COVID-19 Science Update

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Asymptomatic Transmission

The prevalence of asymptomatic COVID-19 cases may vary by population. Examining duration of viral persistence, amount of virus and transmissibility of virus in asymptomatic individuals is relevant for infection control. Below we summarize three studies that discuss SARS-CoV-2 prevalence and clinical characteristics in asymptomatic and symptomatic persons.

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A. Comparison of clinical characteristics of patients with asymptomatic vs symptomatic coronavirus disease 2019 in Wuhan, China. Yang *et al.* JAMA Network Open(May 27, 2020; Correction on June 26, 2020).

Key findings:

- Among 78 early patients in Wuhan with similar exposure histories and treatment course, 33 (42%) were asymptomatic.
- Asymptomatic patients shed the virus for a shorter time than symptomatic patients.
- Asymptomatic patients were more likely to be younger, have faster lung recovery per CT scans, and demonstrate less fluctuation of SARS-CoV-2 testing results.

Methods: 78 patients with RT-PCR-confirmed COVID-19 with exposure to the Hunan seafood market or close contact with a patient hospitalized for COVID-19. NP swabs for RT-PCR were collected every 24 to 48 hours. *Limitations*: Single hospital; clinical differences between asymptomatic and symptomatic patients may have been subject to provider bias; "fluctuation" not well defined but may refer to negative tests followed by positive tests.

Table:

Characteristic	Asymptomatic (n=33)	Symptomatic (n=45)	P-value
Age, median, years	37	56	0.001
Women	22	14	0.002
Incubation period, median, days	NA	3	NA
Baseline liver injury [a]	1	9	0.03
Duration of viral shedding, median, days [b]	8	19	0.001
Duration of lung recovery, median, days [c]	9	15	0.001
Maximum difference of CD4 cells during treatment, days [d]	203	328	0.04
CD4 cell count during recovery [d]	719	474	0.009
Fluctuated results of PCR test [b]	4	15	0.03
Deaths	0	2	0.22

Note: Adapted from Yang *et al*. Clinical features and prognosis of asymptomatic and symptomatic patients with COVID-19.
[a] Liver injury defined as serum alanine aminotransferase/aspartate aminotransferase levels more than 1.5 U/L; [b] Measured via NP swab; [c] Defined as when lung lesions began to improve by chest computed tomography; [d] Time from admission to the occurrence of 2 consecutive negative results for SARS-CoV-2 from NP swab.

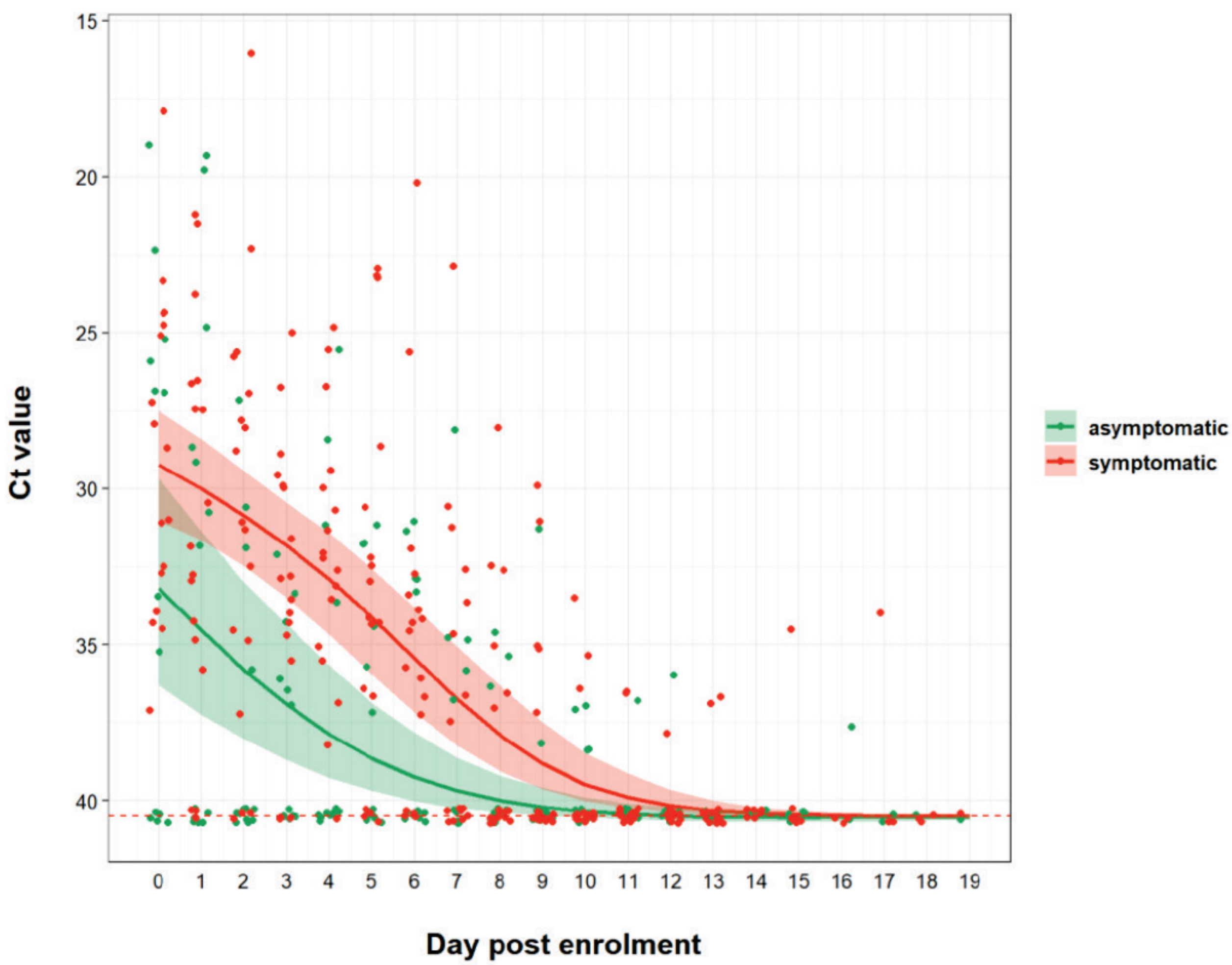
B. The natural history and transmission potential of asymptomatic SARS-CoV-2 infection. Chau *et al.* Clinical Infectious Diseases (June 4, 2020).

