the two viral load peaks in favour of patients on ACEi/ARBs.</p>	<p>Not tested</p>	<p>The authors suggest that the findings from this study demonstrate that ACEi/ARBs reduce viral load and improve clinical outcomes in COVID-19 patients with hypertension. However the study was not designed to test this causal relationship nor was the sample size large enough, hence these findings should be viewed as hypothesis-generating at best.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Nicastri⁽⁶⁸⁾</p> <p>Italy</p> <p>Case report</p> <p>https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.11.2000230</p>	<p>Population setting: 1 hospitalised pre-symptomatic patient identified from a quarantine environment after repatriation from China</p> <p>Demographics: <i>Adult</i> Male in late 20's</p> <p>Clinical characteristics: <i>Presentation</i> No symptoms when tested</p> <p>COVID-19 Clinical syndromes (WHO definition): Mild</p>	<p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: E, RdRp</p> <p>Sample site(s): NP/OP combined, stool, urine, semen, saliva, blood and conjunctival swabs.</p>	<p>From hospitalisation to first of two consecutive negative tests: NP/OP: 7 days (but re-tested positive again for 3 more days).</p> <p>Stool: 9 days</p> <p>Urine, semen, saliva, blood and conjunctival swabs: ND</p>	NR	Not tested	<p>Patient tested positive via NP/OP 1 day prior to development of mild and transient conjunctivitis.</p> <p>Patient treated with lopinavir-ritonavir.</p>

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<p>Saito⁽⁶⁹⁾</p> <p>Japan</p> <p>Case report</p> <p>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa377/5815296</p>	<p>Population setting: 1 hospitalised patient</p> <p>Demographics: <i>Adult</i> 55-year-old male</p> <p>Clinical characteristics: <i>Presentation</i> Mild headache and 5 days of fever.</p> <p>COVID-19 Clinical syndromes (WHO definition): Mild</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): OP swabs and gargle lavage (using 10 mL of normal saline).</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: Day 16**</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>NA</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Scott⁽⁷⁰⁾</p> <p>US</p> <p>Case report plus epidemiological investigation</p> <p>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa374/5815221</p>	<p>Population setting: 1 non-hospitalised patient (presented to a healthcare clinic and subsequently isolated at home) plus 16 contacts (defined as persons exposed to the case, from one day before diagnosis).</p> <p>Demographics: <i>Adult</i> 26-year-old male</p> <p>Clinical characteristics: <i>Presentation</i> Non-productive cough (initially claimed 2 day history of cough but under interview it transpired patient had cough since before travelling to China).</p> <p>COVID-19 Clinical syndromes (WHO definition): Mild</p>	<p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: Three genetic markers of SARS-CoV-2 (not specified).</p> <p>Sample site(s): NP and OP swabs, non-induced sputum and serum for case at time of diagnosis. Paired NP and OP swabs for case and contacts thereafter (Serial testing).</p>	<p>From day of diagnosis to the first of two consecutive negative tests (day of symptom onset unclear): **</p> <p>Case: NP: Day 24 OP: Day 18 Sputum: only tested twice and positive on both occasions (days 1 and 8). Serum: ND</p> <p>10 high-risk contacts who underwent serial testing: ND in all 10 contacts.</p>	<p>Case: OP, Day 1 of diagnosis**, 1st test (Ct values = 26.7–28.1)</p> <p>Sputum, Day 8 of diagnosis**, 2nd test (Ct values = 27.3-27.4)</p> <p>NP, Day 6 of diagnosis, ** 2nd test (Ct values = 25.1-25.6)</p> <p>Contacts: NA</p>	<p>Not tested</p>	<p>All 16 contacts completed 14-day post-exposure symptom monitoring and none tested positive. 6 contacts (including 1 high risk) were not tested but none of these displayed any symptoms.</p> <p>This case investigation suggests COVID-19 illness severity may be associated with SARS-CoV-2 infectivity. The case had repeated intimate contact with 1 person over 36 hours while testing positive for SARS-CoV-2, but the contact still tested negative.</p>

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<p>Yang⁽⁷¹⁾</p> <p>China</p> <p>Case series</p> <p>https://www.medrxiv.org/content/10.1101/2020.02.28.20028068v1</p>	<p>Population setting: 55 hospitalised patients</p> <p>Demographics: <i>Mix of adults and children</i> Sex: Male, 33 (60%) Female, 22 (40%) Age: Median, 44 years (IQR, 34.0-54.0) Range, 3-85 years</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 47 (85.5%), Cough, 28 (50.9%), Fatigue, 15 (27.3%), Myalgia, 11 (20%), Sputum production, 11 (20%) Headache, 6 (10.9%) Sore throat, 9 (16.4%) Dizziness, 9 (16.4%) Diarrhoea, 2 (5.5%) Chest tightness, 3 (5.5%) Dyspnoea, 5 (9.1%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) Mild, 21 (38.2%) Common 20 (36.4%) Severe, 13 (23.6%) Extremely severe, 1 (1.8%)</p>	<p>Test parameters</p> <p>Test: qRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Respiratory samples including throat swab (but unclear whether other respiratory sample sites used).</p>	<p>Duration of virus detection* (Days)</p> <p>From the first positive test to the first of two consecutive negative tests <i>All n=28 patients with reliable PCR test results (and did not have a co-morbid viral infection):</i> Mean (95% CI), 9.71 (8.21-11.22) days.</p> <p><i>Patients without pneumonia (n=17):</i> Mean (95% CI), 9.24 (7.10-11.37) days</p> <p><i>Patients with pneumonia (n=11)</i> Mean (95% CI), 10.45 (8.10-12.81) days.</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>52 patients received antiviral treatment, mostly with lopinavir/ritonavir and or arbidol.</p>

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<p>Yu⁽⁷²⁾</p> <p>China</p> <p>Case series</p> <p>http://dx.doi.org/10.1093/cid/ciaa345</p>	<p>Population setting: 76 COVID-19 confirmed hospitalised patients (323 samples)</p> <p>Demographics: <i>Mix of adults and children</i> Sex: Male, 38 (50%) Female, 38 (50%)</p> <p><i>Age:</i> Median, 40 years (IQR, 32 -63) Range, 6 months -92 years</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 67 (88.2%) Cough, 53 (69.7%) Fatigue, 27 (35.5%) Myalgia, 20 (26.3%) Chills, 12 (15.8) Anorexia, 9 (11.8) Dyspnoea, 8 (10.5%) Pharyngodynia, 7 (9.2%) Headache, 4 (5.3%) Nausea and vomiting, 4 (5.3%) Diarrhoea, 3 (4.0%) No symptoms or sign, 2(2.6%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) Mild, 59 (77.6%)</p>	<p>Test parameters</p> <p>Test: droplet digital PCR (ddPCR) and RT-PCR</p> <p>Thresholds: <i>RT-PCR</i> Ct values ≤ 38: positive Ct values > 38: negative</p> <p><i>ddPCR</i> Limit of detection: 10 copies/test</p> <p>Gene Targets: ORF1ab and N</p> <p>Sample site(s): Nasal, throat, sputum, blood and urine.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: Nasal, throat, sputum: NR</p> <p>Urine and blood: ND</p>	<p>Peak viral load</p> <p>116 sputum samples from 44 confirmed patients</p> <p><i>Early and progressive stages:</i> Mean (± SD) 46,800 (± 17,272) copies/test by <i>ddPCR</i>.</p> <p><i>Recovery stage:</i> Mean (± SD) 1,252 (± 1,027) copies/test by <i>ddPCR</i>.</p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>The average viral load in sputum was found to be significantly higher than in throat or nasal swabs.</p> <p>Sputum: Mean (± SD) 17,429 (± 6,920 copies/test) Throat: Mean (± SD) 2,552 (± 1,965 copies/test) Nasal: Mean (± SD) 651 (± 501 copies/test).</p> <p>2 patients in the progressive stage were each observed 3 times, and the viral load increased over time. 2 patients in the recovery stage were each observed 4 times, and the viral load decreased over time. 2 patients in the recovery phase</p>

	Severe 17 (22.4%)					<p>displayed viral load fluctuations at low levels (≤ 150 copies/test by ddPCR) over a 9 day period.</p> <p>Some patients (unknown number) who had at least twice negative nucleic acid tests and reached the discharge standard were found to be positive again during reexamination</p>
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Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Gao⁽⁵⁴⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1186/s12931-020-01363-7</p>	<p>Population setting: 2 COVID-19 confirmed hospitalised patients</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 2 (100%)</p> <p><i>Age:</i> Case 1: 24 years Case 2: 29 years</p> <p>Clinical characteristics: <i>Presentation</i> Case 1: 7-day history of mild fever, dry coughs, and weakness of unknown cause. Case 2: 3-day history of very mild fever and cough of unknown cause.</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat and sputum</p>	<p>Duration of virus detection* (Days)</p> <p>From day of hospitalisation to the first of two consecutive negative tests: **</p> <p><i>Case 1</i> Throat: day 16 Sputum: day 29</p> <p><i>Case 2</i> Throat: day 8 Sputum: NR</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>Case 1: day 22 sputum was negative, but was positive again day 24. Result changed to negative on day 29 and day 31.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Hu⁽⁵⁵⁾</p> <p>China</p> <p>Retrospective cohort study</p> <p>https://doi.org/10.1016/j.scitotenv.2020.138812</p>	<p>Population setting: 59 COVID-19 confirmed hospitalised patients</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 28 (47.5%) Female, 31 (52.5%)</p> <p><i>Age:</i> Median: 46 years (IQR: 33–57).</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 34 (71.2%) Non-productive cough, 18 (30.5%) Sputum production, 7 (11.9%) Fatigue, 7 (11.9%) Myalgia, 4 (6.8%) Headache, 6 (10.2%) Chest tightness, 5 (8.5%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People’s Republic of China definition) Non-severe (mild to moderate cases): 49 (83.1%) Severe: 10 (16.9%)</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: Ct value <37: positive Ct value ≥ 40: negative Ct value 37-40: requires retesting</p> <p>Gene Targets: N, ORF1ab</p> <p>Sample site(s): Nasopharyngeal</p>	<p>Duration of virus detection* (Days)</p> <p>From first positive test to the first of two consecutive negative tests:</p> <p>Median: 14 (IQR: 10–18) days Range: 4 to 25 days</p> <p>(Intermittent negative status: patients with re-detectable viral RNA after showing negative on RT-PCR test).</p> <p>Median duration for intermittent negative status (n=10): 7 (IQR: 6–10) days</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>The rate of RNA negative conversion within 7 days: 10.2% (95% CI: 2.1%–17.5%) 14 days: 62.7% (95% CI: 48.1%–73.2%) 21 days: 91.2% (95% CI: 80.4%–96.4%).</p> <p>Age older than 45 years was independently associated with delayed clearance of SARS-CoV-2 RNA (HR: 0.38; 95% CI: 0.21–0.70).</p> <p>Chest tightness was independently associated with delayed clearance of SARS-CoV-2 RNA (HR: 0.29; 95%CI: 0.09–0.92) .</p>

