Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Evidence summary for COVID-19 viral load over course of infection

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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 (NPHET) 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. This evidence summary was originally published on 1 April 2020, and has been updated to include a summary of all relevant evidence until 3 April 2020. Data published by national agencies are not included.

Results

A total of 39 studies were included from the original and updated serach (30 December 2019 to 27 March 2020).[1-39] A futher 14 studies were included from the updated search conducted to 3 April 2020, resulting in a total of 53 studies (Table 1).[40-53] Thirty-one studies were conducted in China.[1-3, 5, 7, 13, 14, 16, 17, 22, 23, 25-30, 32, 36, 37, 39, 40, 42, 45-48, 50-53] Four studies were conducted in Singapore[8, 24, 33, 49], three studies were conducted in Taiwan,[4, 11, 31] two studies each were conducted in the United States (US),[6, 10] Vietnam,[18, 35] Hong Kong,[20, 38] Germany,[21, 41] France[43, 44] and South Korea,[9, 12] with one study conducted in each of the following; Australia,[19] Scotland[34] and Canada.[15] Fifty-one studies were observational in nature,[1-27, 29-42, 44-53] one study was a randomised controlled trial (RCT)[28] and one was a non-randomised controlled trial (NRCT).[43] The majority of included observational studies (46) were case reports or series.[1-4, 6-25, 27, 29, 30, 32-36, 39-42, 44-53] Additionally, there were three cohort studies,[26, 37, 38] one epidemiological modelling study[5] and one prospective case-ascertained study.[31] Thirty-six studies contained adults exclusively,[2-6, 9-12, 14, 15, 17-20, 23, 24, 26-29, 32-34, 36, 38, 39, 41, 44, 45, 47-49, 51-53] seven contained children (18 years or younger) exclusively,[1, 8, 22, 35, 37, 42, 50] seven contained a combination of children and adults,[7, 13, 25, 31, 40, 43, 46] and three did not provide demographic information.[16, 21, 30]

Thirty-three studies measured 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.[5, 6, 8-10, 12, 15, 16, 18-21, 23, 24, 27, 28, 30, 33, 34, 36, 38, 40, 42-48, 50-53] In general, the highest viral

loads 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:[44]

1) Patients with mild symptoms, with high upper respiratory tract specimen viral load within the first 24 hours of symptom onset 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 specimens
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.

Additionally, some studies have observed clear differences between the viral loads detected in upper respiratory tract and stool specimens. In general, viral loads from upper respiratory tract 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.[46, 50, 53]

Some studies observed increases in viral loads prior to clinical deterioration, particularly from lower respiratory tract specimens and, similarly, decreases in viral load were observed prior to improvement of symptoms.[9, 16, 21] Four studies reported an association between higher viral loads and more severe symptoms.[16, 36, 38, 44] One of these studies 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.[36] Although another study found numerically higher viral loads in those with severe disease, this relationship was not found to be statistically significant.[38]

Three studies have measured viral load in the pre-symptomatic phase, or in asymptomatic individuals.[8, 41, 43] In one of these studies which was a case report of a child, the child had no symptoms on admission to hospital, with a relatively high viral load (nasopharyngeal sample targeting ORF1ab-gene, peak viral load cycle threshold value (Ct) = 13.73 (note that lower Ct values infer higher viral loads)). 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.[8] Corman *et al.* described two patients who presented with no symptoms and remained asymptomatic for at least two weeks after first testing positive. These patients had peak viral loads (Ct values) of 30.10 and 24.39 respectively.[41] Gautret *et al.* detected 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.[43]

Forty-two 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.[1-5, 7, 9-19, 21, 22, 24-26, 29, 32, 34-40, 42-48, 50-53] Of these 42 studies, 34 reported the duration of virus detection from onset of symptoms using upper respiratory tract specimens.[1-5, 9, 11, 13, 15-19, 21, 24, 26, 29, 32, 34, 35, 39, 40, 42-48, 50-53] At the aggregate study-level, the median duration of virus detection from symptom onset was 12 days; this ranged from five[50] to 52 days.[48] The authors of the study that observed this unusually prolonged period of viral shedding in a patient, speculated that 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.[48] Five of these 42 studies used lower respiratory tract specimens;[4, 9, 12, 16, 21] the median duration of virus detection from symptom onset at the aggregate study-level was 11.5 days (range 10-16 days).[4, 16]

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[1, 8, 9, 13, 21, 24, 34, 38], whereas four studies observed that detection of viral RNA in blood samples was associated with severe disease:[10, 30, 41, 44] three studies detected viral RNA in the blood of patients with severe or critical disease (and not in the blood of those with milder disease)[18, 41, 44] and another study observed greater rates of positive tests in blood samples in intensive care unit (ICU) patients (87.5% (7/8)) compared with non-ICU patients (66.7% (16/24)).[32] However, one case report of a patient with severe pneumonia did not detect viral RNA in the blood.[6] Notably, in several studies, faecal samples were reported to have detectable levels of viral RNA for a prolonged period of time (often greater than three to four weeks after symptom onset),[2, 4, 6, 8, 10, 13, 18, 21, 22, 42, 44, 46, 50, 53] particularly in children.[2, 8, 22, 42, 46, 50] Other sample sites such as urine were used less frequently and gave more inconsistent findings.

Several studies have reported a positive association between the duration of virus detection and disease severity,[2, 7, 29, 36, 40, 44, 47] ICU admission[29, 32] and or old age.[2, 40, 44, 51] However three studies did not observe an association between duration of virus detection and disease severity.[37, 38, 51] There was also some evidence of patients testing positive again for COVID-19 despite having previously had two subsequent negative PCR tests, suggesting that test sensitivity or sampling errors may be an issue when viral load is relatively low.[3, 9, 12, 17, 38, 40, 53] One study 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 tested positive again tended to be younger with milder forms of COVID-19 during their initial hospitalisation.[40]

One study included 24 cases with asymptomatic and pre-symptomatic COVID-19 infections screened from close contacts.[7] The authors reported that the median time from the first positive test to the first of two consecutive negative tests was 9.5 days (range 1-21 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 RT-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). Among all 24 asymptomatic and pre-symptomatic cases, 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).[7] Notably, 23 of the 24 cases had data for at least 14 days after suspected exposure. Another 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.[37] 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.[23, 27, 29, 32, 43, 46, 50]

Some studies observed associations between the administration of certain health products that either accelerated (lopinavir-ritonavir,[12, 14] hydroxychloroquine/azithromycin[43] or convalescent plasma transfusion)[47, 48] or delayed (glucocorticosteroids)[13] viral clearance. However, these relationships require testing in larger more robust studies. Notably, one RCT found that lopinavir-ritonavir treatment did not reduce viral loads or duration of virus detectability as compared with standard supportive care alone, suggesting that this antiviral combination therapy may not be an effective treatment strategy for COVID-19.[28] Another NRCT claimed that administration of hydroxychloroquine was significantly associated with faster viral load reduction and 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.[43]

Although stool samples were consistently reported to contain viral RNA for a prolonged period of time, raising concerns about potential faecal-oral transmission, one study which conducted virus culturing found that while infectious virus was readily isolated from throat and lung-derived samples, it was not isolated from stool samples.[21] This particular study also found that no infectious isolates were obtained from any sample taken after day eight (of symptom onset) in spite of ongoing high viral loads. The authors from this study suggest that early discharge followed by home isolation could be chosen for patients who are beyond day 10 of symptoms with less than 100,000 viral RNA (ribonucleic acid) copies per ml of sputum.[21]

The relationship between viral load and infectivity has not yet been determined for COVID-19. One modelling study based primarily on epidemiological data estimated that 44% of transmission could occur before first symptoms present (starting from 2.5 days before symptom onset and reaching its peak at 0.6 days before symptom onset). The authors also estimated that infectivity declines relatively quickly within seven days of illness onset.[5] A prospective case-ascertained study found that all 12 secondary cases, identified from a total of 1,043 close contacts of 32 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 that the rapid reduction of transmissibility over time implies that prolonged hospitalisation of mild cases might not be necessary in large epidemics.[31] A study conducted in Singapore evaluating seven clusters of COVID-19 found that pre-symptomatic transmission likely occurred between 1-3 days before symptom onset in the presymptomatic source patient in four of these clusters. 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.[49]