Key findings:

- Among a convenience sample of patients admitted to a single hospital, 43% were asymptomatic.
- Asymptomatic patients had overall lower viral burdens (i.e., higher Ct values) that became undetectable faster than among symptomatic patients (Figure 1).
- Asymptomatic patients transmitted infection to contacts (Figure 2).

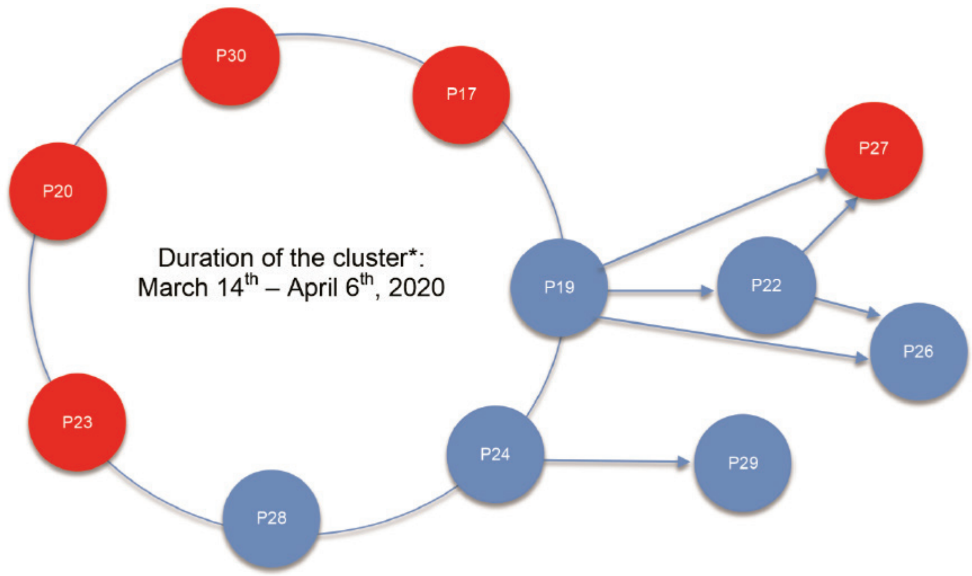
Methods: Prospective study of 30 Vietnamese patients with RT-PCR-confirmed SARS-CoV-2 infection (13 asymptomatic and 17 symptomatic), from whom NP swabs were collected daily from study enrollment to discharge. Transmissibility in asymptomatic patients was assessed through contact tracing. *Limitations*: Small sample size, did not culture virus from RT-PCR positive results to establish infectiousness.

Figure 1:



Note: Adapted from Chau *et al*. Ct values over time for asymptomatic (**green**) and symptomatic (**red**) patients. Asymptomatic patients had overall lower viral burdens (higher Ct values) and cleared virus faster than symptomatic patients. Available via Oxford University Press Public Health Emergency Collection through PubMed Central.

Figure 2:



Note: Adapted from Chau *et al*. Epidemiologic links between patients. Asymptomatic patients are in **blue** and symptomatic patients are in **red**. Patients positioned on the circle attended an event; arrows indicate patients who tested positive for SARS-CoV-2 after contact with a patient who attended the event and whether they were later classified as symptomatic or asymptomatic. Available via Oxford University Press Public Health Emergency Collection through PubMed Central.

C. Pre-procedural surveillance testing for SARS-CoV-2 in an asymptomatic population shows low rates of positivity. Mays *et al.* Journal of Clinical Microbiology. (June 3, 2020).