						Median ORF 1ab Ct values: 26 (IQR: 24–31). Median N gene Ct value: 28 (IQR: 26–31).
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Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Huang⁽⁵⁶⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1101/2020.04.22.20071258</p>	<p>Population setting: 33 COVID-19 confirmed hospitalised patients</p> <p>Demographics: <i>Mix of adults and children</i> <i>Sex:</i> Male, 17 (51.5%) Female, 16 (48.5%)</p> <p><i>Age:</i> Median: 47 years (range, 2-84)</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 19 (57.6%) Cough, 17 (51.5%) Sputum production (expectoration), 4 (12.1%) Fatigue, 3 (9.1%) Diarrhoea, 3 (9.1%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) Moderate: 31 (93.9%) Severe: 2 (6.1%)</p>	<p>Test parameters</p> <p>Test: RT-PCR Antibody testing</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat, sputum, stool (RNA); blood (antibodies).</p> <p>Samples taken during hospitalisation and follow-up after discharge from the hospital (12-38 days, median: 30 days).</p>	<p>Duration of virus detection* (Days)</p> <p>From first positive test to the first of two consecutive negative tests:</p> <p><i>Median (IQR)</i> Throat: 18.5 (13.25-22) days Sputum: 22 (18.5-27.5) days Stool: 17 (11.5-32) days.</p> <p><i>Virus undetectable</i> Throat: undetectable in most patients by three weeks after symptom onset. Sputum: undetectable in most patients by week 5 after onset. Stool: many patients had persistent viral RNA > 5 weeks.</p>	<p>Peak viral load</p> <p>Viral loads in throat samples generally peaked on 1st test and then gradually fell over next 1-3 weeks.</p> <p>Viral loads in sputum samples generally peaked on 1st test but fell much slower, generally over the next 2-4 weeks.</p> <p>Viral loads in stool samples followed a more erratic pattern, often peaking later in the disease and persisting for > 5 weeks.</p> <p>At the early stages of symptom onset, viral load was higher in throat swabs and sputum, but lower in stool.</p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>Compared to throat swabs, viral loads in sputum and stool declined significantly slower (vs stool, P=0.046; vs sputum, P=0.005).</p> <p>One patient had persistent viral RNA for 59 days or longer in sputum samples.</p> <p>The median (IQR) seroconversion time of anti-S IgM, anti-RBD IgM, and anti-N IgM was 10.5 (7.75-15.5) days, 14 (9-24) days, and 10 (7-14) days, respectively. The median (IQR) seroconversion time of anti-S IgG, anti-RBD IgG, and anti-N IgG was 10 (7.25-16.5) days, 13 (9-17) days, and 10 (7-14) days, respectively</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Jing⁽⁵⁷⁾</p> <p>China</p> <p>Statistical transmission model applied the contact-tracing data (from Guangzhou, China)</p> <p>https://www.medrxiv.org/content/10.1101/2020.04.11.20056010v1</p>	<p>Population setting: 349 lab-confirmed COVID-19 cases reported to Guangzhou Municipal CDC, constituting 195 unrelated clusters with 212 primary cases and 137 nonprimary (secondary or tertiary) cases.</p> <p>Demographics: <i>Mix of adults and children</i> <i>Sex:</i> Male, 168 (48.1%) Female, 181 (51.9%)</p> <p><i>Age:</i> <20 years, 20 (5.7%) 20-59 years, 234 (67%) ≥60 years, 95 (27.2%)</p> <p>Clinical characteristics: <i>Presentation</i> NR</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: RT-PCR or genome sequencing</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Respiratory or blood samples</p>	<p>From onset of symptoms to the first of two consecutive negative tests: NR</p>	<p>NR</p>	<p>Not tested</p>	<p>The authors assessed the goodness-of-fit between the observed and model-fitted number of infections for combinations of mean incubation periods of 4-7 days and maximum infectious periods of 13, 16 and 19 days (from day of infection). A mean incubation period of 4 days and a maximum infectious period of 13 days yielded the smallest difference between observed and model-fitted numbers.</p> <p>The authors report that COVID-19 cases were at least as infectious during their incubation period as during their illness period (that is, from symptom onset).</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>La Scola⁽⁵⁸⁾</p> <p>France</p> <p>Cross-sectional study</p> <p>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7185831/</p>	<p>Population setting: 155 patients with lab-confirmed COVID-19, providing 183 samples for testing to a reference centre for highly infectious diseases.</p> <p>Demographics: NR</p> <p>Clinical characteristics: <i>Presentation</i> NR</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: rRT-PCR Virus culture</p> <p>Thresholds: NR</p> <p>Gene Targets: E gene</p> <p>Sample site(s): Sputum and NP swabs</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: Maximum detection of 20 days</p>	<p>Peak viral load</p> <p>Ct value of 13 was reported in one patient sample. However, unclear at what stage of the illness and from what sample site this was obtained.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>The authors found that samples with Ct values of 13–17 all led to positive culture. Culture positivity rate then decreased progressively according to Ct values to reach 12% at 33 Ct. No culture was obtained from samples with Ct > 34.</p> <p>SARS-CoV-2 was detected up to 20 days after onset of symptoms by PCR in infected patients but that the virus could not be isolated after day 8 in spite of ongoing high viral loads of approximately 10⁵ RNA copies/mL of sample</p>

Author	Population setting	Primary outcome results				
Country						
Study design						
Study URL						
<p>Lavezzo⁽⁵⁹⁾</p> <p>Italy</p> <p>Repeated cross-sectional study</p> <p>https://www.medrxiv.org/content/10.1101/2020.04.17.20053157v1</p>	<p>Population setting: Samples from 2,812 and 2,343 subjects collected on 2 separate occasions less than 2 weeks apart from a municipality in Italy (Vo', Veneto Region). This corresponds to 85.9% and 71.5% of the eligible study population (n=3,275) respectively.</p> <p>Demographics of those testing positive at the 1st (n=73, 2.6%), and 2nd time points (n=29, 1.2%) <i>Mix of adults and children</i> <i>Sex, 1st time point (n=73), and 2nd time point (n=29):</i> Males, 43 (58.9%), 20 (69%) Females, 30 (41.1%), 9 (31%)</p> <p><i>Age, 1st time point (n=73), and 2nd time point (n=29):</i> 0-10 years, 0 (0%), 0 (0%) 11-20 years, 3 (4.1%), 2 (6.9%) 21-30 years, 4 (5.5%), 2 (6.9%) 31-40 years, 7 (9.6%), 2 (6.9%) 41-50 years, 5 (6.8%), 2 (6.9%) 51-60 years, 16 (21.9%), 7 (24.1%) 61-70 years, 15 (20.5%), 6 (20.7%) 71-80 years, 19 (26%), 6 (20.7%) >80 years, 4 (5.5%), 2 (6.9%)</p> <p>Clinical characteristics (aggregated data from both time points):† <i>Presentation, median (95% CI)</i> Fever, 26% (17-37%) Cough, 20% (12-30%) Headache, 9% (4-17%)</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: The sensitivity of the E gene and RdRp gene assays was 5.0 and 50 genome equivalent copies per reaction at 95% detection probability, Respectively.</p> <p>Gene Targets: RdRp and E genes</p> <p>Sample site(s): NP swabs</p>	<p>Duration of virus detection* (Days)</p> <p>The time to viral clearance (time from the earliest positive sample for the subjects with more than one sample in the first survey and a negative sample in the second survey) ranged from 8 to 13 days and was on average 9.3 days, with standard deviation 2.0 days.</p>	<p>Peak viral load</p> <p>Authors found no statistically significant difference in the viral load (as measured by genome equivalents inferred from Ct data) of symptomatic versus asymptomatic infections.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Estimated serial interval mean 6.90 days (95% CI 2.56-13.39) before lockdown and 10.12 days (95% CI 1.67-25.90) after the lockdown.</p> <p>43.2% (95% CI 32.2-54.7%) of the confirmed SARS-CoV-2 infections detected across the two surveys were asymptomatic.</p>

Sore throat, 8% (3-16%) Discomfort, 3% (0-9%) Conjunctivitis, 1% (0-7%) Diarrhoea, 1% (0-7%) COVID-19 Clinical syndromes: NR					
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Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
Li ⁽⁶⁰⁾ China Case series DOI: 10.1002/jmv.25905	Population setting: 13 discharged COVID-19 patients who were quarantined for 4-weeks at home Demographics: <i>Adults</i> <i>Sex:</i> Male, 6 (46%) Female, 7 (54%) <i>Age:</i> Mean: 52.8 (± 20.2) Clinical characteristics: <i>Presentation</i> Fever, 13 (100%) Cough, 9 (69.2%) Fatigue, 3 (23.1%) Sore throat, 3 (23.1%) Diarrhoea, 1 (7.7%) COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) NR	Test: RT-PCR Thresholds: NR Gene Targets: RdRP, E, N Sample site(s): Oral, nasal, sputum, blood, faeces, urine, vaginal secretions and milk.	From onset of symptoms to the first of two consecutive negative tests: Respiratory sample (unclear whether upper or lower): Mean (±SR): 25 (±6) days Range: 18-44 Blood, urine, vaginal secretions and milk: ND <i>Post discharge</i> Faeces: 2 (15.4%) patients tested positive at day 14 day and 15 after sputum was negative. Sputum: 4 (30.7%) patients positive between 5 – 14 days after discharge	NR	NR	One of the patients experienced recurrence followed by a negative test result, which turned positive again at a later stage.

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Segar⁽⁶¹⁾</p> <p>US</p> <p>Case report</p> <p>DOI: 10.21203/rs.3.rs-24578/v1</p>	<p>Population setting: 1 COVID-19 patient who was evacuated from Wuhan, China and developed signs of infection in quarantine</p> <p>Demographics: <i>Adult</i> <i>Sex:</i> Female <i>Age:</i> 51</p> <p>Clinical characteristics: <i>Presentation</i> 1 day history of fevers, chills, sweats, nonproductive cough</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People’s Republic of China definition) NR</p>	<p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Serial nasopharyngeal and oropharyngeal, taken every other day. Sputum samples taken on day 10 and 11.</p>	<p>From onset of symptoms to the first of two consecutive negative tests:**</p> <p>NP and OP: Day 1</p> <p>NP and OP samples of patient from hospital day 1 onwards all tested negative for COVID-19, despite having severe symptoms at times.</p> <p>Sputum: Positive on days 10 and 11</p>	<p>NR</p>	<p>NR</p>	<p>NP swab was negative for usual viral pathogens, including influenza A/B, respiratory syncytial virus, human rhinovirus/enterovirus, human metapneumovirus, parainfluenza, and 4 common coronavirus strains previously known to cause human illness (229E, HKU1, NL63, and OC43).</p> <p>Initiation of remdesivir: day 6</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Wang⁽⁶²⁾</p> <p>China</p> <p>Cohort study</p> <p>https://europepmc.org/article/PPR/PPR150648</p> <p>DOI: 10.21203/rs.3.rs-22829/v1</p>	<p>Population setting: 182 post-discharge patients recovering from COVID-19 under medical isolation (20 of whom (11%) re-tested again for SARS-CoV-2 within 14 days of meeting discharge criteria).</p> <p>Demographics (n=20 re-detected patients): <i>Mix of children and adults</i> Sex: Male, 7 (35%) Female, 13 (65%)</p> <p>Age: Median, 41.5 (Range 1-72)</p> <p>Initial Infection: <i>Initial presentation:</i> NR</p> <p>COVID-19 Clinical syndromes (n=20 re-detected patients) (Definition not reported): Non-severe, 20 (100%)</p>	<p>Test: RT-PCR (BioGerm) Total Ig, IgA, IgG and IgM (WANTAI BioPharm)</p> <p>Thresholds: Ct-value < 37 = positive Ct-value ≥ 40 was defined as negative. A medium load, more than 37 and less than 40, was defined as weak positive and required re-testing.</p> <p>Gene Targets: ORF1ab and N genes</p> <p>Sample site(s): NP and anal. Blood for antibody testing.</p>	<p>From onset of symptoms to the first of two consecutive negative tests: Only provided in full for one patient (8-year-old boy), 21 days (but patient fluctuated between positive and negative anal swab results over the next 4 weeks. NP swabs remained negative over this same 4 week period).</p>	<p>NR</p>	<p>Not tested</p>	<p>14/20 re-detected patients underwent antibody testing: Total immunoglobulin, IgA, IgG were positive in all 14 patients, IgM was positive in 10 of these patients.</p> <p>13/20 tested to be re-positive on the 7th day, and another 7 on the 14th day; 14 were tested as nasopharyngeal swabs positive, and 6 were anal swabs positive, none has found both swabs positive.</p>

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		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Wei⁽⁶³⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1016/j.cgh.2020.04.030</p>	<p>Population setting: 84 COVID-19 confirmed hospitalised health-care workers (17 doctors, 66 nurses, 1 allied health worker). 26 (31%) had diarrhoea, 58 (69%) patients had no diarrhoea.</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 28 (33%) Female, 56 (67%) <i>Age:</i> Median: 37 years (range: 24-74)</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 72 (86%) Headache, 28 (33%) Myalgia or fatigue, 37 (44%) Cough, 48 (57%) Sputum production, 26 (31%) Dyspnoea, 32 (38%) Nausea, 16 (19%) Vomiting, 6 (7%) Abdominal pain, 2 (2%) Abdominal distension, 3 (4%) Tenesmus (cramping rectal pain), 1 (1%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Nasal, pharyngeal and stool.</p>	<p>From onset of symptoms to the first of two consecutive negative tests:**</p> <p>Throat swab: Mean (±SD) diarrhoea group (n=26): 12.5 (±4.0) days Mean (±SD) non-diarrhoea group (n=58): 9.2 (±3.9) days.</p> <p>Stool: NR</p> <p>Elimination of SARS-CoV-2 from stool took longer than elimination from the nose and throat.</p>	<p>NR</p>	<p>NR</p>	<p>A significantly higher proportion of patients with diarrhoea had virus RNA in stool than patients without diarrhoea.</p> <p>Of 76 COVID-19 patients who had a negative result from their latest throat swab test during hospitalisation, a significantly higher proportion of patients with diarrhoea (45%) had a positive result from the retest for SARS-CoV-2 in stool than patients without diarrhoea (20%) (P=.039).</p>

