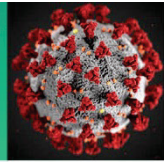


COVID-19 Science Update



From the Office of the Chief Medical Officer, CDC COVID-19 Response, and the CDC Library, Atlanta, GA.
Intended for use by public health professionals responding to the COVID-19 pandemic.

*** Available on-line at <https://www.cdc.gov/library/covid19> ***

Epidemiology

PEER-REVIEWED

[Retinal findings in patients with COVID-19](#). Marinho *et al.* Lancet (May 12, 2020).

Key findings:

- Lesions of the retina (the tissue lining the back of the inner eye that converts light into neural signals) were observed among 12 assessed COVID-19 patients (Figure 1).
 - No eye inflammation was observed, and no one reported vision changes or pain.
- Retinal lesions included:
 - Microhemorrhage (bleeding vessels) (n = 4 patients, Figure 2).
 - Cotton wool spots (which indicates damage to the nerves) (n = 4 patients, Figure 3).

Methods: Case series of 12 symptomatic adult COVID-19 patients. Investigators used radiographic imaging to detect abnormalities of the retina. **Limitations:** Small case series; no repeat imaging to detect ongoing or permanent retinal changes.

Implications: This is the first report of retinal abnormalities detected among COVID-19 cases. In this case series, no patients reported symptoms or showed signs of vision changes, but lasting effects are unknown.

Figure 1

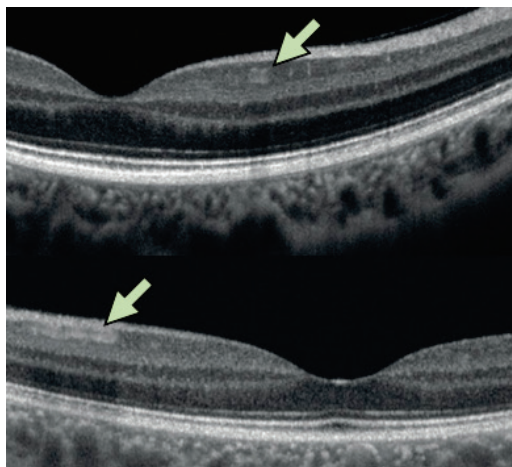


Figure 2



Figure 3



Note: From Marinho *et al.* **Figure 1** shows hyper-reflective lesions of the retina, present in all patients. **Figure 2** illustrates microhemorrhage of the blood vessels, present in 4 patients and **Figure 3** shows cotton wool spots on the retina, present in 4 patients. In all three figures, the **light green arrow** points to the **retinal abnormality**. This article was published in Lancet, Vol 395, Marinho *et al.*, Retinal findings in patients with COVID-19, P1610, Copyright Elsevier 2020. This article is currently available at the Elsevier COVID-19 resource center: <https://www.elsevier.com/connect/coronavirus-information-center>.

Epidemiology of the 2020 pandemic of COVID-19 in the state of Georgia: inadequate critical care resources and impact after seven weeks of community spread. Moore *et al.* Journal of the American College of Emergency Physicians (May 12, 2020).