Key findings:

- <1% of asymptomatic individuals in the Seattle region seeking medical care without known exposure to COVID-19 tested positive for SARS-CoV-2 RNA.
    - This rate was lower than the rate observed among symptomatic hospitalized patients (10%) and asymptomatic patients with known exposure (8%) in the same region.

Methods: In the University of Washington hospital system, 2,056 asymptomatic individuals without known exposure had RT-PCR testing before undergoing a surgical or aerosol-generating procedure. *Limitations:* No follow-up of RT-PCR positive asymptomatic individuals to verify whether they developed symptoms later.

Implications for 3 studies (Yang *et al.*, Chau *et al.*, & Mays *et al.*): Prevalence of SARS-CoV-2 in asymptomatic persons may depend on the level of community spread and is likely to vary by region. Asymptomatic persons can transmit to others although virus in the respiratory tract of asymptomatic persons appears to be present in lower concentrations and for a shorter period than in symptomatic persons, suggesting a shorter period of infectiousness. Infection control practices, including self-isolation and contact tracing, remain necessary for asymptomatic infected persons.

See Oran *et al.* for a summary of findings from studies on asymptomatic SARS-CoV-2 infection.

Epidemiology

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Characteristics of U.S. nursing homes with COVID -19 cases. Abrams *et al.* Journal of the American Geriatrics Society (June 2, 2020).

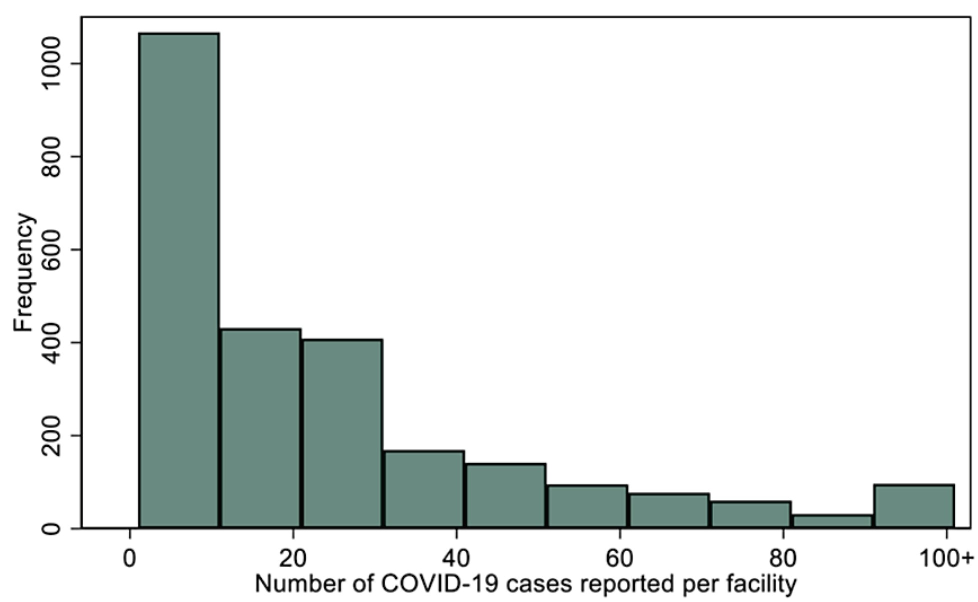
Key findings:

- In an analysis of 9,395 nursing homes, 31.4% had ≥1 documented COVID-19 case.
  - Among nursing homes with at least one COVID-19 case, average number of cases per facility was 19.8 (Figure 1).
- Larger facility size, urban location, greater percentage of African-American residents, non-chain status, and state were associated with having COVID-19 cases.
- Five-star rating, prior infection control violation, Medicaid dependency and ownership (i.e., for-profit, nonprofit, government), were not associated with having COVID-19 cases.
- Outbreak size was associated with facility size, for-profit status, and state.

Methods: A retrospective analysis of US nursing homes using publicly available data sources. ***Limitations***: Lack of a centralized national reporting system for nursing homes, incomplete and variable reporting of COVID-19 and related characteristics.

Implications: Nursing homes with certain characteristics (e.g., larger size, urban location, higher proportion African-American residents) were at an increased likelihood of having COVID-19 cases and may merit heightened vigilance for infections and their prevention to protect the health of residents and staff.

Figure:



Note: From Abrams *et al*. Frequency distribution of COVID-19 cases in 2,575 U.S. nursing homes with ≥1 case reported through May 2020 located in 21 states. Available via Wiley Public Health Emergency Collection through PubMed Central.

Racial disparities in knowledge, attitudes and practices related to COVID-19 in the USA. Alobuia *et al.* Journal of Public Health. (June 3, 2020).