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<p>Yongchen⁽⁶⁴⁾</p> <p>China</p> <p>Case series</p> <p>doi.org/10.1080/22221751.2020.1756699</p>	<p>Population setting: 21 individuals infected with SARS-CoV-2 in 2 medical centres</p> <p>Demographics: <i>Mix of adults and children</i> <i>Sex</i> Total: Female 8 (38.1%), male 13 (61.9%) Non-severe cases: Female, 5 (45.5%), male 6 (54.5%) Severe cases: Female 1 (20%), Male 4 (80%) Asymptomatic carriers: Female 2 (40%), male 3 (60%)</p> <p><i>Age median (range)</i> Total: 37 (10–73) Non-severe cases: 35 (24–73) Severe cases: 54 (30–68) Asymptomatic carriers: 25 (10–61)</p> <p>Clinical characteristics: <i>Presentation:</i> NR</p> <p>COVID-19 Clinical syndromes (Chinese management guideline for COVID-19 (version 6.0)): 11 (52.4%) non-severe, 5 (23.8%) severe, 5 (23.8%) asymptomatic carriers.</p>	<p>Test parameters</p> <p>Test: qualitative rRT-PCR (BGI Genomics, Beijing, China) (two sequential positive respiratory tract sample results) Antibody testing.</p> <p>Thresholds: Not defined</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat swab, anal swab (blood for antibody testing).</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:**</p> <p><i>Overall (throat samples):</i> Median – Day 15 of symptoms</p> <p><i>Non severe cases (throat sample):</i> Median: Day 11.5 of symptoms.</p> <p><i>Severe cases (throat sample):</i> Median Day 15 of symptoms.</p> <p><i>Asymptomatic carriers (throat sample):</i> Median Day 20 of symptoms.</p> <p>Duration of positive viral RNA in throat swab sample (days): Non severe cases median (range): 10 (2 – 21) Severe cases median (range): 14 (9–33) Asymptomatic carriers median (range): 18 (5–28).</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>NR</p>	<p>Other relevant findings</p> <p>Seroconversion: 8/11 (72.7%) non severe patients seroconverted during the period when swab samples converted to RNA negative, suggesting that antibody responses might facilitate the viral clearance. 3/5 severe patients generated viral specific IgG responses prior to viral clearance.</p> <p>Only 1/5 asymptomatic cases generated SARS-CoV-2 specific antibody responses and this patient was not seroconverted until week 3 of her diagnosis.</p> <p>3/15 anal swabs remained positive for SARS-CoV-2 after respiratory swab samples turned negative.</p> <p>Prolonged viral shedding for asymptomatic cases.</p>

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Zheng⁽⁶⁵⁾ China Retrospective cohort study https://www.bmj.com/content/369/bmj.m1443	<p>Population setting: 96 hospitalised patients providing 3,497 samples.</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 58 (60.4%) Female, 38 (39.6%)</p> <p><i>Age:</i> Median (IQR), 55 (44.3-64.8)</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 85 (89%) Cough, 54 (56%) Sputum, 26 (27%) Chest distress, 12 (13%) Dizziness, 7 (7%) Headache, 4 (4%) Nausea, 5 (5%) Vomiting, 2 (2%) Diarrhoea, 10 (10%) Myalgia, 19 (20%) Fatigue, 9 (9%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition): Mild, 22 (22.9%) Severe, 74 (77.1%)</p>	<p>Test parameters</p> <p>Test: qRT-PCR</p> <p>Thresholds: Ct value ≤ 38 = positive Ct value > 38 = re-tested Ct value repeatedly > 38 or undetected = negative.</p> <p>Detection limit: 1000 copies per millilitre.</p> <p>Gene Targets: ORF1ab</p> <p>Sample site(s): Respiratory (sputum or saliva), serum, stool, and urine samples.</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests:† Respiratory samples (both upper and lower): Median (IQR): 18.5 (13-29) days Range: 4-55 days.</p> <p>From first detection to the first of two consecutive negative tests: Stool, median (IQR): 22 (17-31) days.</p> <p>Respiratory, median (IQR): 18 (13-29) days.</p> <p>Serum, median (IQR): 16 (11-21) days.</p> <p>Urine: only detected in 1 sample.</p>	<p>Peak viral load</p> <p>In the mild group, the viral loads peaked in respiratory samples in the 2nd week from disease onset, whereas viral load continued to be high during the 3rd week in the severe group. Of note, viral loads from lower respiratory tract samples peaked after 2 weeks from symptom onset.</p> <p>The viral load of stool samples was highest during the 3rd and 4th weeks after disease onset. Viral load differed significantly by sample type, with respiratory samples showing the highest, followed by stool samples, and serum samples showing the lowest.</p> <p>In respiratory samples, patients with severe</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>The median duration of virus in stool samples was significantly longer than in respiratory and serum samples (P<0.001).</p> <p>In the respiratory samples, the 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), whereas no significant difference was observed in the duration of virus between stool and serum samples among patients with different disease severities.</p> <p>In the severe group, the duration of the virus was significantly higher in patients treated with glucocorticoids continuously for more than 1 longer in patients older than 60 years and in male patients in the severe group.</p> <p>The authors found that the duration of virus shedding in</p>

				disease had significantly higher viral loads than patients with mild disease. Viral loads in stool and serum samples showed no significant difference between patients with mild disease and patients with severe disease.		lower respiratory tract samples was longer than previously reported in other studies, and peak viral shedding occurred after about two weeks from symptom onset.
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Author Country Study design Study URL	Population setting	Primary outcome results				
Studies found in updated search (up to 12.05.20) (n=41 additional studies)						
<p>Arons⁽⁷³⁾</p> <p>US</p> <p>Repeated cross-sectional study</p> <p>https://www.nejm.org/doi/full/10.1056/NEJMoa2008457</p>	<p>Population setting: 76 residents in a skilled nursing facility. 48 (63%) testing positive and 28 (37%) testing negative. Of these 48 positive residents, 27 (56%) were asymptomatic at the time of testing; 24 subsequently developed symptoms.</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 28 (36.8%) Female, 48 (63.2%)</p> <p><i>Age:</i> Mean (\pmSD), 76.8\pm10.5 years\ddagger</p> <p>Clinical characteristics: <i>Presentation (1st test)</i> <u>Typical symptoms:</u> Fever, 9 (11.8%) Cough, 20 (26.3%) Shortness of breath, 4 (5.3%) <u>Atypical symptoms:</u> Sore throat, 5 (6.6%) Chills, 0 (0%) Confusion, 3 (3.9%) Rhinorrhoea or congestion, 2 (2.6%) Myalgia, 0 (0%) Dizziness, 2 (2.6%)</p>	<p>Test parameters</p> <p>Test: rRT-PCR and viral culturing</p> <p>Thresholds: Ct values < 40 = positive</p> <p>Gene Targets: N1 and N2 genes</p> <p>Sample site(s): NP and OP</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests: NR</p>	<p>Peak viral load</p> <p>Highest viral load of any resident (Ct value) = 13.7. This occurred in a resident with typical symptoms on initial testing.</p> <p>Of the 12 residents who had two consecutive positive RT-PCR results: 4 had viral loads peaking prior to symptom onset (up to 5 days before symptom onset), 1 had peak viral load on day of symptom onset and 7 had viral load peaking after symptom onset (up to 6</p>	<p>Pre-symptomatic viral load</p> <p>Median Ct values for the four symptom status groups were similar (asymptomatic residents, 25.5; pre-symptomatic residents, 23.1; residents with atypical symptoms, 24.2; and residents with typical symptoms, 24.8).</p>	<p>Other relevant findings</p> <p>More than half of residents testing positive on initial testing were asymptomatic or pre-symptomatic.</p> <p>Viable virus was isolated from asymptomatic, pre-symptomatic and symptomatic residents. Viable virus was isolated from specimens collected 6 days before to 9 days after the first evidence of typical symptoms. In relation to both typical and atypical symptoms, viable virus was collected 6 days before to 13 days after the first evidence of any symptoms.</p> <p>The lowest viral load (Ct value) for which there was positive culture growth was 34.3 (and this occurred in a pre-symptomatic resident).</p> <p>The authors concluded that Transmission from asymptomatic and pre-symptomatic residents infected with SARS-CoV-2 most likely contributed to the rapid and extensive spread of infection to</p>

<p>Malaise, 9 (11.8%) Headache, 1 (1.3%) Nausea, 4 (5.2%) Diarrhoea, 4 (5.2%) No symptoms, 27 (35.5%)</p> <p>COVID-19 Clinical syndromes : NR</p>			<p>days after symptom onset).</p>		<p>other residents and staff.</p>
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<p>M.G. Chang⁽⁷⁴⁾</p> <p>China</p> <p>Case series</p> <p>https://www.atsjournals.org/doi/pdf/10.1164/rccm.202003-0524LE</p>	<p>Population setting: 16 hospitalised patients</p> <p>Demographics: <i>Mix of adults and children</i> <i>Adults:</i> 15 <i>Children:</i> 1 (3 years) <i>Sex:</i> Male, 11 (69%) Female, 5 (31%) <i>Age:</i> Median (IQR), 35.5 (24-43) <i>Comorbidities:</i> Diabetes (2 of 16) Tuberculosis (1 of 16)</p> <p>Clinical characteristics: <i>Presentation:</i> Fever, 14 (88%) Cough, 11 (69%) Pharyngalgia, 5 (31%) Dyspnoea, 2 (13%) Diarrhoea, 1 (6%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests:</p> <p>Median (IQR): 10.5 (6-12) days</p> <p>From first detection to the first of two consecutive negative tests:</p> <p>Median (IQR): 5.5 (4-8) days</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Half (8 of 16) of the patients remained virus positive, even after the resolution of symptoms (median, 2.5 d; range, 1–8 days).</p> <p>The mean duration of symptoms was estimated to be 8 days (interquartile range, 6.25–11.5).</p>

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<p>Y. Chen⁽⁷⁵⁾</p> <p>China</p> <p>Case series</p> <p>https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25825</p>	<p>Population setting: 42 hospitalised COVID-19 patients</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 15 (35.7%) Female, 27 (64.3%) <i>Age:</i> Median (IQR), 51 (42.75-62)</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 36 (85.7%) Dry cough, 22 (52.4%) Fatigue, 22 (52.4%) Myalgia, 10 (23.8%) Dyspnoea, 9 (21.4%) Sputum production, 7 (16.7%) Pharyngalgia, 6 (14.3%) Headache or dizziness, 5 (11.9%) Gastrointestinal symptoms, 8 (19.1%) Diarrhoea, 7 (16.67%) Abdominal pain, 5 (11.9%) Nausea, 4 (9.5%) Vomiting, 3 (7.1%)</p> <p>COVID-19 Clinical syndromes (WHO definitions): Uncomplicated, 2 (4.8%) Mild, 29 (69.1%) Severe, 11 (29.2%)</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Pharyngeal swab, stool, and urine.</p>	<p>Duration of virus detection* (Days)</p> <p>From first positive test to the first of two consecutive negative tests:</p> <p>Pharyngeal samples: median (IQR), 8 (5-12) days</p> <p>Stool samples: 9 days in uncomplicated cases, 8 (4.5-14) days in mild cases, and 14 (9.5- 18) days in severe cases.</p> <p>Urine: ND</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>18 patients remained positive for viral RNA from faecal samples for a median of 7 (IQR 6-10) days after the pharyngeal swabs turned negative.</p> <p>More severe cases were associated with a significantly longer virus shedding period for pharyngeal samples, but not for faecal samples.</p>

