

# The Daily COVID-19 Literature Surveillance Summary

**June 23, 2020**



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# COVID-19 Daily Literature Surveillance

COVID19LST



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# LEVEL OF EVIDENCE

## Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

| Question   | Step 1<br>(Level 1*)  | Step 2<br>(Level 2*)   | Step 3<br>(Level 3*)   | Step 4<br>(Level 4*)   | Step 5 (Level 5)          |
|--|---|--|--|--|---------------------------|
| <b>How common is the problem?</b>                                  | Local and current random sample surveys (or censuses)   | Systematic review of surveys that allow matching to local circumstances**                    | Local non-random sample**  | Case-series**  | n/a                       |
| <b>Is this diagnostic or monitoring test accurate? (Diagnosis)</b> | Systematic review of cross sectional studies with consistently applied reference standard and blinding  | Individual cross sectional studies with consistently applied reference standard and blinding | Non-consecutive studies, or studies without consistently applied reference standards**   | Case-control studies, or *poor or non-independent reference standard**         | Mechanism-based reasoning |
| <b>What will happen if we do not add a therapy? (Prognosis)</b>    | Systematic review of inception cohort studies   | Inception cohort studies   | Cohort study or control arm of randomized trial*   | Case-series or case-control studies, or poor quality prognostic cohort study** | n/a                       |
| <b>Does this intervention help? (Treatment Benefits)</b>           | Systematic review of randomized trials or n-of-1 trials   | Randomized trial or observational study with dramatic effect                                 | Non-randomized controlled cohort/follow-up study**   | Case-series, case-control studies, or historically controlled studies**        | Mechanism-based reasoning |
| <b>What are the COMMON harms? (Treatment Harms)</b>                | Systematic review of randomized trials, systematic review of nested case-control studies, n-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect | Individual randomized trial or (exceptionally) observational study with dramatic effect      | Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)* | Case-series, case-control or historically controlled studies**                 | Mechanism-based reasoning |
| <b>What are the RARE harms? (Treatment Harms)</b>                  | Systematic review of randomized trials or n-of-1 trial  | Randomized trial or (exceptionally) observational study with dramatic effect                 | Non-randomized controlled cohort/follow-up study**   | Case-series, case-control or historically controlled studies**                 | Mechanism-based reasoning |
| <b>Is this (early detection) test worthwhile? (Screening)</b>      | Systematic review of randomized trials  | Randomized trial   | Non-randomized controlled cohort/follow-up study**   | Case-series, case-control or historically controlled studies**                 | Mechanism-based reasoning |

\* Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.

\*\* As always, a systematic review is generally better than an individual study.

## How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group\*. "The Oxford 2011 Levels of Evidence". Oxford Centre for Evidence-Based Medicine. <http://www.cebm.net/index.aspx?o=5653>

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# EXECUTIVE SUMMARY

## Climate

- A study conducted by the Center for Disease Control and Prevention of 2,402 Americans in May found [widespread support](#) of the implementation of public health orders such as stay-at-home orders, use of face coverings, and business closures, in response to the COVID-19 pandemic.
- Public health experts from New York describe how health disparities, including access, socioeconomic status, language, citizenship status, and education level, experienced by immigrants of color throughout the United States are dramatically worsened during the pandemic and have made providing [sexual and reproductive health services](#) extremely difficult for this population.

## Epidemiology

- The CDC and US Department of Agriculture report the first two cases [of RT-PCR confirmed COVID-19 in companion animals](#) in the U.S. in two domestic cats. In both instances, human cases preceded feline cases and there was no evidence to suggest additional feline-human transmission. Therefore, they believe animals have an insignificant role in the transmission of SARS-CoV-2 to humans.
- A cross-sectional study in Indianapolis found [that 3.1% of 2,953 asymptomatic adults tested positive for SARS-CoV-2](#) by nasopharyngeal swab testing. Of the 81 SARS-CoV-2 positive participants who completed a follow-up interview, 71.6% remained asymptomatic at 14 days while the other 28.4% reported one or more symptoms.

## Understanding the Pathology

- A group of researchers in Toronto suggest SARS-CoV-2 disruption of the renin angiotensin aldosterone system (RAAS) leads to an [endothelial imbalance](#) that leaves the endothelium susceptible to inflammation, vasoconstriction, platelet activation, and thrombosis thus playing a major role in the disease.

## Transmission and Prevention

- Researchers and physicians conducted a retrospective analysis of 49 studies with [666 neonates and 655 pregnant persons with confirmed or suspected COVID-19](#) and concluded that postnatal SARS-CoV-2 mother-to-neonate transmission is low, that infection in neonates largely presents asymptotically, and that vaginal births do not seem to increase infection risk compared with Caesarean section.
- Researchers from University of California, Berkeley examined the effects of large-scale measures, including 1,717 local, regional, and national policies, on the transmission rate of COVID-19 using established reduced-form econometric modeling techniques and estimate that these measures [prevented as many as 285 million infections](#).

## Management

- A retrospective study in France of 268 hospitalized COVID-19 patients found that patients treated at baseline with a [renin-angiotensin system inhibitor](#) had more than twice the risk of an ICU admission when controlled for age, sex, BMI, and coronary artery disease, though the authors recognize that further study is needed to account for unmeasured confounders.

## Adjusting Practice During COVID-19

- Guidelines and recommendations for practice during the pandemic includes management of [fever in infants and young children](#).
- Researchers in Spain conducted a retrospective analysis of 26,131 patients with rheumatic disease in seven different facilities and found that patients with [chronic inflammatory disease](#) had higher incidence of polymerase chain reaction positive COVID-19 compared with a hospital reference population.

## R&D: Diagnosis and Treatments

- A study of 190 patients found that [oropharyngeal/nares swabs](#) and nasopharyngeal swabs had sensitivities of 91.7% and 94.4%, respectively, suggesting that oropharyngeal/nares sampling, which may be more readily

available during the COVID-19 pandemic, is an effective alternative to nasopharyngeal swabs in ambulatory settings

#### **Mental Health and Resilience Needs**

- Psychiatrists and addiction medicine experts from Germany conducted a survey of 2,102 German citizens and found that 34.7% of respondents have consumed “more or much more” [alcohol during the pandemic](#) compared to their baseline, and indicated that increased alcohol consumption during this time is associated with lower educational status and increased stress.

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# PUBLIC ATTITUDES, BEHAVIORS, AND BELIEFS RELATED TO COVID-19, STAY-AT-HOME ORDERS, NONESSENTIAL BUSINESS CLOSURES, AND PUBLIC HEALTH GUIDANCE - UNITED STATES, NEW YORK CITY, AND LOS ANGELES, MAY 5-12, 2020

32555138. Public Attitudes, Behaviors, and Beliefs Related to COVID-19, Stay-at-Home Orders, Nonessential Business Closures, and Public Health Guidance - United States, New York City, and Los Angeles, May 5-12, 2020  
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

### BLUF

In this population-based study across New York City, Los Angeles, and the broader U.S., 2,402 adults were surveyed during May 5-12, 2020 to assess public attitudes regarding the implementation of public health orders such as stay-at-home orders, use of face coverings, and business closures, in response to the COVID-19 pandemic. They found there was widespread support of these public health guidelines to minimize transmission (Table 2), which can inform future government decisions if additional outbreaks occur.

### ABSTRACT

SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), is thought to be transmitted mainly by person-to-person contact (1). Implementation of nationwide public health orders to limit person-to-person interaction and of guidance on personal protective practices can slow transmission (2,3). Such strategies can include stay-at-home orders, business closures, prohibitions against mass gatherings, use of cloth face coverings, and maintenance of a physical distance between persons (2,3). To assess and understand public attitudes, behaviors, and beliefs related to this guidance and COVID-19, representative panel surveys were conducted among adults aged  $\geq 18$  years in New York City (NYC) and Los Angeles, and broadly across the United States during May 5-12, 2020. Most respondents in the three cohorts supported stay-at-home orders and nonessential business closures\* (United States, 79.5%; New York City, 86.7%; and Los Angeles, 81.5%), reported always or often wearing cloth face coverings in public areas (United States, 74.1%, New York City, 89.6%; and Los Angeles 89.8%), and believed that their state's restrictions were the right balance or not restrictive enough (United States, 84.3%; New York City, 89.7%; and Los Angeles, 79.7%). Periodic assessments of public attitudes, behaviors, and beliefs can guide evidence-based public health decision-making and related prevention messaging about mitigation strategies needed as the COVID-19 pandemic evolves.

### FIGURES

| Attitudes, behaviors, and beliefs  |   |                  |                 | p-value <sup>a</sup> | p-value <sup>b</sup> | p-value <sup>c</sup> |                    |
|--|---|------------------|-----------------|----------------------|----------------------|----------------------|--------------------|
|  | (U.S.<br>(N = 1,676)                                    | NYC<br>(N = 286) | LA<br>(N = 259) | U.S. vs NYC          | U.S. vs LA           | NYC vs LA            |                    |
| Attitudes, no. of respondents (%)  |   |                  |                 |                      |                      |                      |                    |
| Support stay-at-home order and nonessential business closures                              | Yes   | 1,332 (79.5)     | 248 (86.7)      | 211 (81.5)           | <0.05 <sup>d</sup>   | 0.5097               | 0.1187             |
|  | No  | 344 (20.5)       | 38 (13.3)       | 49 (18.5)            |                      |                      |                    |
| Nonesential workers should stay home   | Agree   | 1,128 (67.3)     | 219 (76.6)      | 179 (69.1)           | <0.05 <sup>d</sup>   | 0.6722               | <0.05 <sup>d</sup> |
|  | Neither agree nor disagree                              | 283 (16.9)       | 41 (14.3)       | 34 (14.7)            |                      |                      |                    |
|  | Disagree  | 265 (15.8)       | 26 (9.1)        | 42 (16.2)            |                      |                      |                    |
| Persons should always keep 6-ft of physical distance                                       | Agree   | 1,470 (87.7)     | 262 (91.6)      | 234 (90.3)           | 0.1242               | 0.4707               | 0.6377             |
|  | Neither agree nor disagree                              | 127 (7.6)        | 17 (5.9)        | 15 (5.8)             |                      |                      |                    |
|  | Disagree  | 79 (4.7)         | 7 (2.4)         | 10 (3.9)             |                      |                      |                    |
| Groups of 10 or more persons should not be allowed   | Agree   | 1,381 (82.4)     | 247 (86.4)      | 226 (87.3)           | 0.1245               | 0.1374               | 0.8130             |
|  | Neither agree nor disagree                              | 302 (17.6)       | 42 (14.0)       | 25 (8.9)             |                      |                      |                    |
|  | Disagree  | 139 (8.3)        | 14 (4.9)        | 14 (5.4)             |                      |                      |                    |
| Dining inside restaurants should not be allowed  | Agree   | 1,117 (66.0)     | 233 (81.3)      | 186 (71.8)           | <0.05 <sup>d</sup>   | 0.1769               | <0.05 <sup>d</sup> |
|  | Neither agree nor disagree                              | 302 (18.6)       | 36 (12.8)       | 31 (11.9)            |                      |                      |                    |
|  | Disagree  | 315 (18.8)       | 25 (8.7)        | 37 (14.3)            |                      |                      |                    |
| Behaviors, no. of respondents (%)  |   |                  |                 |                      |                      |                      |                    |
| In self-isolation <sup>e</sup>   | Yes   | 1,296 (77.3)     | 242 (84.6)      | 215 (83.0)           | <0.05 <sup>d</sup>   | <0.05 <sup>d</sup>   | 0.6954             |
|  | No  | 380 (22.7)       | 44 (15.4)       | 44 (17.0)            |                      |                      |                    |
| Keep 6 ft apart from others  | Always  | 975 (58.2)       | 191 (66.8)      | 177 (66.4)           | 0.0653               | 0.1576               | 0.8331             |
|  | Often   | 357 (21.3)       | 54 (19.1)       | 40 (14.7)            |                      |                      |                    |
|  | Sometimes   | 138 (8.2)        | 16 (5.6)        | 17 (6.6)             |                      |                      |                    |
|  | Rarely  | 69 (4.1)         | 10 (3.5)        | 10 (3.9)             |                      |                      |                    |
|  | Never   | 137 (8.2)        | 15 (5.2)        | 18 (6.9)             |                      |                      |                    |
| Avoid groups of 10 or more persons   | Always  | 1,259 (75.1)     | 222 (77.6)      | 196 (75.7)           | 0.7621               | 0.9568               | 0.8975             |
|  | Often   | 181 (10.8)       | 32 (11.2)       | 24 (8.7)             |                      |                      |                    |
|  | Sometimes   | 39 (2.3)         | 5 (1.7)         | 7 (2.7)              |                      |                      |                    |
|  | Rarely  | 39 (2.3)         | 5 (1.7)         | 5 (1.9)              |                      |                      |                    |
|  | Never   | 138 (8.2)        | 18 (6.3)        | 22 (8.5)             |                      |                      |                    |
| Been to a public area in the previous week   | Yes   | 1,533 (91.5)     | 260 (90.9)      | 235 (90.7)           | 0.8436               | 0.7851               | 0.9381             |
|  | No  | 143 (8.5)        | 26 (9.1)        | 24 (9.3)             |                      |                      |                    |
| Wear cloth face covering when in public**  | Always  | 925 (60.3)       | 208 (80.0)      | 181 (77.9)           | <0.05 <sup>d</sup>   | <0.05 <sup>d</sup>   | 0.7659             |
|  | Often   | 212 (13.8)       | 25 (8.6)        | 20 (11.9)            |                      |                      |                    |
|  | Sometimes   | 134 (8.7)        | 14 (4.6)        | 16 (8.8)             |                      |                      |                    |
|  | Rarely  | 63 (4.1)         | 5 (1.9)         | 3 (1.3)              |                      |                      |                    |
|  | Never   | 199 (13.0)       | 8 (3.1)         | 5 (2.1)              |                      |                      |                    |
| Beliefs, no. of respondents (%)  |   |                  |                 |                      |                      |                      |                    |
| Believe community mitigation strategies are  |   |                  |                 |                      |                      |                      |                    |
| Not effective/nothing  |   | 302 (18.0)       | 49 (17.4)       | 43 (16.3)            | 0.0500               | 0.1699               | <0.05 <sup>d</sup> |
| The right balance  |   | 1,112 (66.3)     | 204 (72.3)      | 163 (63.4)           |                      |                      |                    |
| Too restrictive  |   | 262 (15.6)       | 29 (10.3)       | 52 (20.2)            |                      |                      |                    |
| Would feel safe if community mitigation strategies were lifted nationwide at the same time | Yes   | 431 (25.7)       | 53 (18.5)       | 69 (26.6)            | <0.05 <sup>d</sup>   | 0.8102               | 0.0304             |
|  | No  | 1,245 (74.3)     | 233 (81.5)      | 190 (73.4)           |                      |                      |                    |
|  | No, but would like restrictions lifted and accept risks | 287 (17.1)       | 36 (12.6)       | 33 (12.7)            |                      |                      |                    |

<sup>a</sup>Abbreviations: COVID-19 = coronavirus disease 2019.

<sup>b</sup>The U.S. survey group did not exclude respondents from New York City and Los Angeles.

<sup>c</sup>Calculated with Chi-squared test of independence.

<sup>d</sup>P value is statistically significant ( $p < 0.05$ ).

<sup>e</sup>For the survey, "self-isolation" means staying at home and having no contact with others outside of the respondent's household unless required for essential services.

\*\*Of respondents who reported having been in a public area in the preceding week.

## SHOULD SCHOOLS REOPEN EARLY OR LATE? - TRANSMISSION DYNAMICS OF COVID-19 IN CHILDREN

Kuttiatt VS, Menon RP, Abraham PR, Sharma S.. Indian J Pediatr. 2020 Jun 16. doi: 10.1007/s12098-020-03401-0. Online ahead of print.

Level of Evidence: Other - Expert Opinion

### BLUF

A letter to the editor by authors from India is in favor of early reopening of schools for children due to low rates of transmission and contraction of COVID-19 in the pediatric population as evidenced by case reports. The authors also urge for more studies on asymptomatic pediatric patients with COVID-19 and for strict preventative measures (e.g. social distancing, wearing masks) to still be in place when schools reopen.

## GLOBAL

## FLATTENING THE EMOTIONAL DISTRESS CURVE: A BEHAVIORAL HEALTH PANDEMIC RESPONSE STRATEGY FOR COVID-19

Kaslow NJ, Friis-Healy EA, Cattie JE, Cook SC, Crowell AL, Cullum KA, Del Rio C, Marshall-Lee ED, LoPilato AM, VanderBroek-Stice L, Ward MC, White DT, Farber EW.. Am Psychol. 2020 Jun 15. doi: 10.1037/amp0000694. Online ahead of print.

Level of Evidence: Other - Expert Opinion

### BLUF

In this article, experts from Emory University School of Medicine highlight aspects of emotional and behavioral distress exacerbated by the COVID-19 pandemic while illustrating ways in which public leaders can help improve the behavioral health of all people (Table 1, Figure 1). They describe several steps that can be taken to "flatten the emotional distress curve," such as collecting information regarding behavioral health during the pandemic, launching public health and medical intervention efforts to address health discrepancies, and utilizing community health programs to improve behavioral health. Ultimately, the authors argue for the integration of psychological and behavioral health practices into public health policies.

## ABSTRACT

This article proposes a framework for managing the behavioral health impacts of the COVID-19 global pandemic. This framework aligns and should be integrated with an existing public health pandemic intervals model. It includes six phases of a behavioral health pandemic response strategy: preplanning, response readiness, response mobilization, intervention, continuation, and amelioration. The ways behavioral health specialists can capitalize on their competence in the leadership, prevention, education, service, research, and advocacy domains within each behavioral health pandemic response phase are articulated. Behavioral health expertise can help ensure a more comprehensive, effective pandemic response that facilitates the flattening of the curve of disease spread, along with the corresponding emotional distress curve. A case illustration, the Caring Communities (CC) initiative, is offered as an exemplar of action steps in the leadership, prevention, education, service, research, and advocacy domains that behavioral health professionals can take within each of the behavioral health pandemic response phases. Key CC action steps include providing support groups, offering virtual wellness breaks, participating in educational outreach, creating and disseminating wellness guides, launching and leading a virtual behavioral health clinic for health care staff, participating in behavioral health research and program evaluation, and engaging in advocacy initiatives aimed at improving behavioral health care and addressing and reducing health disparities. Finally, recommendations for optimizing behavioral health contributions to future pandemic responses are proffered. (PsycInfo Database Record (c) 2020 APA, all rights reserved).