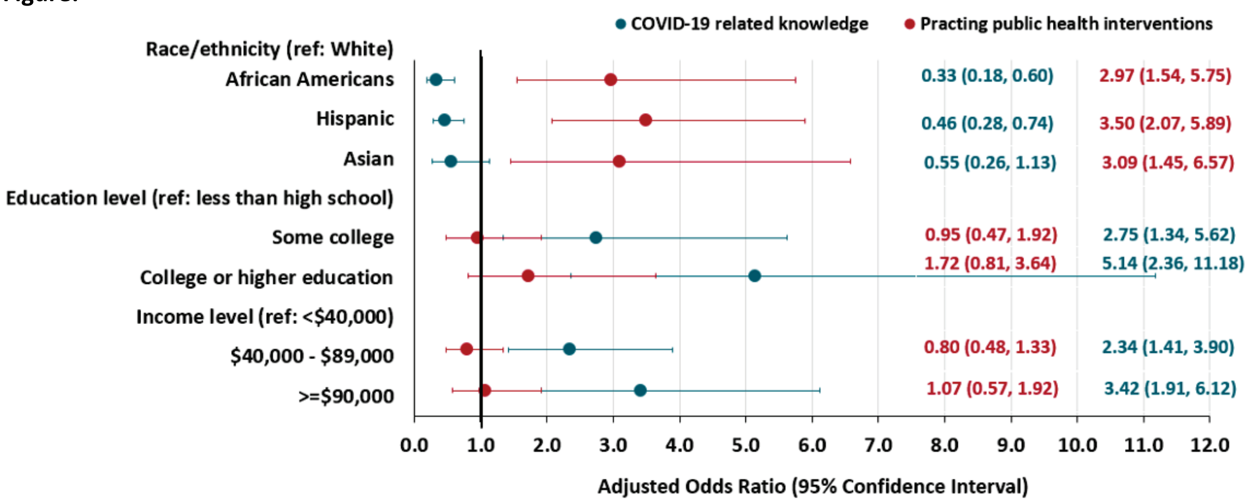
Key findings:

- Although African American and Hispanic persons were less knowledgeable about COVID-19 when compared with White persons, they were more likely to practice social distancing and other interventions that reduce the spread of infection (Figure).
- Persons with higher levels of education or higher income were more knowledgeable about COVID-19 but were not more likely to engage in public health interventions to reduce transmission (Figure).

Methods: A multivariate regression analysis using phone survey results from 1,216 persons who participated in the March 2020 Kaiser Family Foundation 'Coronavirus Poll' to identify predictors of COVID-19-related knowledge, attitudes and practices. *Limitations:* Response bias, cross-sectional survey.

Implications: Racial and socioeconomic disparities exist in COVID-19-related knowledge and practice. Expanded messaging on the public health benefits of social distancing may be needed. Educational resources on COVID-19 should be tailored to minority racial and ethnic groups and those of lower socioeconomic status.

Figure:



Note: Adapted from Alobuia *et al*. Adjusted odds ratio and 95% confidence intervals on COVID-19-related knowledge (**blue**) and practicing public health interventions (**red**) stratified by various demographic characteristics. Odds ratio calculations adjusted for race, sex, age, marital status, education level, income, insurance coverage and political views. Reproduced by permission of Oxford University Press on behalf of the Royal Colleges of Physicians of the United Kingdom. Please visit: https://academic.oup.com/jpubhealth/article/42/3/470/5850538.

African American children are at higher risk for COVID-19 infection. Bandi *et al.* Pediatric Allergy and Immunology (May 29, 2020).

Key findings:

- 5.3% (25/474) children tested positive for SARS-CoV-2 RNA.
    - 5 were hospitalized; 3 of whom were admitted to pediatric ICU (PICU).
        - 80% (4/5) of hospitalized children and all children admitted to PICU were African American (AA).
- Age and race/ethnicity were associated with positive SARS-CoV-2 RNA results.
    - Children with positive results were older than those with negative results (9.3 vs. 4.9 years, respectively).

    - Percent testing positive was higher for AA (6.8% (14/250)) and Hispanic (6.6% (2/119)) compared with non-Hispanic white children (1.7% (2/119)).
- Asthma was not associated with positive test result.

Methods: 474 children (<18 years old) in Chicago with fever, cough, dyspnea, myalgia, sore throat, or anosmia were tested by RT-PCR. Demographics, risk factors, and asthma status were recorded. Associations were evaluated by unadjusted and adjusted (age, race, gender) logistic regression and random step-wise matching. *Limitations*: Small sample size; asymptomatic children not tested.

Implications: AA and Hispanic children might be at higher risk for COVID-19 infection, and AA children may have a more severe infection course. Older children might also be at higher risk for COVID-19 infection. Studies are needed to corroborate these findings.

Modeling & Transmission

PEER-REVIEWED

Evaluating the effectiveness of social distancing interventions to delay or flatten the epidemic curve of coronavirus disease. Matrajt *et al.* Emerging Infectious Diseases. (April 21, 2020).

Key findings:
- In a modeling exercise, social distancing implemented early in the epidemic would delay the time to the peak number of cases while social distancing implemented later would decrease the number of cases (Figure 1).
- A 25% reduction in social contacts among adults age <60 years coupled with substantial social distancing in children and adults age ≥60 years could avert an estimated 90% of COVID-19 cases, hospitalizations and deaths (Figure 2).
- Reducing social contacts among children as part of social distancing interventions could decrease overall number of cases, hospitalizations, and deaths by 60–70% (Figures 1 and 2).
- Cases would rebound after the end of all interventions, a finding that emphasizes the need for a multipronged public health approach that includes testing, isolation of infected cases and contact tracing once social distancing restrictions are eased (Figure 1).