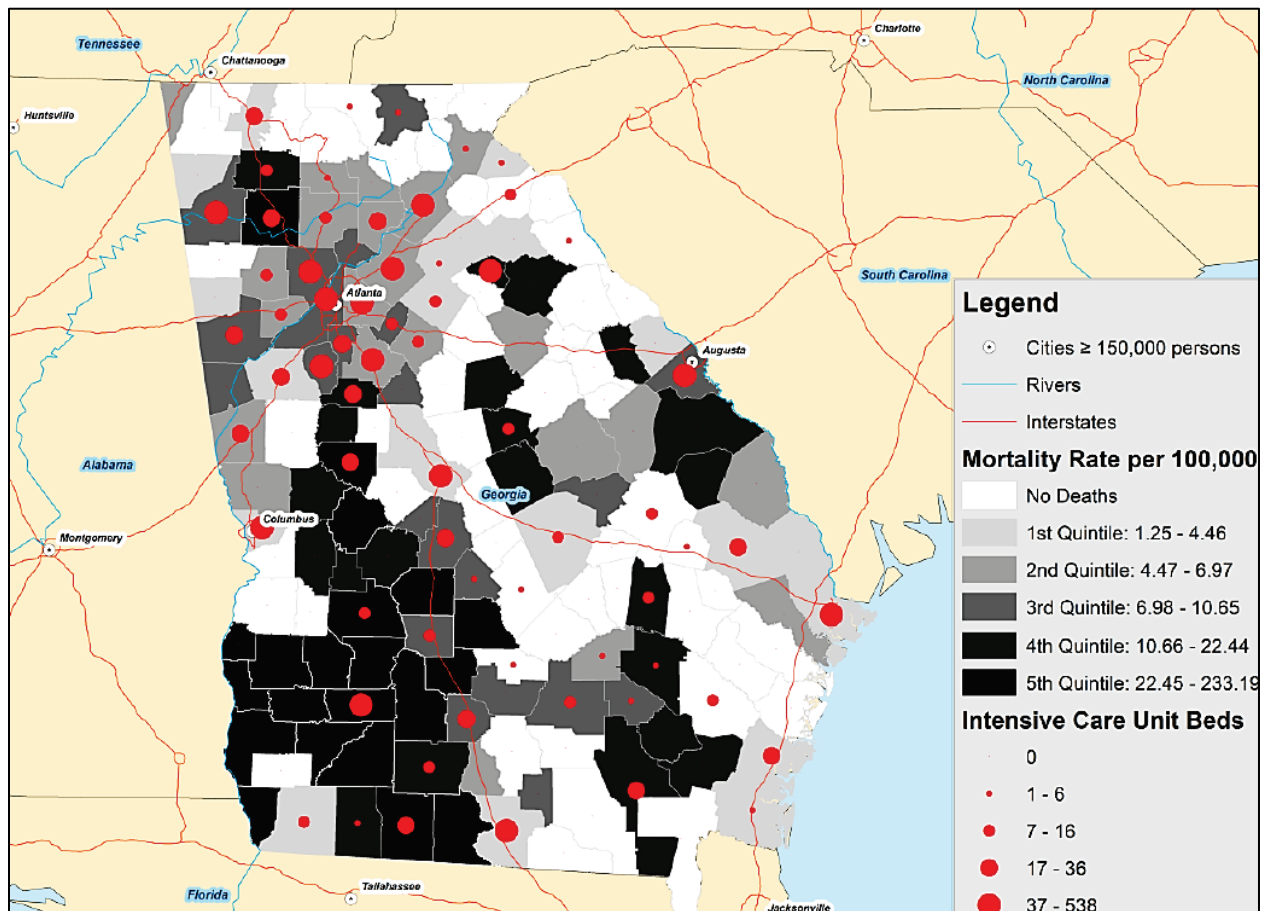
Key findings:

- Although metropolitan Atlanta had the highest number of confirmed COVID-19 cases in Georgia, southwestern rural areas of the state had the greatest increases in incidence rate.
- Compared with counties with lower mortality rates (MRs), counties with the highest MRs (22.5 – 2,332 per 100,000) had proportionately more non-Hispanic Black residents, adults aged ≥60 years, and residents living in rural communities, and proportionately fewer ICU beds (Figure).

Methods: A descriptive study of 159 Georgia counties from March 3 through April 24, 2020. Geographic variation in COVID-19 cases assessed by extracting data on incidence and mortality from national and state datasets. County-level mortality rates per 100,000 population were contrasted with county-level factors. **Limitations:** Prevalence, incidence, and mortality rates may be underestimated due to undiagnosed, asymptomatic cases.

Implications: Rural counties in the state of Georgia have higher COVID-19 mortality rates and lower critical care capacity. Targeted allocation of resources may be warranted to adequately control COVID-19 in these areas.

Figure:



Note: From Moore *et al.* Mapping of mortality rates per 100,000 population, overlaid with estimated number of available ICU beds in the state of Georgia. Licensed under CC-BY-NC-ND 4.0.

Transmission

PEER-REVIEWED

[A study on infectivity of asymptomatic SARS-CoV-2 carriers](#). Gao *et al.* Respiratory Medicine (May 13, 2020).

Key findings:

- Of 455 people who had contact with an asymptomatic SARS-CoV-2 positive patient:
 - 19/35 (54%) of hospitalized patients and 1/196 (0.5%) of family members had respiratory symptoms.
 - None had chest CT scans consistent with SARS-CoV-2 infection.
 - None tested positive for SARS-CoV-2, even after multiple tests.
- Hospital staff in contact with patients in the emergency department wore personal protective equipment; patients and family members wore masks.