The studies were of moderate quality and were generally well conducted. However, there are some concerns relating to how cases were selected[11, 14, 16-21, 27, 30, 32, 36, 41, 46, 48, 52, 53] and the pre-print status of some studies.[2, 5, 10, 18, 21, 22, 25, 31, 40, 41, 48, 51, 53] Furthermore, given the case series and or report nature of these studies, their findings should be viewed with caution and will require confirmation using larger more robust study designs. In relation to the included RCT, there are some concerns regarding the open label nature of this trial, specifically the lack of blinding of physicians, patients and outcome assessors.[28] 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.[43] 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 finding from this study should be interpreted with extreme caution.[43]

Discussion

The available evidence to date would appear to suggest that viral load throughout the duration of COVID-19 peaks around symptom onset and decreases within one to three weeks, though different patterns have been observed and may describe different clinical evolutions of the disease. Although the duration of detection and the size of the viral load appears to differ from patient to patient, it seems that the viral RNA becomes undetectable (from upper respiratory tract specimens) about two weeks after symptom onset, but is prolonged and sometimes erratic in stool samples. There is also increasing evidence that asymptomatic patients and those in pre-symptomatic phases have detectable levels of viral RNA. There appears to be a relationship between severity of symptoms and viral load, and potentially the presence of viral RNA in blood samples. There also appears to be evidence emerging regarding the association between the duration of viral RNA detection and severity of disease, ICU admission and old age. However, these associations were not consistently found and more evidence is required in this regard. There is also some evidence of prolonged periods of viral shedding from upper respiratory tract samples in individuals with mild disease, the reasons for which are not understood.[48]

The relationship between SARS-CoV-2 viral load and infectivity is also not fully understood, as the presence of viral RNA may not represent transmissible infectious viral cells. However, there is emerging evidence that there is a reduction in infectivity after 7-10 days of symptoms. One study suggests that transmission may even be limited to five days after symptom onset,[31] and another suggests that pre-symptomatic transmission may start one to three days prior to symptom onset,[49] though more research is required to confirm these findings. Finally, concerns have been raised about the potential for faecal-oral transmission of SARS-CoV-2,

particularly among children. However, there is currently insufficient evidence to suggest this is a viable route of transmission.

Conclusion

The updated evidence largely corroborates earlier findings, providing more evidence of the high transmissibility near and potentially before symptom onset. Although the evidence initially suggested a somewhat consistent trajectory of the viral load of SARS-CoV-2 over the course of the disease, peaking around the time of symptom onset, the updated evidence does suggest that different patterns of viral clearance have been observed and may relate to different clinical evolutions of COVID-19.

There is increasing evidence regarding virus detectability, viral loads and infectivity in pre-symptomatic phases and asymptomatic patients. In general, the virus appears to be detectable in asymptomatic individuals, in the pre-symptomatic phases and for around two weeks from symptom onset in symptomatic individuals. However, some evidence suggests that affected patients may not be infectious for this entire period. The evidence suggests a more nuanced relationship between viral load, detection of viral RNA in blood, duration of virus detection and outcomes such as disease severity. The differences between children and adults in terms of viral loads and duration of detection are still not well understood. Furthermore, there are also limited data regarding the duration of infectivity.

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Table 1 Characteristics of included studies

Author Country Study design Study URL	Population setting	Primary outcome results				
Studies found in original search (30.12.19 to 20.03.20) (n=27 studies)						
J. Cai[(1)] **China** **Case series** https://doi.org/10.1093/cid/ciaa198	**Population setting:** 10 patients admitted to a Children's Hospital **Demographics:** Children *Age:* 3-131 months (mean: 74 months) *Sex:* Male 4, female 6 **Clinical characteristics:** *Presentation:* Fever, 8 (80%); cough, 6 (60%); sore throat, 4 (40%); stuffy nose, 3 (30%); sneezing and rhinorrhea, 2 (20%). **COVID-19 Clinical syndromes (WHO definition):** Mild, 10 (100%).	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: rRT-PCR **Thresholds:** Ct < 35 = positive **Gene Targets:** N, ORF **Sample site(s):** NP, Throat, (faecal in 6 patients, urine and serum in 5)	**From onset of symptoms to the first of two consecutive negative tests:** *NP/Throat* Median (IQR),12 (8-15) days Range, 6-22 *Faeces* Range, >18 and >30 days (and still detected) *Urine/serum:* ND	NR	Not tested	NA

Author Country Study design Study URL	Population setting	Primary outcome results				
Q. Cai[2] **China** **Case series** https://www.medrxiv.org/content/medrxiv/early/2020/02/19/2020.02.17.20024018.full.pdf	**Population setting:** 298 confirmed COVID-19 cases admitted to a designated hospital **Demographics:** Adults *Age:* Median, 47 years (IQR, 33-61) *Sex:* Male, 149 (50%); female, 149 (50%) **Clinical characteristics:** *Presentation:* 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%). **COVID-19 Clinical syndromes (American Thoracic Society and Infectious Disease Society of America definitions for pneumonia) :** Non-severe, 240 (80.6%); severe, 58 (19.4%)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: rqRT-PCR **Thresholds:** Not defined **Gene Targets:** N, ORF1ab **Sample site(s):** Nasal	**From onset of symptoms to the first of two consecutive negative tests:** *Nasal* Median (IQR), 14 (9-19)	NR	Not tested	Old age and severe COVID-19 symptoms independently associated with delayed viral clearance.

Author Country Study design Study URL	Population setting	Primary outcome results				
D. Chen[3] **China** **Case report** http://www.sciencedirect.com/science/article/pii/S1201971220301223	**Population setting:** 1 patient admitted to hospital **Demographics:** Adult *Age:* 46 years *Sex:* Female **Clinical characteristics:** *Presentation:* Fever, sore throat, cough, chest distress **COVID-19 Clinical syndromes:** NR	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: qualitative rRT-PCR **Thresholds:** Not defined **Gene Targets:** N, ORF1ab **Sample site(s):** OP	**From onset of symptoms to the first of two consecutive negative tests:** ** *OP* Day 12	NR	Not tested	Patient subsequently tested positive again on day 17. Subsequent tests on days 20, 22 and 32 were negative.

Author Country Study design Study URL	Population setting	Primary outcome results				
S. Cheng[4] **Taiwan** **Case report** http://www.sciencedirect.com/science/article/pii/S0929664620300449	**Population setting:** 1 patient admitted to hospital (after being quarantined at the airport) **Demographics:** Adult *Age:* 55 years *Sex:* Female **Clinical characteristics:** *Presentation*: Sore throat, dry cough, fatigue, low-grade fever. **COVID-19 Clinical syndromes (WHO definition):** Severe pneumonia	**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):** OP, sputum, stool and urine	**From onset of symptoms to the first of two consecutive negative tests::** ** *OP:* Day 21 *Sputum: Day 17* *Stool/urine*: Day 25 (but earlier samples not tested). **From hospitalisation to the first of two consecutive negative tests::**** *OP:* Day 12 *Sputum*: Day 8 *Stool/urine*: Day 16 (but earlier samples not tested). **From first detection to the first of two consecutive negative tests::** *OP:* 10 days *Sputum:* 6 days	NR	Not tested	NA