## FIGURES

| Interval      | Pandemic event  | Example actions  |
|---------------|---|--|
| Investigation | Emergence of a newly identified influenza virus that may portend a human health risk      | Monitor and evaluate for pandemic threat potential   |
| Recognition   | Determination of a heightened likelihood for continued viral transmission                 | Ramp up of efforts to control outbreak   |
| Initiation    | Efficient and sustained viral spread demarcating the starting point for a “pandemic wave” | Ongoing case-based control efforts; surveillance monitoring to evaluate when to implement mitigation strategies; encouragement of hand hygiene as a preventive measure   |
| Acceleration  | Rapid climb in the epidemiological curve based on a steady increase in new cases          | Mitigation strategies (e.g., school closures, social distancing measures); voluntary quarantine of persons with viral exposure; isolation and medical intervention for infected persons; use of pharmacological agents and vaccines if available |
| Deceleration  | Downward trajectory of the epidemiological curve based on a decline in new cases          | Continued epidemiological monitoring and medical intervention; assessment of readiness to suspend or retract mitigation initiatives, particularly in geographic areas where few or no new cases are being reported                               |
| Preparation   | Low pandemic infection rates  | Aggressive epidemiological monitoring and response to new outbreaks; planning for possible recurrences of pandemic waves   |

*Note.* Information in this table builds upon the work of Holloway and colleagues (2014) and the CDC (<https://www.cdc.gov/flu/pandemic-resources/national-strategy/intervals-framework.html>).

Table 1. Centers for Disease Control and Prevention Pandemic Intervals Framework

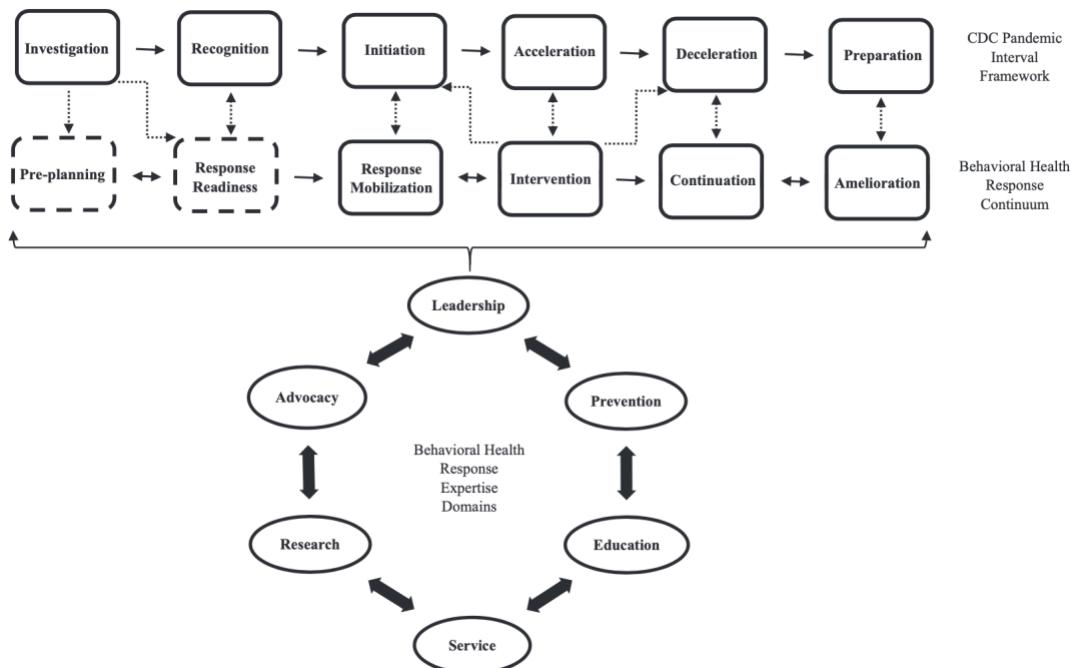


Figure 1. Behavioral health pandemic response strategy.

# DISPARITIES

## SPATIAL DISPARITIES IN CORONAVIRUS INCIDENCE AND MORTALITY IN THE UNITED STATES: AN ECOLOGICAL ANALYSIS AS OF MAY 2020

Zhang CH, Schwartz GG.. J Rural Health. 2020 Jun 16. doi: 10.1111/jrh.12476. Online ahead of print.

Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

### BLUF

A meta-analysis conducted by researchers at the University of Louisville and the University of North Dakota using US county COVID-19 data up to May 1, 2020, found evidence of a higher incidence and mortality rate in metropolitan areas compared to non-metropolitan areas. There was also evidence of increased risk of infection and mortality in areas with high population density, elderly population, and lack of testing (see summary for more details). The results suggest the current pandemic carries disproportionate risk to certain populations secondary to underlying ecologic factors.

### SUMMARY

The authors analyzed COVID-19 cases and mortality using John Hopkins University county-level data for 2,814 US counties with at least one case of infection. Urban-rural locale codes were used to examine disparities between metropolitan and non-metropolitan areas and multiple regression analyses were used to examine the variables. From their analyses, the researchers found the following:

- The New York metropolitan area was the most affected with about 37% of the country's infections
- The top 10 metropolitan areas contained 61% of confirmed cases in the US
- Metropolitan areas had a higher incidence and mortality than non-metropolitan areas (Figure 1)
- Within metropolitan areas themselves, urban areas were more affected than suburban or rural areas (Figure 2).

Although this was the general trend, there were some smaller non-metropolitan counties that had relatively high incidence and mortality rates. The authors mapped the county data to give a better idea of the distribution (Figures 3). In relation to incidence, the population density was the strongest predictor, with percent of the population over 65 and testing rates also being significant. For mortality, the population density was again the strongest predictor, along with the elderly population and poverty. Percent of minority populations was shown to be a negative predictor.

### ABSTRACT

**PURPOSE:** This ecological analysis investigates the spatial patterns of the COVID-19 epidemic in the United States in relation to socioeconomic variables that characterize US counties. **METHODS:** Data on confirmed cases and deaths from COVID-19 for 2,814 US counties were obtained from Johns Hopkins University. We used Geographic Information Systems (GIS) to map the spatial aspects of this pandemic and investigate the disparities between metropolitan and nonmetropolitan communities. Multiple regression models were used to explore the contextual risk factors of infections and death across US counties. We included population density, percent of population aged 65+, percent population in poverty, percent minority population, and percent of the uninsured as independent variables. A state-level measure of the percent of the population that has been tested for COVID-19 was used to control for the impact of testing. **FINDINGS:** The impact of COVID-19 in the United States has been extremely uneven. Although densely populated large cities and their surrounding metropolitan areas are hotspots of the pandemic, it is counterintuitive that incidence and mortality rates in some small cities and nonmetropolitan counties approximate those in epicenters such as New York City. Regression analyses support the hypotheses of positive correlations between COVID-19 incidence and mortality rates and socioeconomic factors including population density, proportions of elderly residents, poverty, and percent population tested. **CONCLUSIONS:** Knowledge about the spatial aspects of the COVID-19 epidemic and its socioeconomic correlates can inform first responders and government efforts. Directives for social distancing and to "shelter-in-place" should continue to stem the spread of COVID-19.

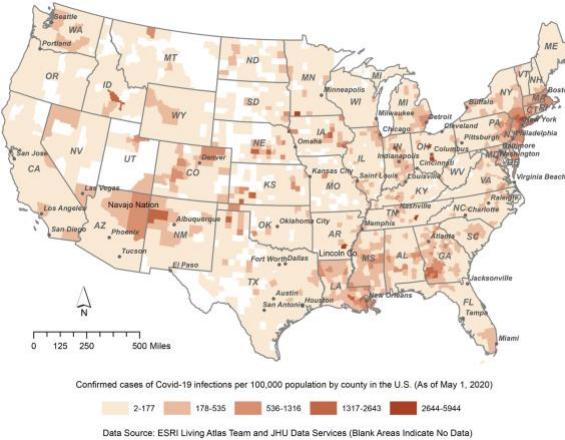


Figure 2. Average Incidence and Mortality Rates in Urban, Suburban, and Rural Counties in the United States.

## IMPACT OF COVID-19 ON FAMILY PLANNING SERVICES IN INDIA

32552622. Impact of COVID-19 on family planning services in India

Level of Evidence: Other - Expert Opinion

### BLUF

These authors from Ahmedabad, India evidence the impact of the COVID-19 pandemic on family planning services in India through presenting health management information system (HMIS) data from public sector health facilities. This data reveals reductions in the provision of injectable contraception-first dose by 36%, IUD insertions by 21%, combined oral pill cycles by 15%, condom pieces by 23%, and abortion procedures by 28% in March 2020 compared to December 2019, although there was reduced reporting of data in this time period. The Foundation for Reproductive Health Services India's estimates that reduced contraceptive access may lead to about 2.4 million unintended pregnancies, 1,700 additional maternal deaths, and 1.45 million abortions, half of which would be performed in an unsafe environment. These observations suggest that the pandemic has reduced access in an already strained family planning system in India, leading the authors to call for a comprehensive, rights-based health system response to mitigate further mortality and morbidity of women.

## ADDRESSING INEQUITIES IN COVID-19 MORBIDITY AND MORTALITY: RESEARCH AND POLICY RECOMMENDATIONS

Wang ML, Behrman P, Dulin A, Baskin ML, Buscemi J, Alcaraz KI, Goldstein CM, Carson TL, Shen M, Fitzgibbon M.. Transl Behav Med. 2020 Jun 16:ibaa055. doi: 10.1093/tbm/ibaa055. Online ahead of print.

Level of Evidence: Other - Guidelines and Recommendations

### BLUF

United States public health researchers affiliated with the Society of Behavioral Medicine promote recommendations to alleviate racial, ethnic, and socioeconomic health disparities exasperated by the COVID-19 pandemic. They outline recommendations for equity-driven research that utilizes a social determinants and health equity lens, policy actions that prioritize resources for high-risk communities, and legislation that addresses barriers to well-being faced by vulnerable populations during a pandemic.

## SUMMARY

Research recommendations:

- Data collection should be standardized, accurate, and reflect race/ethnicity and socioeconomic status (SES) measures.
- Public health messaging should be timely, accessible, and understandable at all levels of health literacy.
- Funding for research to understand social determinants of COVID-19-related morbidity and mortality should be increased.
- COVID-19-related clinical trials should have equitable recruitment to fairly represent racial and ethnic minorities.

Short-term policy recommendations:

- Governments at all levels should provide free and accessible SARS-CoV-2 testing and prioritize at-risk communities.
- Leadership and media should consult and collaborate with experts in medicine and public health.
- Governments at all levels should work with internet providers to provide free and accessible internet access to address

disparities in information, education, healthcare, and connectedness.

- Occupation and public health departments should implement standardized and frequent inspections of open business to enforce COVID-19 safety policies.
- Employees should be protected in the case of COVID-19 sick leave or if they need to take time off to care for a sick family member.
- Government and healthcare system coordination should work to protect insurance coverage of COVID-19 diagnostic and treatment interventions, including preventive health and the treatment of underlying conditions.
- Hospital leadership must identify and address any biases in treatment algorithms for COVID-19, such as ventilator use.

Intermediate- and long-term policy recommendations:

- Policymakers should prioritize development of affordable, culturally sensitive, multilingual, and accessible health-related outreach education.
- Policymakers should restore funding and/or the equivalent of expected patient reimbursements to community health systems.
- Policymakers should increase funding for developing innovative, accessible, and culturally sensitive healthcare delivery options, such as mobile clinics.

## ABSTRACT

The COVID-19 pandemic is the greatest global public health crisis since the 1918 influenza outbreak. As of early June, the novel coronavirus has infected more than 6.3 million people worldwide and more than 1.9 million in the United States (US). The total number of recorded deaths due to COVID-19 are growing at an alarming rate globally (3383,000) and nationally (3109,000). Evidence is mounting regarding the heavier burden of COVID-19 infection, morbidity, and mortality on the underserved populations in the US. This commentary focuses on this global health pandemic and how mitigation of the virus relies heavily on health behavior change to slow its spread, highlighting how the pandemic specifically affects the most socially and economically disadvantaged populations in the US. The commentary also offers short, intermediate and long-term research and policy focused recommendations. Both the research and policy recommendations included in this commentary emphasize equity-driven: (1) research practices, including applying a social determinants and health equity lens on monitoring, evaluation, and clinical trials activities on COVID-19; and (2) policy actions, such as dedicating resources to prioritize high-risk communities for testing, treatment, and prevention approaches and implementing organizational, institutional, and legislative policies that address the social and economic barriers to overall well-being that these populations face during a pandemic. It is our hope that these recommendations will generate momentum in delivering timely, effective, and lifesaving changes.

## COVID-19 AND IMMIGRANTS' ACCESS TO SEXUAL AND REPRODUCTIVE HEALTH SERVICES IN THE UNITED STATES

Desai S, Samari G.. Perspect Sex Reprod Health. 2020 Jun 12. doi: 10.1363/psrh.12150. Online ahead of print.  
Level of Evidence: Other - Expert Opinion

### BLUF

Public health experts from New York describe how health disparities, including access, socioeconomic status, language, citizenship status, and education level, experienced by immigrants of color throughout the United States are dramatically worsened during this COVID-19 pandemic and have made providing sexual and reproductive health (SRH) services extremely difficult for this population. The authors suggest that SRH care must remain accessible and directed towards all populations and that policies should be put in place to protect the rights of all people including immigrants.

## THE COVID-19 PANDEMIC EXPOSES LIMITED UNDERSTANDING OF AGEISM

Reynolds L.. J Aging Soc Policy. 2020 Jun 12:1-7. doi: 10.1080/08959420.2020.1772003. Online ahead of print.  
Level of Evidence: Other - Expert Opinion

### BLUF

A professor of Gerontology in Sacramento, CA explains how the COVID-19 pandemic has exacerbated the negative social impacts of ageism by devaluing older people and generating negative subconscious attitudes about aging. They discuss the following policy changes and initiatives to reduce these negative impacts:

- The Elder Justice Act of 2009 can be revised to address abuse, neglect, and exploitation of the older population.
- The Reframing Aging Initiative spreads positive images of aging to counteract the negative priming that people experience.

- The Age Friendly University Movement helps institutions become more age friendly.
- Ageism First Aid is an online course providing knowledge and awareness about ageism.

## **ABSTRACT**

During the COVID-19 pandemic, justification for orders to shelter in place have emphasized the vulnerability of older people. Although other at-risk groups were sometimes mentioned, the emphasis on older people could have effects on attitudes about aging and older people for decades to come. This essay provides a comprehensive biopsychosocial description of ageism and discusses the pandemic as a "focusing event" that exemplifies the extreme social consequence of ageism for the entire older population. It suggests revisions to the Elder Justice Act and utilization of programs such as the Reframing Aging, Age-Friendly University, and Ageism First Aid initiatives to reduce ageism in the wake of the pandemic.

### SARS-COV-2 GENOMIC SURVEILLANCE IN TAIWAN REVEALED NOVEL ORF8-DELETION MUTANT AND CLADE POSSIBLY ASSOCIATED WITH INFECTIONS IN MIDDLE EAST

Gong YN, Tsao KC, Hsiao MJ, Huang CG, Huang PN, Huang PW, Lee KM, Liu YC, Yang SL, Kuo RL, Chen KF, Liu YC, Huang SY, Huang HI, Liu MT, Yang JR, Chiu CH, Yang CT, Chen GW, Shih SR.. Emerg Microbes Infect. 2020 Jun 16:1-37. doi: 10.1080/22221751.2020.1782271. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

#### BLUF

The authors analyze and compare 20 genomes derived from 3 specimens and 17 virus isolates in Taiwan to global strains. They identify a new open reading frame 8 deletion mutation which was similar to observations made of 8 patients in Singapore indicating early spread of that strain, and a new virus clade that may be associated with infections in the Middle East (Table 2, Figure S1). These findings may provide insight into viral genome information regarding SARS-CoV-2 outbreaks in that region.

#### ABSTRACT

Taiwan experienced two waves of imported infections with Coronavirus Disease 2019 (COVID-19). This study aimed at investigating the genomic variation of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Taiwan and compared their evolutionary trajectories with the global strains. We performed culture and full-genome sequencing of SARS-CoV-2 strains followed by phylogenetic analysis. A 382-nucleotides deletion in open reading frame 8 (ORF8) was found in a Taiwanese strain isolated from a patient on February 4, 2020 who had a travel history to Wuhan. Patients in the first wave also included several sporadic, local transmission cases. Genomes of 5 strains sequenced from clustered infections were classified into a new clade with ORF1ab-V378I mutation, in addition to 3 dominant clades ORF8-L84S, ORF3a-G251V and S-D614G. This highlighted clade also included some strains isolated from patients who had a travel history to Turkey and Iran. The second wave mostly resulted from patients who had a travel history to Europe and Americas. All Taiwanese viruses were classified into various clades. Genomic surveillance of SARS-CoV-2 in Taiwan revealed a new ORF8-deletion mutant and a virus clade that may be associated with infections in the Middle East, which contributed to a better understanding of the global SARS-CoV-2 transmission dynamics.

#### FIGURES

**Table 2. Genomic mutations of Taiwanese and Singapore strains with the ORF8-deletion.**

| Strain name               | Nucleotide (amino acid) mutation   |
|---------------------------|--|
| CGMH-CGU-02               | ORF1ab-C8517T, ORF1ab-A16577G (K5526R), S-C145T (H49Y), S-C2651T (S884F) |
| hCoV-19/Singapore/12/2020 | ORF1ab-C8517T, S-T2449C (F817L), ORF3a-C176A (A59D)                      |
| hCoV-19/Singapore/13/2020 | ORF1ab-C8517T, ORF1ab-T17459C (V5820A), N-C595T (P199S)                  |
| hCoV-19/Singapore/14/2020 | ORF1ab-C8517T  |

\* Nucleotide or amino acid position was based on gene position of the reference strain (Wuhan-1).