Methods: A 22-year-old female patient (case A) was hospitalized in a Chinese hospital for shortness of breath and chest distress presumed to be related to congenital heart disease. She tested positive for SARS-CoV-2 via RT-PCR and was assumed to be an asymptomatic carrier. Authors described characteristics of her 455 contacts, including 224 hospital staff, 196 family members, and 35 other patients who were hospitalized in the same hospital as case A. All contacts were tested for SARS-CoV-2 via RT-PCR. **Limitations:** Results based on one asymptomatic carrier; Ct values, which could indicate level of infectivity, not reported for case A; detailed exposure information for contacts not reported.

Implications: Person-to-person transmission did not occur between an asymptomatic COVID-19 carrier and her 455 contacts. However, level of infectivity was not determined, and it was uncertain where this individual was in terms of disease course.

[Contact tracing assessment of COVID-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset](#). Cheng *et al.* JAMA Internal Medicine (May 1, 2020; [Correction](#) on September 2020).

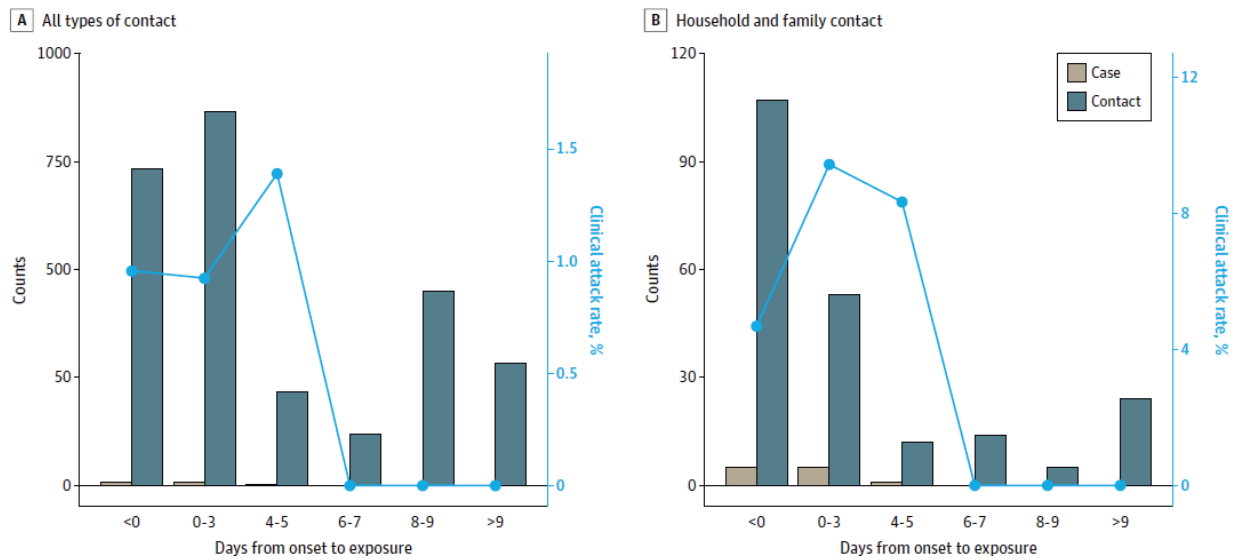
Key findings:

- 2,761 close contacts of 100 index cases were identified: 5.5% household, 2.8% non-household, and 25.3% healthcare.
- 22 secondary cases were identified through contact tracing; four were asymptomatic.
- The secondary clinical attack rate (excluding four asymptomatic infections) was 18/2,761 (0.7%), with infections occurring among persons with contact before cases' symptoms onset, as well as immediately after (Figure).

Methods: Prospective study in Taiwan of 100 index cases with RT-PCR confirmed SARS-CoV-2 infection and their close contacts. Close contacts were tested for SARS-CoV-2 when symptoms manifested, or they were deemed high risk during their 14-day quarantine period at home. The authors calculated secondary clinical attack rates (ratio of symptomatic confirmed cases among close contacts) for the period from the first day to the last day of exposure to the index case, and for different exposure settings (household, family, health care, and other). **Limitations:** Incomplete examination of contacts before symptom onset of the index cases.

Implications: SARS-CoV-2 transmission occurred before and immediately after symptom onset. This finding supports efforts to identify contacts exposed prior to illness onset in cases.

Figure:



Note: From Cheng *et al.* **Number of contacts**, **secondary cases**, and **secondary clinical attack rate** by the time of first exposure for all types of contact (Figure A), and household and family contact (Figure B). Licensed under CC-BY.