Author Country Study design Study URL	Population setting	Primary outcome results				
He[5] **China** **Epidemiological modelling study** https://www.medrxiv.org/content/medrxiv/early/2020/03/18/2020.03.15.20036707.1.full.pdf	**Population setting:** 94 COVID-19 confirmed patients admitted to hospital **Demographics:** Adults *Age:* Median, 47 years *Sex:* Male 47 (50%); Female 47 (50%) **Clinical characteristics:** *Presentation*: Moderate illness (with fever and/or respiratory symptoms and radiographic evidence of pneumonia), 61 (66%) **COVID-19 Clinical syndromes:** Developed to severe or critical, 20 (21%) (not defined)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: qRT-PCR **Thresholds:** Ct < 40 = positive **Gene Targets:** N **Sample site(s):** Throat	**From onset of symptoms to the first of two consecutive negative tests:** Approximately 21 days after onset of illness (using spline analysis)	Highest viral loads detected soon after illness onset (1st test) (Peak trend value, Ct = 30.73)†	Infectiousness in pre-symptomatic phase estimated using modelling approaches.	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 2.5 days before symptom onset and reached its peak at 0.6 days before symptom onset)*** Infectiousness was estimated to decline relatively quickly within 7 days of illness onset.***

Author Country Study design Study URL	Population setting	Primary outcome results				
Holshue[6] **US** **Case report** https://www.nejm.org/doi/pdf/10.1056/NEJMoa2001191?articleTools=true	**Population setting:** 1 patient initially presenting to an urgent care clinic and subsequently hospitalised **Demographics:** Adult *Age:* 35 years *Sex:* Male **Clinical characteristics:** *Presentation*: 4-day history of cough and subjective fever **COVID-19 Clinical syndromes (WHO definition):** Severe pneumonia	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: rRT-PCR **Thresholds:** NR **Gene Targets:** N **Sample site(s):** NP, OP, serum, urine, stool	**From onset of symptoms to the first of two consecutive negative tests:** NR	*Viral load peaked at first test for all sites* *NP:* Day 4 of illness (Ct, 18-20)*** *OP:* Day 4 of illness (Ct, 21-22) *Stool:* Day 7 of illness (Ct, 36-38) *Urine and Serum:* All tests negative	Not tested	NA

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

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

Author Country Study design Study URL	Population setting	Primary outcome results				
Kim[9] **South Korea** **Case series** https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7036338/pdf/jkms-35-e86.pdf	**Population setting:** 2 hospitalised patients **Demographics:** Adults **Patient 1:** 35 year old woman **Patient 2:** 55 year old man **Clinical characteristics:** *Presentation*: **Patient 1:** fever, chills, and myalgia **Patient 2:** sore throat and intermittent myalgia **COVID-19 Clinical syndromes:** Patient 1: Moderate Patient 2: Mild (not defined)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: rRT-PCR **Thresholds:** Ct > 37 = negative **Gene Targets:** RdRp, E **Sample site(s):** URT, LRT, serum, plasma, urine, stool	**From onset of symptoms to the first of two consecutive negative tests:**** **<u>Patient 1:</u>** *URT(RdRp):* Day 14 *URT:(E):* Day 14 *LRT(RdRp)*: Day 13 *LRT(E)*: Day 11 *Stool(E): Day 10* *Serum,* *Urine, Stool(RdRp):* *ND on multiple initial tests but fluctuated from positive to negative at several times* *Plasma:* ND at any stage **<u>Patient 2:</u>** *URT (RdRp):* Day 17 *URT: (E):* Day 17 (both turned positive again on day 25) *LRT: (E) Day 14 (turned positive again on day 26)* *Plasma(RdRp), Stool(RdRp), Serum and urine:* ND at any stage *LRT(RdRp),Plasma(E), Stool (E)*: Only 1 positive test each despite near daily testing	Viral load was highest during the early phase of the illness. **Patient 1:** Days 3-5 **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).	Not tested	Increase and decrease in viral loads may signal worsening and improvement of clinical symptoms respectively.

Author Country Study design Study URL	Population setting	Primary outcome results				
Kujawski[10] **US** **Case series** https://www.medrxiv.org/content/medrxiv/early/2020/03/12/2020.03.09.20032896.full.pdf	**Population setting:** 12 patients with COVID-19 (7 were hospitalised) **Demographics:** Adults *Age:* Median: 53 Range 21-68 *Sex:* Male 8 (67%), Female 3 (33%) **Clinical characteristics:** *Presentation*: cough (n=8), fever (n=7), diarrhoea (n=1) and sore throat (n=1) **COVID-19 Clinical syndromes:** Mild to moderate, 12 (100%) (not defined)	**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):** NP, OP, sputum, serum, urine, stool	**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	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.	Not tested	Among 98 pairs of simultaneous NP and OP specimens, only 58 (59%) had concordant results. The only patient with detected RNA in serum experienced the most severe clinical deterioration during the second week of illness. 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.

Author Country Study design Study URL	Population setting	Primary outcome results				
Lee[11] **Taiwan** **Case report** http://www.sciencedirect.com/science/article/pii/S1684118220300608	**Population setting:** 1 patient presenting to emergency department **Demographics:** *Adult* 46 year old woman **Clinical characteristics:** *Presentation*: 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[12] **South Korea** **Case report** https://www.ncbi.nlm.nih.gov/pubmed/32056407	**Population setting:** 1 patient admitted to hospital **Demographics:** *Adult:* 54 year old man **Clinical characteristics:** *Presentation*: 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) *However virus became detectable again on days 13 to 16 of illness (Days 11-14 of hospitalisation)*	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				
Ling[13] **China** **Case series** https://journals.lww.com/cmj/Fulltext/publishahead/Persistence_and_clearance_of_viral_RNA_in_2019.99362.aspx	**Population setting:** 66 COVID-19 patients admitted to hospital who have recovered **Demographics:** *Mix of adults and children (predominantly adults)* Age: Median (IQR) 44.0 (34.0-62.0) Range: 16-78 *Sex:* Females, 28(42.4%); males 38 (57.6%) **Clinical characteristics:** *Presentation*: NR **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):** OP, stool, urine, and serum	**From onset of symptoms to the first of two consecutive negative tests:** OP: Median (IQR) 9.5 (6.0-11.0) days. Range 2-22 days Faecal (n=55): Median (IQR): 11 (9.0-16.0) days	NR	Not tested	The authors report that administration of corticosteroids was associated with delayed clearance of viral RNA in both OP and stool samples. 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

Author Country Study design Study URL	Population setting	Primary outcome results				
F. Liu[14] **China** **Case series** http://www.sciencedirect.com/science/article/pii/S1201971220301326	**Population setting:** 10 patients admitted to hospital **Demographics:** *Adults* Age: Median (IQR) 42 (34–50). *Sex:* Females, 6 (60%), males 4 (40%) **Clinical characteristics:** *Presentation*: 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%). **COVID-19 Clinical syndromes:** Mild, 5 (50%), Moderate, 3 (30%), Severe, 2 (20%) (not defined)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-PCR **Thresholds:** Ct value ≤35 = positive **Gene Targets:** E, N, RdRp **Sample site(s):** Nasal, throat	**From first day of hospitalisation to the first of two consecutive negative tests:**** Median (IQR): Day 11 (10-13) Range: Days 7 - 18	NR	Not tested	Authors claim that administration of lopinavir/ritonavir was associated with an increase in viral clearance; however, this hypothesis remains to be tested in RCTs.

Author Country Study design Study URL	Population setting	Primary outcome results				
Marchand-Senécal[15] **Canada** **Case report** https://doi.org/10.1093/cid/ciaa227	**Population setting:** 1 patient admitted to hospital **Demographics:** *Adult* 56 year old male **Clinical characteristics:** *Presentation*: new onset fever and non-productive 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: RT-PCR **Thresholds:** Ct value <40 = positive **Gene Targets:** RdRp, E, N, ORF3a **Sample site(s):** NP, mid-turbinate, throat	**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	*Viral load increased slightly on 2nd day of testing for both throat and NP and then fell. Highest viral load for mid-turbinate detected on first test.* 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)†	Not tested	NA

Author Country Study design Study URL	Population setting	Primary outcome results				
Pan[16] **China** **Case series** http://www.sciencedirect.com/science/article/pii/S1473309920301134	**Population setting:** 2 patients admitted to hospital (plus samples from 80 patients at different stages of COVID-19) **Demographics:** *NR* **Clinical characteristics:** *NR* **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):** Nasal, Throat, sputum, Urine and stool.	**From onset of symptoms to the first of two consecutive negative tests:** Patient 1: Sputum: 8 days Throat: 9 days Urine/stool: ND Patient 2: Sputum: 12 days Throat: 9 Days Urine/stool: ND	The viral loads in throat swab and sputum samples peaked at around 5–6 days after symptom onset, ranging from around 10^4 to 10^7 copies per mL during this time	Not tested	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. An individual who subsequently died had very high viral load 8 days after symptom onset. Lower viral loads in stool samples than from other sites.