Methods: Modeled effectiveness of four 6-week social distancing interventions to reduce COVID-19 cases, hospitalizations, and deaths in Seattle, WA during the first 100 days of the epidemic:
- 95% reduction in social contacts in adults age ≥60 years (first scenario)
- First scenario and 85% reduction in social contacts in children (second scenario)
- First scenario and 25%, 75% or 90% reduction in social contacts in adults <60 years (third scenario)
- Second scenario and 25%, 75% or 90% reduction in social contacts in adults <60 years (fourth scenario)

Limitations: Did not consider transmission from asymptomatic individuals.

Implications: Social distancing alone is insufficient to reduce COVID-19-associated morbidity and mortality and should be coupled with increased testing, self-isolation, when appropriate, and contact tracing. The relative infectiousness of children compared to adults is important to understand and incorporate into models.

Figure 1

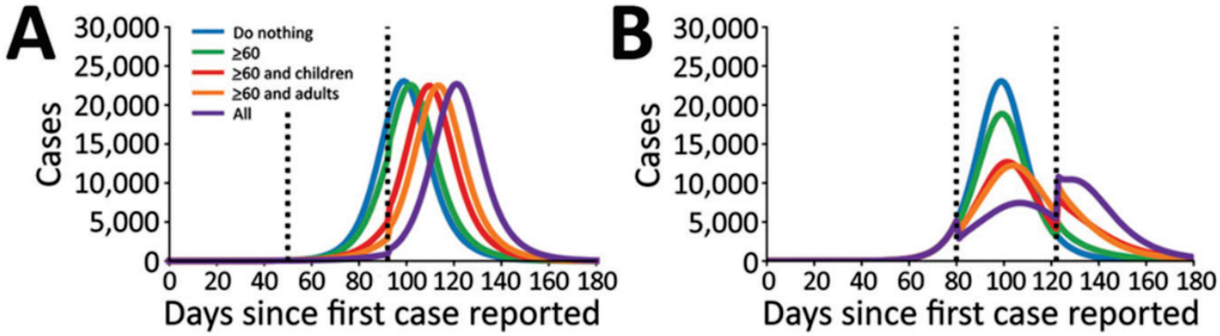
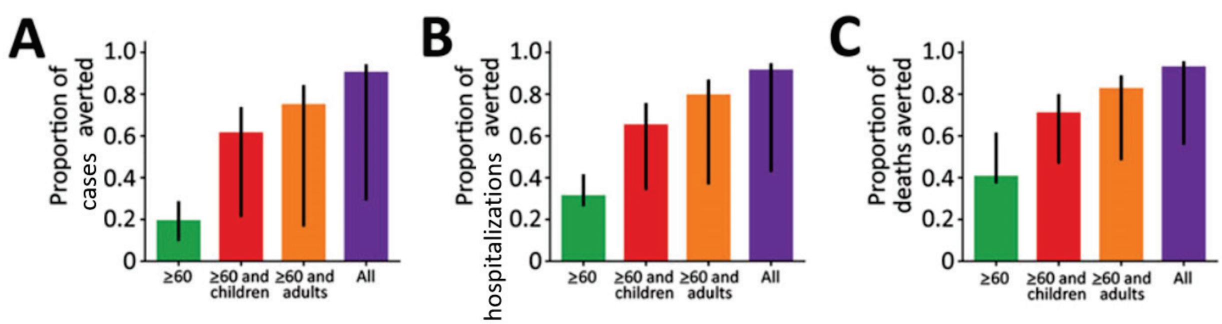


Figure 2



Note: Adapted from Matrajt *et al*. **Figure 1**: Number of projected COVID-19 cases if social distancing interventions started 50 (A) or 80 (B) days after the first case was reported. Dotted lines indicated the start and end of 6-week social distancing interventions. As per scenarios mentioned in Methods, **green** indicates the first scenario; **red** indicates the second scenario, **orange** and **purple** indicate the third and fourth scenarios, respectively with 25% reduction in social contacts in adults <60 years. **Figure 2**: Number of averted COVID-19 cases (A), hospitalizations (B) and deaths (C) due to social distancing interventions. Same color schema as in Figure 1. Open access journal; all content freely available.

Clinical Treatment & Management

PEER-REVIEWED

[Pathological findings in the testes of COVID-19 patients: Clinical implications](). Yang *et al.* European Urology Focus (May 31, 2020).