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<p>C.Y. Cheng⁽⁷⁶⁾</p> <p>Taiwan</p> <p>Case series</p> <p>https://www.sciencedirect.com/science/article/pii/S168411822030092X?via%3Dihub</p>	<p>Population setting: 5 hospitalised COVID-19 patients</p> <p>Demographics: <i>Adults</i> Case 1: 56 year old female Case 2: 53 year old male Case 3: 52 year old female Case 4: 50 year old male Case 5: 46 year old female</p> <p>Clinical characteristics: <i>Presentation</i> Case 1: 2-day history of subjective fever and dry cough Case 2: fever Case 3: acute onset of fever Case 4: mild rhinorrhoea for one day Case 5: intermittent fever and severe headache for 3 days.</p> <p>COVID-19 Clinical syndromes (not defined): Mild pneumonia</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: Ct value ≤ 34 = positive</p> <p>Gene Targets: N, E and RdRP genes</p> <p>Sample site(s): OP and sputum samples.</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests**</p> <p>Sputum (E gene): Day 16 OP (E gene): Day 16</p>	<p>Peak viral load</p> <p>For sputum samples, the 1st or 2nd test had the highest viral load (day 1-6 of symptoms). Median peak viral load, Ct = 20.9[†].</p> <p>For OP samples, the 1st, 2nd or 3rd test had the highest viral load (days 1-8 of symptoms). Median peak viral load, Ct = 24.7[†].</p> <p>Authors found higher viral loads in sputum samples compared with OP samples.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Authors concluded that lopinavir-ritonavir was not associated with a reduction in the duration of SARS-CoV-2 viral shedding in patients with mild pneumonia compared with patients who did not receive these antivirals.</p>

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<p>Fu⁽⁷⁷⁾</p> <p>China</p> <p>Case series</p> <p>https://www.medrxiv.org/content/10.1101/2020.04.03.20051763v1</p>	<p>Population setting: 50 COVID-19 patients in recovery, 21 (42%) had been discharged, 29 (58%) were still hospitalised.</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> 23 Female, 27 male <i>Age:</i> median, 64 (range 37–87) years.</p> <p>Clinical characteristics: <i>Presentation</i> Shortness of breath 50 (100%); Fatigue, 39 (78%); loss of appetite, 33 (66%); dizzy, 29 (58%); Cough, 24 (48%); Sleep disorder, 16 (32%); Diarrhoea, 11 (22%); Sputum production, 10 (20%); Nausea or vomiting, 7 (14%); Myalgia or arthralgia, 6 (12%); Conjunctivitis, 1 (2%); sore throat, 1 (2%).</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People’s Republic of China definition) Severe, 50 (100%)</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Nasal, throat and anal</p>	<p>Duration of virus detection◊ (Days)</p> <p>From onset of symptoms to the first of three consecutive negative tests:</p> <p>Any sample site: Median duration of viral shedding: 31 (IQR, 27–34 days).</p> <p>Any sample site: Longest duration of viral shedding: 57 days.</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>The interval of viral shedding in patients with poor recovery (n= 29) was markedly prolonged.</p> <p>All participants had antiviral drug treatment, 33 (66.0%) had antibiotics.</p> <p>Patients with poor recovery had a higher frequency of corticosteroid therapy and albumin administration than patients with good recovery.</p>

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Jahan⁽⁷⁸⁾ Bangladesh Case report https://www.ncbi.nlm.nih.gov/pubmed/32363143	Population setting: 1 hospitalised patient Demographics: <i>Adult</i> <i>Sex: Male</i> <i>Age: 34</i> Clinical characteristics: <i>Presentation:</i> Runny nose, fever and breathing difficulty. COVID-19 Clinical syndromes: NR	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		Test: RT-PCR Thresholds: NR Gene Targets: NR Sample site(s): Nasal and throat	From symptom onset to the first of two consecutive negative tests: 10 days	NR	Not tested	

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		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
Jiang⁽⁷⁹⁾ China Case report https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25941	Population setting: 1 paediatric asymptomatic COVID-19 patient Demographics: <i>Child</i> <i>Sex: Female</i> <i>Age: 8</i> Clinical characteristics: <i>Presentation</i> Asymptomatic COVID-19 Clinical syndromes: NR	Test: qRT-PCR Thresholds: NR Gene Targets: NR Sample site(s): Nasopharyngeal and anal.	From first positive test to the first negative tests: NP: ND Anal: 41 days (until first negative test).	NR	Not tested	Asymptomatic SARS-CoV-2 infected case found to persistently test positive in stool samples, but negative in NP swabs for a long time.

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Jones⁽⁸⁰⁾ Germany Cross-sectional study https://zoonosen.charite.de/fileadmin/user_upload/microsites/m_cc05/virologie-ccm/dateien_upload/Weitere_Datien/analysis-of-SARS-CoV-2-viral-load-by-patient-age.pdf	Population setting: 3,712 patients with confirmed COVID-19 from routine testing at a large laboratory testing centre in Berlin (screened from a total of 59,831 patients). Demographics: <i>Mix of Adults and Children</i> <i>Sex:</i> <i>Age:</i> 0-10 years, 49 11-20 years, 78 21-30 years, 536 31-40 years, 630 41-50 years, 575 51-60 years, 662 61-70 years, 431 71-80 years, 420 81-90 years, 314 91-100 years, 17 Clinical characteristics: <i>Presentation</i> NR COVID-19 Clinical syndromes: NR	Test parameters Test: rRT-PCR Thresholds: NR Gene Targets: NR Sample site(s): Sputum and swabs from unknown sample site	Duration of virus detection* (Days) From symptom onset to the first of two consecutive negative tests: NR	Peak viral load <i>Mean base-10 logarithm of viral load per age group (SD, 95% CI)</i> 0-10 years, 4.64 (1.83, 95% CI 4.12-5.15) 11-20 years, 4.80 (1.79, 95% CI 4.40-5.20) 21-30 years, 5.26 (1.94, 95% CI 5.10-5.43) 31-40 years, 5.21 (2.02, 95% CI 5.06-5.37) 41-50 years, 4.99 (1.87, 95% CI 4.83-5.14) 51-60 years, 5.26 (1.91, 95% CI 5.11-5.40) 61-70 years, 5.28 (1.87, 95% CI 5.10-5.46) 71-80 years, 5.17 (1.78, 95% CI 5.00-5.35) 81-90 years, 5.34 (1.90, 95% CI 5.13-5.55) 91-100 years, 5.61 (2.05, 95% CI 4.61-6.61)	Pre-symptomatic viral load Not tested	Other relevant findings While younger age groups have lower detection rates this does not imply an age-based estimate of infection prevalence because of mostly symptom-directed testing. The authors conclude that no significant differences in viral load exists across age groups. These data indicate that viral loads in the very young do not differ significantly from those of adults, though the sample of young children was relatively small. However viral load measurement is an indirect measurement of infectivity and may not translate to transmissibility.

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<p>T.Q.M. Le⁽⁸¹⁾</p> <p>Vietnam</p> <p>Case series</p> <p>https://wwwnc.cdc.gov/eid/article/26/7/20-0591_article#suggestedcitation</p>	<p>Population setting: 12 hospitalised patients (involving 2 clusters)</p> <p>Demographics: <i>Mix of adults and children</i> Sex: Males, 4 (33%) Females, 8 (67%)</p> <p><i>Age: Median (range), 29.5 years (3 months – 55 years)</i> Average, 31.2 years</p> <p>Clinical characteristics: <i>Presentation</i> Clinical signs, including fever and cough, were demonstrated by 11 patients.</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: Ct values ≥ 40 = negative</p> <p>Gene Targets: E, N, and RdRp gene</p> <p>Sample site(s): Throat</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests: Throat: Median (range) 8.5 (6-12) days</p> <p>From first positive test to the first of two consecutive negative tests: Throat: Median (range), 7 (1-9) days</p>	<p>Peak viral load</p> <p>Using best fit curve of the median Ct values for all 3 target genes, the viral load in all patient samples peaked earlier in the disease trajectory (Ct = 28 ~ 7 days after potential exposure) and fell thereafter (negative ~ 22 days after potential exposure).</p>	<p>Pre-symptomatic viral load</p> <p>One asymptomatic patient (who did not show symptoms for at least 14 days) had a median (of all 3 target genes) peak viral load (Ct = 28) 7 days after first testing positive.</p> <p>Virus shedding was detected for up to 9 days after first diagnosis in this individual.</p>	<p>Other relevant findings</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>L'Huillier⁽⁸²⁾</p> <p>Switzerland</p> <p>Case series</p> <p>https://www.medrxiv.org/content/10.1101/2020.04.27.20076778v1</p>	<p>Population setting: 23 hospitalised symptomatic neonates, children and teenagers with lab-confirmed COVID-19</p> <p>Demographics: <i>Children</i> Sex: NR Age: Median (IQR), 12 (3.8-14.5) years</p> <p>Clinical characteristics: <i>Presentation</i> Upper respiratory tract Infection, 13 (56.5%) Fever, 2 (8.7%) Pneumonia, 2 (8.7%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: RT-PCR and virus culturing</p> <p>Thresholds: NR</p> <p>Gene Targets: E gene</p> <p>Sample site(s): NP</p>	<p>From symptom onset to the first of two consecutive negative tests:</p> <p>NR</p>	<p>Median viral load at time of diagnosis was 3.0×10^6 copies/ml (mean 4.4×10^8, IQR 6.9×10^3-4.4×10^8)</p> <p>Virus isolation was successful from NP samples from all age groups, with a median initial VL of 1.7×10^8 copies/ml (mean 7.9×10^8, IQR 4.7×10^6-1.0×10^9).</p> <p>Viral loads were higher in NP samples that were culture positive compared with those that were culture negative.</p>	<p>Not tested</p>	<p>Virus isolation was successful in 12/23 (52%) of the children.</p> <p>The youngest patient that SARS-CoV-2 was isolated from was a 7-day old neonate.</p> <p>No correlation between disease presentation and success of virus isolation was observed.</p> <p>The authors concluded that initial viral loads at diagnosis in symptomatic children is comparable to those seen in adults. Infectious virus isolation success was largely comparable to that of adults, although two specimens yielded an isolate at a lower viral load (1.2×10^4 and 1.4×10^5 copies/ml) than what was observed in adults.</p>

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<p>N. Li ⁽⁸³⁾</p> <p>China</p> <p>Case series</p> <p>https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25952</p>	<p>Population setting: 36 confirmed COVID-19 patients with prolonged viral shedding of > 30 days.</p> <p>Early onset group (symptoms before Feb 1st) and late onset group (symptoms after Feb 1st)</p> <p>Demographics: <i>Adults</i> <i>Age median (range)</i> 57.5 years (IQR 52-65); 0-40 years 11.1% 41-64 years 61.1% ≥65 years 27.8%</p> <p><i>Sex</i> Male, 23 (63.9%) Female, 13 (36.1%)</p> <p>Clinical characteristics: NR</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition): Mild, 33 (91.7%) Severe, 3 (8.3%)</p>	<p>Test parameters</p> <p>Test: Real time RT-PCR (BioGerm, Shanghai, China)</p> <p>Thresholds: Not defined</p> <p>Gene Targets: NR</p> <p>Sample site(s): Respiratory tract (site not reported).</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:</p> <p>Median: 53.5 days (IQR 47.75-60.5)</p> <p>Maximum duration, 83 days</p> <p>Early onset group (number of patients with viral RNA shedding): 41-50 days (n = 2) 51-60 days (n = 12) 61-70 days (n = 6) 71-80 days (n = 2) >81 days (n = 1)</p> <p>Late onset group (number of patients with viral RNA shedding):: 30-40 days (n = 4) 41-50 days (n = 7) 51-60 days (n = 2)</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings:</p> <p>Patients in the early-onset group had longer durations of viral shedding and more severe illnesses.</p> <p>Treatment: The majority of patients received antiviral therapy at the onset of infection for at least one week, including arbidol 34 (91.7%), ribavirin 1 (2.8%) and remdesivir 2 (5.6%). 17 patients received antiviral treatment again at the final stage; 13 received chloroquine phosphate therapy and 4 received chloroquine and favipiravir combined therapy for at least 5 days until rRT-PCR turned negative.</p>