Author Country Study design Study URL	Population setting	Primary outcome results				
Qu[17] **China** **Case report** http://www.sciencedirect.com/science/article/pii/S1477893920300879	**Population setting:** 1 patient admitted to hospital **Demographics:** *Adult* 49 year old man **Clinical characteristics:** *Presentation*: 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
LV Tan[18] **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:** *Adult* 73 year old man **Clinical characteristics:** *Presentation*: 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				
Thevarajan[19] **Australia** **Case report** https://www.nature.com/articles/s41591-020-0819-2.pdf	**Population setting:** 1 patient hospitalised **Demographics:** *Adult* 47 year old female **Clinical characteristics:** *Presentation*: lethargy, sore throat, dry cough, pleuritic chest pain, mild dyspnoea and subjective fevers **COVID-19 Clinical syndromes:** Mild-to-moderate (not defined)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-PCR, Anti IgM, Anti IgG **Thresholds:** Ct value < 45 = positive **Gene Targets:** E **Sample site(s):** NP, Faecal, sputum, rectal, urine, throat	**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	*Viral load highest on first testing* NP: Ct =33.03 (Day 4 of illness) Sputum: Ct = 31.87 (Day 6 of illness) Faeces: Ct = 40.11 (Day 6 of illness)†	Not tested	Anti-IgM antibodies first detected at day 7 of illness. Anti-IgG antibodies first detected at day 9 of illness.
K. To[20] **Hong Kong** **Case series** https://doi.org/10.1093/cid/ciaa149	**Population setting:** 12 hospitalised patients **Demographics:** *Adults* *Age:* Median, 62.5 Range, 37-75 Sex: female, 5 (42%); males, 7 (58%) **Clinical characteristics:** *Presentation*: NR **COVID-19 Clinical syndromes:** NR	**Test:** qRT-PCR **Thresholds:** NR **Gene Targets:** S **Sample site(s):** Saliva	**From onset of illness to the first of two consecutive negative tests:** NR	*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)* Viral load on first test: median, 3.3 × 106 copies/mL (range, 9.9 × 102 - 1.2 × 108 copies/mL)	Not tested	RNA detected in 11/12 saliva samples that were otherwise confirmed to have COVID-19. Authors suggest that saliva testing could be a viable alternative to NP or OP testing.

Author Country Study design Study URL	Population setting	Primary outcome results				
Woelfel[21] **Germany** **Case series** https://www.medrxiv.org/content/medrxiv/early/2020/03/08/2020.03.05.20030502.full.pdf	**Population setting:** 9 cases (samples taken from inpatients) **Demographics:** "young- to middle-aged professionals" **Clinical characteristics:** *Presentation*: NR **COVID-19 Clinical syndromes:** Mild to moderate (not defined)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: qRT-PCR IgG/IgM immunofluorescence **Thresholds:** 10^2 copies/ml **Gene Targets:** E- and RdRp **Sample site(s):** OP, NP, sputum urine, serum, stool	**From onset of illness to the first of two consecutive negative tests:** Sputum: median 11.5 days OP/NP Swab: median 9.5 days Stool: persistently positive	OP/NP: The average viral RNA load was $6.76x10^5$ copies per whole swab until day 5 of illness (maximum, $7.11X10^8$ copies/swab). Swab samples taken after day 5 had an average viral load of $5.13x10^3$ copies per swab 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. Urine and serum: ND	Not tested	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. No infectious isolates were obtained from any sample taken after day 8 in spite of ongoing high viral loads. Seroconversion occurred after 6-12 days, but was not followed by a rapid decline of viral loads. 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.

Author Country Study design Study URL	Population setting	Primary outcome results				
Xing[22] **China** **Case series** https://www.medrxiv.org/content/medrxiv/early/2020/03/13/2020.03.11.20033159.full.pdf	**Population setting:** 3 hospitalised children **Demographics:** *Children* *Case 1:* 18 month old male *Case 2:* 5 year old male *Case 3:* 6 year old female **Clinical characteristics:** *Presentation*: Fever, 3 (100%) **COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition). :** Mild to moderate, 3 (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 and faecal	**From day of hospitalisation to the first of two consecutive negative tests:**** Throat: median Day 14 Faeces: median Day 31	NR	Not tested	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.

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

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

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

Author Country Study design Study URL	Population setting	Primary outcome results				
Zhou[26] **China** **Retrospective cohort study** http://www.sciencedirect.com/science/article/pii/S0140673620305663	**Population setting:** 191 adult (≥18 years old) inpatients in two hospitals (Wuhan) **Demographics:** *Adults* *Age:* Median (IQR) 56.0 (46.0 - 67.0) *Sex:* Male 119 (62%); Female 72 (38%) **Clinical characteristics:** *Presentation*: 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%). *Outcome:* Died 54 (28.3%); discharged 137 (71.7%) **COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition):** General: 72 (38%) Severe: 66 (35%) Critical: 53 (28%)	**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):** Throat-swab	**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) Survivors (n=137) Median (IQR) 20.0 days (17.0–24.0) Non-survivors (n=54) Median (IQR) 18.5 days (15.0–22.0) Shedding continued until death	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				
Zou[27] **China** **Case series** https://www.nejm.org/doi/full/10.1056/NEJMc2001737	**Population setting:** 18 patients **Demographics:** *Adults* *Age:* median (range) 59 (26 to 76) *Sex:* Male 9 (50%); female 9 (50%) **Clinical characteristics:** *Presentation:* 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). **COVID-19 Clinical syndromes:** 13 with evidence of pneumonia CT. Mild-to-moderate illness with 3 ICU admissions. (not defined)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: rRT-PCR **Thresholds:** Negative = Ct value > 40 **Gene Targets:** N and Orf1b **Sample site(s):** 72 nasal swabs (sampled from the mid-turbinate and nasopharynx); 72 throat swabs. 1 - 9 sequential samples obtained from each patient.	**From onset of symptoms to the first of two consecutive negative tests:** NR	When data from all 18 patients (Ct values) are aggregated viral loads peaked in the early stage of the illness Throat: Day 1 of illness onset (Ct = 25.98 Nasal: Day 3 of illness onset (Ct = 21.10)†	NR	Higher viral loads were detected in the nose than in the throat.

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)						
Cao[28] **China** **RCT** https://www.nejm.org/doi/full/10.1056/NEJMoa2001282	**Population setting:** 199 patients with severe COVID-19 ($Sao_2 \leq 94\%$ while breathing ambient air or a ratio of Pao_2 to $Fio_2 < 300$ mm Hg) **Demographics:** *Adults* *Age:* Median (IQR), 58 (49–68) *Sex:* Male, 120 (60.3%) Female (all non-pregnant), 79 (39.7%) **Clinical characteristics:** *Presentation:* Fever 182 (91.5%), Respiratory rate >24/min, 37 (18.8%) **COVID-19 Clinical syndromes (Chinese CDC definition):** Severe, 199 (100%)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: qRT-PCR **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 log^{10} copies/mL; results of patients with viral negative RNA are imputed with 0 log^{10} copies/mL **Gene Targets:** RdRP, N and E **Sample site(s):** Throat (n=130)	**From onset of symptoms to the first of two consecutive negative tests:** NR	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: †** *Mean ±SD log^{10} copies per ml* ***Day 1:*** *Total population:* 4.0±2.1 *Lopinavir–Ritonavir arm:* 4.4±2.0 *Standard care arm:* 3.7±2.1 ***Day 5:*** *Total population:* NR *Lopinavir–Ritonavir arm:* 2.4 *Standard care arm:* 1.7 ***Day 10:*** *Total population:* NR *Lopinavir–Ritonavir arm:* 1.5 *Standard care arm:* 1.5 ***Day 14:*** *Total population:* NR *Lopinavir–Ritonavir arm:* 1.3	Not tested	Authors found that adding lopinavir–ritonavir treatment did not reduce viral RNA loads or duration of viral RNA detectability as compared with standard supportive care alone. 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%).