Transmission: Household pets

The following two peer-reviewed studies reported on transmission of SARS-CoV-2 from people to animals in their household or between cohabitating animals. Neither study reported transmission of the virus from an infected animal to a person.

PEER-REVIEWED

A. [Infection of dogs with SARS-CoV-2](#). Sit *et al.* Nature (May 14, 2020).

Key findings:

- In households with confirmed human cases of COVID-19, two dogs tested positive for SARS-CoV-2 by RT-PCR and serology; virus was isolated from one of the dogs.
 - Only one infected dog had known pre-existing conditions, including chronic kidney disease and systemic and pulmonary hypertension.
 - Both dogs showed no signs of COVID-19.
 - A dog that lived with one of the infected dogs did not test positive for SARS-CoV-2 RNA.
- Viral genome sequencing results were identical for the dogs and their respective owners.

Methods: The Hong Kong Department of Agriculture quarantined 15 dogs and 7 cats from 15 households with confirmed human COVID-19 cases and tested respiratory, blood, and fecal samples for SARS-CoV-2 by RT-PCR, serology, viral genome sequencing, and viral isolation.

B. Transmission of SARS-CoV-2 in domestic cats. Halfman *et al.* NEJM (May 13, 2020).

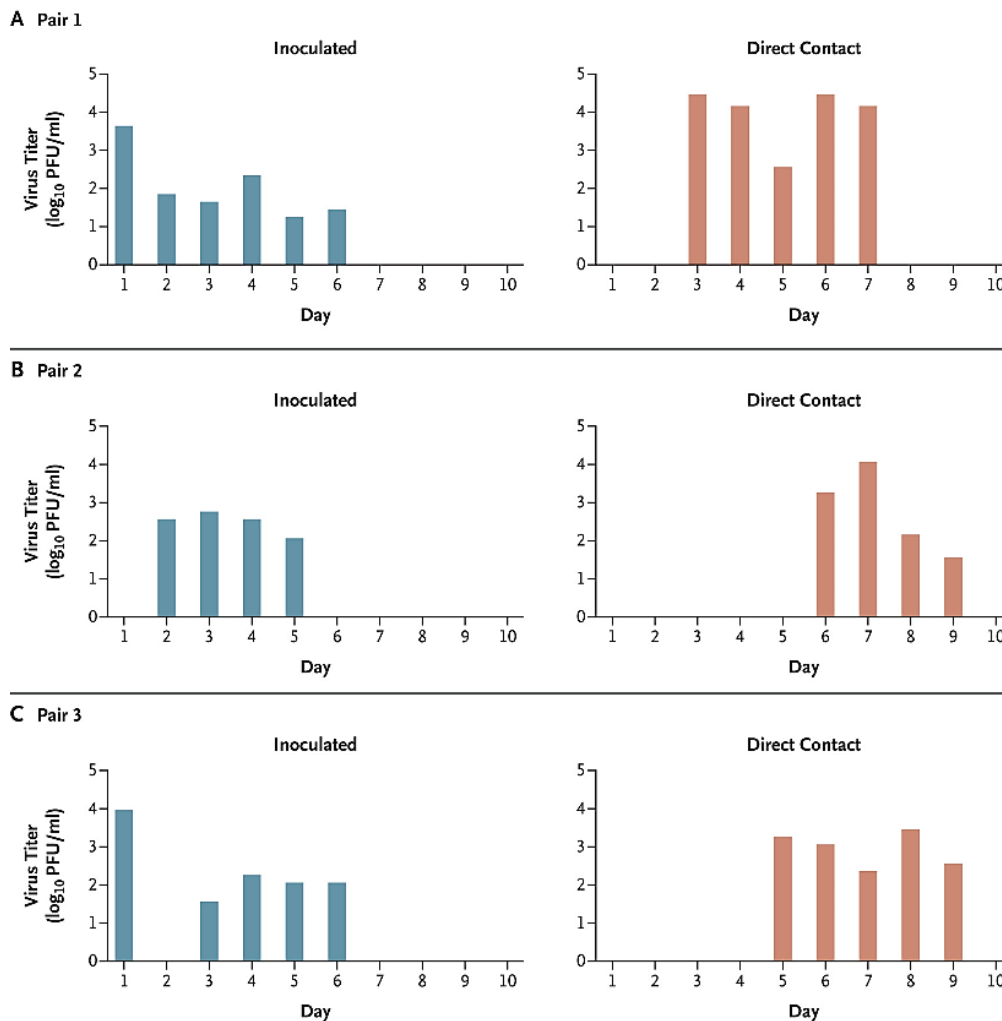
Key findings:

- Three cats inoculated and infected with SARS-CoV-2 transmitted the infection to 3 uninfected cats during 5 days of cohabitation.
- None of the cats exhibited illness.
- No cat shed viral RNA for more than 6 days; viral RNA was never detected in rectal samples.