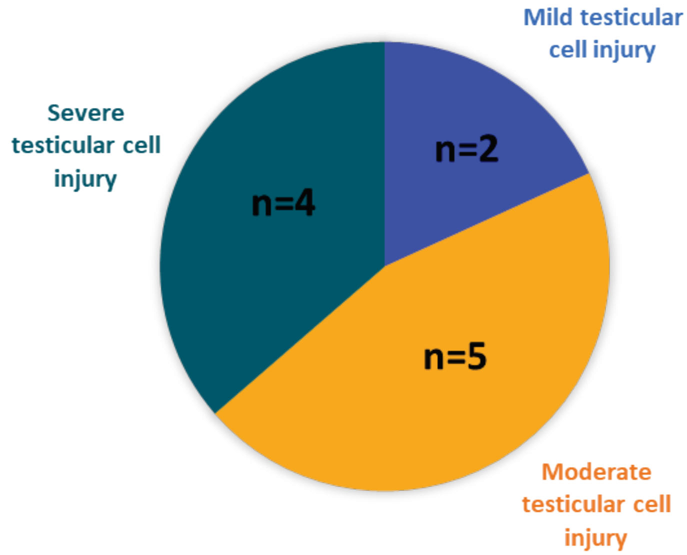
Key findings:

- In a series of 11 male autopsies, seminiferous tubular injury was mild (<10% seminiferous tubules affected), moderate (10%-50% tubules affected) or severe (>50% tubules affected) (Figure 1).
- The ACE2 receptor (a target for SARS-CoV-2 virus) was expressed on cells in testicular tissues (Figure 2).
- SARS-CoV-2 RNA was detected in 1 of 11 testicular samples; virus was not visualized by electron microscopy in any samples.

Methods: A postmortem analysis of testicular samples from 11 COVID-19 cases from Tongji Medical College in China. Samples were analyzed by light and electron microscopy, immunohistochemistry and RT-PCR for SARS-CoV-2 RNA. *Limitations*: Limited samples from one hospital.

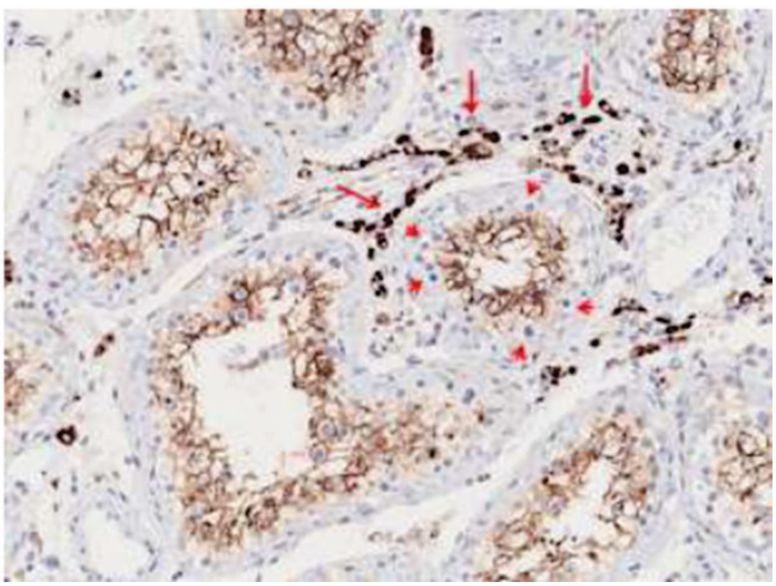
Implications: There may be a pathological effect of SARS-CoV-2 infection on testicular tissue. Further study is needed to determine the mechanism of injury.

Figure 1



Note: Adapted from Yang *et al*. Extent of seminiferous tubular injury in postmortem testicular samples from COVID-19 cases. Licensed under CC-BY-NC-ND 4.0

Figure 2



Note: From Yang *et al.* ACE2 cells expressed in Sertoli cells and strongly expressed in Leydig cells (**long arrows**) according to immunohistochemistry. Spermatogonia are negative for staining (**short arrows**). Licensed under CC-BY-NC-ND 4.0.

Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19. Li *et al.* JAMA (June 3, 2020; Correction on August 4, 2020).

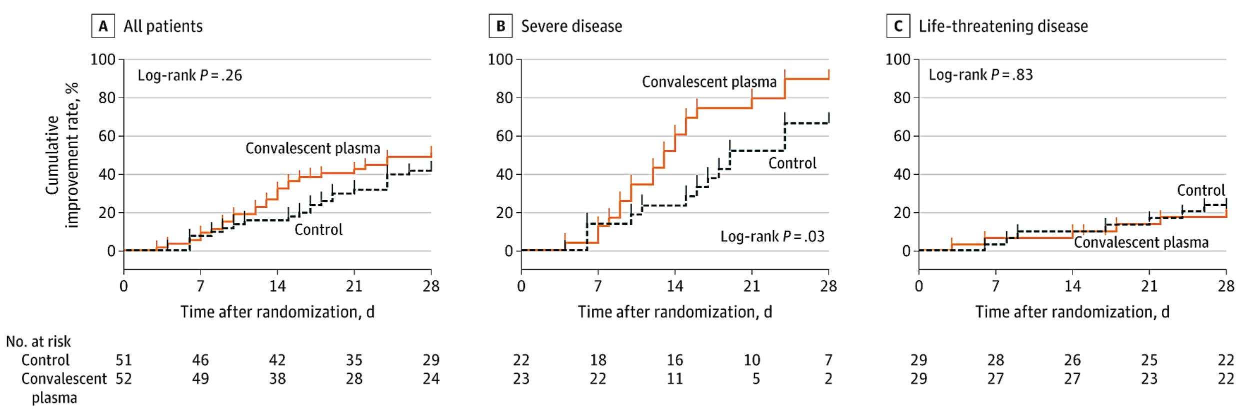
Key findings:

- Overall, no difference was observed in clinical improvement with administration of convalescent plasma: treatment group 51.9% (27/52) vs control group 43.1% (22/51), hazard ratio (HR), 1.40 (95% CI 0.79-2.49).
    - In patients with severe disease, convalescent plasma treatment was associated with improved outcome (HR 2.15, p = 0.03) but not in patients with advanced life-threatening disease (HR 0.88, p = 0.30).
- Overall, convalescent plasma treatment was associated with higher rates of negative NP RT-PCR at 24, 48, and 72 hours.

Methods: Open-label, randomized trial of convalescent plasma versus standard treatment in 103 participants with severe or life-threatening laboratory-confirmed COVID-19 in 7 medical centers in Wuhan, China. The trial was terminated early after 103 of 200 planned enrollments due to the containment of COVID-19 in Wuhan. *Limitations*: Small sample that did not reach predetermined enrollment; open label; median time between symptom onset and randomization was 30 days; standard therapy in both groups was not uniform.

Implications: Convalescent plasma did not result in clinical improvement within 28 days of administration; higher rates of conversion to negative RT-PCR may indicate antiviral activity of convalescent plasma.

Figure:



Note: from Li *et al*. Rate of cumulative clinical improvement over time for all patients (A), those with severe disease (B) and those with life-threatening disease (C) for **convalescent plasma** and **control** groups. Reproduced with permission from JAMA. doi:10.1001/jama.2020.10044.

Laboratory Science

PEER-REVIEWED

Swabs collected by patients or health care workers for SARS-CoV-2 testing. Tu *et al.* NEJM (June 3, 2020).

Key findings:

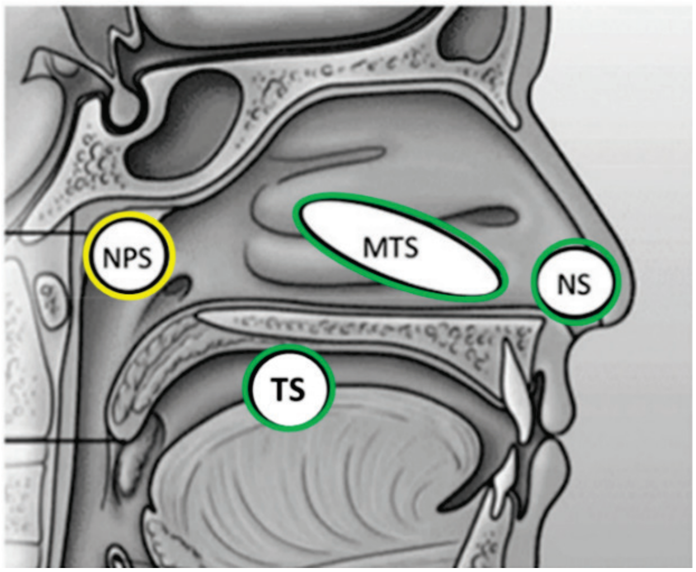
- Using healthcare worker (HCW)-collected NP samples (NPS) as the standard, the sensitivities of self-collected mid-turbinate samples (MTS), tongue samples (TS), and anterior nares or nasal samples (NS) were high and comparable (Figure 1).

- RT-PCR Ct values for self-collected MTS (r = 0.86) were more highly correlated with Ct values for HCW-collected NPS than TS (r = 0.48) or NS (r = 0.78) (Figure 2).

Methods: A prospective study in Washington State of 530 participants designed to compare self-collected TS, NS and MTS to HCW-collected NPS for detection of SARS-CoV-2 RNA. ***Limitations***: Small number of positive SARS-CoV-2 RNA results.

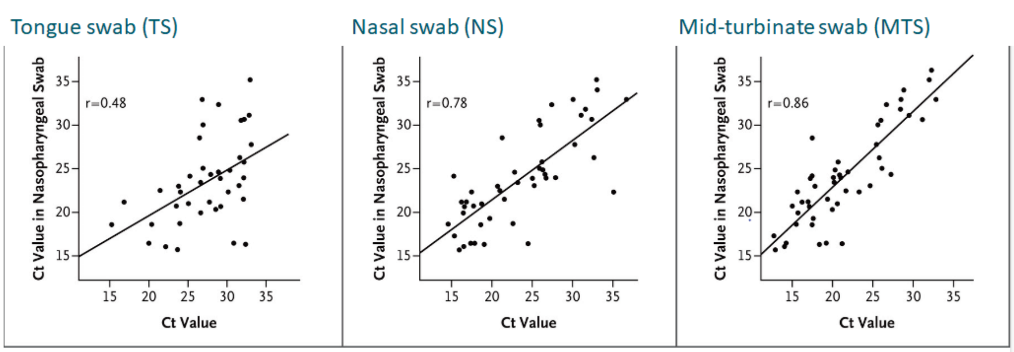
Implications: This study and a study presented in a the May 22, 2020 Science Update by Wehrhahn *et al*. indicate that self-collected samples can provide a reliable alternative to HCW-collected samples. Use of self-collected samples can lower HCW exposure to SARS-CoV-2 and reduce demand for PPE.