				Standard care arm: 0.6 ***Day 21:*** *Total population:* NR *Lopinavir–Ritonavir arm:* 0.08 *Standard care arm:* 0.06 ***Day 28:*** *Total population:* NR *Lopinavir–Ritonavir arm:* 0 *Standard care arm:* 0		

Author Country Study design Study URL	Population setting	Primary outcome results				
J. Chen[29] **China** **Case series** https://www.sciencedirect.com/science/article/pii/S0163445320301195	**Population setting:** 249 hospitalised patients **Demographics:** *Adults* *Age:* Median 51 (IQR, 36–64 years) *Sex:* Male, 126 (50.6%), Female, 123 (49.7%) **Clinical characteristics:** *Presentation:* 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%). **COVID-19 Clinical syndromes:** Authors report that "nearly 10% were severe and critical". The rest (~90%) were considered mild or asymptomatic. (not defined)	**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):** Upper respiratory tract	**From onset of symptoms to the first of two consecutive negative tests:** Median, 11 days (95% CI, 10-12 days) **From hospital admission to the first of two consecutive negative tests:** *Asymptomatic patients (n=7):* median 2 days (95% CI, 1-3)	NR	Not tested	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).

Author Country Study design Study URL	Population setting	Primary outcome results				
W. Chen[30] **China** **Case series** https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1732837	**Population setting:** 57 hospitalised patients (including 6 patients testing positive for RNA in blood samples) **Demographics:** *NR* **Clinical characteristics:** *Presentation:* NR **COVID-19 Clinical syndromes (Chinese CDC definition):** Mild, 39 (68.4%) Severe, 18 (31.6%). Patients with at least one of the following symptoms were classified as severe cases, 1) distress of respiratory with respiratory rate > = 30/min; 2) Oxygen saturation < = 93% in the rest state, and 3) PaO_2 / FIO_2 of less than 300 mm Hg.	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-PCR **Thresholds:** NR **Gene Targets:** ORF1ab, N **Sample site(s):** Pharyngeal, blood, anal	**From onset of symptoms to the first of two consecutive negative tests:** NR	***Patient 1:*** Pharyngeal sample peaked day 11 of illness while in ICU (ORF1ab, Ct = 15) (4^{th} day of testing) N target: Ct = 25 both on 1^{st} and 4^{th} 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) ***Patient 2:*** Pharyngeal sample peaked day 10 of illness while in ICU (ORF1ab, Ct = 23; N, Ct = 24) (2^{nd} 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) ***Patient 3:*** Pharyngeal sample peaked day 12 of illness while in ICU	Not tested	Authors report that the presence of viral RNA in the blood and anal swab is positively correlated with severity of disease.

				(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 ***Patient 4:*** No pharyngeal test conducted. Blood test positive on day 8 (ORF1ab, Ct = 32; N, Ct = 37) Anal: Not tested ***Patient 5:*** All three pharyngeal tests negative. Blood test positive for ORF1ab on day 6 (Ct = 38). Negative for N target. Anal: not tested ***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.		

Author Country Study design Study URL	Population setting	Primary outcome results				
H. Cheng[31] **Taiwan** **Prospective case-ascertained study** https://www.medrxiv.org/content/10.1101/2020.03.18.20034561v1.full.pdf	**Population setting:** 32 confirmed cases and 12 paired cases (index-secondary cases) identified from 1,043 close contacts **Demographics of n=12 secondary cases:** *Index cases (n=12):* NR *Secondary cases (n=12)* *Mixture of Adults and Children:* *Age range:* 0-19: 1 (8.3%) 20-39: 3 (25%) 40-59: 5 (41.7%) ≥ 60: 3 (25%) ***Close contacts (n=1,043)*** *Mixture of Adults and Children:* *Sex:* Male, 493 (47.3%) Female, 508 (48.7%) Unknown, 42 (4%) ***Age range:*** 0-19: 70 (6.7%) 20-39: 462 (44.3%) 40-59: 350 (33.6%) ≥ 60: 82 (7.9%) Unknown: 79 (7.6%) **Clinical characteristics:** *Presentation:* NR **COVID-19 Clinical syndromes (WHO definition):** *Index cases (n=12)* Mild, 4 (33%) Mild pneumonia, 2 (16.7%) Severe pneumonia, 0 ARDS, Sepsis, 6 (50%) Secondary cases (n=12): 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):** NR	**From onset of symptoms to the first of two consecutive negative tests:** NR	NR	Not tested	Authors estimated that the mean incubation period was 4.9 days (95% CrI, 2.7–8.4), and the mean serial interval was 7.0 days (95% CrI, 3.7–13.2). All 12 secondary cases 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. Of all identified contacts (n=1,043), none were infected if exposure first occurred after five days of the index case's symptom onset. 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.

Author Country Study design Study URL	Population setting	Primary outcome results				
Fang[32] **China** **Case series** https://www.sciencedirect.com/science/article/pii/S0163445320301390	**Population setting:** 32 hospitalised adults (8 ICU and 24 non-ICU patients) **Demographics:** *Adults* *Age:* Median, 41 Range: 34-54 *Sex:* Male, 16 (50%), Female, 16 (50%) **Clinical characteristics:** *Presentation:* Cough, 24(75%), fever, 17 (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%) **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, blood, faecal, urine, saliva and tears	**From onset of symptoms to the first of two consecutive negative tests:** Conversion time of nasal samples was significantly longer than that of blood or saliva Non-ICU patients (n=24): *Nasal*: 15.67±6.68 days *Blood:* 10.17±6.13 days *Saliva:* 13.33±5.27 days ICU patients (n=8): *Nasal:* 22.25±3.62 days *Blood:* 14.63±5.88 days *Saliva:* 16.50±6.19 days	NR	Not tested	In ICU patients, the conversion time of blood, nasal and saliva samples all exceeded two weeks.

Author Country Study design Study URL	Population setting	Primary outcome results				
Goh[33] **Singapore** **Case report** https://www.ncbi.nlm.nih.gov/pubmed/32200400	**Population setting:** 1 hospitalised adult **Demographics:** *Adult* 64 year old male **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, he deteriorated rapidly with severe hypoxemic respiratory failure) **COVID-19 Clinical syndromes (WHO definition):** ARDS	**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, Endotracheal tube aspirate (ETT), stool	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

Author Country Study design Study URL	Population setting	Primary outcome results				
Hill[34] **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:** *Adult:* 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**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-PCR **Thresholds:** Ct Value > 40 = negative **Gene Targets:** NR **Sample site(s):** Nose, throat, (combined nose/throat), urine, faeces, blood	**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	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	Not tested	NR
Le[35] **Vietnam** **Case report** https://doi.org/10.1016/S2352-4642(20)30091-2	**Population setting:** 1 hospitalised infant **Demographics:** *Child:* 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				
Y. Liu[36] **China** **Case series** https://doi.org/10.1016/S1473-3099(20)30232-2	**Population setting:** 76 hospitalised patients **Demographics:** *Adults* 48 (63.2%) male 28 (36.8%) female Mean age 48.3 years **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%) **COVID-19 Clinical syndromes (author definition):** 46 (61%) mild 30 (39%) severe Patients who had any of the following were classified as severe cases: (1) respiratory distress (≥30 breaths per min); (2) oxygen saturation at rest ≤93%; (3) ratio of partial pressure of arterial oxygen to fractional concentration of oxygen inspired air ≤300 mm Hg; or (4) severe disease complications (eg, respiratory failure, requirement of mechanical ventilation, septic shock, or non-respiratory organ failure).	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-PCR **Thresholds:** **Gene Targets:** **Sample site(s):** nasopharyngeal	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.	Initial viral load (Ct_{sample}-Ct_{Ref}): Mean (SD) 4.44 (3.99) in mild cases Mean (SD) -1.42 (3.62) in severe cases The ΔCt values of severe cases remained significantly lower for the first 12 days after onset than those of corresponding mild cases.	Not tested	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. 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.