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<p>Lillie⁽⁸⁴⁾</p> <p>UK</p> <p>Case series</p> <p>https://www.journalofinfection.com/article/S0163-4453(20)30102-X/abstract</p>	<p>Population setting: 2 cases admitted to the regional infectious diseases unit at Castle Hill Hospital.</p> <p>Demographics: <i>Adults</i> <i>Case A:</i> 50 year-old female. No past medical history and no regular medications.</p> <p><i>Case B:</i> 23 year-old male. Previously fit and well.</p> <p>Clinical characteristics: Clinically stable. <i>Case A:</i> fever, malaise, sore throat, dry cough. <i>Case B:</i> fever (38.5 °C), myalgia, dry cough, malaise, sinus congestion.</p> <p>COVID-19 Clinical syndromes: Relatively mild and short-lived, with no evidence of parenchymal lung disease (reflected by normal oxygenation and the absence of radiological infiltrates).</p>	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		<p>Test: PCR testing</p> <p>Thresholds: Not defined</p> <p>Gene Targets: NR</p> <p>Sample site(s): Nose and throat (daily sampling).</p>	<p>From onset of symptoms to the first of two consecutive negative tests:**</p> <p>Case A: Day 8 of illness.</p> <p>Case B: Day 9 of illness (throat swabs from this individual were negative throughout).</p>	NR	Not tested	<p>Authors conclude that there was no evidence of prolonged asymptomatic shedding, although discordance between nose and throat samples in case B highlights the need to sample both areas.</p>

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W. D. Liu ⁽⁸⁵⁾ Taiwan Case report https://www.ncbi.nlm.nih.gov/pubmed/32283147	Population setting: 1 hospitalised patient Demographics: <i>Adult</i> 50 year old female Clinical characteristics: <i>Presentation</i> Acute onset fever COVID-19 Clinical syndromes: NR	Test parameters Test: RT-PC, antibody testing and virus culturing Thresholds: NR Gene Targets: RdRp, E and N genes Sample site(s): Sputum or gargle, throat, stool and plasma.	Duration of virus detection* (Days) From symptom onset to the first of two consecutive negative tests: Sputum (E gene): 62 days Sputum (N gene): 30 days Sputum (RdRp gene): 44 days. Throat (E gene):47 days Throat (N gene): 6 days Throat (RdRp gene): 6 days. Gargle (E gene): 30 days Gargle (N gene): 26 days Gargle (RdRp gene): 26 days. Stool: only detected in one sample (3 days after symptom onset) before repeatedly testing negative thereafter. Plasma: ND	Peak viral load Viral load highest in sputum compared with all other samples. <i>Peak viral load (E gene)</i> Sputum, 1 st test (1 day after symptom onset), = 7.3 log ₁₀ copies/ml Throat, 2 nd test (2 days after symptom onset) = 5.8 log ₁₀ copies/ml Gargle, 1 st test (2 days after symptom onset) = 5.4 log ₁₀ copies/ml A drop of 3 log ₁₀ of viral loads was observed among all specimens within one week after admission.	Pre-symptomatic viral load Not tested	Other relevant findings SARS-CoV-2 persisted to be detectable on 63 rd day of symptoms. SARS-CoV-2 could be isolated from cell cultures in throat swab collected upon admission, and all sputum specimens collected within 18 days of symptoms. Authors concluded that the contagious period of COVID-19 might last more than one week after "clinical recovery". Unspecified antibody to SARS-CoV-2 was firstly identified on the tenth day after symptom Onset.

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<p>Paoli⁽⁸⁶⁾</p> <p>Italy</p> <p>Case report</p> <p>https://link.springer.com/content/pdf/10.1007/s40618-020-01261-1.pdf</p>	<p>Population setting: 1 suspected case voluntarily participated in the study (no hospitalisation)</p> <p>Demographics: Adult <i>Age:</i> 31 years</p> <p>Clinical characteristics: <i>Presentation:</i> Fever Myalgia Anosmia Ageusia</p> <p>COVID-19 Clinical syndromes: Mild disease which did not require hospitalisation</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: E, S</p> <p>Sample site(s): Pharyngeal Semen Urine</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests: Pharyngeal: 16 days</p> <p>From first detection to the first of two consecutive negative tests: Pharyngeal: 9 days</p> <p>Urine and semen: ND</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Semen and urine samples were negative for SARS-CoV-2 RNA. Although this should be interpreted cautiously, it may be possible that either the viral clearance kinetics in these fluids matches the progressive clinical recovery of the patient or that the virus was never present in these fluids at the time of the laboratory diagnosis.</p>

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		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
Peng⁽⁸⁷⁾ China Case report https://www.sciencedirect.com/science/article/pii/S1876034120304391?via%3Dihub	Population setting: A hospitalised mother and her preterm new born baby. Demographics: <i>Mix of adult and child</i> Mother: 25 year old female New born: Female (born at 35 ⁺³ weeks' gestation by caesarean section). Clinical characteristics: <i>Presentation:</i> Mother: Fever, fatigue, shortness of breath New born: Tachypnoea, moaning, and periodic breath immediately after being delivered (unrelated to COVID-19). COVID-19 Clinical syndromes: NR	Test: RT-PCR Thresholds: Ct value < 30 = positive Gene Targets: ORF1ab and N genes Sample site(s): Mother: Amniotic fluid, vaginal secretions, cord blood, placenta, serum, anal swab, breast milk and throat swab. New born: Throat swab, anal swab, serum, sputum, urine.	From symptom onset to the first of two consecutive negative tests: Mother: Only detected in throat swab. Throat (both genes): Day 16** New born: ND in any sample (tested for 14 days)	Highest viral load detected in 1 st test (day 6 of symptoms) Throat (ORF1ab gene): Ct value = 22.69 Throat (N gene): Ct value = 22.37	Not tested	This study found no evidence of vertical transmission from mother to new born.

Author Country Study design Study URL	Population setting	Primary outcome results				
Pongpirul⁽⁸⁸⁾ Thailand Case series https://wwwnc.cdc.gov/eid/article/26/7/20-0598_article	Population setting: 11 hospitalised patients (3 detected through airport screening, 1 through contact tracing and 7 voluntarily sought medical care) Demographics: <i>Adults</i> <i>Sex:</i> Male, 6 (55%) Female, 5 (45%) <i>Age:</i> Median (range), 61 (28-74) Clinical characteristics: <i>Presentation:</i> Cough, 10 (91%) Malaise/fatigue, 10 (91%) Fever, 10 (91%) Sore throat, 9 (82%) Rhinorrhoea, 10 (91%) Headache, 6 (55%) Vomiting, 3 (27%) Diarrhoea, 2 (18%) COVID-19 Clinical syndromes (not defined): All: Pneumonia Mild to moderate disease	Test parameters Test: Conventional RT-PCR and rRT-PCR Thresholds: NR Gene Targets: NR Sample site(s): Nasopharyngeal Oropharyngeal Sputum.	Duration of virus detection* (Days) From symptom onset to the first of two consecutive negative tests: NP/OP: 14 days (IQR, 9-26 days) From first detection to the first of two consecutive negative tests: NP/OP: 10 days (IQR, 6-22.75 days)	Peak viral load NR	Pre-symptomatic viral load Not tested	Other relevant findings Patients became afebrile 6 days after illness onset, with a median of 9 (3–19.75) additional days of detectable SARS-CoV-2 RNA in respiratory specimens after resolution of fever.

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Qian⁽⁸⁹⁾</p> <p>China</p> <p>Case report</p> <p>https://www.tandfonline.com/doi/full/10.1080/23744235.2020.1748705</p>	<p>Population setting: 1 hospitalised patient</p> <p>Demographics: Adult Sex: Male Age: 47 years old</p> <p>Clinical characteristics: Mild cough</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: RT-PCR</p> <p>Thresholds: Ct > 30 = negative</p> <p>Gene Targets: RdRP, N and E</p> <p>Sample site(s): Throat Rectal</p>	<p>From symptom onset to the first of two consecutive negative tests: Throat: 42 days</p> <p>From first detection to the first of two consecutive negative tests: Throat: 34 days – 1 adult male patient</p> <p>Median (IQR) of 24 patients: 12 (9-14) days</p> <p>Rectal: Only detected once.</p>	<p>Unclear as test results from day of diagnosis are not provided.</p>	<p>Not tested</p>	<p>Although this patient had been treated by multiple antiviral drugs and did not take any corticosteroid, his RT-PCR was still positive after 34 days.</p>

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<p>Shi⁽⁹⁰⁾</p> <p>China</p> <p>Cross-sectional study</p> <p>https://www.sciencedirect.com/science/article/pii/S0042682220300787?via%3Dihub#appsec1</p>	<p>Population setting: 114 hospitalised COVID-19 patients with paired pharyngeal and serum results</p> <p>Demographics: <i>Mix of adults and children</i></p> <p><i>Sex:</i> Male, 59 (51.7%) Female, 55 (48.3%)</p> <p><i>Age:</i> Median (range), 43.5 (6–79)</p> <p>Clinical characteristics: <i>Presentation</i> NR</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People’s Republic of China definition): Non-pneumonia, 32 (28.1%) Pneumonia, 74 (64.9%) Severe pneumonia, 8 (7%)</p>	<p>Test parameters</p>	<p>Test: rRT-PCR and antibody testing</p>	<p>Thresholds: NR</p>	<p>Gene Targets: N gene</p>	<p>Sample site(s): Pharyngeal (RT-PCR) Serum (antibody)</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests: NR</p>	<p>Peak viral load</p> <p>The mean viral load/mL (log₁₀) was lower in pneumonia cases (5.15), followed by non-pneumonia cases (5.22), and highest in severe pneumonia cases (5.58), but no significant differences were found.</p> <p>No statistical significance was found between male and female cases with the same severity in the non-pneumonia, pneumonia and severe pneumonia groups (mean, 5.36, 5.20 and 5.36 for male cases; 5.06, 5.10 and 5.81 for female case, respectively).</p> <p>Mean viral loads tended to increase along with the age of patients (<30 years, 30-59 years and ≥60 years), but all the differences were not significant.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>The viral load of IgM negative patients showed an upward trend with time after onset - this may reflect the potential antiviral effect of the IgM antibodies.</p> <p>However, the viral load of IgM (+) patients in severe cases remained high 12 days after onset, which might indicate that the antiviral effect of IgM antibodies is weak, or there are other factors involved in the early resistance to the virus.</p> <p>The viral load of CRP(+)/SAA(+) non-pneumonia patients was significantly lower than that of CRP (+)/SAA(+) severe pneumonia patients, and it was also lower than that of other types of non-pneumonia patients. For severe pneumonia patients, the viral load of CRP(+)/SAA(+) cases was about the same as that of CRP(-)/SAA(+) patients.</p> <p>The authors found that both CRP and SAA showed trends of increase along with the worsening of severity, hence the authors suggest that these biomarkers may be useful indicators for severity. For example, the authors suggest that a CRP(-), SAA(-), IgM (+) patient may have a better prognosis than a patient with the converse test results. However data is needed from</p>

						larger studies to validate these findings.
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Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Song⁽⁹¹⁾</p> <p>China</p> <p>Case series</p> <p>https://www.sciencedirect.com/science/article/pii/S0163445320302292?via%3Dihub</p>	<p>Population setting: 24 hospitalised patients within 4 family clusters</p> <p>Demographics: <i>Mix of adults and children</i> Sex: Male, 9 (37.5%) Female, 15 (62.5%) Age: Median (range), 36 years (9 months – 86 years)</p> <p>Clinical characteristics: <i>Presentation (prior to testing):</i> Family 1 (n=6 family members): Fever and cough in index case only</p> <p>Family 2 (n=9 family members): Fever, 7 family members Muscle ache, 3 family members Fatigue, 1 family member</p> <p>Family 3 (n=6 family members) Cough, 3 family members Fever, 3 family members Fatigue, 2 family members</p> <p>Family 4 (n=3 family members) Fever, 2 family members</p> <p>COVID-19 Clinical syndromes (no definition): Moderate to severe, 2 adults patients Asymptomatic to mild, 22 patients (adults and children)</p>	<p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat swabs</p>	<p>From first positive test to the first of two consecutive negative tests: Throat: median (range), 15 (5 – 30) days</p> <p>However, 5 patients were still positive at end of the study i.e. > 30 days</p>	NR	Not tested	Study found evidence of patients testing positive again after negative tests.