Figure 1



Note: Adapted from **Frazee *et al.*** Sample collection sites for use in SARS-CoV-2 RT-PCR. **Nasopharyngeal (NPS) samples** were collected by healthcare workers and **tongue (TS)**, **nasal (NS)** and **mid-turbinate (MTS) samples** were self-collected. This article was published in Annals of Emergency Medicine, Vol 71, Frazee *et al*., Accuracy and Discomfort of Different Types of Intranasal Specimen Collection Methods for Molecular Influenza Testing in Emergency Department Patients, P509-517, Copyright American College of Emergency Physicians 2020. This article is currently available at the Elsevier COVID-19 resource center: https://www.elsevier.com/connect/coronavirus-information-center.

Figure 2



	Tongue swab (TS)	Nasal swab (NS)	Mid-turbinate swab (MTS)
Sensitivity	89.8%	94.0%	96.2%
(One-sided 97.5% confidence interval)	(78.2, 100)	(83.8, 100)	(87.0, 100)

Note: Adapted from Tu *et al.* Cycle threshold values for SARS-CoV-2 RT-PCR results from healthcare worker-collected nasopharyngeal swabs (y-axis) and self-collection of tongue, nasal and mid-turbinate swabs. From NEJM. 383:494-496. DOI: 10.1056/NEJMc2016321. Copyright ©2020 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

In Brief

Lockdowns and School Closures

- Angoulvant *et al*. **COVID-19 pandemic: Impact caused by school closure and national lockdown on pediatric visits and admissions for viral and non-viral infections, a time series analysis**. Clinical Infectious Diseases. An analysis of pediatric emergency room visits that indicates that there has been a significant decrease in diseases transmitted via airborne or fecal oral route since the COVID-19 shutdown.
- Sharfstein *et al*. **The urgency and challenge of opening K-12 schools in the fall of 2020**. JAMA. Maintains that it is critical to open schools in the fall to ensure disadvantaged children have access to meals and services and can receive in-person learning.
- Lesser *et al*. **The impact of COVID-19 on physical activity behavior and well-being of Canadians**. International Journal of Environmental Research and Public Health. An evaluation of the effect of COVID-19 restrictions on the physical activity level and well-being of Canadians.
- Melnick *et al*. **Should governments continue lockdown to slow the spread of COVID-19?** BMJ. Pros and cons of government shutdowns.

COVID-19 Data Quality

- Mayo-Yanez M. **Research during SARS-CoV-2 pandemic: to "preprint" or not to "preprint", that is the question**. Medicina Clinica. Describes the need for peer-review and the difference between a peer-reviewed and a preprint manuscript.
- Segal *et al*. **Building an international consortium for tracking coronavirus health status**. Nature Medicine. Proposes an international consortium (Coronavirus Census Collective) to collect self-reported data on COVID-19 symptoms and integrate it with other COVID-19 data to improve epidemiological models and measures.
- Holmdahl *et al*. **Wrong but useful — What COVID-19 epidemiologic models can and cannot tell us**. NEJM. A description of the various epidemiological models and how to determine if they are high quality and have useful information.

Other Topics

- Shippee *et al*. **COVID-19 pandemic: Exacerbating racial/ethnic disparities in long-term services and supports**. Journal of Aging & Social Policy. Existing racial/ethnic barriers to receiving high-quality long-term care services and support may be heightened with COVID-19.
- Bartels *et al*. **COVID-19 emergency reforms in Massachusetts to support behavioral health care and reduce mortality of people with serious mental illness**. Psychiatric Services. Describes reforms designed to enhance access to medical services for persons with mental illness and to support community-based behavioral health services.
- Wolfler *et al*. **Acute myocardial injury: a novel clinical pattern in children with COVID-19**. The Lancet Child & Adolescent Health. Characterizes myocardial injury in children with COVID-19 admitted to the pediatric ICU.
- Nardell *et al*. **Airborne spread of SARS-CoV-2 and a potential role for air disinfection**. JAMA. Air disinfection in hospitals may be used to reduce potential airborne transmission of SARS-CoV-2.
- Watson C. **How countries are using genomics to help avoid a second coronavirus wave**. Nature. Genotyping SARS-CoV-2 sequences of infected persons alongside contact tracing can elicit information not captured through traditional contact tracing alone.

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