Methods: Three cats were inoculated with SARS-CoV-2 and placed separately in shared housing a day later with a cat not previously infected with the virus. Nasal and rectal swabs were obtained from all cats each day for 10 days to determine if they became infected with SARS-CoV-2.

Implications (Sit *et al.* & Halfman *et al.*): SARS-CoV-2 can be transmitted from humans to dogs, but dog-to-dog or dog-to-human virus transmission is uncertain. In contrast, cat-to-cat transmission has been documented, while cat-to-human transmission is uncertain. Cats and dogs may not show signs of illness and infection might only be identified through testing.

Figure:



Note: From Halfman *et al.* Figures A, B and C each represent a pair of **inoculated** and **not inoculated cats put in direct contact**. Day 1 on the x-axis is the day of inoculation for the **inoculated** cats. Viral titer is shown on the y-axis. All cats tested positive for SARS-CoV-2 RNA by 5 days post exposure, and none shed viral RNA for longer than 6 days. From NEJM. 383:592-594. DOI: 10.1056/NEJMc2013400. Copyright © 2020 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Clinical Treatment & Management

PEER-REVIEWED

[Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19](#). Liang *et al.* JAMA Internal Medicine (May 12, 2020).

Key findings:

- 10 of 72 variables independently predicted critical COVID-19 illness and were chosen to construct a risk score (Table).
- The mean area under the curve (AUC) was 0.88.

Methods: Medical record data of 1,590 patients hospitalized with COVID-19 from 575 hospitals in China were used to develop a COVID risk score (COVID-GRAM) to predict development of critical illness (composite measure of admission to the intensive care unit, invasive ventilation, or death). 72 epidemiological, clinical, laboratory, and imaging variables ascertained at hospital admission were assessed using a logistic regression model. Accuracy of the score was measured by mean area under the receiver operating characteristic curve, or AUC. COVID-GRAM was validated in an additional 710 COVID-19 patients. **Limitations:** Potentially limited generalizability.

Implications: Use of a risk prediction score may help to identify patients who are likely to develop critical COVID-19 illness and to optimize use of resources.

Table:

Variables	Odds ratio (95% CI)
X-ray abnormality (yes vs no)	3.39 (2.14-5.38)
Age, per y	1.03 (1.01-1.05)
Hemoptysis (yes vs no)	4.53 (1.36-15.15)
Dyspnea (yes vs no)	1.88 (1.18-3.01)
Unconsciousness (yes vs no)	4.71 (1.39-15.98)
No. of comorbidities	1.60 (1.27-2.00)
Cancer history (yes vs no)	4.07 (1.23-13.43)
Neutrophil to lymphocyte ratio	1.06 (1.02-1.10)
Lactate dehydrogenase, U/L	1.002 (1.001-1.004)
Direct bilirubin, $\mu\text{mol/L}$	1.15 (1.06-1.24)

Note: From Liang *et al.* Multivariable logistic regression model for predicting development of critical illness in 1,590 patients hospitalized with COVID-19 in China. All ORs were significant at $p < 0.05$. X-ray refers to chest radiography, hemoptysis to coughing up blood, and dyspnea to shortness of breath. Neutrophil-to-lymphocyte ratio is an indicator of inflammatory status, lactate dehydrogenase of tissue damage, and direct bilirubin of liver damage or blocked bile ducts. Reproduced with permission from JAMA Intern Med. doi:10.1001/jamainternmed.2020.2033. Copyright©2020 American Medical Association. All rights reserved.

[An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study](#). Verdoni *et al.* Lancet (May 13, 2020).

Key findings:

- After the start of the COVID-19 epidemic, incidence rate of multisystem inflammatory syndrome in children (**MIS-C**) (which has signs and symptoms similar to Kawasaki disease) exceeded the incidence rate of Kawasaki disease prior to the start of the epidemic (10 vs 0.3 cases/month respectively).
 - 8/10 (80%) MIS-C cases had a positive RT-PCR and/or serology test result for COVID-19.
- Compared with those with Kawasaki disease, patients with MIS-C were:
 - Older (average: 7.5 vs 3 years), and had higher BMIs, lower white blood cell and platelet counts, heart abnormalities measured via echocardiogram (60% vs 10%), multiple markers of systemic inflammation, and a severe drop in blood pressure (50% vs 0%).