Author Country Study design Study URL	Population setting	Primary outcome results				
Stebbing ⁽⁹²⁾ Italy Case series	Population setting: 4 hospitalised patients Demographics: <i>Adults</i>	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
https://www.researchsquare.com/article/rs-23195/v1	<p>Patient A: 29 year old female Patient B: 76 year old male Patient C: 57 year old male Patient D: 51 year old male</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 3 Dry cough, 3 Myalgia, 1 Dyspnoea, 1 NR, 1</p> <p>COVID-19 Clinical syndromes (WHO criteria): Bilateral COVID-19 pneumonia, 4 Moderate-to-severe disease, 3</p>	<p>Test: rRT-PCR</p> <p>Thresholds: Ct values ≤ 40 = positive Ct values > 40 = negative</p> <p>Gene Targets: RdRp, N and E genes</p> <p>Sample site(s): NP and blood samples</p>	<p>From symptom onset to the first of two consecutive negative tests:</p> <p>NP (N gene): median, 16 days</p> <p>Blood (N gene): median, 17 days</p>	<p><i>Patient A:</i> Peaked in NP and blood samples on 1st test (4 days after symptom onset) NP (N): Ct = 24 Blood (N): Ct = 31</p> <p><i>Patient B:</i> Peaked in NP on 1st test (1 day after symptom onset) NP (N): Ct = 21 Blood: ND.</p> <p><i>Patient C:</i> Peaked in NP on 7th test (16 days after symptom onset) and on 1st test in blood sample (9 days after symptom onset), though viral loads in blood samples peak again 13 and 18 days after symptom onset. NP (N): Ct = 23 Blood (N): Ct = 37</p> <p><i>Patient D:</i> Peaked in NP and on 1st test (7 days after symptom onset). Was only detected in blood once 14 days after symptom onset. NP (N): Ct= 31 Blood (N): Ct = 38</p>	Not tested	Authors claim that administration of baricitinib was associated with improved lung function, illness resolution, and reductions in viral load, plasma IL-6, ferritin, and CRP levels. However, this drug warrants clinical trial evaluation through an RCT before effectiveness for the treatment of COVID-19 can be determined.

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		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>Su⁽⁹³⁾</p> <p>China</p> <p>Case series</p> <p>https://www.tandfonline.com/doi/full/10.1080/2221751.2020.1744483</p>	<p>Population setting: 23 hospitalised patients with lab-confirmed COVID-19 (including 9 children and their 14 adult family members).</p> <p>Demographics: <i>Mix of adults and children</i> <i>Sex:</i> Males, 11 (47.8) Females, 12 (52.2%)</p> <p><i>Age:</i> Mean (range), 27.8 years[†] (11 months – 72 years)</p> <p>Clinical characteristics: <i>Presentation</i> <i>Children (n=9):</i> Mild dry cough, 1 (11.1%) Fever, 2 (22.2%) NR, 6 (66.7%)</p> <p><i>Adults (n=14):</i> Fever, 8, (57.1%) Cough, 5 (35.7%) Chest tightness/pain, 3 (21.4%) Fatigue, 3 (21.4%) Sore throat, 1 (7.1%) No symptoms, 4 (28.6%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: ORF1ab and N genes.</p> <p>Sample site(s): Stool, Sputum and NP.</p>	<p>From hospital admission to the first of two consecutive negative tests: <i>Children (NP sample):</i> Median, 11.5 days</p> <p><i>Children (sputum):</i> ND <i>Children (stool):</i> turned positive for 5 discharged patients.</p> <p><i>Adults (any sample):</i> NR</p>	NR	Not tested	<p>Five discharged children were admitted again because their stool re-tested positive.</p> <p>Authors found that all the children were diagnosed after their families, which indicated that they were infected by the household contact.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
Li Tan⁽¹²⁵⁾ China Case series https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7235581/	Population setting: 142 hospitalised COVID-19 patients (including 15 patients who subsequently died) Demographics: <i>Adults</i> <i>Sex:</i> NR <i>Age:</i> NR Clinical characteristics: <i>Presentation</i> NR COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition): Moderate, 96 (67.6%) Severe, 21 (14.8%) Critically ill, 25 Critically ill (and subsequently died), 15 (10.6%)	Test parameters Test: RT-PCR Thresholds: NR Gene Targets: ORF1ab Sample site(s): OP	Duration of virus detection* (Days) From symptom onset to the first of two consecutive negative tests Virus detection persisted for 27 days longer in patients who subsequently died (n=15) compared with survivors (n=55). Virus detection persisted for 15 days longer in critically ill patients (n=25) compared with moderate disease patients (n=40) There were no obvious differences in the duration of viral shedding between the severe (n=15) and moderate patients (n=40), and between critically ill (n=25) and severe disease patients (n=15).	Peak viral load From 10 days after disease onset onwards, the patients who subsequently died (n=15) had significantly higher levels of viral load than the survivors did (n=55) (Ct values, 27.7 vs. 34.0, p<0.005).† From 8 days after disease onset onwards, critically ill patients (n=25) had significantly higher levels of viral load than moderate disease patients did (n=40) (Ct values, 22.7 vs. 31.9, p<0.05).† There were no significant differences in viral loads between critically ill (n=25) and severe disease patients (n=15), or between severe disease (n=15) or moderate disease patients (n=40).	Pre-symptomatic viral load Not tested	Other relevant findings The authors concluded that viral load (as measured targeting the ORF1ab gene) may be useful for disease classification and prognosis in COVID-19. The authors concluded that LYM% was the most sensitive and reliable predictor of those tested (LYM%, CRP, IL-6, PCT, LA and viral load) for disease typing and prognosis of COVID-19.

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>X. Tan⁽⁹⁵⁾</p> <p>China</p> <p>Case series</p> <p>http://www.zgddk.com/CN/abstract/html/2020-4-294.htm</p>	<p>Population setting: 13 hospitalised children with COVID-19</p> <p>Demographics: <i>Children</i> <i>Sex:</i> Males, 4 (30.8%) Females, 9 (69.2%)</p> <p><i>Age:</i> Median (range), 8 (1-17) years</p> <p>Clinical characteristics: <i>Presentation</i> No symptoms, 2 (15.4%) Fever, 6 (46.2%) Respiratory symptoms, 7 (53.8%) Diarrhoea, 2 (15.4%) Convulsions, 1 (7.7%) Vomiting, 1 (7.7%) Abdominal pain, 1 (7.7%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition): Mild, 7 (53.8%) Common, 5 (38.5%) Severe, 1 (7.7%)</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): NP, stool, blood.</p>	<p>Duration of virus detection* (Days)</p> <p>From first positive test to the first of two consecutive negative tests:</p> <p>NP: Median (range): 13 (5-25) days</p> <p>Blood: ND</p> <p>Stool: Only detected for unknown duration in 1 child.</p> <p>The asymptomatic children had positive NP samples for 5 and 16 days respectively.</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>SARS-CoV-2 RNA remained detectable in stools for 12 days after the nasopharyngeal swab test yielded a negative result in 3 children.</p> <p>Potential overlap of several patients with the study by Y.P. Tan et al.⁽⁹⁶⁾</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
Y.P. Tan ⁽⁹⁶⁾ China Case series https://www.sciencedirect.com/science/article/pii/S1386653220300950?via%3Dihub	<p>Population setting: 10 hospitalised children with COVID-19</p> <p>Demographics: <i>Children</i> <i>Sex:</i> Males, 3 (30%) Females, 7 (70%)</p> <p><i>Age:</i> Average (range), 7 (1-12) years</p> <p>Clinical characteristics: <i>Presentation</i> No symptoms, 2 (20%) Fever, 4 (40%) Cough, 3 (30%) Abdominal pain, 1 (10%) Vomiting, 1 (10%) Constipation, 1 (10%) Convulsion, 1 (10%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: RT-PCR or high-throughput viral gene sequencing</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat, sputum, blood and stool.</p>	<p>Duration of virus detection* (Days)</p> <p>From symptom onset to the first of two consecutive negative tests</p> <p>Throat: Median (range), 14 (5-24) days.</p> <p>Sputum and blood: ND</p> <p>Stool: detected inconsistently in 3 children.</p> <p>One asymptomatic child had positive throat samples for 17 days. The other did not have 2 consecutively negative tests before being discharged.</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Stool samples tested positive on discharge for 1 patient.</p> <p>Potential overlap of several patients with the study by X. Tan et al.⁽⁹⁵⁾</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Tu (97)</p> <p>China</p> <p>Case Series</p> <p>https://europepmc.org/article/ppr/ppr140932</p>	<p>Population setting: 40 hospitalised COVID-19 patients. Group A, shedding time < 10 days: n=14 Group B, shedding time ≥10 days: n= 26</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> Male, 21 (52.5%) Female, 19 (47.5%)</p> <p><i>Age mean (±SD):</i> Overall (n=40), 43.88 (±12.82) years‡ Group A (n=14), 40.86 (±8.26) Group B (n=26), 45.50 (±14.60)</p> <p>Clinical characteristics: <i>Presentation</i> Fever, 34 (85%); Cough, 20 (50%); Sputum, 9 (22.5%); Mild chest tightness after exercise, 5 (12.5%); Fatigue, 6 (15%); Diarrhoea, 1 (2.5%); Sore throat, 2 (5%).</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) Common, 40 (100%)</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Pharyngeal</p>	<p>Duration of virus detection* (Days)</p> <p>From first positive test to the first of two consecutive negative tests:</p> <p>Group A, shedding time < 10 days: n=14 Median (range) viral shedding: 7 (3-9) days</p> <p>Group B, shedding time ≥10 days: n=26 Median (range) viral shedding: 16 (10-36) days</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Epidemiological risk history, serum glucose and CD4/8 on admission were significantly associated with longer viral shedding time (OR=7.5, 11.41, 9.21 respectively, P<0.05). However very small sample size (n=40).</p> <p>All patients were treated with antiviral medicines, 4 with antibiotics and 5 with Corticoid.</p> <p>All patients were tested for nine respiratory pathogens, influenza A and B, and bacteria and fungi culture. None positive.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
Wan ⁽⁹⁸⁾ China	Population setting: 2 asymptomatic COVID-19 patients	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
Case series https://doi.org/10.1016/j.ijid.2020.03.041	Demographics: <i>Adults</i> Case 1 <i>Sex: Male</i> <i>Age: 36</i> Case 2 <i>Sex: Male</i> <i>Age: 19</i> Clinical characteristics: <i>Presentation</i> Asymptomatic COVID-19 Clinical syndromes: NR	Test: rRT-PCR Thresholds: Ct > 40 = negative Gene Targets: ORF1ab Sample site(s): Throat	From first positive test to the first of two consecutive negative tests: Case 1: 7 days Case 2: 23 days	Case 1: Ct = 29.96 (day 1) Case 2: Ct = 23.32 (day 1)	Both patients were asymptomatic and had peak viral loads (Ct values) of 29.96 and 23.32, respectively.	