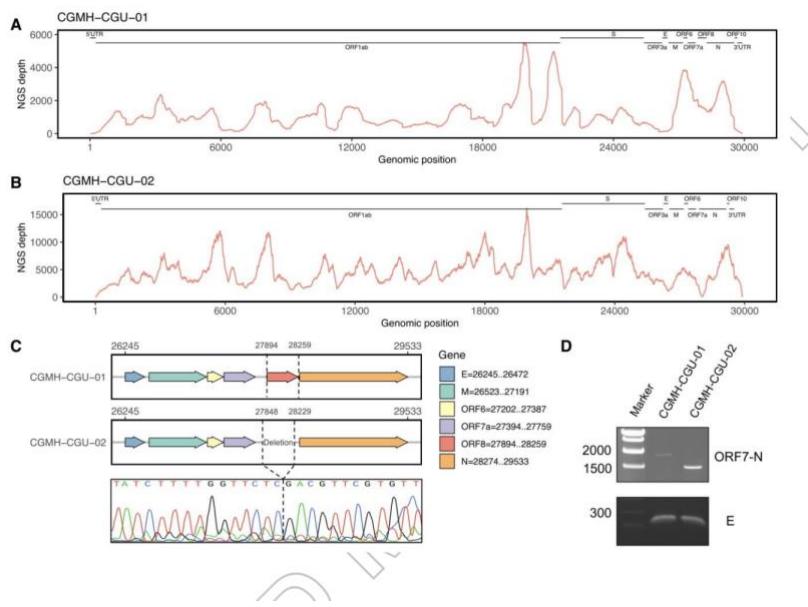


Figure S1. RNA expression levels of the ORF8-deletion strain. RNA expression levels of A) RdRp and B) E genes in CGMH-CGU-02 infected cells compared with CGMH-CGU-01 were measured.

## PANGOLINS HARBOR SARS-COV-2-RELATED CORONAVIRUSES

Han GZ.. Trends Microbiol. 2020 Jul;28(7):515-517. doi: 10.1016/j.tim.2020.04.001. Epub 2020 Apr 6.  
Level of Evidence: Other - Expert Opinion

### BLUF

This author reviews evidence suggesting that Malayan pangolins could be an intermediate host that transmitted SARS-CoV-2 to humans from its natural reservoir in bats due to the similarity in amino acid sequence of receptor binding domains (RBDs) between SARS-CoV-2 and CoVs isolated from populations of pangolins that were obtained by anti-smuggling groups in China, which suggests a scenario where SARS-CoV-2 related coronaviruses from pangolins could be readily transmitted to humans (Figure 1) and highlights the risks of handling and trafficking pangolins.

### ABSTRACT

The pandemic of coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 has posed a severe threat to global public health. Yet, the origin of SARS-CoV-2 remains mysterious. Several recent studies (e.g., Lam et al., Xiao et al.) identified SARS-CoV-2-related viruses in pangolins, providing novel insights into the evolution and diversity of SARS-CoV-2-related viruses.

### FIGURES

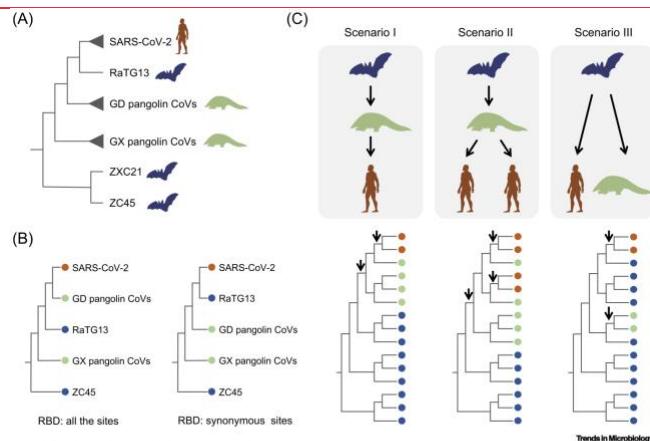


Figure 1. The Evolution of Pangolin Coronaviruses (CoVs). (A) The phylogenetic relationship among SARS-CoV-related viruses at the genome level. (B) The phylogenetic relationship among SARS-CoV-related viruses based on all the sites (left panel) or the synonymous sites (right panel) of the receptor-binding domain (RBD). (C) Cross-species transmission scenarios and their expected phylogenetic patterns. Pangolin CoVs might ultimately originate from cross-species transmission from bats. Pangolins serve as the intermediate host, and SARS-CoV-2 arose through spillover from pangolins to humans once (scenario I) or multiple times (scenario II). SARS-CoV and pangolin CoVs originated independently through cross-species transmission from bats (scenario III). Black arrows indicate cross-species transmission events.

# MODELING

## AN UPDATED ANALYSIS OF TURNING POINT, DURATION AND ATTACK RATE OF COVID-19 OUTBREAKS IN MAJOR WESTERN COUNTRIES WITH DATA OF DAILY NEW CASES

Wei W, Zhang X.. Data Brief. 2020 Aug;31:105830. doi: 10.1016/j.dib.2020.105830. Epub 2020 Jun 11.

Level of Evidence: Other - Modeling

### BLUF

Researchers describe an updated version of their previously published segmented Poisson model with sections based on the dates of major government COVID-19 interventions (Table 1) in six Western countries (USA, Canada, Italy, France, Germany, and the UK) to make updated predictions for turning point, duration, final size, and attack rate of COVID-19 (Figure 2 and Table 2). They analyze daily COVID-19 case data from Wind Database and unspecified US and Canada COVID-19 live update sites from 21 January 2020 to 21 May 2020 in their model. The authors suggest this updated segmented Poisson model may be a useful predictor of future COVID-19 cases and would be able to incorporate new data as the pandemic evolves.

### ABSTRACT

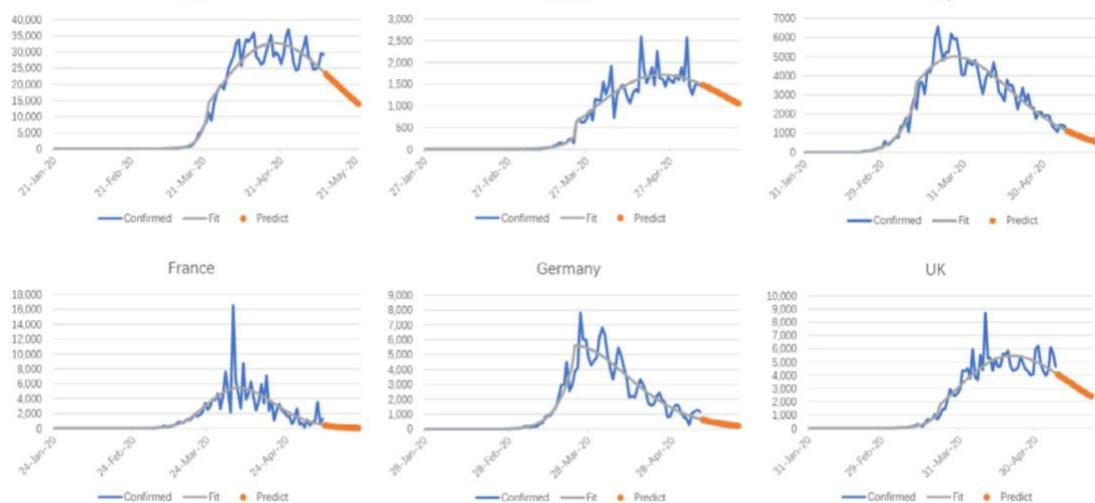
As coronavirus spreads around the world, the study of its effects is of great practical significance. We collated data on daily new cases of the COVID-19 outbreaks in the six Western countries of the Group of Seven and the dates of governments' interventions. We studied the periods before and after the dates of major governments' interventions integrally based on a segmented Poisson model. The relevant results are published in the paper of "Predicting turning point, duration and attack rate of COVID - 19 outbreaks in major Western countries" [1]. Our method can be used to update prediction daily as COVID-19 outbreaks evolve. In this article, we illustrate an updated analysis with our method to facilitate reproducibility. Both datasets used and updated are provided.

### FIGURES

**Table 1**

Dates of government's interventions.

| USA      | Canada   | Italy   | France   | Germany  | UK       |
|----------|----------|---------|----------|----------|----------|
| 16-March | 16-March | 6-March | 13-March | 22-March | 23-March |



**Fig. 2.** Daily new confirmed cases, fitted and predictive values in each country.

**Table 2**

Updated prediction of turning point, duration, final size and attack rate of COVID-19.

| Country | Turning point(Range)  | Final size | Duration      | Attack rate |
|---------|-----------------------|------------|---------------|-------------|
| USA     | Apr.18(Apr.16–Apr.20) | 1,817,322  | Jan.21–Sep.16 | 0.55%       |
| Canada  | Apr.24(May.02–Apr.20) | 108,641    | Jan.27–Sep.12 | 0.29%       |
| Italy   | Mar.28(Mar.25–Mar30)  | 233,301    | Jan.31–Aug.01 | 0.39%       |
| France  | Apr.05(Apr.04–Apr.07) | 179,204    | Jan.24–Jun.13 | 0.27%       |
| Germany | Mar.23(Mar.19–Mar27)  | 178,723    | Jan.28–Jul.13 | 0.21%       |
| UK      | Apr.21(Apr.17–Apr.25) | 297,167    | Jan.31–Aug.27 | 0.44%       |

## ARIMA MODELLING AND FORECASTING OF IRREGULARLY PATTERNED COVID-19 OUTBREAKS USING JAPANESE AND SOUTH KOREAN DATA

Duan X, Zhang X.. Data Brief. 2020 Aug;31:105779. doi: 10.1016/j.dib.2020.105779. Epub 2020 May 26.

Level of Evidence: Other - Modeling

### BLUF

Authors from China employed an Auto Regressive Integrated Moving Average (ARIMA) model to analyze the daily new confirmed COVID-19 cases from Japan and South Korea from January 20-April 26, 2020 in order to predict their daily new confirmed cases from April 27-May 3, 2020 (Figure 3). By using their model, authors were able to forecast the upper and lower limits of the predicted COVID-19 cases under a 95% confidence level (Table 1), suggesting that other countries could apply this ARIMA model to quickly collect, disseminate, track, and analyze COVID-19 data during the pandemic.

### ABSTRACT

The World Health Organization (WHO) upgraded the status of the coronavirus disease 2019 (COVID-19) outbreak from epidemic to global pandemic on March 11, 2020. Various mathematical and statistical models have been proposed to predict the spread of COVID-2019 [1]. We collated data on daily new confirmed cases of the COVID-19 outbreaks in Japan and South Korea from January 20, 2020 to April 26, 2020. Auto Regressive Integrated Moving Average (ARIMA) model were introduced to analyze two data sets and predict the daily new confirmed cases for the 7-day period from April 27, 2020 to May 3, 2020. Also, the forecasting results and both data sets are provided.

### FIGURES

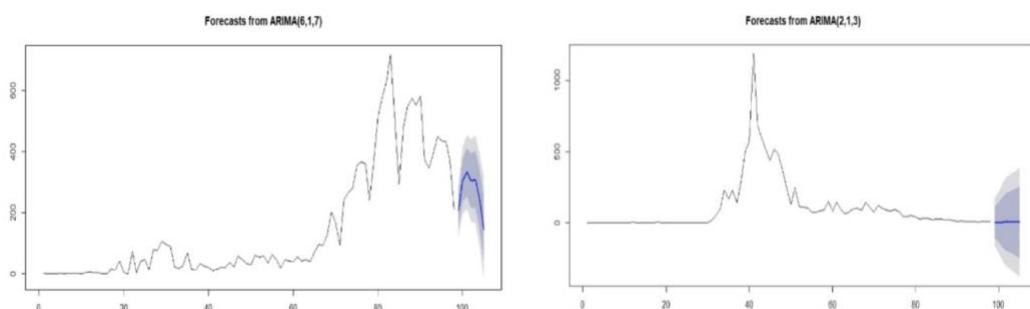


Figure 3. 7-day period prediction of the daily new confirmed cases for Japan and Korea plot.

**Table 1**  
Predicted value under the 95% confidence level of the daily new confirmed cases for the 7-day period

| Japan      | date      | lowwer   | mean     | upper | Korea      | date      | lowwer   | mean     | upper |
|------------|-----------|----------|----------|-------|------------|-----------|----------|----------|-------|
| 2020-04-27 | 122.68342 | 207.5012 | 292.319  |       | 2020-04-27 | -161.9685 | 6.36643  | 174.7014 |       |
| 2020-04-28 | 194.68068 | 303.4768 | 412.2729 |       | 2020-04-28 | -210.9135 | 2.035784 | 214.9851 |       |
| 2020-04-29 | 211.76786 | 333.6616 | 455.5554 |       | 2020-04-29 | -272.6349 | 4.635792 | 281.9065 |       |
| 2020-04-30 | 170.06375 | 304.8661 | 439.6684 |       | 2020-04-30 | -308.2444 | 7.649637 | 323.5437 |       |
| 2020-05-01 | 164.28963 | 308.5206 | 452.7516 |       | 2020-05-01 | -330.465  | 7.153191 | 344.7714 |       |
| 2020-05-02 | 93.39579  | 244.7979 | 396.1999 |       | 2020-05-02 | -354.1099 | 5.432586 | 364.975  |       |
| 2020-05-03 | -22.66019 | 143.4524 | 309.565  |       | 2020-05-03 | -381.2896 | 5.198718 | 391.687  |       |

# QUANTIFY THE ROLE OF SUPERSpreadERS -OPINION LEADERS- ON COVID-19 INFORMATION PROPAGATION IN THE CHINESE SINA-MICROBLOG

Yin F, Xia X, Song N, Zhu L, Wu J.. PLoS One. 2020 Jun 8;15(6):e0234023. doi: 10.1371/journal.pone.0234023. eCollection 2020.

Level of Evidence: Other - Modeling

## BLUF

A group of experts from China and Canada developed an opinion-leader susceptible-forwarding-immune (OL-SFI) dynamics model to quantify the rate of information spread about COVID-19 from a Chinese Sina-microblog. Through this model, the designers illustrated the large role that opinion leaders (or "social media superspreaders"), individuals with many followers on social media, play in the propagation of information online and suggest that early recruitment of opinion leaders may be beneficial in the dissemination of important public health information. The authors conducted this modeling with the assumption that users are fixed in their ability to spread social media, and only focused on the forwarding of information from users.

## ABSTRACT

**BACKGROUND:** Effective communication of accurate information through social media constitutes an important component of public health interventions in modern time, when traditional public health approaches such as contact tracing, quarantine and isolation are among the few options for the containing the disease spread in the population. The success of control of COVID-19 outbreak started from Wuhan, the capital city of Hubei Province of China relies heavily on the resilience of residents to follow public health interventions which induce substantial interruption of social-economic activities, and evidence shows that opinion leaders have been playing significant roles in the propagation of epidemic information and public health policy and implementations.

**METHODS:** We design a mathematical model to quantify the roles of information superspreaders in single specific information which outbreaks rapidly and usually has a short duration period, and to examine the information propagation dynamics in the Chinese Sina-microblog. Our opinion-leader susceptible-forwarding-immune (OL-SFI) model is formulated to track the temporal evolution of forwarding quantities generated by opinion leaders and normal users.

**RESULTS:** Data fitting from the real data of COVID-19 obtained from Chinese Sina-microblog can identify the different contact rates and forwarding probabilities (and hence calculate the basic information forwarding reproduction number of superspreaders), and can be used to evaluate the roles of opinion leaders in different stages of the information propagation and the outbreak unfolding.

**CONCLUSIONS:** The parameterized model can be used to nearcast the information propagation trend, and the model-based sensitivity analysis can help to explore important factors for the roles of opinion leaders.

## FIGURES

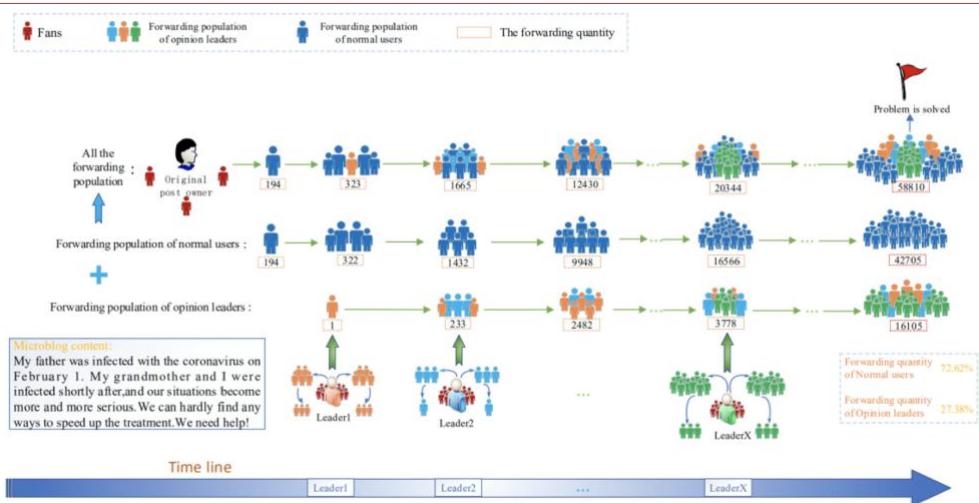
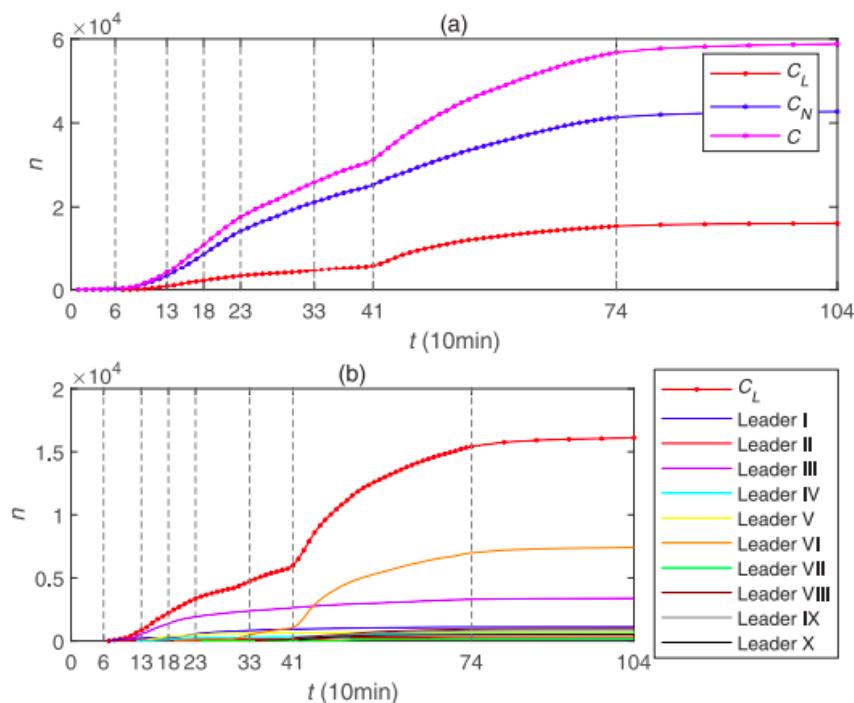


Figure 1: An illustration of a message receiving public attention after the involvement of several opinion leaders.