Methods: In one Italian hospital, 10 cases of MIS-C were identified after the start of the COVID-19 epidemic. Authors compared clinical presentation and treatment of these 10 cases with 19 cases of Kawasaki disease diagnosed before the outbreak. RT-PCR and serologic testing for SARS-CoV-2 was conducted among cases identified after the start of the epidemic. *Limitations:* Small sample size; one hospital.

Implications: MIS-C is a new inflammatory syndrome that has been described among children and is likely related to SARS-CoV-2 infection. Given its severity, further research is urgently needed to fully understand the epidemiology, treatment, and prevention of MIS-C.

Laboratory Science

PEER-REVIEWED

[Variation in false-negative rate of reverse transcriptase polymerase chain reaction-based SARS-CoV-2 tests by time since exposure](#). Kucirka *et al.* Annals of Internal Medicine (May 13, 2020).

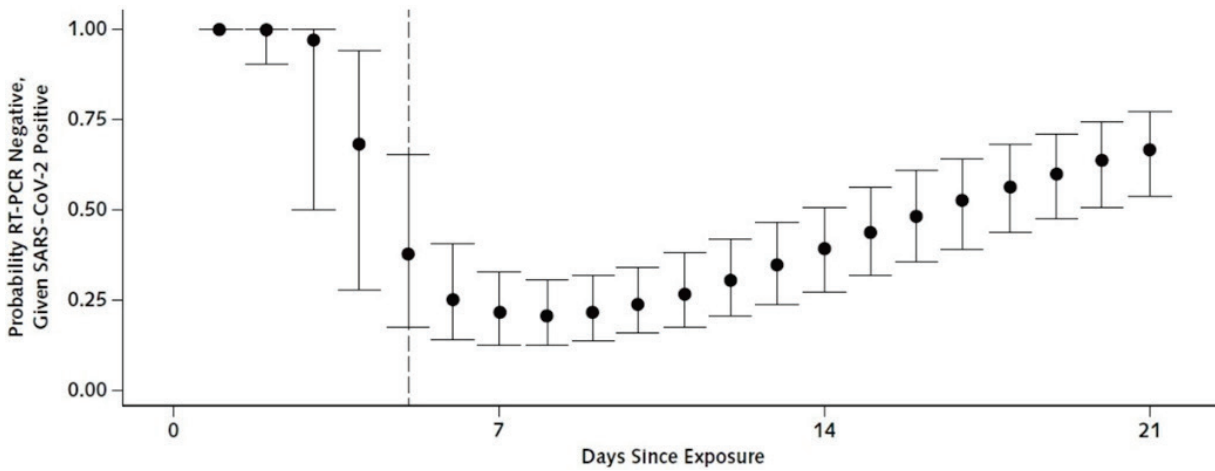
Key findings:

- Pooled analysis of 7 studies found that among persons who were infected with SARS-CoV-2, the probability of a false negative RT-PCR SARS-CoV-2 test result was highest immediately after exposure; it decreased until day 8 after exposure (Figure 1).
- In cases with high clinical suspicion of SARS-CoV-2 infection (pretest probability of infection), a negative test result immediately after exposure provided little additional information about the likelihood of infection (posttest probability of infection) (Figure 2).

Methods: The false negative rate was calculated using a Bayesian hierarchical model based on a pooled analysis of 7 studies evaluating RT-PCR performance of 1330 upper respiratory tract samples. *Limitations:* Most studies tested at time of symptom onset, leading to high variability in the estimated false negative rate before symptom onset.