Author Country Study design Study URL	Population setting	Primary outcome results				
Qiu[37] **China** **Cohort study** https://doi.org/10.1016/S1473-3099(20)30198-5	**Population setting:** 36 hospitalised children **Demographics:** *Children* *Age:* Mean 8.3 years (SD 3.5) Range: 1-16 *Sex:* Males, 23 (64%) Females, 13 (36%) **Clinical characteristics:** Fever, 13 (36%), cough, 7 (19%), headache, 3 (8%), sore throat, 2 (6%), vomiting/diarrhoea, 2 (6%) asymptomatic, 10 (28%) **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%)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-PCR **Thresholds:** NR **Gene Targets:** *ORF1ab, N* **Sample site(s):** Upper nasopharyngeal	**From hospitalisation to the first of two consecutive negative tests:** All patients (n=36): mean 10 days (SD 2, range 7-22). 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) 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)	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				
K. To[38] **Hong Kong** **Cohort study** http://www.sciencedirect.com/science/article/pii/S1473309920301961	**Population setting:** 23 patients at two hospitals in Hong Kong **Demographics:** *Adults* 13 male, 10 female Median age 62 years (range 37–75) **Clinical characteristics:** Fever, 22 (96%), cough, 5 (22%), chills, 4 (17%), dyspnoea, 4 (17%) **COVID-19 Clinical syndromes (author definitions):** Severe disease, 10 (43%), Mild disease, 13 (57%) Severe disease defined as the need for supplemental oxygen, admission to ICU, or death.	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-qPCR **Thresholds:** NR **Gene Targets:** NR **Sample site(s):** posterior oropharyngeal saliva or endotracheal aspirate, blood, urine, rectal	**From onset of symptoms to the first of two consecutive negative tests:** NR for most of the sample. 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. Urine: ND Blood: Only detected in 5 (22%) patients Rectal: Only detected in 4 (17%) patients 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.	*Salivary viral load was highest during the first week after symptom onset and subsequently declined with time.* The median viral load at presentation was 5.2 log_{10} copies per mL (IQR 4.1–7.0). Peak viral load was 6.91 log_{10} copies per mL (IQR 4.27–7.40) in those with severe disease, and 5.29 log_{10} copies per mL (IQR 3.91–7.56) in those with mild disease.	Not tested	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. An increase was noted in IgG or IgM antibody levels against NP or RBD for most patients at 10 days or later after symptom.

Author Country Study design Study URL	Population setting	Primary outcome results				
Wu[39] **China** **Case series** **https://doi.org/10.1016/S2468-1253(20)30083-2**	**Population setting:** 74 hospitalised patients **Demographics:** *Adults* Female 35 (47.3%) Male 39 (52.7%) Mean age 43.5 years **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%) **COVID-19 Clinical syndromes** Severe (not defined), 18 24.3%	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: Real-time RT-PCR **Thresholds:** NR **Gene Targets:** *RdRp, N, E* **Sample site(s):** Throat, faecal	**From onset of symptoms to the first of two consecutive negative tests:** *For all 74 patients: Throat: Mean ± SD, 16.1 ± 6.7 day‡* For 33 (45%) of 74 patients with negative faecal samples, respiratory swabs remained positive for a mean of 15.4 days (SD 6.7) from first symptom onset. 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. For 41 patients who tested positive on both swabs,	NR	Not tested	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.

			throat swabs remained positive for a median of 16 days (IQR 12.3, 20.8) from symptom onset. Faecal swabs remained positive for a median of 29 days (IQR 18.3, 36.8).			

Author Country Study design Study URL	Population setting	Primary outcome results				
Studies found in updated search (up to 03.04.20) (n=14 additional studies)						
An[40] **China** **Case series** **https://www.medrxiv.org/content/10.1101/2020.03.26.20044222v1**	**Population setting:** 262 discharged COVID-19 patients (38 (14.5%) of whom had tested positive again for SARS-CoV-2 within 14 days) **Demographics:** *Mix of adults and children* *Sex:* *n=242 mild and moderate patients* Male, 116 (47.9%) Female, 126 (52.1%) *Severe disease:* NR *Age* *Mild disease, Median (range)* Re-dected patients (n=11), 20 (5-64) Not re-detected (n=19), 23 (2-63) *Moderate disease, Median (range)* Re-dected patients (n=27), 38 (2-60) Not re-detected (n=185), 48 (1-86) Severe disease: NR **Clinical characteristics:**	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		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:** *Mild disease, Median (range)* Re-dected patients (n=11), 17 (11-22) Not re-detected (n=19), 15 (8-24) *Moderate disease, Median (range)* Re-dected patients (n=27), 18 (9-30) Not re-detected (n=185), 20 (5-47) Severe disease: 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.

	Presentation (n=242 mild and moderate patients): Fever, 165 (68.1%) Upper respiratory symptoms, 45 (18.6%) Lower respiratory symptoms, 121 (50%) Digestive tract symptoms, 20 (8.3%) Severe patients: NR **COVID-19 Clinical syndromes (National Health Commission of the People's Republic of China definition):** *All 262 patients:* Mild, 30 (11.4%) Moderate, 212 (81%) Severe, 20 (7.6%) *38 re-detected patients* Mild, 11 (28.9%) Moderate, 27 (71.1%) Severe, 0 (0%)					The hypersensitive Sherlock assay test had higher rates of positive RNA detection than commercial tests. No differences were found between the two groups in terms of levels of IgG and Ig M antibodies in the plasma.

Author Country Study design Study URL	Population setting	Primary outcome results				
Corman[41] **Germany** **Case series** **https://www.medrxiv.org/content/10.1101/2020.03.29.20039529v1**	**Population setting:** 18 patients (hospital and quarantine settings) **Demographics:** *Adults* *Sex:* Male, 12 (66.7%) Female, 6 (33.3%) *Age:* All between 18-65 years **Clinical characteristics:** *Presentation:* 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%) **COVID-19 Clinical syndromes (WHO definition):** ARDS, 1 (5.6%) Unclear for remainder (but at least 2 developed some level of pneumonia)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-PCR **Thresholds:** NR **Gene Targets:** E, RdRp **Sample site(s):** OP, sputum, blood	**From onset of symptoms to the first of two consecutive negative tests:** NR	Mean (± SD) peak viral load of 17/18 patients with detectable OP/Sputum RNA: 27.9 ± 6.4 (days tested unknown) .	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. Peak Ct values during quarantine/ hospitalisation = 30.10, 24.39 and 30.25 respectively.	The authors report only one positive RNA test from all blood samples (77 in total). This positive sample was in the patient with ARDS. 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.

Author Country Study design Study URL	Population setting	Primary outcome results				
Fan[42] **China** **Case report** **https://onlinelibrary.wiley.com/doi/10.1002/ped4.12186**	**Population setting:** 1 hospitalised child **Demographics:** *Child* 3 month old girl **Clinical characteristics:** *Presentation:* Diarrhoea and fever **COVID-19 Clinical syndromes (WHO definition)**: Mild	**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):** OP, anal	**From onset of symptoms to the first of two consecutive negative tests:** OP: 14 days Anal: Still positive at 28 days	NR	Not tested	Authors describe the potential for prolonged faecal-oral transmission in children.