**Table 2. The number of fans and forwarding population of each opinion leaders.**

|             | t(10min) | The number of fans | The number of final forwarding population |
|-------------|----------|--------------------|---|
| Leader I    | 7        | 1905854            | 1145                                      |
| Leader II   | 9        | 352392             | 319                                       |
| Leader III  | 10       | 1744183            | 3567                                      |
| Leader IV   | 12       | 78406              | 721                                       |
| Leader V    | 14       | 2144029            | 690                                       |
| Leader VI   | 19       | 1269890            | 8167                                      |
| Leader VII  | 24       | 5741               | 257                                       |
| Leader VIII | 34       | 409299             | 1090                                      |
| Leader XI   | 42       | 1561825            | 955                                       |
| Leader X    | 42       | 817185             | 548                                       |



**Fig 3.** The cumulative number of forwarding population: (a) the cumulative forwarding population affected by opinion leaders, normal users and their sum; (b) the cumulative forwarding population affected by each opinion leader and their sum.

## SYMPTOMS AND CLINICAL PRESENTATION

### FIRST REPORTED CASES OF SARS-COV-2 INFECTION IN COMPANION ANIMALS - NEW YORK, MARCH-APRIL 2020

Newman A, Smith D, Ghai RR, Wallace RM, Torchetti MK, Loiacono C, Murrell LS, Carpenter A, Moroff S, Rooney JA, Barton Behravesh C.. MMWR Morb Mortal Wkly Rep. 2020 Jun 12;69(23):710-713. doi: 10.15585/mmwr.mm6923e3.  
Level of Evidence: Other - Case Report

#### BLUF

A case series in New York describes two domestic cats with the first confirmed SARS-CoV-2 infection in two different households in March 2020 (diagnosis confirmed with SARS-CoV-2 RT-PCR, see Figure for timeline). Both animals were exposed to symptomatic household members (fevers, chills, and cough) suspected of SARS-CoV-2 infection (household B had a confirmed case) 8-9 days prior to the cats showing respiratory symptoms (sneeze, cough, and nasal/ocular discharge). The authors report human cases preceded both feline cases and there was no evidence at the time of report to suggest feline-

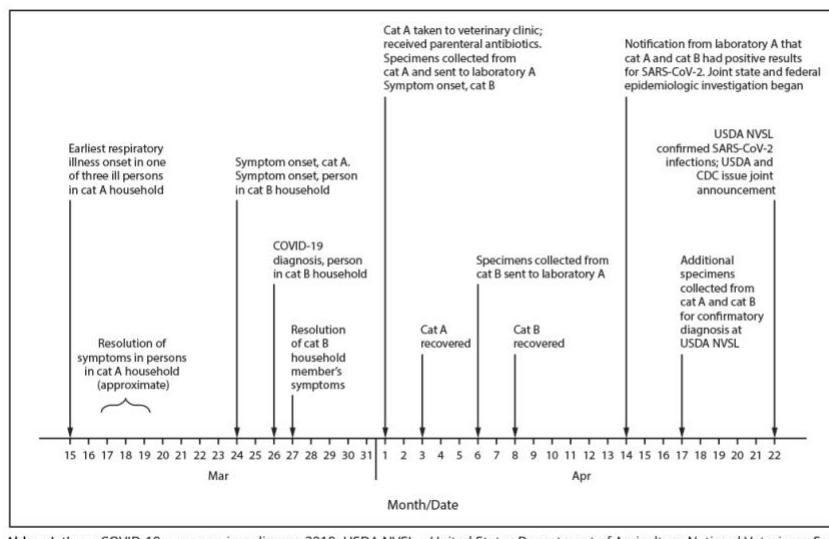
human transmission. Therefore, they believe animals have an insignificant role in the transmission of SARS-CoV-2 to humans; however human-to-animal transmission is uncertain and they recommend persons with SARS-CoV-2 infection limit contacts with animals.

## ABSTRACT

On April 22, CDC and the U.S. Department of Agriculture (USDA) reported cases of two domestic cats with confirmed infection with SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19). These are the first reported companion animals (including pets and service animals) with SARS-CoV-2 infection in the United States, and among the first findings of SARS-CoV-2 symptomatic companion animals reported worldwide. These feline cases originated from separate households and were epidemiologically linked to suspected or confirmed human COVID-19 cases in their respective households. Notification of presumptive positive animal test results triggered a One Health\* investigation by state and federal partners, who determined that no further transmission events to other animals or persons had occurred. Both cats fully recovered. Although there is currently no evidence that animals play a substantial role in spreading COVID-19, CDC advises persons with suspected or confirmed COVID-19 to restrict contact with animals during their illness and to monitor any animals with confirmed SARS-CoV-2 infection and separate them from other persons and animals at home (1).

## FIGURES

FIGURE. Timeline of events related to SARS-CoV-2 infections in two domestic cats (cats A and B) kept as pets in two different households — New York, March 15–April 22, 2020



Abbreviations: COVID-19 = coronavirus disease 2019; USDA NVSL = United States Department of Agriculture National Veterinary Services Laboratories.

Figure. Timeline of events related to SARS-CoV-2 infections in two domestic cats (cats A and B) kept as pets in two different households — New York, March 15–April 22, 2020.

## ADULTS

### A CROSS-SECTIONAL COMMUNITY-BASED OBSERVATIONAL STUDY OF ASYMPTOMATIC SARS-COV-2 PREVALENCE IN THE GREATER INDIANAPOLIS AREA

Meyers KJ, Jones ME, Goetz IA, Botros FT, Knorr J, Manner DH, Woodward B.. J Med Virol. 2020 Jun 16. doi: 10.1002/jmv.26182. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

## BLUF

A cross-sectional community-based observational study conducted in the Indianapolis metropolitan area from April 6 to May 16, 2020 found that 3.1% (95% CI, 2.5%-3.7%) of 2,953 asymptomatic (no fever, cough, or shortness of breath in the last 7 days) adults tested positive for SARS-CoV-2 by nasopharyngeal swab testing. Of the 81 SARS-CoV-2 positive participants who completed a follow-up interview, 71.6% remained asymptomatic at 14 days while the other 28.4% reported one or more

symptoms (Table 2). These findings highlight that further investigation is needed to better understand SARS-CoV-2 transmission among asymptomatic and pre-symptomatic individuals and the impact this is having on the spread of disease.

## ABSTRACT

The Asymptomatic novel CORonavirus iNfection (ACORN) study was designed to investigate the prevalence of SARS-CoV-2 infection in the asymptomatic adult population of the Indianapolis metropolitan area, to follow individuals testing positive for the development of symptoms, and to understand duration of positive test results. ACORN is a cross-sectional community-based observational study of adult residents presenting asymptomatic for COVID-like illness, defined as the self-reported absence of the following 3-symptoms in the last 7-days: fever ( $\geq 100$  F), new onset or worsening cough, and new onset or worsening shortness of breath. SARS-CoV-2 infection was determined by RT-PCR in nasopharyngeal swab samples. SARS-CoV-2 infection prevalence was expressed as a point estimate with 95%-CI. Test results are reported for 2953 participants who enrolled and underwent nasopharyngeal swab testing between April 7, 2020 and May 16, 2020. Among tested participants, 91 (3.1%; 95%-CI; 2.5%-3.7%) were positive for SARS-CoV-2. Overall, baseline characteristics, medical history, and infection risk factors were comparable between SARS-CoV-2 positive and negative participants. Within the ongoing 14-day follow-up period for positive participants, 58 (71.6%) of 81-assessed participants remained asymptomatic while others (n=23, 28.4%) reported one or more symptoms. Indiana had "Stay-at-Home" orders in place during nearly the entire test period reported here, yet 3.1% of asymptomatic participants tested positive for SARS-CoV-2. These results indicate screening questions had limited predictive utility for testing in an asymptomatic population and suggest broader testing strategies are needed. Importantly, these findings underscore that more research is needed to understand the viral transmission and the role asymptomatic and pre-symptomatic individuals play in this global pandemic. This article is protected by copyright. All rights reserved.

## FIGURES

| Reported Symptoms                               | n (%)     |
|---|-----------|
| Subjects with $\geq 1$ Symptom                  | 23 (28.4) |
| Fever (temperature $\geq 100^{\circ}\text{F}$ ) | 4 (4.9)   |
| Chills  | 3 (3.7)   |
| Fatigue and/or muscle aches                     | 9 (11.1)  |
| Sore throat                                     | 4 (4.9)   |
| Cough   | 6 (7.4)   |
| Shortness of breath                             | 7 (8.6)   |
| Headache  | 10 (12.3) |
| Gastrointestinal symptoms <sup>a</sup>          | 4 (4.9)   |
| Loss of smell or taste                          | 6 (7.4)   |

<sup>a</sup>Nausea, vomiting, or diarrhea

Table 2. Symptoms development within approximately 14 days after SARS-CoV-2 diagnosis among participants who completed follow-up at the time of the interim analysis (N=81).

## COVID-19 IN A PATIENT WITH SEVERE ASTHMA TREATED WITH OMALIZUMAB

Lommatsch M, Stoll P, Christian Virchow J.. Allergy. 2020 Jun 16. doi: 10.1111/all.14456. Online ahead of print.  
Level of Evidence: 5 - Case Report

## BLUF

Authors affiliated with the University of Rostock in Germany presented a case of a 52-year-old male previously diagnosed with severe, early-onset allergic asthma treated with fixed doses of Fluticasone furoate, Vilanterol, Tiotropium, and Omalizumab (anti-IgE antibody). On March 9, the patient presented with a dry cough, chills, myalgia, headache, fever, fatigue, loss of appetite, and anosmia. Laboratory tests returned positive for SARS-CoV-2 on March 13, 2020 and the patient began home

quarantine since symptoms of dyspnea, pneumonia, and worsening asthma were not reported. Omalizumab was then self-administered at home on March 19th and the patient has been symptom-free and tested negative for SARS-CoV-2 on March 30th. Thus, the authors hypothesize that either allergic asthma or Omalizumab protected the patient against acute asthma exacerbation or pneumonia during COVID-19.

## UNDERSTANDING THE PATHOLOGY

### OVERCOMING BARRIERS: THE ENDOTHELIUM AS A LINCHPIN OF CORONAVIRUS DISEASE 2019 PATHOGENESIS?

Gustafson D, Raju S, Wu R, Ching C, Veitch S, Rathnakumar K, Boudreau E, Howe KL, Fish JE.. Arterioscler Thromb Vasc Biol. 2020 Jun 8;ATVBAHA120314558. doi: 10.1161/ATVBAHA.120.314558. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

#### BLUF

A review article conducted by the Toronto General Hospital Research Institute, Canada highlights the current evidence and proposed mechanisms of cardiovascular risk in COVID-19, focusing on the role of endothelial cells. The authors suggest SARS-CoV-2 disruption of the renin angiotensin aldosterone system (RAAS) leads to an endothelial imbalance that plays a major role in the infection and dysfunctions of the disease. The imbalance leaves the endothelium susceptible to inflammation, vasoconstriction, platelet activation, and thrombosis. Future research is warranted to determine the specific roles and potential treatments relating to this disruption, angiotensin converting enzyme 2 (ACE2), and the RAAS pathway.

#### SUMMARY

The review covers the evidence and mechanisms of the following:

- The mechanism of viral entry to the endothelium via ACE2 seen in Figure 1.
- An imbalance in the RAAS contributes to endothelial dysfunction.
- Comorbidities of diabetes mellitus, hypertension, coronary artery disease, or cerebrovascular disease increase infection risk.
- Endothelial dysfunction contributes to cytokine storms which can damage lung and heart tissue.
- Atypical Kawasaki disease has been reported in pediatric COVID-19 patients presenting with acute vasculitis and hyper-inflammatory shock, suggesting an infectious trigger.
- Cardiac biomarkers are suggestive of poor cardiovascular outcomes in COVID-19 patients (Table 1).
- Endothelial dysfunction and resulting cytokine storms are contributing factors to hypercoagulability and disseminated intravascular coagulation seen in COVID-19.
- Endothelial-derived biomarkers can be used to predict ARDS (Table 3).
- Therapies strengthening the endothelial barrier may limit cardiovascular damage.
- Long-term cardiovascular complications may be seen in viral pneumonia and exacerbated by comorbidities.

#### ABSTRACT

**OBJECTIVE:** Coronavirus disease 2019 (COVID-19) is a global pandemic involving >5 500 000 cases worldwide as of May 26, 2020. The culprit is the severe acute respiratory syndrome coronavirus-2, which invades cells by binding to angiotensin-converting enzyme 2. While the majority of patients mount an appropriate antiviral response and recover at home, others progress to respiratory distress requiring hospital admission for supplemental oxygen. In severe cases, deterioration to acute respiratory distress syndrome necessitating mechanical ventilation, development of severe thrombotic events, or cardiac injury and dysfunction occurs. In this review, we highlight what is known to date about coronavirus disease 2019 and cardiovascular risk, focusing in on the putative role of the endothelium in disease susceptibility and pathogenesis.

**Approach and Results:** Cytokine-driven vascular leak in the lung alveolar-endothelial interface facilitates acute lung injury in the setting of viral infection. Given that the virus affects multiple organs, including the heart, it likely gains access into systemic circulation by infecting or passing from the respiratory epithelium to the endothelium for viral dissemination. Indeed, cardiovascular complications of coronavirus disease 2019 are highly prevalent and include acute cardiac injury, myocarditis, and a hypercoagulable state, all of which may be influenced by altered endothelial function. Notably, the disease course is worse in individuals with preexisting comorbidities that involve endothelial dysfunction and may be linked to elevated ACE2 (angiotensin-converting enzyme 2) expression, such as diabetes mellitus, hypertension, and cardiovascular disease.

**CONCLUSIONS:** Rapidly emerging data on coronavirus disease 2019, together with results from studies on severe acute respiratory syndrome coronavirus-1, are providing insight into how endothelial dysfunction may contribute to the pandemic that is paralyzing the globe. This may, in turn, inform the design of biomarkers predictive of disease course, as well as therapeutics targeting pathogenic endothelial responses.

## FIGURES

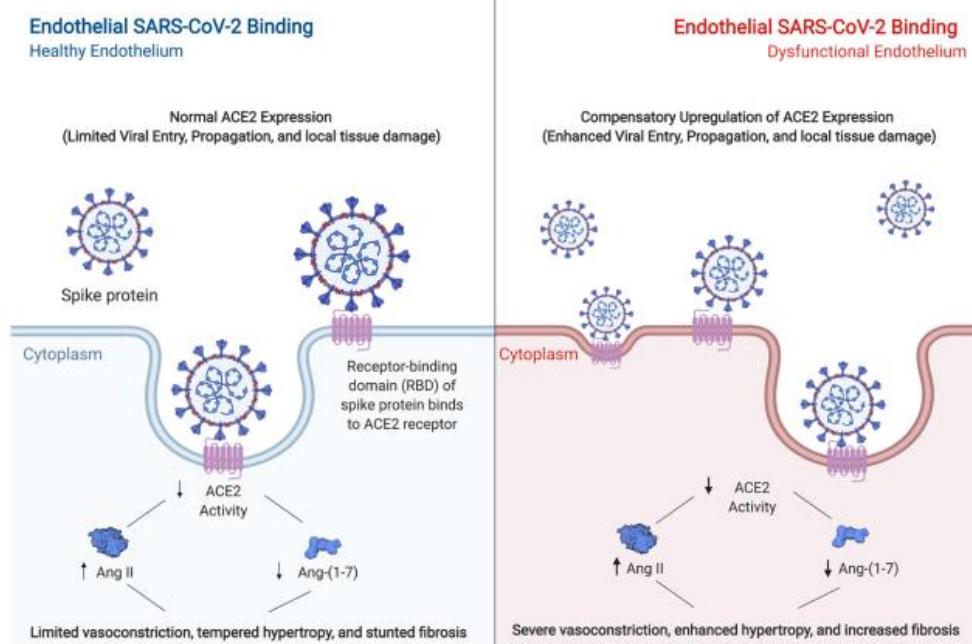


Figure 1. Proposed model of the pathological effect of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) on the endothelium. Left, under conditions of endothelial quiescence binding of SARS-CoV-2 is mediated in part by ACE2 (angiotensin-converting enzyme 2). Internalization of ACE2, and subsequent receptor interference, results in an upregulation of Ang-II (angiotensin II) and downregulation of Ang-(1-7) (angiotensin-[1-7]). Although contributing to vasoconstriction, hypertrophy, and fibrosis, limited expression of ACE2 within a relatively quiescent endothelium may result in limited viral entry and local and systemic dysfunction. Right, paradoxically, although a dysfunctional endothelium may have higher baseline levels of ACE2, enhanced viral entry may increase the degradation of ACE2 in the lysosome, enhancing inflammation and tissue damage. The resulting downregulation of ACE2 activity, upregulation of Ang-II, and downregulation of Ang-(1-7) thereby may have a starker induction of vasoconstriction, hypertrophy, inflammation, and fibrosis as compensatory mechanisms are abrogated. Arrow width corresponds to intensity. This figure was created with the assistance of [www.BioRender.com](http://www.BioRender.com).

| Biomarker                                  | Potential Mechanistic Insight   | Predicted Clinical Outcomes            |
|--|---|--|
| B-type natriuretic peptide (NT-proBNP/BNP) | Released into the circulation by cardiomyocytes in response to volume overload, increased cardiac stress, and hormone stimulation <sup>67</sup>   | Myocardial stress and dysfunction      |
| CK-MB                                      | Released by cardiomyocytes following cardiac damage or myocardial injury <sup>68</sup>  | Cardiac muscle damage                  |
| C-reactive protein                         | C-reactive protein is produced by the liver following IL-6 <sup>69</sup>  | Inflammation                           |
| D-dimer                                    | Fibrin degradation product that is produced during resolution of blood clot through fibrinolysis <sup>70</sup>  | Inflammation and coagulation           |
| Ferritin                                   | Released by the liver as a protective mechanism depriving microbes of iron <sup>71</sup>  | Associated with in-hospital mortality  |
| IL-6                                       | Proinflammatory cytokine that is elevated promptly following infection or tissue injury <sup>71</sup>   | Inflammation, elevated immune response |
| Troponin I/T                               | Troponin proteins anchor within the actin filaments of the heart to facilitate muscle contraction. It is normally present at low levels in the circulation, and it is released into the blood upon cardiomyocyte injury <sup>72</sup> | Cardiomyocyte damage                   |
| vWF  | vWF, predominantly released into the circulation by endothelial cells, may reflect the extent of endothelial activation or injury <sup>73</sup>   | Inflammation and risk of thrombosis    |