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>C. Wang⁽⁹⁹⁾</p> <p>China</p> <p>Retrospective, cohort study</p> <p>https://www.researchsquare.com/article/rs-24743/v1</p>	<p>Population setting: 4 cases with a longer course of illness (>40 days) from Wuhan Pulmonary Hospital</p> <p>Demographics: <i>Adults</i> <i>Age, Mean (±SD)</i> 41.25 ± 8.1 years</p> <p><i>Sex</i> Males, 2 Females, 2</p> <p>Clinical characteristics: Case 1: Cough, dizziness. Case 2: Cough, sore throat and myalgia. Case 3: Cough, and fever, and later diarrhoea. Case 4: Cough and chest tightness, and later short of breath. Respiratory failure.</p> <p>COVID-19 Clinical syndromes (not defined); 2 moderate (case 1 and 2), 2 severe (case 3 and 4).</p>	<p>Test: qualitative rRT-PCR</p> <p>Thresholds: Not defined</p> <p>Gene Targets: ORF1ab and N genes.</p> <p>Sample site(s): Nasal and pharyngeal swab (cases 1, 3 and 4). Stool, sputum and throat swab (case 2).</p>	<p>From onset of symptoms to the first of two consecutive negative tests:**</p> <p>Case 1: Still testing positive at Day 48.</p> <p>Case 2: Sputum: Day 40 Faeces: Still testing positive at Day 35.</p> <p>Case 3: Throat: Day 20</p> <p>Case 4: Throat: Day 20</p> <p>Course of illness ≥40 days for all cases. >50 days in 1 patient (case 4).</p>	NR	Not tested	<p>The authors report the case of 4 relatively young patients, with prolonged viral shedding – for reasons for which are unclear.</p> <p>Treatment: Antiviral drugs, Mechanical ventilation, Immunotherapy, oxygen therapy were administered to all patients. IV antibiotics and corticosteroids were given to 2 severe patients.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>L. Wang ⁽¹⁰⁰⁾</p> <p>China</p> <p>Case series</p> <p>https://erj.ersjournals.com/content/early/2020/03/17/13993003.00398-2020</p>	<p>Population setting: 18 hospitalised COVID-19 patients, 6 (33.3%) patients had been discharged</p> <p>Demographics: <i>Mix of adults and children</i> <i>Sex:</i> Male 10 (55.6%) Female, 8 (46.4%)</p> <p><i>Age:</i> median 39 (IQR, 29-55), (2 children aged 7 and 9)</p> <p>Clinical characteristics: Presentation Fever, 17 (94.4%); Cough, 10 (55.6%); Shortness of breath, 4 (22.2%), Haemoptysis, 1 (5.6%), Muscle ache, 2 (11.1%), Headache, 1 (5.6%), Sore throat, 1 (5.6%), Diarrhoea, 3 (16.7%), Nausea and vomiting, 1 (5.6%).</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat</p>	<p>From onset of symptoms to the first of two consecutive negative tests:</p> <p>Median time of RT-PCR conversion (n=6): 19.5 (range 17-24) days.</p>	NR	Not tested	

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<p>Y. Wang⁽¹⁰¹⁾</p> <p>China</p> <p>Case report</p> <p>https://europepmc.org/article/ppr/ppr152908</p>	<p>Population setting: Case report of patient admitted to admitted to QianJiang Central Hospital</p> <p>Demographics: <i>Adult</i> 37-year-old male</p> <p>Clinical characteristics: Fever (38.5°C), dry cough, fatigue, dizziness, runny nose and diarrhoea.</p> <p>COVID-19 Clinical syndromes (China Health Authority's interim criteria): moderate COVID-19 pneumonia.</p>	<p>Test parameters</p> <p>Test: Real time RT-PCR (Sansure Biotech, Hunan, China)</p> <p>Thresholds: Not defined</p> <p>Gene Targets: ORF1ab and N protein</p> <p>Sample site(s): Throat and NP swab</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:</p> <p>32 days (Throat swab)</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Time from symptom onset to recover: 36 days</p> <p>Viral shedding from other sites: Positive stool sample: Days 13,15, 25, 27 Positive anal swab: Day 7.</p> <p>Treatment: Antiviral treatment including arbidol (0.2 g, tid, po), Kaletra (lopinavir 400 mg/ritonavir 100 mg, q12h, po), IFN-α (interferon-α 50 µg, q12h, hypo).</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>X. Wei⁽¹⁰²⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1016/j.jmii.2020.04.013</p>	<p>Population setting: 14 health care workers (12 nurses, 2 doctors) in a neurosurgery department, 12 confirmed cases, and 2 suspected cases.</p> <p>Demographics: <i>Adults</i> <i>Sex:</i> male, 4 Female, 10 <i>Age:</i> mean (\pmSD) 36 \pm6 years</p> <p>Clinical characteristics: <i>Presentation</i> Myalgia or fatigue, 14 (100%); Fever, 12 (86%); Headache, 8 (57%); Pharyngalgia, 7 (50%); Dry cough, 10 (71%); Sputum, 5 (36%); Dyspnoea 2 (14%); Diarrhoea, 9 (64%); Vomiting (14%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test: rRT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat</p>	<p>From first positive test to the first of two consecutive negative tests:</p> <p>Throat: Median (range), 12 (4-16) days</p>	<p>NR</p>	<p>Not tested</p>	<p>Influenza virus A test was positive in one patient.</p> <p>All 14 HCWs received antibiotic and antiviral treatments.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
A.T. Xiao⁽¹⁰³⁾ China Case series https://www.sciencedirect.com/science/article/pii/S1386653220300883?via%3Dihub	Population setting: 301 confirmed COVID-19 patients hospitalised at Tongji Hospital Demographics: <i>Adults</i> <i>Age median (range)</i> 58 years (IQR, 44–68; range, 10–92 years) ≥65 years: 110 (36.5%) <i>Sex</i> Male, 154 (51.2%) Female, 147 (48.8%) Clinical characteristics: NR COVID-19 Clinical syndromes (Diagnosis and treatment of 2019-nCoV pneumonia in China. (Version 5)): Mild to moderate, 301.	Test parameters Test: rRT-PCR Thresholds: Positive: Ct-value < 35 Negative: Ct-value >39.2 Confirmatory retest: Ct-value 35 to <39.2 Gene Targets: ORF1ab and N protein Sample site(s): throat and/or nasal swabs (92.7 % throat swabs)	Duration of virus detection* (Days) From onset of symptoms to the first of two consecutive negative tests: Available for 216 patients: 20 days (IQR 17–24; range, 7–44) <i>Patients <65 years</i> 19 days (IQR 17–23) <i>Patients ≥65 years</i> 22 days (IQR, 19–26) <i>Male</i> 21 days (IQR 17–25) <i>Female</i> 19 days (IQR 17–24) Positive rate of RT-PCR: Day 0-7: 97.9% (137/140) Day 8-14: 68.8% (152/221) Day 15-21: 36.3% (127/350) Day 22-28: 30.0 % (92/307) Day >28: 26.3% (25/95)	Peak viral load NR	Pre-symptomatic viral load Not tested	Other relevant findings Authors reported that older patients had a longer duration of viral detection than younger patients (22 days vs 19 days, $p = 0.015$) 85 (28.2 %) patients still tested positive results at the last follow-up. Re-detection positive rate: Older (≥65 years) patients had a higher re-testing positive rate (32 %, 7/22) than younger (29 %, 14/48) patients had, although the difference is not significant ($p = 0.82$). The authors conclude that longer observation period and >2 consecutive negative viral test may be necessary for patients ≥65 years.

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>Y. Xing⁽¹⁰⁴⁾</p> <p>China</p> <p>Case series</p> <p>https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000191</p>	<p>Population setting: 2 Healthcare workers with COVID-19; post-discharge surveillance after clinical recovery</p> <p>Demographics: <i>Adults</i></p> <p>Case 1 (doctor) <i>Sex:</i> Male <i>Age:</i> in his 40s</p> <p>Case 2 (nurse) <i>Sex:</i> Female <i>Age:</i> in her 20s</p> <p>Clinical characteristics: <i>Presentation</i> Case 1: fever (up to 39.3 °C), chill and fatigue Case 2: headache and pharyngalgia.</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) NR</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: Ct <37 = positive Ct > 40 = negative Ct value 37–40 = intermediate</p> <p>Gene Targets: ORF1ab, N</p> <p>Sample site(s): Throat, stool.</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests:</p> <p>Case 1 Throat: 23 days</p> <p>Case 2 Throat: 12 days.</p>	<p>Peak viral load</p> <p>Exact Ct values were unavailable.</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>After discharge patients tested positive on several occasions using throat samples.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>K. Xu⁽¹⁰⁵⁾</p> <p>China</p> <p>Retrospective cohort study</p> <p>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa351/5818308</p>	<p>Population setting: 113 symptomatic patients from two hospitals outside Wuhan.</p> <p>Early viral RNA clearance (<15 days): n = 37 Prolonged (≥15 days) viral RNA shedding: n = 76</p> <p>Demographics: <i>Adults</i> <i>Age median (IQR)</i> 52 (43-63) years</p> <p><i>Sex</i> Male, 66 (58.4%) Female, 47 (41.6%)</p> <p>Clinical characteristics: 91 patients with fever</p> <p>COVID-19 Clinical syndromes (Diagnosis and treatment of 2019-nCoV pneumonia in China. (Version 5)): Majority of patients had mild symptoms. 28.3% had severe.</p>	<p>Test parameters</p> <p>Test: Real time RT-PCR (Shanghai Bio-germ Medical Technology Co Ltd).</p> <p>Thresholds: Positive: Ct-value < 37. Negative: Ct-value >40 Confirmatory retest: Ct-value 37-40</p> <p>Gene Targets: NR</p> <p>Sample site(s): sputum, NP or throat swab (NP or throat samples <10% of all samples).</p>	<p>Duration of virus detection ♦ (Days)</p> <p>From onset of symptoms to the first of three consecutive negative tests:</p> <p><i>All patients (N=113) (based on predominantly sputum samples)</i> Median 17 days (IQR 13-22)</p> <p><i>Female</i> Median 15 days (IQR, 12–17 days) <i>Male</i> Median 18.5 days (IQR, 15–25 days) (P = .013).</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Risk factors of prolonged viral RNA shedding: Male sex, delayed admission to hospital after illness onset, and invasive mechanical ventilation.</p> <p>The authors did not find an association between corticosteroid use and prolonged viral shedding.</p> <p>Clinical recovery and viral shedding: Prolonged RNA shedding was associated with delayed recovery on radiological image (median days, 12 vs. 16, p<0.001) delayed recovery of body temperature (median days, 7 vs. 11, p<0.001). Prolonged hospital stay (median days, 13.5 vs. 22, p<0.001).</p> <p>Treatment: Corticosteroid (p=0.025) and invasive mechanical ventilation (p=0.006) treatments were related to prolonged viral RNA shedding time.</p>

						Infection severity and viral shedding: The ratio of severe patients at admission in the group with prolonged shedding (≥ 15 days) was significantly higher than that in the group with early viral RNA clearance (< 15 days) (34.2% vs. 16.2%, $p=0.049$).
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Author Country Study design Study URL	Population setting	Primary outcome results				
<p>T. Xu⁽¹⁰⁶⁾</p> <p>China</p> <p>Case series</p> <p>https://doi.org/10.1002/jmv.25944</p>	<p>Population setting: 15 asymptomatic COVID-19 patients</p> <p>Demographics: <i>Mix of adults and children</i> Sex: Male, 10 (66.7%) Female, 5 (33.3%)</p> <p><i>Age:</i> median, 27 (IQR 17-36) years 4 (36.7%) were children or adolescents.</p> <p>Clinical characteristics: <i>Presentation</i> Asymptomatic, 15 (100%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) Mild 15 (100%)</p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat and anal</p>	<p>Duration of virus detection* (Days)</p> <p>From first positive test to the first of two consecutive negative tests:</p> <p>Median: 7 (IQR: 4-9) days</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>One patient was tested positive for SARS-CoV-2 only in anal swab samples.</p> <p>13 (86.7%) patients were treated with antiviral therapy, 4 (26.7%) received empirical antibiotic treatment.</p> <p>Patients remained asymptomatic throughout disease course, except 2 patients who required oxygen.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
J. Yang⁽¹⁰⁷⁾ China Case report https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25940	Population setting: 1 COVID-19 patient admitted to a hospital in Wuhan. Transferred to another hospital on day 56. Demographics: <i>Adult</i> 44-year-old male Clinical characteristics: Fever, malaise, and fatigue for 11 days. COVID-19 Clinical syndromes (not defined): Moderate to mild respiratory symptoms.	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		Test: RT-qPCR Thresholds: Ct-value = 33.2 Gene Targets: ORF1 and N Sample site(s): Throat swabs. (saliva and urine samples on day 40)	From onset of symptoms to the first of two consecutive negative tests: Patient is still testing positive after 74 days of symptoms Virological course of SARS-CoV-2 (Ct-value of throat swab): Day 15: 33.2 (mild-to-moderate symptoms) Days 18-32: 34.0, 34.6 Day 32: >40 (mild-to-moderate symptoms) Day 36: 23.2 (Asymptomatic) Day 43: 29.9 Day 48: 30.4 Day 52: 30.9 Day 54: 18.7 (saliva), >40 (urine), urinary sediment (36.4) Day 56: 31.1 Day 63: Positive (viral load NR) Day 74: Positive (viral load NR)	Day 36: Ct-value 23.2	Not tested	The authors report the case of a patient where the viral RNA reappeared and additionally persisted in throat swabs for more than 70 days. The authors found antibodies and suggest that the coexistence of viral RNA and viral specific antibodies may imply an immune evasion of SARS-CoV-2 from host's immune system. However this requires further large scale investigation. Treatment Methylprednisolone (may prolong the clinical course) and oxygen therapies, and anti-infective therapy including ganciclovir, arbidol and moxifloxacin. Interferon nebulisation, thymalfasin, and chloroquine diphosphate were sequentially initiated on day 49 to inhibit viral replication. Conclusions:

							High load of salivary virus during the recovery period indicates that this patient could potentially be a hidden infectious source for close contact transmission.
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Author Country Study design Study URL	Population setting	Primary outcome results				
X. Yu⁽¹⁰⁸⁾ China Case Series https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-02893-8	Population setting: 92 hospitalised COVID-19 patients. Demographics: <i>Adults</i> <i>Sex:</i> Male, 57 (62%) Female, 35 (38%) <i>Age:</i> mean, 55 (SD ± 16) Clinical characteristics: <i>Presentation</i> Fever, 84 (91.3%); Cough, 58 (63%); Fatigue, 6 (6.5%); Diarrhoea, 7 (7.6%); Nausea and vomiting 4 (4.3%); Shortness of breath 25 (92.2%) COVID-19 Clinical syndromes (not defined) <i>Admission</i> Severe, 30 (32.6%) Mild-moderate, 62 (67.4%) <i>During hospitalisation</i> Persistent mild-moderate, 51 Mild-moderate that became severe, 11.	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		Test: rRT-PCR Thresholds: NR Gene Targets: NR Sample site(s): Sputum	From onset of symptoms to the first of two consecutive negative tests: NR	<i>Ct values at admission, median</i> Severe: 25 Mild-moderate: 28 (p = 0.017) <i>Ct value during hospitalisation</i> Mild-moderate that became severe: 24 Persistent mild-moderate: 29 (p = 0.008).	Not tested	The authors found a positive association between sputum viral load and disease severity as well as risk of progression. Ct values negatively correlated with the probability of progression to severe type in all the patients representing mild-to-moderate at admission. Severe patients had significantly lower Ct values than mild-moderate cases at admission (25 vs. 28, p = 0.017), suggesting a higher viral load in the lower respiratory tract. A higher viral load was observed in sputum specimens from patients who became severe during hospitalisation than those did not.

Author Country Study design Study URL	Population setting	Primary outcome results				
Y. Yuan ⁽¹⁰⁹⁾ China Case series https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25796	<p>Population setting: 6 hospitalised COVID-19 patients</p> <p>Demographics: <i>Adults</i> <i>Age median (range)</i> 64 years (36-71)</p> <p><i>Sex</i> Males, 2 (33%) Females, 4 (67%)</p> <p>Clinical characteristics: Cough, 4 (67%), Fever 2 (33%) White phlegm 2 (33%) No symptoms, 1 (16.7%)</p> <p>COVID-19 Clinical syndromes: NR</p>	<p>Test parameters</p> <p>Test: rRT-PCR</p> <p>Thresholds: Not defined</p> <p>Gene Targets: RdRP, E, and N</p> <p>Sample site(s): NP and faeces</p>	<p>Duration of virus detection* (Days)</p> <p>From first positive test to the first of two consecutive negative tests:</p> <p><i>Time to negative NP swab result (median (range))</i> Day 10.5 (7-18) after the onset of treatment (n=6).</p> <p><i>Time to negative faeces swab result (median (range))</i> Day 10 (10-14) after the onset of treatment (n=3).</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Faeces samples were persistently positive in some patients.</p> <p>All patients with 2 consecutive negative tests later retested positive for SARS-CoV-2 infection using NP samples.</p> <p>Treatment: Combination therapy including nutritional support.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
Zha ⁽¹¹⁰⁾ China Case series https://onlinelibrary.wiley.com/doi/full/10.5694/mja2.50577	Population setting: 31 hospitalised COVID-19 patients. Demographics: <i>Adults</i> <i>Sex:</i> Male, 20 (64%) Female, 11 (36%) <i>Age:</i> median 39 (IQR, 32–54) years Clinical characteristics: <i>Presentation</i> Fever, 25 (81%); Cough, 19 (61%); Myalgia or fatigue, 18 (58%); Headache, 4 (13%); Diarrhoea, 5 (16%); Dyspnoea, 4 (13%) COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) Mild, 31 (100%)	Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
		Test: RT-PCR Thresholds: NR Gene Targets: NR Sample site(s): Throat	From onset of symptoms to the first of two consecutive negative tests: <i>Median (IQR) virus clearance time</i> All (n=31): 14 (11.5–16) days Range. 7-26 days Non-corticosteroid group (n=20): 14 (11–17) days Corticosteroid group (n=11): 15 (14–16) days.	NR	Not tested	11/31 (35.5%) patients received corticosteroid treatment. All patients received lopinavir/ ritonavir (protease inhibitors) and interferon alfa (an antiviral agent) by inhalation. No association between corticosteroid treatment and virus clearance time found (HR, 1.26; 95% CI, 0.58–2.74). But sample size was small.

Author Country Study design Study URL	Population setting	Primary outcome results				
		Test parameters	Duration of virus detection* (Days)	Peak viral load	Pre-symptomatic viral load	Other relevant findings
<p>T. Zhang⁽¹¹¹⁾</p> <p>China</p> <p>Case series</p> <p>https://onlinelibrary.wiley.com/doi/10.1002/jmv.25795</p>	<p>Population setting: 3 cases of SARS-CoV-2 infected children discharged from hospital</p> <p>Demographics: <i>Children</i> <i>Age median (range)</i> Median 8 (range 6-9) years</p> <p><i>Sex</i> Male, 3</p> <p>Clinical characteristics: Fever, 2 Nasal obstruction, 2 Runny nose, 2 Digestive tract symptoms, 2 Cough, 1 Expectoration, 1 Wheeze, 1</p> <p>COVID-19 Clinical syndromes(New Coronavirus Infected Pneumonia Diagnosis and Treatment Program (Fifth Edition): Common type, 3</p>	<p>Test: rRT-PCR (BioGerm)</p> <p>Thresholds: Not defined</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat and faecal swab</p>	<p>From onset of symptoms to the first of two consecutive negative tests:</p> <p><i>Median (range)</i> Throat: 15 days (14-25)</p>	NR	Not tested	<p>Persistent detection of viral RNA in faeces of children was observed despite negative test results from throat samples.</p> <p>Follow up No positive result was found in subsequent PCR tests using throat samples post-discharge, but stool samples were positive after 10 days.</p> <p>Treatment Interferon atomisation, vitamin C, oral Chinese medicine treatment.</p>

Author Country Study design Study URL	Population setting	Primary outcome results				
B. Zhou⁽¹¹²⁾ China Case series https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa451/5821307	Population setting: 41 patients with severe COVID-19 discharged in the west district, Union Hospital, Tongji Medical College <i><65 years</i> n=31 (75.6%) <i>≥65 years</i> n=10 (24.4%) Demographics: <i>Predominantly adults</i> <i>Age median (IQR)</i> 58 (IQR: 48-62) years Range, 17-75 years <i>Sex</i> Male, 22 (53.7%), Female, 19 (46.3%) COVID-19 Clinical syndromes (New Coronavirus Pneumonia Prevention and Control Program in China (4th edition): Severe infection, 41 (100%)	Test parameters Test: rRT-PCR Thresholds: Ct-value < 37 = positive Ct-value of >40 = negative Ct-value 37 - <40 = confirmatory retest Gene Targets: ORF1ab and N Sample site(s): Throat	Duration of virus detection* (Days) From onset of symptoms to the first of two consecutive negative tests: <i>Median duration</i> 31 days (IQR 24 – 40) Range, 18-48 days Male 29 days (IQR: 23.3-38) Female 32 days (IQR: 25.5-40.5) <65 years 31 days (IQR: 23.5-40.5) ≥65 years 31 days (IQR: 24.3-38)	Peak viral load NR	Pre-symptomatic viral load Not tested	Other relevant findings Risk factors for prolonged viral shedding No significant difference in viral shedding time when analysed according to sex or age group.

Author Country Study design Study URL	Population setting	Primary outcome results				
<p>L. Zhu⁽¹¹³⁾</p> <p>China</p> <p>Case series</p> <p>https://www.sciencedirect.com/science/article/pii/S0302283820302141</p>	<p>Population setting: 20 COVID-19 patients, 10 renal transplant recipients and 10 family members</p> <p>Demographics: <i>Adults</i> <i>Overall (n=20)</i> <i>Sex:</i> Male, 13 (65%) Female, 7 (35%) <i>Age,</i> Mean (\pmSD) 43.7 (\pm13.9) years[‡]</p> <p><i>Transplant group</i> <i>Sex:</i> Male, 8 (80%) Female, 2 (20%) <i>Age:</i> Mean(\pmSD) 45 (\pm14.0) years</p> <p><i>Family members</i> <i>Sex:</i> Male, 5 (50%) Female, 5 (50%) <i>Age:</i> Mean(\pmSD), 42.3 (\pm14.4) years</p> <p>Clinical characteristics: <i>Presentation: Transplant group</i> Cough, 9 (90%); Fatigue, 9 (90%); Shortness of breath, 9 (90%); Fever, 9 (90%); Diarrhoea, 3 (30%)</p> <p><i>Family members:</i> Fever, 7 (70%)</p> <p>COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition) <i>Overall:</i></p>	<p>Test parameters</p> <p>Test: RT-PCR</p> <p>Thresholds: NR</p> <p>Gene Targets: NR</p> <p>Sample site(s): Throat</p>	<p>Duration of virus detection* (Days)</p> <p>From onset of symptoms to the first of two consecutive negative tests: <i>Overall (n=18, as 1 transplant patient died and 1 was still testing positive)</i> 19.4 \pm 10.7 days</p> <p><i>Transplant group (n=8):</i> 28.4 \pm 9.3 days</p> <p><i>Family members (n=10):</i> 12.2 \pm 4.6 days</p>	<p>Peak viral load</p> <p>NR</p>	<p>Pre-symptomatic viral load</p> <p>Not tested</p>	<p>Other relevant findings</p> <p>Transplant patients had significantly longer duration of viral shedding than family members ($p < 0.01$). But very small, unmatched groups.</p>

Mild, 11 (55%) Severe, 6 (30%) Critical, 3 (15%) <i>Transplant group</i> Mild, 2 (20%) Severe, 5 (50%) Critical, 3 (30%) <i>Family members</i> Mild, 9 (90%) Severe, 1 (10%)					
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Key: ARDS – acute respiratory distress syndrome; CD4/8 – Cluster of differentiation T-cells 4/8; CDC – Centre for Disease Control and Prevention; COVID-19 – Coronavirus disease 2019; CrI – credible Interval; CRP - C-reactive protein; CT – computed tomography; ddPCR - droplet digital PCR; ELISA - enzyme-linked immunosorbent assay; ETT - Endotracheal tube aspirate; Ct – cycle threshold; Fio₂ - fraction of inspired oxygen; ICU – intensive care unit; IgG/IgM – immunoglobulin G/M; IL-6 – interleukin 6; IQR – interquartile range; LA- lactic acid; LRTI – lower respiratory tract infection; LYM% - lymphocyte percentage; NA – not applicable; NP – nasopharyngeal; ND – not detected; OP – oropharyngeal; Pao₂ – partial pressure of oxygen; PCT – procalcitonin; (q)(r)RT-PCR – (quantitative) (real-time) reverse transcriptase polymerase chain reaction; RCT – randomised controlled trial; RNA - ribonucleic acid; SAA - Serum amyloid A; Sao₂ – oxygen saturation; SARS-CoV-2 - severe acute respiratory syndrome coronavirus 2; SOB – shortness of breath; URTI – upper respiratory tract infection; UK – United Kingdom; WHO – World Health Organization.

- * Viral clearance defined as two consecutive negative results with PCR detection at an interval of 24 hours (counting the first day of negative results as the final day)
- ** Counting Day 1 as the first day of illness/hospitalisation/randomisation
- *** Viral load was not used in the estimation but showed similar monotonic decreasing pattern after symptom onset
- ◇ Viral clearance defined as three consecutive negative results with PCR detection at an interval of 24 hours (counting the first day of negative results as the final day)
- † Data extracted from graphs using webplot digitiser <https://automeris.io/WebPlotDigitizer/>
- ‡ Data analysed using online data calculator https://www.statstodo.com/CombineMeansSDs_Pgm.php

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