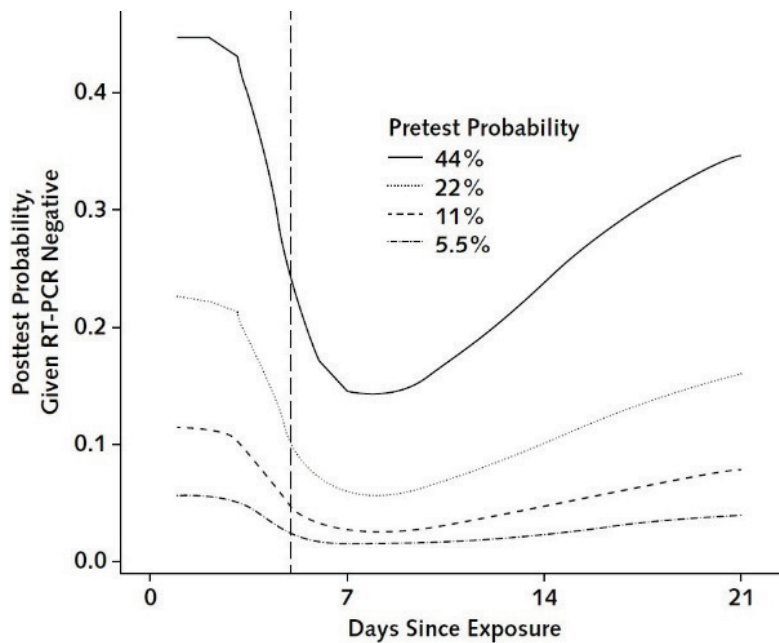
Implications: Negative SARS-CoV-2 RT-PCR test results should be interpreted with caution in the days immediately after exposure, particularly when there is a high clinical suspicion of SARS-CoV-2 infection.

Figure 1



Note: Adapted from Kucirka *et al.* Probability of having a negative RT-PCR test result given SARS-CoV-2 infection, by days since exposure in a pooled analysis of 7 studies evaluating RT-PCR performance of 1330 upper respiratory tract samples. Point estimates and confidence intervals are displayed. Available via American College of Physicians Public Health Emergency Collection through PubMed Central.

Figure 2



Note: From Kucirka *et al.* Posttest probability of SARS-CoV-2 infection after a negative RT-PCR result, by pretest probability of infection. Available via American College of Physicians Public Health Emergency Collection through PubMed Central.

Self-collection: An appropriate alternative during the SARS-CoV-2 pandemic. Wehrhahn *et al.* Journal of Clinical Virology (May 4, 2020).

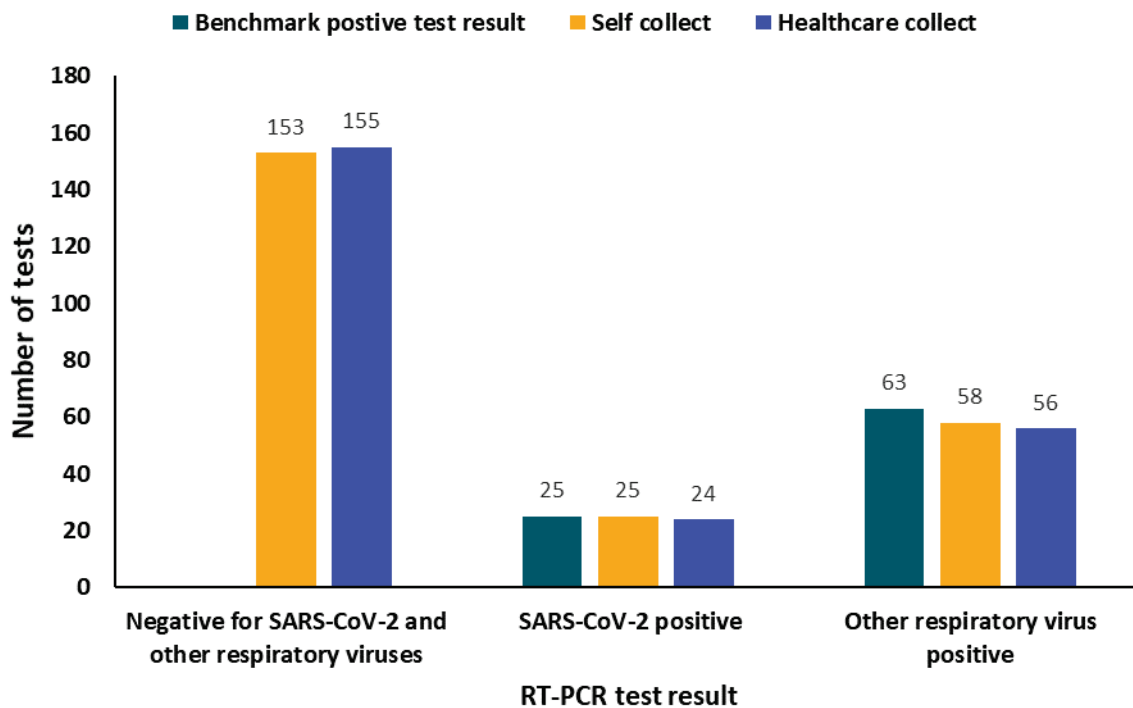
Key findings:

- Self-collected throat and nasal swabs from study participants yielded as many positive test results for SARS-CoV-2 and other respiratory viruses as swabs collected by healthcare workers (Figure).