Table 1. Emerging Biomarkers of Poor Cardiovascular Outcomes in COVID-19

| Biomarker  | Disease                      | Potential Mechanistic Insight  | Predicted Clinical Outcomes  |
|--|------------------------------|--|--|
| Angiopoietin-2 (Angpt2)                                | Acute lung injury (ALI)/ARDS | Angpt2 is a growth factor produced by endothelial cells that regulates vascular permeability, promotes cell death, and disrupts vascularization  | Early increase of Angpt2 predicted the development of ARDS and identified patients at high risk for ALI <sup>77</sup>  |
|  |                              | Hypoxia and inflammation induce Angpt2 expression, suggesting the presence of endothelial injury <sup>78</sup>   | Angpt2 correlated with increased pulmonary oedema and mortality in patients with ARDS <sup>78</sup>  |
| Endocan or endothelial cell-specific molecule 1 (ESM1) | ARDS                         | ESM1 is a dermatan sulfate proteoglycan that is mainly secreted by pulmonary and kidney vascular endothelial cells in response to inflammatory cytokines <sup>79</sup>   | Elevated ESM1 can predict multiple organ dysfunction and mortality in ARDS patients <sup>80</sup>  |
|  |                              | GAGs are a component of the endothelial glycocalyx and circulating fragments suggest endothelial glycocalyx degradation<br><br>Heparin sulfate was increased following indirect lung injury (ie, sepsis and pancreatitis) and hyaluronic acid was increased following direct lung injury (ie, pneumonia) <sup>81</sup> | GAGs, heparan sulfate and hyaluronic acid, did not correlate with the severity of ALI/ARDS, however there was a correlation between plasma heparan sulfate concentration and length of stay in ICU <sup>81</sup>   |
| Soluble thrombomodulin (sTM)                           | ARDS                         | TM is an integral membrane protein expressed by endothelial cells and sTM is released following EC injury in ARDS patients <sup>82</sup>   | Higher levels of plasma sTM are associated with increased mortality in ARDS <sup>82</sup>  |
| Soluble intercellular adhesion molecule-1 (sICAM-1)    | ALI                          | sICAM-1 is widely secreted by multiple cell types, including vascular endothelial cells and respiratory epithelial cells at low levels   | Patients with ALI have higher levels of sICAM-1 in plasma and edema fluid than patients with hydrostatic pulmonary edema. Also, higher sICAM-1 levels were associated with poor clinical outcomes <sup>83</sup><br> |
|  |                              | Proinflammatory cytokines significantly increase sICAM-1 expression permitting its use as a marker of endothelial activation/dysfunction <sup>83</sup>   |  |
| von Willebrand Factor (vWF)                            | ARDS                         | vWF is a glycoprotein produced predominantly by endothelial cells and to a lesser extent by platelets  | Elevated plasma vWF levels in patients with ALI/ARDS were associated adverse outcomes, including death and organ failure <sup>73,84</sup>  |
|  |                              | vWF is released from preformed stores into the circulation in the context of endothelial activation or injury <sup>78</sup>  |  |

Table 1. Emerging Biomarkers of Poor Cardiovascular Outcomes in COVID-19

## MATERNAL TRANSMISSION OF SARS-COV-2 TO THE NEONATE, AND POSSIBLE ROUTES FOR SUCH TRANSMISSION: A SYSTEMATIC REVIEW AND CRITICAL ANALYSIS

Walker KF, O'Donoghue K, Grace N, Dorling J, Comeau JL, Li W, Thornton JG.. BJOG. 2020 Jun 12. doi: 10.1111/1471-0528.16362. Online ahead of print.

Level of Evidence: 3 - Local non-random sample

### BLUF

Researchers and physicians conducted a retrospective analysis of 49 studies with 666 neonates and 655 pregnant persons with confirmed or suspected COVID-19 across several countries from April through May 2020. They found that 28 out of 666 (4%) of neonates had SARS-CoV-2 infection postnatally, and 8 out of 28 (28.6%) positive neonates exhibited symptoms. 2.7% of vaginal births had SARS-CoV-2 positive neonates compared to 5.3% of Caesarean (Table 2). These results support evidence that postnatal SARS-CoV-2 mother-to-neonate transmission is low, that infection in neonates largely presents asymptotically, and suggests vaginal births do not seem to increase infection risk compared with Caesarean section.

### ABSTRACT

**BACKGROUND:** Early reports of COVID-19 in pregnancy described management by caesarean, strict isolation of the neonate and formula feeding, is this practise justified?

**OBJECTIVE:** To estimate the risk of the neonate becoming infected with SARS-COV-2 by mode of delivery, type of infant feeding and mother-infant interaction

**SEARCH STRATEGY:** Two biomedical databases were searched between September 2019 - June 2020.

**SELECTION CRITERIA:** Case reports or case series of pregnant women with confirmed COVID-19, where neonatal outcomes were reported.

**DATA COLLECTION AND ANALYSIS:** Data was extracted on mode of delivery, infant infection status, infant feeding and mother-infant interaction. For reported infant infection a critical analysis was performed to evaluate the likelihood of vertical transmission.

**MAIN RESULTS:** We included 49 studies which included 666 neonates and 655 women where information was provided on the mode of delivery and the infant's infection status. 28/666 (4%) neonates had confirmed COVID-19 infection postnatally. Of the 291 women who delivered vaginally, 8/292 (2.7%) neonates were positive. Of the 364 women who had a Caesarean birth, 20/374 (5.3%) neonates were positive. Of the 28 neonates with confirmed COVID-19 infection, 7 were breast fed, 3 formula fed, 1 was given expressed breast milk and in 17 neonates the method of infant feeding was not reported.

**CONCLUSIONS:** Neonatal COVID-19 infection is uncommon, uncommonly symptomatic, and the rate of infection is no greater when the baby is born vaginally, breastfed or allowed contact with the mother.

### FIGURES

**Table 2.** Mode of delivery and neonatal outcomes

|              | Centre/hospital (Study numbers from Appendix S1)   | Vaginal        |          |              |            |      | Caesarean      |          |              |         |      |
|--------------|--|----------------|----------|--------------|------------|------|----------------|----------|--------------|---------|------|
|              |  | Total neonates | Infected | Not infected | Not tested | Died | Total neonates | Infected | Not infected | No test | Died |
| <b>China</b> | Zhongnan Hospital of Wuhan University (1)  | 0              | 0        | 0            | 0          | 0    | 9              | 0        | 6            | 3       | 0    |
|              | Wuhan Children's Hospital (8)  | 0              | 0        | 0            | 0          | 0    | 3              | 3        | 0            | 0       | 0    |
|              | Maternal and Child Hospital of Hubei Province (30)   | 2              | 0        | 0            | 2          | 0    | 15             | 0        | 3            | 12      | 0    |
|              | Central Hospital of Wuhan (73)   | 5              | 0        | 5            | 0          | 0    | 18             | 0        | 18           | 0       | 0    |
|              | Union Hospital, Tongji Medical College, Huazhong University of Science and Technology (2a and 6) | 1              | 0        | 0            | 0          | 0    | 13             | 0        | 3            | 0       | 0    |
|              | Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (15)      | 0              | 0        | 0            | 0          | 0    | 7              | 1        | 2            | 4       | 0    |
|              | First Affiliated Hospital of Sun Yat-sen University (3)  | 3              | 0        | 3            | 0          | 0    | 10             | 0        | 10           | 0       | 1    |
|              | Renmin Hospital of Wuhan University (36 and 37)  | 3              | 0        | 3            | 0          | 0    | 17             | 0        | 17           | 0       | 0    |
|              | Affiliated Infectious Hospital of Soochow University, Suzhou. No GRID listing (19)               | 0              | 0        | 0            | 0          | 0    | 1              | 0        | 1            | 0       | 0    |
|              | Beijing YouAn Hospital (34)  | 1              | 0        | 1            | 0          | 0    | 0              | 0        | 0            | 0       | 0    |

|            |   |    |   |    |    |   |    |   |    |   |   |
|------------|---|----|---|----|----|---|----|---|----|---|---|
| USA        | No. 2 People's Hospital of Hefei City Affiliated to Anhui Medical University (62) | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
|            | New York Presbyterian & Columbia (27)   | 10 | 0 | 10 | 0  | 0 | 8  | 0 | 8  | 0 | 0 |
|            | MedStar Washington Hospital Center (21)   | 1  | 0 | 1  | 0  | 0 | 0  | 0 | 0  | 0 | 0 |
|            | Good Samaritan Hospital, Ohio (50)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
|            | Hospital of the University of Pennsylvania (65)                                   | 0  | 0 | 0  | 0  | 0 | 3  | 0 | 3  | 0 | 0 |
|            | Washington University in St. Louis, Missouri (69)                                 | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
|            | New York Winthrop Hospital (93)   | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
|            | New York University, Langone Health (85)  | 7  | 0 | 7  | 0  | 0 | 4  | 0 | 4  | 0 | 0 |
|            | San Francisco (89)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
|            | Livingstone, New Jersey (111)   | 0  | 0 | 0  | 0  | 0 | 2  | 1 | 1  | 0 | 0 |
|            | Stanford University Hospital (115)  | 1  | 0 | 1  | 0  | 0 | 0  | 0 | 0  | 0 | 0 |
|            | Weill Cornell Medicine, New York (118)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
|            | Michigan (123)  | 8  | 0 | 8  | 0  | 0 | 4  | 0 | 4  | 0 | 0 |
|            | Maimonides Medical Center, Brooklyn (113)   | 46 | 0 | 30 | 16 | 0 | 22 | 0 | 18 | 4 | 0 |
| Honduras   | Hospital Escuela de Tegucigalpa (18)  | 1  | 0 | 1  | 0  | 0 | 0  | 0 | 0  | 0 | 0 |
| Sweden     | Southern General Hospital, Stockholm (20)   | 0  | 0 | 0  | 0  | 0 | 2  | 0 | 2  | 0 | 0 |
| Korea      | Daegu Fatmal Hospital (22)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
| Turkey     | Ankara University (31)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
| Italy      | IRCCS Fondazione Policlinico Universitario Agostino Gemelli, Rome (76)            | 0  | 0 | 0  | 0  | 0 | 2  | 1 | 1  | 0 | 0 |
|            | Sant'Anna Hospital, Turin (79)  | 1  | 1 | 0  | 0  | 0 | 0  | 0 | 0  | 0 | 0 |
|            | Palma (109)   | 3  | 0 | 2  | 1  | 0 | 1  | 0 | 1  | 0 | 0 |
|            | 12 Italian hospitals (117)  | 34 | 3 | 31 | 0  | 0 | 22 | 1 | 21 | 0 | 0 |
| Portugal   | Hospital Pedro Hispano in Porto (105)   | 4  | 0 | 4  | 0  | 0 | 6  | 0 | 6  | 0 | 0 |
| Australia  | Gold Coast University Hospital (45)   | 1  | 0 | 1  | 0  | 0 | 0  | 0 | 0  | 0 | 0 |
| Canada     | Mount Sinai Hospital (48A)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 0  | 1 | 0 |
|            | Toronto (103)   | 0  | 0 | 0  | 0  | 0 | 1  | 1 | 0  | 0 | 0 |
| France     | Antoine Béclère hospital (48B)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 0  | 1 | 0 |
| Spain      | Madrid (125)  | 18 | 0 | 18 | 0  | 0 | 5  | 0 | 5  | 0 | 0 |
| Lima, Peru | British American Hospital (51)  | 0  | 0 | 0  | 0  | 0 | 1  | 1 | 0  | 0 | 0 |
| India      | Designated COVID hospital (58)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |
| Iran       | Vali-e-asr Hospital, Zanjan (43)  | 1  | 0 | 0  | 1  | 1 | 0  | 0 | 0  | 0 | 0 |
|            | Tehran/Raftab/Qom/Zanjan (67)   | 1  | 0 | 0  | 1  | 1 | 7  | 1 | 5  | 1 | 0 |
|            | Imam Khomeini Hospital, Sari (70)   | 0  | 0 | 0  | 0  | 0 | 1  | 1 | 0  | 0 | 0 |
|            | Imam Reza hospital of Tabriz (101)  | 0  | 0 | 0  | 0  | 0 | 1  | 0 | 1  | 0 | 0 |

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|             |  |     |   |     |    |   |     |    |     |    |   |
|-------------|--|-----|---|-----|----|---|-----|----|-----|----|---|
| UK          | UKOSS (92)                               | 107 | 4 | 102 | 0  | 5 | 161 | 8  | 148 | 0  | 0 |
| Belgium     | Cliniques Universitaires Saint Luc (100) | 0   | 0 | 0   | 0  | 0 | 1   | 1  | 0   | 0  | 0 |
| Netherlands | NethOSS (141)                            | 33  | 0 | 33  | 0  | 0 | 16  | 0  | 16  | 0  | 0 |
|             | TOTAL                                    | 292 | 8 | 261 | 21 | 7 | 374 | 20 | 313 | 26 | 1 |

## PREVENTION IN THE COMMUNITY

### THE EFFECT OF LARGE-SCALE ANTI-CONTAGION POLICIES ON THE COVID-19 PANDEMIC

Hsiang S, Allen D, Annan-Phan S, Bell K, Bolliger I, Chong T, Druckenmiller H, Huang LY, Hultgren A, Krasovich E, Lau P, Lee J, Rolf E, Tseng J, Wu T.. Nature. 2020 Jun 8. doi: 10.1038/s41586-020-2404-8. Online ahead of print.

Level of Evidence: Other - Modeling

#### BLUF

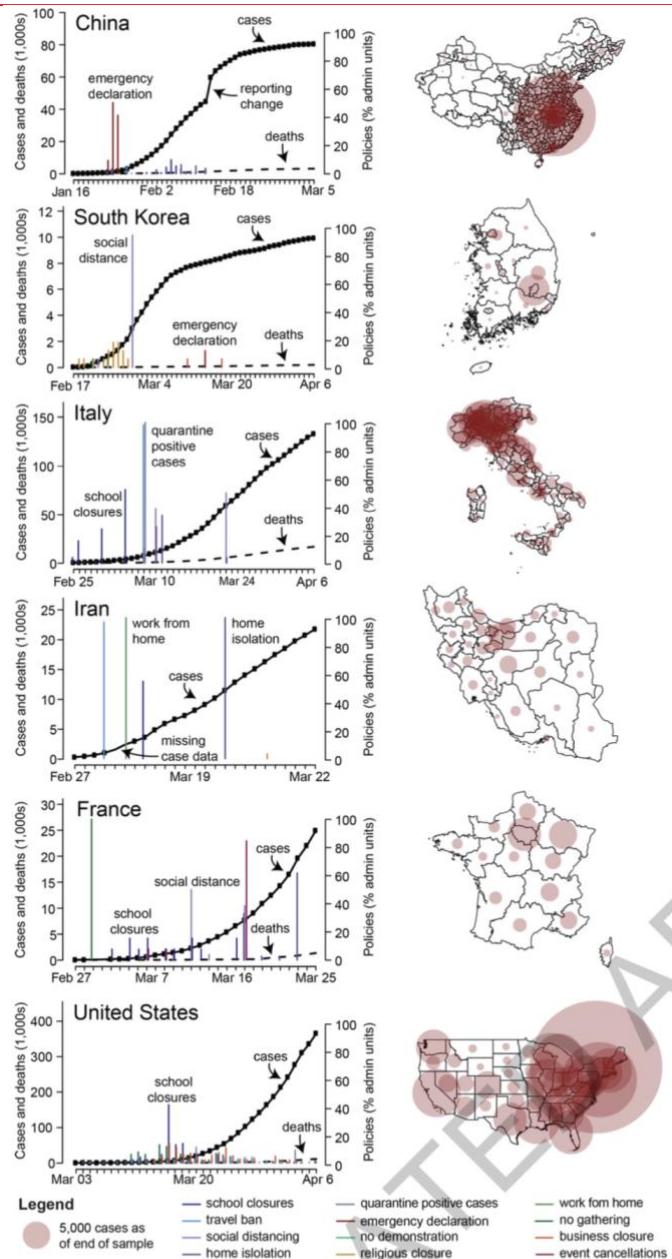
Authors from University of California, Berkeley examine the effects of wide-scale measures, comprising 1,717 local, regional, and national policies across six countries (China, France, Italy, Iran, South Korea, and US), on the transmission rate of COVID-19 using established reduced-form econometric modeling techniques and panel regression models, which revealed that these anti-contagion policies effectively lowered the transmission rate of the virus (Figures 1,2,3). The authors estimate that the measures implemented at the time of this study limited the expected rapid exponential growth and prevented as many as 285 million additional infections, suggesting that the anti-contagion policies implemented in these six countries had a measurable and beneficial effect and can be used to guide policy decisions in other countries around the world.

#### ABSTRACT

Governments around the world are responding to the novel coronavirus (COVID-19) pandemic1 with unprecedented policies designed to slow the growth rate of infections. Many actions, such as closing schools and restricting populations to their homes, impose large and visible costs on society, but their benefits cannot be directly observed and are currently understood only through process-based simulations2-4. Here, we compile new data on 1,717 local, regional, and national non-pharmaceutical interventions deployed in the ongoing pandemic across localities in China, South Korea, Italy, Iran, France, and the United States (US). We then apply reduced-form econometric methods, commonly used to measure the effect of policies on

economic growth<sup>5,6</sup>, to empirically evaluate the effect that these anti-contagion policies have had on the growth rate of infections. In the absence of policy actions, we estimate that early infections of COVID-19 exhibit exponential growth rates of roughly 38% per day. We find that anti-contagion policies have significantly and substantially slowed this growth. Some policies have different impacts on different populations, but we obtain consistent evidence that the policy packages now deployed are achieving large, beneficial, and measurable health outcomes. We estimate that across these six countries, interventions prevented or delayed on the order of 62 million confirmed cases, corresponding to averting roughly 530 million total infections. These findings may help inform whether or when these policies should be deployed, intensified, or lifted, and they can support decision-making in the other 180+ countries where COVID-19 has been reported<sup>7</sup>.