Author Country Study design Study URL	Population setting	Primary outcome results				
Gautret[43] **France** **Non-randomised controlled trial** **http://dx.doi.org/10.1016/j.ijantimicag.2020.105949**	**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 hydroxycholoquine, 6 were treated with hydroxycholorquine and azithromycin, 16 were treated with neither) **Demographics:** *Mixt of adults and children* *Sex:* Male, 15 (41.7%) Female, 21 (58.3%) *Age:* 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). **Clinical characteristics:** *Presentation:* No symptoms, 6 (16.7%) URTI symptoms, 22 (61.1%) LRTI symptoms, 8 (22.2%) **COVID-19 Clinical syndromes:** NR	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: rRT-PCR **Thresholds:** Ct value >35 = negative **Gene Targets:** NR **Sample site(s):** NP	**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). **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). 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.	Where viral loads were reported (n=26 patients) these most commonly peaked on first day of testing (n=15 patients): Median (IQR) viral load (Ct value) of first day of testing from the reporting 26 patients = 26.5 (23.25-29)	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.	The authors conclude that hydoxycholoroquine was significantly associated with viral load reduction and this effect was reinforced by addition of azithromycin. However, due to critical flaws with the conduct and reporting of this trial, we strongly maintain that it is not possible to determine any causal relationship between these drugs and viral load reduction from this study. Better designed studies are required to investigate the efficacy of these drugs in COVID-19 patients.

			For hydoxychloroquine patients: 7/14 tested negative on 2 consecutive tests by the end of the 6 day period. For hydorxychloroquine + azithromycin patients: All 6 patients tested negative in 2 consecutive tests by the end of the 6 day period.			

Author Country Study design Study URL	Population setting	Primary outcome results				
Lescure[44] **France** **Case series** **https://www.sciencedirect.com/science/article/pii/S1473309920302000?via%3Dihub**	**Population setting:** 5 hospitalised patients **Demographics:** *Adults* *Sex:* Male, 3 (60%) Female, 2 (40%) *Age:* Median, 46 Range: 30-80 **Clinical characteristics:** *Presentation:* Cough, 4 (80%) Fever, 3 (60%) Conjunctivitis, 1 (20%) Diarrhoea, 1 (20%) Shortness of breath, 1 (20%) **COVID-19 Clinical syndromes (Chinese CDC)**: Mild, 2 (40%) Severe, 2 (40%) Critical 1 (20%)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: Semi-quantitative rRT-PCR **Thresholds:** **Quantification limit =** 2 log_{10} copies per 1000 cells **Gene Targets:** E, GAPDH, dRp-IP1 and RdRp **Sample site(s):** Upper respiratory tract, lower respiratory tract (where possible), blood, urine, conjunctival, pleural, stool (or anal swab)	**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 Median for the 5 patients = 11 days Urine and conjunctival: ND for all patients	<u>Mild disease patients</u> Patient 4 and 5 NP RdRp target: Viral load peaked within the first few days and then declined gradually over next 12 or 16 days respectively. (6.2† log_{10} copies per 1000 cells for patient 4 on day 4, and 7.4 log_{10} copies per 1000 cells for patient 5 on day 2 after symptom onset). Stool samples: Peaked on day 3 for patient 4 (6.8 log_{10} copies/g stool) and day 6 for patient 5 (8.1 log_{10} copies/g stool) <u>Severe disease patients</u>	Not tested	Three different clinical evolutions are described by the authors: (1) two 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 two 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

				NP RdRp target: Patient 1 peaked on day 6 (1st day of testing) (7.1 log_{10} copies/1000 cells). Patient 2 had a detectable not 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. <u>Critical disease</u> Viral load peaked in patient 3 on day 8 (first day of testing)(6.7 log_{10} copies/1000 cells) and remained high and stable for the duration of his illness before he died on day 24.		towards 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). RNA was only detected in blood and pleural fluids of the critical patient who subsequently died. 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.

Author Country Study design Study URL	Population setting	Primary outcome results				
Lv[45] **China** **Case report** **https://www.sciencedirect.com/science/article/pii/S0009898120301340?via%3Dihub**	**Population setting:** 1 hospitalised patient **Demographics:** *Adult* 54 year old male **Clinical characteristics:** *Presentation:* Fever 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: RT-PCR **Thresholds:** Ct value <37 = positive **Gene Targets:** ORF1ab, N (Positive result is determined by two positive target genes in the same specimen. Result of single positive gene is assessed as pending (requires retest), and the result of two negative genes is assessed as negative) **Sample site(s):** OP, sputum and anal	**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	OP (N gene): Ct value = 31.54 (4th day of testing, 16 days after symptom onset). OP (ORF1ab): Ct value = 33.78, 5th day of testing, 22 days after symptom onset.	Not tested	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				
Ma[46] **China** **Case series** **http://dx.doi.org/10.1016/j.jmii.2020.03.010**	**Population setting:** 8 patients in a hospital and post-discharge setting **Demographics:** *Mix of Adults (n=2) and Children (n=6)* *Sex:* Females, 6 (75%) Males, 2 (25%) *Age:* Median (IQR): 70 months old (40.5 -180 months) Range (11 months – 39 years) **Clinical characteristics:** *Presentation:* Fever, 3 (37.5%) No symptoms, 5 (62.5%) **COVID-19 Clinical syndromes (not defined)**: Mild to moderate, 8 (100%)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: rRT-PCR **Thresholds:** NR **Gene Targets:** ORF1ab and N **Sample site(s):** Stool, Nasal, Throat	**From onset of symptoms to the first of two consecutive negative tests:** Nasal: week 2-3 Throat: week 2-3 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.	NR	Not tested	Authors note the prolonged shedding of virus from stool samples (even when throat and nasal samples are negative) in both adults and children.

Author Country Study design Study URL	Population setting	Primary outcome results				
Shen[47] **China** **Case series** **http://dx.doi.org/10.1001/jama.2020.4783**	**Population setting:** 5 hospitalised patients **Demographics:** *Adults* *Sex:* Females, 2 (40%) Males, 3 (60%) *Age:* Range, 36-65 years **Clinical characteristics:** *Presentation:* NR **COVID-19 Clinical syndromes (author definition):** Critical, 5 (100%) 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)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: qRT-PCR **Thresholds:** Ct value ≤ 37 = positive **Gene Targets:** NR **Sample site(s):** NP	**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 **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.	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). 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). One patient experienced their highest viral day just prior to transfusion (21 days since symptom onset) (Ct value, 26.6).	Not tested	Patients received transfusion with convalescent plasma with a SARS-CoV-2–specific antibody (IgG) binding titer greater than 1:1000 and a neutralization titer greater than 40 that had been obtained from 5 patients who recovered from COVID-19. After the transfusion of convalescent plasma, the titers of IgG and IgM in the sera of these patients increased in a time-dependent manner. The authors observed improvement in

						patients' clinical status and viral load post transfusion, but state that RCTs are required to determine efficacy.