Methods: A prospective study in Australia of 236 participants to compare self-collection of throat and nasal (anterior 2-3 centimeters inside the nostril) swabs to healthcare worker collection for use in the detection of SARS-CoV-2 RNA and other respiratory viruses. **Limitations:** Small number of positive test results.

Implications: Self-collection of throat and nasal swabs for SARS-CoV-2 appears to be a reliable alternative to collection by healthcare workers. Self-collection may ease the testing process for patients, lower healthcare worker exposures, and reduce the need for PPE.

Figure:



Note: Adapted from Wehrhahn *et al.* RT-PCR results from **healthcare collection** and **self-collection** of nasal, throat or nasopharyngeal samples tested for SARS-CoV-2 or other respiratory viruses. A positive result on either a healthcare collection or self-collection was considered a **benchmark positive test result**. This article was published in Journal of Clinical Virology, Vol 128, Wehrhahn *et al.*, Self-collection: An appropriate alternative during the SARS-CoV-2 pandemic, 104417, Copyright Elsevier 2020. This article is currently available at the Elsevier COVID-19 resource center: <https://www.elsevier.com/connect/coronavirus-information-center>.

In Brief

- Poillon *et al.* **Cerebral venous thrombosis associated with COVID-19 infection: causality or coincidence?** Journal of Neuroradiology. Reports on two COVID-19 patients with novel symptoms; two weeks after symptom onset, both patients had cerebral venous thrombosis.

- Ruetzler *et al.* [Respiratory protection among healthcare workers during cardiopulmonary resuscitation in COVID-19 patients](#). American Journal of Emergency Medicine. Editorial highlighting the need for healthcare workers performing CPR to use a face shield in addition to an N95 respirator.
- Hooper *et al.* [COVID-19 and racial/ethnic disparities](#). JAMA. Describes the disproportionate burden of coronavirus in African American and Latino populations in the US.
- Shore *et al.* [Telepsychiatry and the coronavirus disease 2019 pandemic — Current and future outcomes of the rapid virtualization of psychiatric care](#). JAMA. Telepsychiatry had already grown in use prior to the coronavirus pandemic, but the pandemic may permanently alter how psychiatric care is delivered.
- Maxmen A. [Coronavirus is spreading under the radar in US homeless shelters](#). Nature. Approximately 1.4 million Americans stay in homeless shelters each year; robust testing policies are needed.
- Pollett *et al.* [Social media and the new world of scientific communication during the COVID-19 pandemic](#). Clinical Infectious Diseases. Use of Twitter to communicate scientific information facilitates information spread and fuels debate; however, great care should be taken by scientists who use social media to share their research.
- Pitas *et al.* [Social capital in the response to COVID-19](#). American Journal of Health Promotion. Social networks are critical during physical distancing measures, but many communities in America lack strong social capital.
- Wise J. [COVID-19: Known risk factors fail to explain the increased risk of death among people from ethnic minorities](#). BMJ. Known risk factors are not enough to explain why Asian and black people in the UK are at greater risk of death from COVID-19.
- Ready T. [COVID-19: The US state copying a global health template for contact tracing success](#). BMJ. Contact tracing efforts, a key component to ending the epidemic, are described for Massachusetts.
- Dooley *et al.* [Low-income children and coronavirus disease 2019 \(COVID-19\) in the US](#). JAMA. Compared to children in middle or high income brackets, low income children are disproportionately impacted by school closures, as well as disruptions to learning, loss of nutritional support, and reduced social development.
- Khamsi R. [If a coronavirus vaccine arrives, can the world make enough?](#) Nature. Vaccine production will struggle to meet the global demand by billions of people; distribution equity and the continuity of vaccine production for other infectious diseases should be considered now.
- Janvier *et al.* [Medically vulnerable clinicians and unnecessary risk during the COVID-19 pandemic](#). Bioethics. Describes a scoring system that could help to place medical providers most at risk of COVID-19 (older males) in the least risky response roles (e.g. telemedicine).
- Glasziou *et al.* [Waste in COVID-19 research](#). BMJ. The demand for COVID-19 research is high and pre-prints provide access to critical information; however, the speed of research may contribute to poor study design and conduct, and outcomes that may spread false or inaccurate information.

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