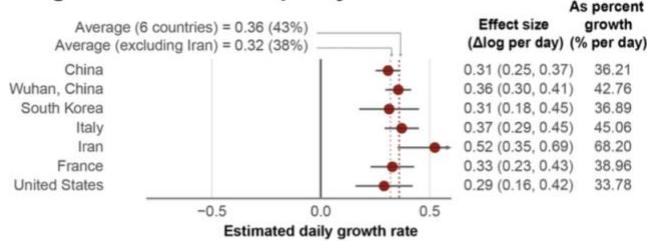
## FIGURES



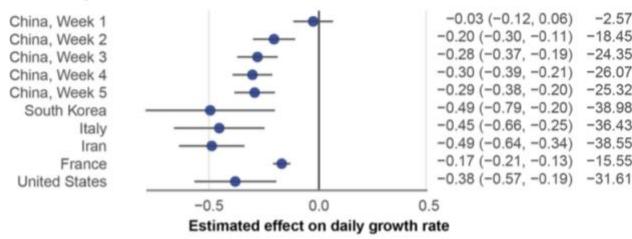
**Fig. 1 | Data on COVID-19 infections and large-scale anti-contagion policies.**

Left: Daily cumulative confirmed cases of COVID-19 (solid black line, left axis) and deaths (dashed black line) over time. Vertical lines are deployments of anti-contagion policies, with height indicating the number of administrative units instituting a policy that day (right axis). For display purposes only,  $\leq 5$  policy types are shown per country and missing case data are imputed unless all sub-national units are missing. Right: Maps of cumulative confirmed cases by administrative unit on the last date of each sample.

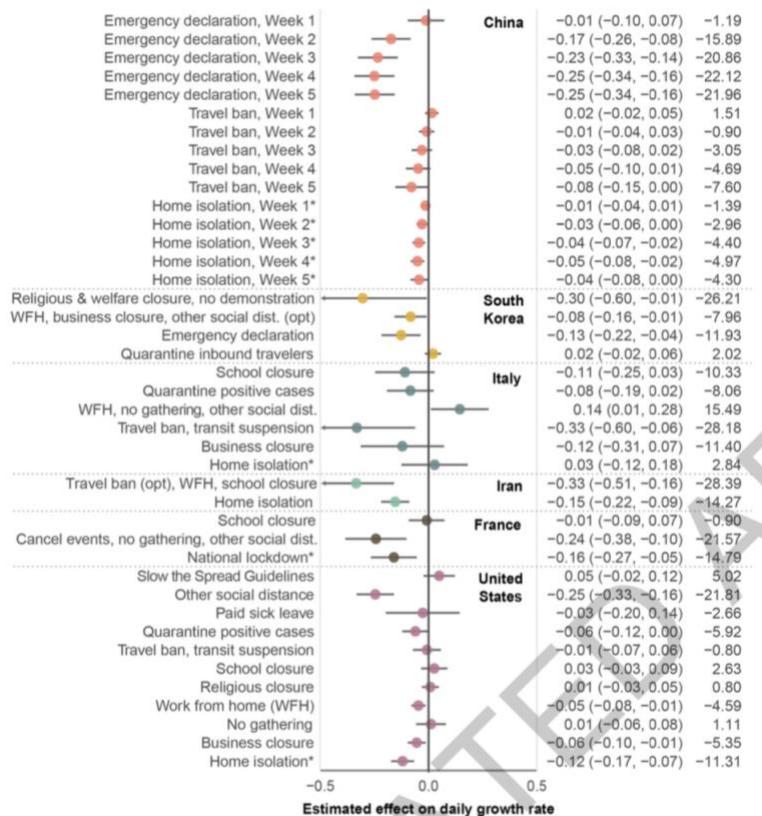
### a Infection growth rate without policy



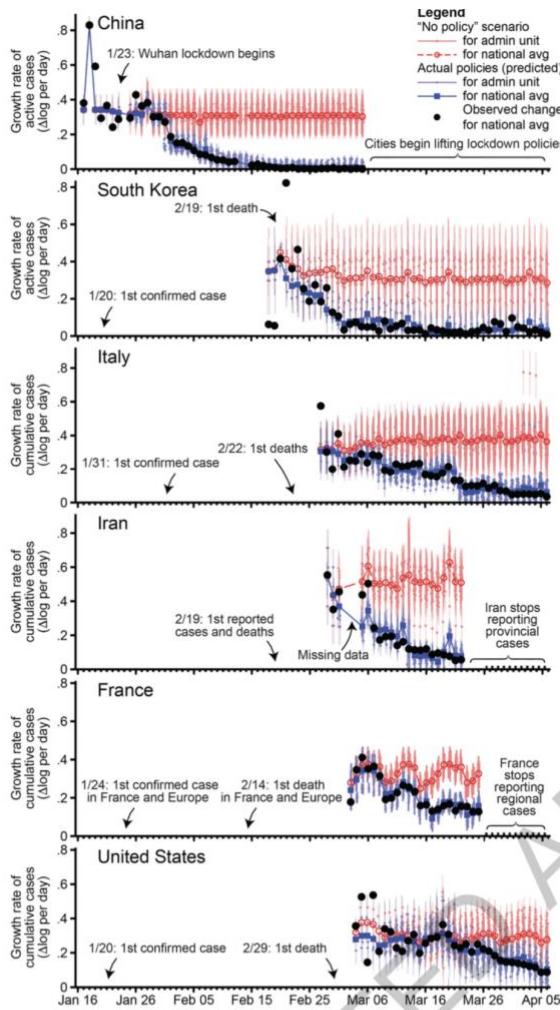
### b Effect of all policies combined



### c Effect of individual policies



**Fig. 2 | Empirical estimates of unmitigated COVID-19 infection growth rates and the effect of anti-contagion policies.** Markers are country-specific estimates, whiskers are 95% CI. Columns report effect sizes as a change in the continuous-time growth rate (95% CI in parentheses) and the day-over-day percentage growth rate. (a) Estimates of daily COVID-19 infection growth rates in the absence of policy (dashed lines = averages with and without Iran, both excluding Wuhan-specific estimate). (b) Estimated combined effect of all policies on infection growth rates. (c) Estimated effects of individual policies or policy groups on the daily growth rate of infections, jointly estimated and ordered roughly chronologically within each country. \*Reported effect of “home isolation” includes effects of other implied policies (see Methods). China: N = 3669; South Korea: N = 595, Italy: N = 2898, Iran: N = 548, France: N = 270, US: N = 1238.



**Fig. 3 | Estimated infection growth rates based on actual anti-contagion policies and in a “no policy” counterfactual scenario.** Predicted daily growth rates of active (China, South Korea) or cumulative (all others) COVID-19 infections based on the observed timing of all policy deployments within each country (blue) and in a scenario where no policies were deployed (red). The difference between these two predictions is our estimated effect of actual anti-contagion policies on the growth rate of infections. Small markers are daily estimates for sub-national administrative units (vertical lines are 95% CI). Large markers are national averages. Black circles are observed daily changes in  $\log(\text{infections})$ , averaged across administrative units. Sample sizes are the same as Figure 2.

## PREVENTION IN THE HOSPITAL

### PERSONAL PROTECTIVE EQUIPMENT AND CONCERN OVER AIRBORNE TRANSMISSION OF COVID-19: A REPLY

Cook TM.. Anaesthesia. 2020 Jun 11. doi: 10.1111/anae.15143. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

#### BLUF

This English author who proposed a guideline for PPE use in high-risk procedures replied to correspondence from J. Brown and C. Pope about the risk of transmission of SARS-CoV-2 from cough/sneeze compared to high-risk procedure-related aerosol generation. Contrary to current body of evidence, the author reports cough/sneeze will generate aerosol particles but does not believe these would be sufficient for viral transmission. He recommends PPE in high-risk procedures (tracheal intubation,

mask ventilation, and tracheostomy/non-invasive ventilation) and advises rationing PPE in basic clinical interactions or other procedures (see Table 2 from doi:10.1111/anae.15071).

## FIGURES

Table 2 Modes of viral transmission, settings where they are relevant and matched types of personal protective equipment.

| Mode of transmission              | When to use in a patient being treated at COVID-19 +ve | What is it?   |
|-----------------------------------|--|---|
| Contact precautions               | > 2 m away from patient                                | Gloves<br>Apron   |
| Droplet precautions               | Within 2 m of patient                                  | Gloves<br>Apron<br>Fluid-resistant surgical mask<br>± Eye protection <sup>a</sup> (risk assess) |
| Airborne precautions <sup>b</sup> | Aerosol generating procedure                           | Gloves<br>Fluid-repellent long sleeved gown<br>Eye protection <sup>c</sup><br>FFP3 mask         |

The levels of protection are increasing: droplet precautions are also designed to prevent contact transmission; airborne precautions also cover contact and droplet transmission.

<sup>a</sup>Eye protection may be goggles or a visor. Personal spectacles are not sufficient.

<sup>b</sup>In "hot spots" where aerosol generating procedure are regularly undertaken airborne precautions may be worn on a sessional basis: the normal attire is supplemented by a plastic gown and this and the gloves are changed between patients [2].

Table 2. Modes of viral transmission, settings where they are relevant and matched types of personal protective equipment.  
From original article Brown and Cook 2020, doi:10.1111/anae.15071

## CRITICAL CARE

## CLEARANCE OF CHLOROQUINE AND HYDROXYCHLOROQUINE BY THE SERAPH® 100 MICROBIND® AFFINITY BLOOD FILTER - APPROVED FOR THE TREATMENT OF COVID-19 PATIENTS

Seffer MT, Martens-Lobenhoffer J, Schmidt JJ, Eden G, Bode-Böger SM, Kielstein JT.. Ther Apher Dial. 2020 Jun 19. doi: 10.1111/1744-9987.13549. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

### BLUF

Researchers from Germany investigated the clearance of chloroquine and hydroxychloroquine from human plasma by the Seraph 100 Microbind Affinity blood filter (a U.S. Food and Drug Administration approved extra-corporeal blood purification device) on plasma samples obtained from 5 patients receiving therapeutic plasma exchange for various indications, to determine if the Seraph would alter blood levels of these medications. Using UV detection of these samples at 5, 10, 15, 30, 60, and 120 minute intervals (Figure), They found the median plasma clearance for chloroquine and hydroxychloroquine was statistically insignificant at the end of 120 min with 1.71 and 1.79 ml/min, respectively. The authors conclude that these results suggest that standard dose adjustments for these drugs are not necessary in COVID-19 patients receiving Seraph treatment.

### ABSTRACT

On April 17th 2020 the US Food and Drug Administration granted Coronavirus Disease 2019 (COVID-19) emergency use authorizations for the Seraph 100 Microbind Affinity Blood Filter. The medical device is aimed to treat critically ill COVID-19 patients with confirmed or imminent respiratory failure. The aim of this life size in vitro pharmacokinetic study was to investigate the in-vitro adsorption of chloroquine and hydroxychloroquine from human plasma using equipment that is also used at the bedside. After start of the hemoperfusion Pre (C<sub>Pre</sub>) Seraph plasma levels were obtained at 5 (C<sub>5</sub>), 10 (C<sub>10</sub>), 15 (C<sub>15</sub>), 30 (C<sub>30</sub>), 60 (C<sub>60</sub>) and 120 (C<sub>120</sub>) minutes into the procedure. At two timepoints (5 min and 120 min) post (C<sub>Post</sub>) Seraph plasma levels were determined that were used to calculate the plasma clearance. Both drugs were determined using a validated HPLC method Median [IQR] plasma clearance of the Seraph for chloroquine / hydroxychloroquine was 1.71 [0.51-4.38] ml/min / 1.79 [0.21-3.68] ml/min respectively. The lack of elimination was also confirmed by the fact that plasma levels did not change over the 120 min treatment. As neither chloroquine nor hydroxychloroquine were removed by the treatment with the Seraph dose adjustments in COVID-19 patients undergoing this treatment are not necessary. This article is protected by copyright. All rights reserved.

### FIGURES

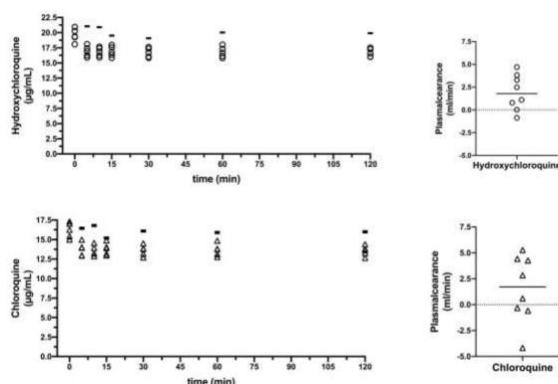


Figure 1. Time course of hydroxychloroquine and chloroquine plasma concentrations during hemoperfusion using the Seraph® 100 Microbind® Affinity blood filter (left upper and lower graph; n=5). The horizontal bar in both graphs is

depicting the control sample that was not pumped through the Seraph®. The right upper and lower graph depict the calculated plasma clearance of the Seraph® for hydroxychloroquine and chloroquine (n=8)."

## MEDICAL SUBSPECIALTIES

### CARDIOLOGY

#### ASSOCIATION BETWEEN RENIN-ANGIOTENSIN SYSTEM INHIBITORS AND COVID-19 COMPLICATIONS

Liabeuf S, Moragny J, Bennis Y, Batteux B, Brochot E, Schmit JL, Lanoix JP, Andrejak C, Ganry O, Slama M, Maizel J, Mahjoub Y, Masmoudi K, Gras-Champel V.. Eur Heart J Cardiovasc Pharmacother. 2020 Jun 12:pva062. doi: 10.1093/eihcvp/pva062. Online ahead of print.

Level of Evidence: 4 - Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)

#### BLUF

This retrospective cohort study conducted at Amiens University Hospital in Amiens, France evaluated 268 hospitalized COVID-19 confirmed patients between 28 February 2020 and 30 March 2020 to identify factors associated with poor outcomes as measured by Intensive Care Unit (ICU) requirements. Notably, treatment with renin-angiotensin system inhibitors (RASIs; i.e. angiotensin-converting enzyme inhibitors [ACEIs] and angiotensin II type I receptor blockers [ARBs]) was associated with an increased risk of severe COVID-19 exacerbation among patients taking RASI compared to patients who are not (odds ratio [OR] 1.97, 95% confidence interval [CI] 1.03–3.78). Patients treated at baseline with a RASI had more than twice the risk of an ICU admission when controlled for age, sex, BMI, and coronary artery disease (Figure 2), (OR 2.28, 95% CI 1.17–4.42). The authors acknowledge the limitations of their study, explaining that the observed associations may be attributed to unknown or unmeasured confounders. Thus, future studies are needed to evaluate the association of RASI use and COVID-19 disease severity.

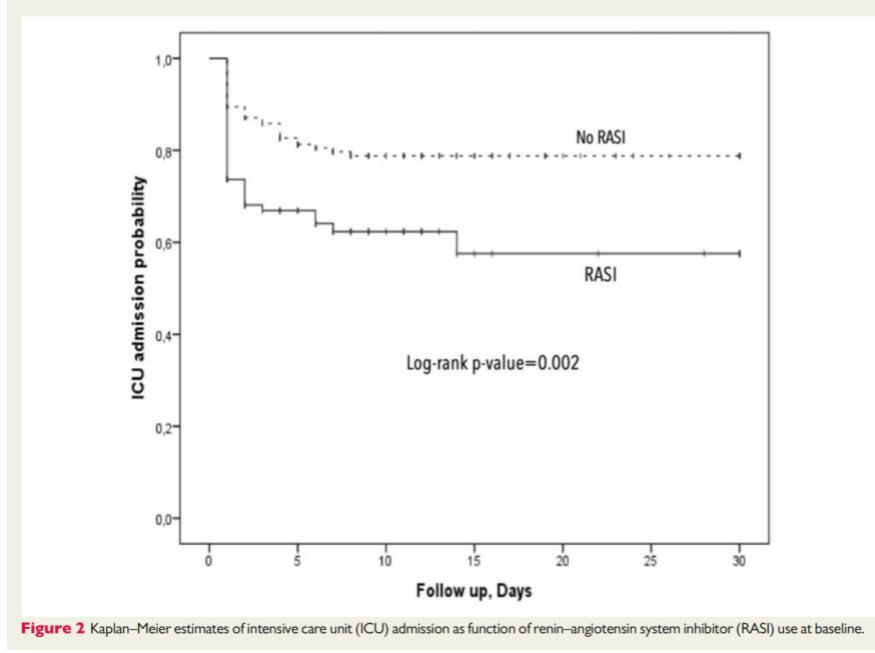
#### ABSTRACT

**AIMS:** To describe the characteristics of patients hospitalized with COVID-19 (including their long-term at-home medication use), and compare them with regard to the course of the disease. To assess the association between renin-angiotensin system inhibitors (RASIs) and disease progression and critical outcomes.

**METHODS AND RESULTS:** All consecutive hospitalized patients with laboratory-confirmed COVID-19 in a university hospital in Amiens (France) were included in this study. The primary composite endpoint was admission to an intensive care unit (ICU) or death before ICU admission. Univariable and multivariable logistic regression models were used to identify factors associated with the composite endpoint. Between 28 February 2020 and 30 March 2020, a total of 499 local patients tested positive for SARS-CoV-2. Of these, 231 were not hospitalized {males 33%; median [interquartile range (IQR)] age: 44 (32-54)}, and 268 were hospitalized [males 58%; median (IQR) age: 73 (61-84)]. A total of 116 patients met the primary endpoint: 47 died before ICU admission, and 69 were admitted to the ICU. Patients meeting the primary endpoint were more likely than patients not meeting the primary endpoint to have coronary heart disease and to have been taking RASIs; however, the two subsets of patients did not differ with regard to median age. After adjustment for other associated variables, the risk of meeting the composite endpoint was 1.73 times higher (odds ratio 1.73, 95% confidence interval 1.02-2.93) in patients treated at baseline with a RASI than in patients not treated with this drug class. This association was confirmed when the analysis was restricted to patients treated with antihypertensive agents.

**CONCLUSIONS:** We highlighted a potential safety signal for RASIs, the long-term use of which was independently associated with a higher risk of severe COVID-19 and a poor outcome. Due to the widespread use of this important drug class, formal proof based on clinical trials is needed to better understand the association between RASIs and complications of COVID-19.

## FIGURES



**Figure 2** Kaplan-Meier estimates of intensive care unit (ICU) admission as function of renin-angiotensin system inhibitor (RASI) use at baseline.