Author Country Study design Study URL	Population setting	Primary outcome results				
L. Tan[48] **China** **Case series** **https://doi.org/10.1101/2020.03.22.20040071**	**Population setting:** 2 hospitalised patients **Demographics:** *Adults* *Age:* Case 1, 40-50 years; Case 2, 70-80 years *Sex:* Case 1, Male; Case 2, Female **Clinical characteristics:** *Presentation:* Case 1: Asymptomatic; history of intermittent fever for one week. Case 2: Intermittent fever and dry cough 10 days prior to presentation. **COVID-19 Clinical syndromes (National Health Commission of China definitions):** Case 1: moderate Case 2: moderate	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: RT-PCR nucleic acid amplification test (NAPT) **Thresholds:** Ct > 40 = negative **Gene Targets:** NR **Sample site(s):** OP	**From onset of symptoms to the first of two consecutive negative tests:** Case 1: 52 days Case 2: 24 days	**Peak viral load (Case 1):** Day 27 (Ct value = 21.03) † **Case 2:** NR	Not tested	Authors describe how treatment with convalescent plasma was associated with faster clearance of the virus. This treatment requires testing in RCTs. A relatively mild case had excessive virus shedding (52 days). Authors speculate that 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. IgG detectable from Case 1, 27 days after symptom onset

Author Country Study design Study URL	Population setting	Primary outcome results				
Wei[49] **Singapore** **Case series** **https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm?s_cid=mm6914e1_w**	**Population setting:** 7 clusters of COVID-19 cases in which pre-symptomatic transmission was likely (n=18 patients) **Demographics:** *Adultsy* *Sex:* Female, 11 (61.1%); Male, 7 (38.9%) *Age:* Median 52.5 years (range 26 to 63) **Clinical characteristics:** *Presentation:* 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%) **COVID-19 Clinical syndromes:** NR	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: PCR **Thresholds:** NR **Gene Targets:** NR **Sample site(s):** NR	**From onset of symptoms to the first of two consecutive negative tests:** NR	NR	Not tested	In the four 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 three clusters (C, D, and E), the exact timing of transmission exposure could not be ascertained because the persons lived together, and exposure was continual.

Author Country Study design Study URL	Population setting	Primary outcome results				
Y. Xu[50] **China** **Case series** **https://www.nature.com/articles/s41591-020-0817-4.pdf**	**Population setting:** 10 paediatric cases admitted to hospital **Demographics:** Children *Sex:* Male, 6; Female, 4 *Age:* Range 2 months to 15 years **Clinical characteristics:** Fever, 7 (70%), cough, 5 (50%), sore throat, 4 (40%), diarrhoea, 3 (30%), nasal congestion and rhinorrhoea, 2 (20%). Asymptomatic, 1 (10%). **COVID-19 Clinical syndromes:** NR	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load*†**	**Other relevant findings**
		Test: rRT-PCR **Thresholds:** Ct ≥40 = negative **Gene Targets:** Orf1ab, N **Sample site(s):** Nasopharyngeal, rectal	**From onset of symptoms to the first of two consecutive negative tests:** Nasopharangeal swab: Median 5 days (IQR 3.5-13.0) Rectal: Median 22 days (IQR 7-23) [could be longer as 7 positive at study end]	NP: Viral load generally peaked in all cases on the 1st day of testing (Average Ct valie = 33.60 on Day 0 since admission) † Rectal: Viral loads from rectal swabs dynamics followed a more heterogenous patterns and peaked on Day 18 since hospital admission (average Ct value = 27.86) †	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, one was ~33 and the other ~39) † 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) †	Eight of ten patients demonstrated persistently positive real-time RT–PCR tests of rectal swabs after their nasopharyngeal testing had become negative. Authors suggest the potential for faecal-oral transmission but acknowledge that cell culturing is required to confirm. Tends to be more consistent viral kinetics with NP samples than with rectal swabs. Virus detectable in both pre-symptomatic and asymptomatic individuals.

Author Country Study design Study URL	Population setting	Primary outcome results				
Yan[51] **China** **Case series** **https://doi.org/10.1101/2020.03.22.20040832**	**Population setting:** 120 laboratory confirmed patients admitted to isolation wards of a hospital in Hubei **Demographics:** *Adult* *Age:* Median 52 years Sex: Male, 54 (45%); Female 66 (55%) **Clinical characteristics:** NR **COVID-19 Clinical syndromes (Chinese management guideline for COVID-19 version 6.0 definition):** General, 89 (74%); Severe, 30 (25%); Critical, 1 (0.8%)	**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):** Throat	**From onset of symptoms to the first of two consecutive negative tests:** Median 23 days (IQR 18-23 days) For patients treated with Lopinavir/Ritonavir (n=78), median 22 days (IQR 18-29) For those not treated with LPV/r (n=42) median 28.5 days (IQR 19.5-38)	NR	Not tested	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). 5 patients (4.2%) 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. Authors report that old age and lack of antiviral

						therapy was associated with delayed virus clearance, however this requires evidence from more robust study trials.

Author Country Study design Study URL	Population setting	Primary outcome results				
Yang[52] **China** **Case series** **https://doi.org/10.1016/j.rmed.2020.105935**	**Population setting:** 82 COVID-19 patients **Demographics:** *Adults* *Sex:* Male, 31 (37.8%); Female, 51 (62,2%) *Age*: Median 56 years (IQR 35–65) for patients with respiratory symptoms; median 51 years (IQR 36–64) for group without respiratory symptoms **Clinical characteristics:** Respiratory symptoms, 26 (31.7%); non-respiratory symptoms 56 (68.3%) **COVID-19 Clinical syndromes (WHO definition):** NR	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: NR **Thresholds:** NR **Gene Targets:** NR **Sample site(s):** Nasopharyngeal	**From onset of symptoms to the first of two consecutive negative tests:** For patients with cough: Median duration 17 days (IQR 12-23) For patients without respiratory symptoms: Median 13 days (IQR 6 to 20)	NR	Not tested	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. The authors found that those with respiratory symptoms had longer duration of positive testing.

Author Country Study design Study URL	Population setting	Primary outcome results				
Zhang[53] **China** **Case series** **https://doi.org/10.1101/2020.03.28.20043059**	**Population setting:** 23 patients treated in hospital in Beijing **Demographics:** Adults *Age:* 48 years (IQR 40 to 62) *Sex:* Male, 12 (52.2%); Female, 11 (47.8%) **Clinical characteristics:** *Presentation:* Fever 20 (87.0%), cough 13 (56.5%), weakness 9 (39.1%), myalgia 5 (21.7%), pharyngalgia 5 (21.7%), headache 3 (13.0%) **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%)	**Test parameters**	**Duration of virus detection* (Days)**	**Peak viral load**	**Pre-symptomatic viral load**	**Other relevant findings**
		Test: rRT-PCR **Thresholds:** Ct value > 43 = negative **Gene Targets:** Orf1ab, N, S **Sample site(s):** Upper respiratory (nasal-throat mixed), faeces, urine, plasma	**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) Faeces: 22.0 days (IQR 15.5 to 23.5) At 26 days after discharge, 1 case was detected positive again in faeces samples, but appeared healthy and negative for respiratory swabs.	Nasal-throat swabs peaked at 6-9 days aftr symptom onset (which was generally the 1st or 2nd day of testing), Peak viral load $10^{6.3}$ 64 copies/ml, mean 2535 copies/ml Faecal sample peaked at 14-18 days after symptom onset, peak viral load $10^{5.8}$ copies/ml, mean 5623 copies/ml Faecal samples contained higher viral titres than nasal-throat swabs	Not tested	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). All samples from one severe patient were negative until 21 days, when faeces samples were positive.

Key: ARDS – acute respiratory distress syndrome; CDC – Centre for Disease Control and Prevention; COVID-19 – Coronavirus disease 2019; CrI - credible

Interval; CT – computed tomography; ELISA - enzyme-linked immunosorbent assay; ETT - Endotracheal tube aspirate; Ct – cycle threshold; Fio_2 - fraction of inspired oxygen; ICU – intensive care unit; IgG/IgM – immunoglobulinG/M; IQR – interquartile range; LRTI – lower respiratory tract infection; NA – not applicable; NP – nasopharyngeal; ND – not detected; OP – oropharyngeal; Pao_2 – partial pressure of oxygen; (q)(r)RT-PCR – (quantitative) (real-time) reverse transcriptase polymerase chain reaction; RCT – randomised controlled trial; RNA - ribonucleic acid; Sao_2 – oxygen saturation; SARS-CoV-2 - severe acute respiratory syndrome coronavirus 2; SOB – shortness of breath; URTI – upper respiratory tract infection; 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
† Data extracted from graphs using webplot digitizer https://automeris.io/WebPlotDigitizer/
‡ Data analysed using online data calculator https://www.statstodo.com/CombineMeansSDs_Pgm.php

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