**Table I** Baseline characteristics of the study population

|  | All hospitalized<br>(n = 268) | Achievement of the composite endpoint |                  | P-value | Type of composite endpoint | Patients with missing data |
|--|-------------------------------|---------------------------------------|------------------|---------|----------------------------|----------------------------|
|  |                               | No<br>(n = 152)                       | Yes<br>(n = 116) |         |                            |                            |
| Age (years)                              |                               |                                       |                  |         |                            |                            |
| <18                                      | 73 (61–84)                    | 73 (58–82)                            | 73 (63–86)       | 0.124   | 86 (81–89)                 | 66 (57–74)                 |
| 18 to 44                                 | 4 (2)                         | 4 (3)                                 | 0 (0)            |         | 0 (0)                      | 0 (0)                      |
| 45 to 64                                 | 17 (6)                        | 11 (7)                                | 6 (5)            |         | 0 (0)                      | 6 (8)                      |
| 65 to 74                                 | 62 (23)                       | 34 (22)                               | 28 (25)          |         | 1 (2)                      | 27 (39)                    |
| ≥75                                      | 60 (22)                       | 34 (22)                               | 26 (22)          |         | 7 (15)                     | 19 (28)                    |
| Male sex                                 | 125 (47)                      | 69 (46)                               | 56 (48)          |         | 39 (83)                    | 17 (25)                    |
| Male sex                                 | 156 (58)                      | 83 (55)                               | 73 (63)          | 0.171   | 24 (51)                    | 49 (71)                    |
| Body mass index (kg/m <sup>2</sup> )     | 28 (24–33)                    | 28 (23–33)                            | 28 (24–33)       | 0.348   | 25 (21–30)                 | 29 (26–34)                 |
| ≥ 30 kg/m <sup>2</sup>                   | 82 (39)                       | 44 (38)                               | 38 (40)          |         | 10 (27)                    | 28 (47)                    |
| Lean                                     | 69 (32)                       | 41 (35)                               | 28 (30)          |         | 20 (56)                    | 8 (14)                     |
| Overweight                               | 61 (29)                       | 32 (27)                               | 29 (30)          |         | 6 (17)                     | 23 (39)                    |
| Moderately obese                         | 51 (24)                       | 29 (25)                               | 22 (23)          |         | 7 (19)                     | 15 (25)                    |
| Severely obese                           | 31 (15)                       | 15 (13)                               | 16 (17)          |         | 3 (8)                      | 13 (22)                    |
| Smoking status                           |                               |                                       |                  | 0.699   |                            | 0%                         |
| Non-smoker                               | 215 (80)                      | 124 (82)                              | 91 (78)          |         | 41 (87)                    | 50 (73)                    |
| Former smoker                            | 44 (17)                       | 4 (3)                                 | 20 (17)          |         | 4 (9)                      | 16 (23)                    |
| Current smoker                           | 9 (3)                         | 24 (15)                               | 5 (4)            |         | 2 (4)                      | 3 (4)                      |
| Pregnancy                                | 1 (1)                         | 0 (0)                                 | 1 (1)            | 0.247   | 0 (0)                      | 1 (1)                      |
| Concomitant disorder                     |                               |                                       |                  |         |                            | 0.7%                       |
| Any disorder                             | 221 (83)                      | 121 (79)                              | 100 (87)         | 0.115   | 45 (98)                    | 55 (80)                    |
| Hypertension                             | 152 (57)                      | 80 (53)                               | 71 (62)          | 0.116   | 29 (61)                    | 42 (62)                    |
| Coronary heart disease                   | 33 (12)                       | 11 (7)                                | 22 (19)          | 0.003   | 10 (23)                    | 12 (18)                    |
| Stroke                                   | 37 (14)                       | 22 (15)                               | 15 (13)          | 0.743   | 8 (18)                     | 7 (10)                     |
| Cardiac insufficiency                    | 30 (11)                       | 17 (11)                               | 13 (11)          | 0.955   | 5 (13)                     | 8 (12)                     |
| Cardiac surgery                          | 26 (10)                       | 13 (9)                                | 13 (11)          | 0.438   | 4 (10)                     | 9 (13)                     |
| Other cardiovascular disease             | 74 (28)                       | 40 (26)                               | 34 (30)          | 0.527   | 15 (38)                    | 19 (28)                    |
| Chronic obstructive pulmonary disease    | 26 (10)                       | 11 (7)                                | 13 (13)          | 0.108   | 10 (25)                    | 3 (4)                      |
| Asthma                                   | 14 (5)                        | 8 (5)                                 | 5 (5)            | 0.989   | 3 (8)                      | 2 (3)                      |
| Restrictive lung disease                 | 16 (6)                        | 7 (5)                                 | 7 (7)            | 0.264   | 2 (5)                      | 5 (7)                      |
| Active cancer                            | 16 (6)                        | 12 (8)                                | 3 (4)            | 0.137   | 2 (5)                      | 1 (1)                      |
| Cured cancer                             | 22 (8)                        | 10 (7)                                | 11 (11)          | 0.247   | 7 (18)                     | 4 (6)                      |
| Chronic kidney disease                   | 19 (7)                        | 9 (6)                                 | 10 (9)           | 0.372   | 4 (10)                     | 6 (9)                      |
| Dialysis                                 | 5 (2)                         | 3 (2)                                 | 2 (2)            | 0.896   | 0 (0)                      | 2 (3)                      |
| Cirrhosis                                | 1 (1)                         | 0 (0)                                 | 1 (1)            | 0.247   | 1 (2)                      | 0 (0)                      |
| Type 1 diabetes mellitus                 | 8 (3)                         | 3 (2)                                 | 5 (4)            | 0.254   | 1 (2)                      | 4 (6)                      |
| Type 2 diabetes mellitus                 | 47 (18)                       | 27 (18)                               | 20 (18)          | 0.603   | 1 (2)                      | 19 (27)                    |
| Hypothyroidism                           | 26 (10)                       | 16 (11)                               | 10 (9)           | 0.633   | 7 (18)                     | 3 (4)                      |
| Chronic inflammatory disease             | 9 (3)                         | 4 (3)                                 | 5 (4)            | 0.434   | 1 (2)                      | 4 (6)                      |
| Immunosuppressant drugs                  | 10 (4)                        | 8 (5)                                 | 2 (2)            | 0.402   | 1 (2)                      | 1 (1)                      |
| Immunosuppression due to HIV             | 1 (1)                         | 1 (1)                                 | 1 (1)            | 0.353   | 0 (0)                      | 0 (0)                      |
| Immunosuppression due to transplantation | 2 (1)                         | 1 (1)                                 | 1 (1)            | 0.501   | 0 (0)                      | 1 (1)                      |
| Treated haematological malignancy        | 3 (1)                         | 3 (1)                                 | 0 (0)            | 0.165   | 0 (0)                      | 0 (0)                      |
| Neurodegenerative disease                | 60 (23)                       | 35 (23)                               | 24 (21)          | 0.479   | 23 (51)                    | 1 (1)                      |

Median (IQR) or n (%).  
Body mass index category: lean (18.5 to <25 kg/m<sup>2</sup>), overweight (25 to <30 kg/m<sup>2</sup>), moderately obese (30 to 35 kg/m<sup>2</sup>), and severely obese (≥35 kg/m<sup>2</sup>).

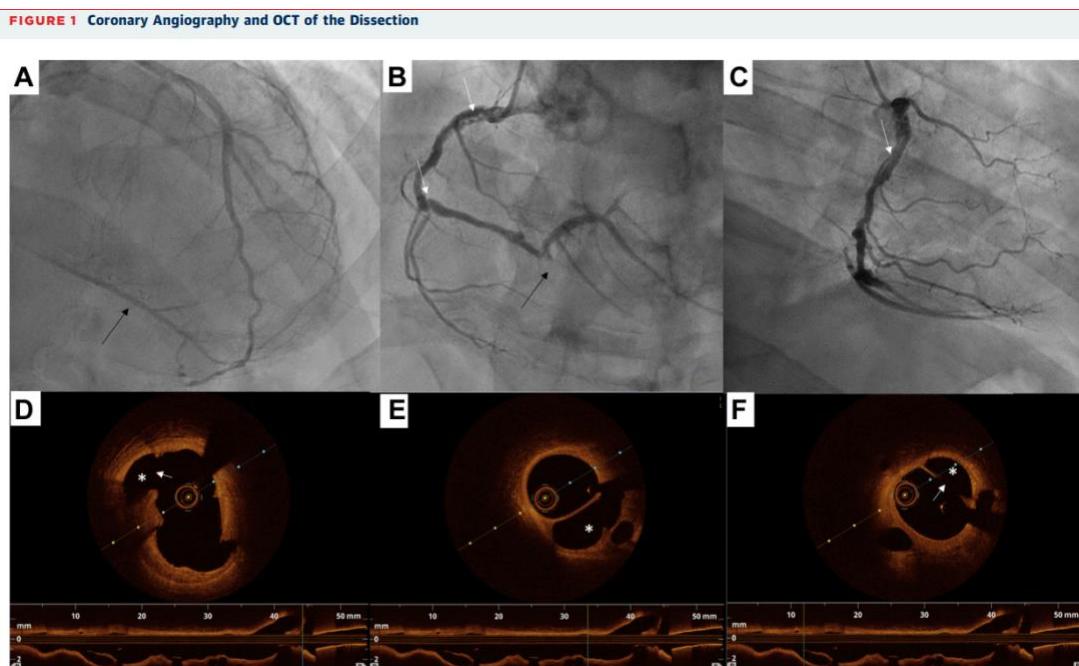
# SPONTANEOUS CORONARY ARTERY DISSECTION IN A PATIENT WITH COVID-19

32553344. Spontaneous Coronary Artery Dissection in a Patient With COVID-19  
Level of Evidence: 5 - Case report

## BLUF

A case report presented by cardiologists at University of Lyon in France describes a 55-year-old man with COVID-19 who developed chest pain 48 hours after admission. A 12-lead ECG displayed inverted T-waves in the inferior leads and coronary angiography demonstrated chronic total occlusion of the posterior descending artery with a spontaneous dissecting coronary hematoma with intimal tear in the mid-right coronary artery (Figure 1). The authors suggest SARS-CoV-2 may trigger acute coronary syndrome via significant systemic and local vascular inflammation and that physicians should be aware of this and other rare sequelae of SARS-CoV-2 infection.

## FIGURES



(A) Coronary angiogram of the left anterior descending artery with epicardial collateral to the posterior descending artery (black arrow). (B and C) Total chronic occlusion of the posterior descending artery (black arrow), and suspected intimal tear in the mid right coronary artery (white arrows). (D, E, and F) Optical coherence tomography (OCT) on the proximal (D), middle (E), and distal (F) part of the dissection (asterisks indicate the false lumen, white arrows show intimal rupture).

## RHEUMATOLOGY

### PREVALENCE OF HOSPITAL PCR-CONFIRMED COVID-19 CASES IN PATIENTS WITH CHRONIC INFLAMMATORY AND AUTOIMMUNE RHEUMATIC DISEASES

Pablos JL, Abasolo L, Alvaro-Gracia JM, Blanco FJ, Blanco R, Castrejón I, Fernandez-Fernandez D, Fernandez-Gutierrez B, Galindo-Izquierdo M, Gonzalez-Gay MA, Manrique-Arija S, Mena Vázquez N, Mera Varela A, Retuerto M, Seijas-Lopez A.. Ann Rheum Dis. 2020 Jun 12:annrheumdis-2020-217763. doi: 10.1136/annrheumdis-2020-217763. Online ahead of print.

Level of Evidence: 1 - Local and current random sample surveys (or censuses)

#### BLUF

Researchers in Spain conducted a retrospective analysis of 26,131 patients with rheumatic disease in seven different facilities between April 7 and April 17, 2020. Patients with chronic inflammatory disease had higher incidence of polymerase chain reaction (PCR) positive COVID-19 compared with a hospital reference population (0.76% vs 0.58%, odds ratio 1.32 p<0.0001; Table 1 and Figure 1). Patients with spondyolarthritis and patients taking a targeted synthetic disease-modifying antirheumatic drug (jakinibs or other biological agents) showed significant increase (p<0.01), while patients with inflammatory arthritis or systemic lupus erythematosus did not. Notably, some diagnostic groups had significant increased age. These results suggest patients with chronic systemic autoimmune or immune-mediated diseases may be at higher risk for SARS-CoV-2 infection, with probable confounding factors such as age, therapies, and disease-specific factors.

#### ABSTRACT

**BACKGROUND:** The susceptibility of patients with rheumatic diseases and the risks or benefits of immunosuppressive therapies for COVID-19 are unknown.

**METHODS:** We performed a retrospective study with patients under follow-up in rheumatology departments from seven hospitals in Spain. We matched updated databases of rheumatology patients with severe acute respiratory syndrome coronavirus 2-positive PCR tests performed in the hospital to the same reference populations. Rates of PCR+ confirmed COVID-19 were compared among groups.

**RESULTS:** Patients with chronic inflammatory diseases had 1.32-fold higher prevalence of hospital PCR+ COVID-19 than the reference population (0.76% vs 0.58%). Patients with systemic autoimmune or immune-mediated disease (AI/IMID) showed a significant increase, whereas patients with inflammatory arthritis (IA) or systemic lupus erythematosus did not. COVID-19 cases in some but not all diagnostic groups had older ages than cases in the reference population. Patients with IA on targeted-synthetic or biological disease-modifying antirheumatic drugs (DMARDs), but not those on conventional-synthetic DMARDs, had a greater prevalence despite a similar age distribution.

**CONCLUSION:** Patients with AI/IMID show a variable risk of hospital-diagnosed COVID-19. Interplay of ageing, therapies and disease-specific factors seem to contribute. These data provide a basis to improve preventive recommendations to rheumatic patients and to analyse the specific factors involved in COVID-19 susceptibility.

#### FIGURES

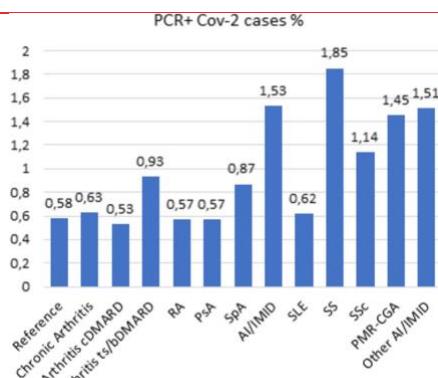


Figure 1: Rates of hospital COVID-19 in patients with chronic arthritis, autoimmune diseases and reference population. Prevalence of hospital PCR-confirmed cases of COVID-19 infection in patients with chronic IA or AI/IMID diseases (n=26 131)

in seven reference hospitals in Spain, compared with that in the reference population of the same hospitals ( $n=2.9$  million). The AI/IMID group includes all diagnoses but PMR-CGA, and other AI/IMID of the less frequent diseases as indicated in the

Patients and methods section. AI/IMID, autoimmune or immune-mediated disease; ts/bDMARD, targeted synthetic or biological disease-modifying antirheumatic drug; cDMARD, conventional disease-modifying antirheumatic drug; csDMARD, conventional-synthetic disease-modifying antirheumatic drug; IA, inflammatory arthritis; PMR-CGA, polymyalgia rheumatica or giant cell arteritis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SpA, spondyloarthritis; SS, Sjögren's syndrome; SSc, systemic sclerosis.

**Table 1**  
Rates of hospital PCR-confirmed COVID-19 cases in patients with different rheumatic diseases

|                          | n            | COVID-19 prevalence % (CI) | OR (CI) versus reference§ | Median age of cases (QI) | Sex (female, %) |
|--------------------------|--------------|----------------------------|---------------------------|--------------------------|-----------------|
| Reference population     | 2 899<br>935 | 0.58 (0.57 to 0.59)        | —                         | 55 (43–69)†              | 44†             |
| All rheumatic diseases   | 26 131       | 0.76 (0.66 to 0.87)        | 1.32 (1.15–1.52)*         | 65 (53–78)*              | 56              |
| Inflammatory arthritis   | 19 975       | 0.63 (0.53 to 0.75)        | 1.06 (0.91–1.30)‡         | 63 (53–75)*              | 50              |
| Arthritis csDMARD        | 7558         | 0.53 (0.38 to 0.72)        | 1.10 (0.80–1.50)‡         | 69 (52–79)*              | 39              |
| Arthritis tsDMARD/bDMARD | 5802         | 0.94 (0.71 to 1.22)        | 1.60 (1.23–2.10)**        | 60 (51–70)***            | 53              |
| RA                       | 10 927       | 0.57 (0.44 to 0.73)        | 0.98 (0.76–1.26)‡         | 67 (56–79)*              | 56              |
| PsA                      | 4777         | 0.57 (0.37 to 0.82)        | 0.97 (0.67–1.43)‡         | 57 (51–78)‡              | 48              |
| SpA                      | 4268         | 0.89 (0.63 to 1.22)        | 1.54 (1.11–2.13)***       | 59 (49–69)‡              | 43              |
| AI/IMID                  | 4781         | 1.11 (0.83 to 1.45)        | 1.92 (1.47–2.53)*         | 60 (51–73)***            | 68              |
| AI/IMID non-SLE          | 2528         | 1.54 (1.10 to 2.10)        | 2.69 (1.96–3.69)*         | 60 (54–76)*              | 65              |
| SLE                      | 2253         | 0.62 (0.34 to 1.04)        | 1.07 (0.63–1.80)‡         | 51 (42–66)*              | 77              |
| PMR-CGA                  | 1378         | 1.45 (0.89 to 2.23)        | 2.53 (1.62–3.93)*         | 84 (75–86)**             | 57              |

• \* $P<0.0001$ , \*\* $p<0.001$ , \*\*\* $p<0.01$ .

• †Calculated in a subset of reference population cases ( $n=3,800$ ).

• ‡Non-significant difference.

• §Odds ratio (OR) with 95% confidence intervals (CI), and all comparisons were between each group and the reference population.

• AI/IMID, autoimmune or immune-mediated disease; bDMARD, biological disease-modifying antirheumatic drug; csDMARD, conventional-synthetic disease-modifying antirheumatic drug; PMR-CGA, polymyalgia rheumatica or giant cell arteritis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SpA, spondyloarthritis; tsDMARD, targeted-synthetic disease-modifying antirheumatic drug.

## PEDIATRICS

### MANAGEMENT OF FEVER IN INFANTS AND YOUNG CHILDREN

Hamilton JL, Evans SG, Bakshi M.. Am Fam Physician. 2020 Jun 15;101(12):721-729.

Level of Evidence: Other - Guidelines and Recommendations

#### BLUF

In this article, experts from Drexel University College of Medicine formulate a set of guidelines and recommendations for evaluation and management of febrile children younger than 3 years old as well as for empiric antibiotic therapy for children younger than 36 months (Tables 3 and 4). The authors also discuss various risk assessment tools for infants one to three months of age, which can inform clinical decisions and management strategies (Table 2).

#### ABSTRACT

Despite dramatic reductions in the rates of bacteremia and meningitis since the 1980s, febrile illness in children younger than 36 months continues to be a concern with potentially serious consequences. Factors that suggest serious infection include age younger than one month, poor arousability, petechial rash, delayed capillary refill, increased respiratory effort, and overall physician assessment. Urinary tract infections are the most common serious bacterial infection in children younger than three

years, so evaluation for such infections should be performed in those with unexplained fever. Abnormal white blood cell counts have poor sensitivity for invasive bacterial infections; procalcitonin and C-reactive protein levels, when available, are more informative. Chest radiography is rarely recommended for children older than 28 days in the absence of localizing signs. Lumbar puncture is not recommended for children older than three months without localizing signs; it may also be considered for those from one to three months of age with abnormal laboratory test results. Protocols such as Step-by-Step, Laboratory Score, or the Rochester algorithms may be helpful in identifying low-risk patients. Rapid influenza testing and tests for coronavirus disease 2019 (COVID-19) may be of value when those diseases are circulating. When empiric treatment is appropriate, suggested antibiotics include ceftriaxone or cefotaxime for infants one to three months of age and ampicillin with gentamicin or with cefotaxime for neonates. For children three months to three years of age, azithromycin or amoxicillin is recommended if pneumonia is suspected; for urinary infections, suggested antibiotics are cefixime, amoxicillin/clavulanate, or trimethoprim/sulfamethoxazole. Choice of antibiotics should reflect local patterns of microbial resistance.

## FIGURES

TABLE 2

**Risk Assessment Tools for Infants One to Three Months of Age**

| Laboratory Score <sup>a</sup> (requires CRP, PCT)                               | Step-by-Step <sup>b</sup> (requires CRP, PCT)   | Rochester Criteria <sup>c,d</sup> (CRP, PCT not required)   |
|---|---|---|
| If ill-appearing: high risk   | Assess the following in the order shown:  | If ill-appearing: high risk   |
| Obtain PCT and CRP measurements and urine dipstick                              | If ill-appearing: high risk   | If signs of soft tissue infection, skeletal infection, or ear infection: high risk  |
| PCT < 0.5 ng per mL: 0 points   | If 21 days or younger: high risk  | Obtain complete blood count with differential and microscopic urinalysis  |
| PCT = 0.5 to 1.9 ng per mL: 2 points  | If PCT ≥ 0.5 ng per mL: high risk   | If WBC count ≥ 15,000 per mm <sup>3</sup><br>(15.0 × 10 <sup>9</sup> per L): high risk  |
| PCT ≥ 2 ng per mL: 4 points   | If leukocyturia is present: high risk   | If WBC count ≤ 5,000 per mm <sup>3</sup><br>(5.0 × 10 <sup>9</sup> per L): high risk  |
| CRP < 40 mg per L: 0 points   | If CRP > 20 mg per L: intermediate risk (treat as high risk)  | If absolute neutrophil count<br>> 10,000 per mm <sup>3</sup> (10.0 × 10 <sup>9</sup> per L): intermediate risk (treat as high risk) |
| CRP = 40 to 99 mg per L: 2 points   | If absolute neutrophil count<br>> 10,000 per mm <sup>3</sup> (10.0 × 10 <sup>9</sup> per L): intermediate risk (treat as high risk) | If bands ≥ 1,500 per mm <sup>3</sup><br>(1.5 × 10 <sup>9</sup> per L): high risk  |
| CRP ≥ 100 mg per L: 4 points  | If none of the criteria apply, treat as low risk  | If urine WBC count per high-power field ≥ 10: high risk   |
| Urine dipstick with leukocyte esterase, nitrites, or both: 1 point              |   | If none of the criteria apply, treat as low risk  |
| If total score is 3 or more, treat as high risk;<br>otherwise treat as low risk |   |   |

CRP = C-reactive protein; PCT = procalcitonin; WBC = white blood cell.

Information from references 40, 43, and 56.

TABLE 3

| <b>Evaluation and Management of Febrile Children Younger Than Three Years</b> |   |   |
|---|---|---|
| Assess risk   | High risk, inpatient evaluation   | Lower risk, consider outpatient evaluation  |
| <b>Younger than one month</b>   | Blood tests<br>CBC with differential<br>Blood culture<br>PCT and CRP if available<br><br>Urine tests<br>Urinalysis<br>Urine culture<br>Lumbar puncture<br>CSF WBC count<br>Protein<br>Glucose<br>CSF culture<br><br>Chest radiography<br>All neonates<br><br>Begin empiric antibiotics after cultures have been obtained  | Not appropriate in this age group   |
| <b>One to three months of age</b>   | Blood tests<br>CBC with differential<br>Blood culture<br>PCT and CRP if available<br><br>Urine tests<br>Urinalysis<br>Urine culture<br>Lumbar puncture for ill-appearing children<br>CSF WBC count<br>Protein<br>Glucose<br>CSF culture<br><br>Chest radiography for ill-appearing children or if WBC count > 20,000 per mm <sup>3</sup> ( $20 \times 10^3$ per L)<br>Begin empiric antibiotics after cultures have been obtained | Consider antibiotic treatment depending on results of studies thus far<br>If good outpatient follow-up available, consider close outpatient monitoring; otherwise admit for inpatient monitoring  |
| <b>Three months to three years of age</b>                                     | Blood tests<br>CBC with differential<br>Blood culture<br>Urine tests<br>Urinalysis<br>Urine culture<br>Lumbar puncture if neurologic or meningeal signs are present<br>CSF WBC count<br>Protein<br>Glucose<br>CSF culture<br><br>Chest radiography if respiratory findings suggestive of pneumonia<br>Begin empiric antibiotics after cultures have been obtained   | During influenza season, perform rapid influenza testing<br>If concern for urinary tract infection or no other source of fever found, perform urine dipstick testing<br>If leukocyte esterase or nitrites present, obtain urinalysis and urine culture<br>Chest radiography if physical examination suggestive of pneumonia<br>Consider antibiotic/antiviral treatment depending on results of studies thus far<br>If good outpatient follow-up available, consider close outpatient monitoring; otherwise admit for inpatient monitoring |

Note: When coronavirus disease 2019 (COVID-19) is circulating, test for that infection.

CBC = complete blood count; CRP = C-reactive protein; CSF = cerebrospinal fluid; PCT = procalcitonin; WBC = white blood cell.

Information from references 8, 11, 18, 24, 37, 42, 43, 45–47, 51, and 53.

TABLE 4

| <b>Recommended Empiric Antibiotic Therapy for Children Younger Than 36 Months</b>    |   |
|--|---|
| Age and findings   | Therapy   |
| Younger than one month   | Ampicillin plus gentamicin:<br>Ampicillin,* 100 to 200 mg per kg per day IM or IV, divided, every six hours<br>Gentamicin,† 2.5 mg per kg IM or IV every eight hours, with adjustments based on serum levels<br>Alternative: Ampicillin plus cefotaxime (Claforan)<br>Ampicillin,* 100 to 200 mg per kg per day IM or IV, divided, every six hours<br>Cefotaxime,* 150 to 200 mg per kg per day IM or IV, divided, every six to eight hours<br>Alternative: Cefotaxime alone, 150 to 200 mg per kg per day IM or IV, divided, every six to eight hours*<br>If <i>Streptococcus pneumoniae</i> meningitis is suspected, add vancomycin, 20 mg per kg IV loading dose, then check creatinine levels:<br>< 0.7 mg per dL, use 15 mg per kg every 12 hours<br>0.7 to 0.9, use 20 mg per kg every 24 hours<br>1.0 to 1.2, use 15 mg per kg every 24 hours<br>1.3 to 1.6, use 10 mg per kg every 24 hours<br>> 1.6, use 15 mg per kg every 48 hours |
| One to three months, meningitis not suspected  | Ceftriaxone (Rocephin), 50 to 75 mg per kg per day IM or IV, divided, every 12 to 24 hours<br>Alternative: Cefotaxime, 75 to 200 mg per kg per day IM or IV, divided, every six to eight hours  |
| One to three months, meningitis a concern  | Ceftriaxone: Initial dose, 100 mg per kg IV; then 80 to 100 mg per kg per day IV, divided, every 12 to 24 hours; maximum dose, 4 g per 24 hours<br>If <i>S. pneumoniae</i> is a concern, add vancomycin, 60 mg per kg per day IV, divided, every six hours  |
| One to three months, urinary findings  | Ceftriaxone, 75 mg per kg IV every 24 hours<br>Alternative: Older than two months, oral cefixime (Suprax),‡ 8 mg per kg per day<br>Alternative: Oral amoxicillin/clavulanate (Augmentin), 30 mg per kg per day (amoxicillin component), divided, every 12 hours   |
| One to three months, suspected bacterial pneumonia, considering outpatient treatment | Oral amoxicillin, 90 mg per kg per day, divided, every 12 hours<br>Alternative: Oral azithromycin (Zithromax), 10 mg per kg in single dose on day 1, then 5 mg per day for days 2 to 5<br>Severe infection: Ceftriaxone, 50 to 200 mg per kg per day IM or IV, divided, every 12 to 24 hours; maximum, 2 g per day  |
| Older than three months, high risk, no localizing signs                              | Ceftriaxone, 50 to 75 mg per kg IV once daily<br>Alternative: Cefotaxime, 150 to 180 mg per kg per day IM or IV, divided, every six to eight hours  |
| Older than three months, suspected bacterial pneumonia                               | Amoxicillin, 90 mg per kg per day orally, divided, every 12 hours; maximum, 500 mg per dose<br>Alternative: Oral azithromycin, 10 mg per kg in single dose on day 1, then 5 mg per kg orally for days 2 to 5<br>Severe infection: Ceftriaxone, 50 to 200 mg per kg per day IM or IV, divided, every 12 to 24 hours; maximum, 2 g per day  |
| Older than three months, urinary findings  | Oral cefixime,§ 8 mg per kg per day<br>Alternative: Oral amoxicillin/clavulanate, 20 to 40 mg per kg per day (amoxicillin component), divided, every eight hours<br>Alternative: Trimethoprim/sulfamethoxazole, 8 to 12 mg per kg per day (trimethoprim component) orally or IV, divided, every six to 12 hours   |

IM = intramuscularly; IV = intravenously.

\*=Dosage for children seven days or older weighing at least 2 kg (4 lb, 7 oz).

†=Dosage for children older than seven days.

‡=Cefixime therapy in children younger than six months is off-label.

Information from references 11, 37, and 60–63.

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## R&D: DIAGNOSIS & TREATMENTS

### CURRENT DIAGNOSTICS

#### SEROLOGICAL DIFFERENTIATION BETWEEN COVID-19 AND SARS INFECTIONS

Chia WN, Tan CW, Foo R, Kang AEZ, Peng Y, Sivalingam V, Tiu C, Ong XM, Zhu F, Young BE, Chen MIC, Tan YJ, Lye DC, Anderson DE, Wang LF.. *Emerg Microbes Infect.* 2020 Jun 12:1-23. doi: 10.1080/22221751.2020.1780951. Online ahead of print.

Level of Evidence: 5 - Mechanism-based reasoning

#### BLUF

This study examined the performance of 3 different proteins (N, S1, and receptor-binding domain) from SARS-CoV-2 and SARS-CoV in four serological tests to assess cross-reactivity between the two virus strains. They found considerable cross-reactivity when the N protein is used, while the S1 and RBD proteins were more specific (Figures 1, 4, 5). These findings suggest that "SARS-CoV-2 HRP-RBD [horseradish-conjugated RBD protein] based capture ELISA will be an effective tool for many applications requiring reliable, simple and specific antibody test."

#### ABSTRACT

In response to the coronavirus disease 2019 (COVID-19) outbreak, caused by the SARS-CoV-2 virus, multiple diagnostic tests are required globally for acute disease diagnosis, contact tracing, monitoring of asymptomatic infection rates and assessing herd immunity. While PCR remains the frontline test of choice in the acute diagnostic setting, serological tests are urgently needed to fulfil the other requirements. Unlike PCR tests which are highly specific for each virus, cross-reactivity could potentially be a major challenge for COVID-19 antibody tests considering there are six other coronaviruses known to infect humans. Among the human pathogens, SARS-CoV is genetically most related to SARS-CoV-2 sharing approximately 80% sequence identity and both belong to the species SARS related coronavirus (SARSr-CoV) in the genus Betacoronavirus of family Coronaviridae. In this study, we developed and compared the performance of four different serological tests to comprehensively assess the cross-reactivity between COVID-19 and SARS patient sera. Our results indicate that there is a significant cross-reactivity when N protein of either SARS-CoV or SARS-CoV-2 is used. The S1 or RBD derived the spike (S) protein offers better specificity. Amongst the different platforms, capture ELISA performed best. Finally, we found that SARS survivors all have significant level of antibodies remaining in their blood 17 years after infection. We discovered that anti-N antibodies waned more than anti-RBD antibodies, and the latter is known to play a more important role in providing protective immunity.

## FIGURES

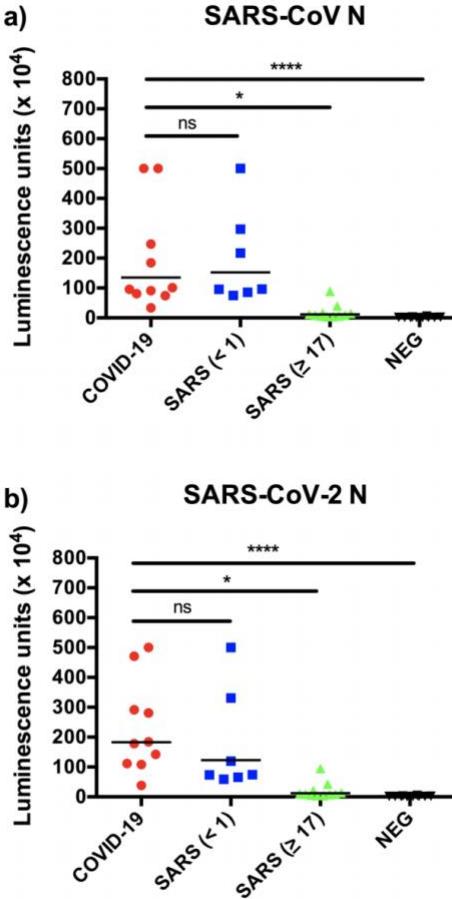


Figure 1. Rapid detection of N-specific antibodies using LIPS. Data presented are luminescence units against N proteins of SARS-CoV (a) and SARS-CoV-2 (b). The SARS sera were divided into those collected in 2003 (<1 year) or 2020 ( $\geq 17$  years).

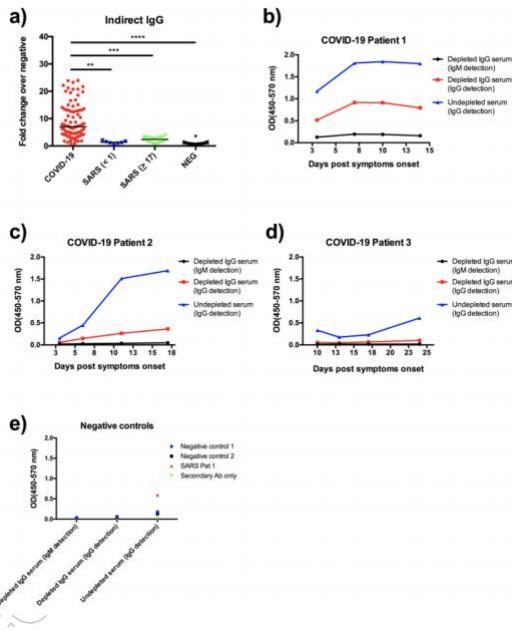


Figure 4. Detection of anti-RBD IgG and IgM antibodies by indirect ELISA. (a) IgG data obtained from the same serum panels as those in Figure 3. IgM testing with or without IgG

depletion from three representative COVID-19 patient sera known to have high (b), medium (c) and low (d) IgG antibody levels. Also included are two healthy controls and one SARS patient serum (e). Data are presented as fold of change (Fc) over the average reading of negative controls.

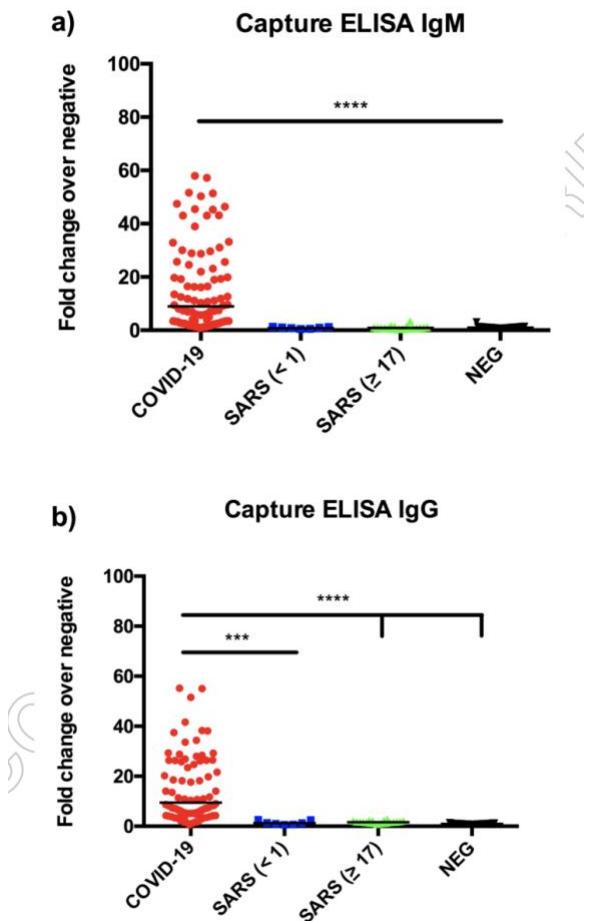


Figure 4. Detection of anti-RBD IgG and IgM antibodies by indirect ELISA. (a) IgG data obtained from the same serum panels as those in Figure 3. IgM testing with or without IgG depletion from three representative COVID-19 patient sera known to have high (b), medium (c) and low (d) IgG antibody levels. Also included are two healthy controls and one SARS patient serum (e). Data are presented as fold of change (Fc) over the average reading of negative controls.

## DEVELOPMENTS IN DIAGNOSTICS

### A COMBINED OROPHARYNGEAL/NARES SWAB IS A SUITABLE ALTERNATIVE TO NASOPHARYNGEAL SWABS FOR THE DETECTION OF SARS-COV-2

LeBlanc JJ, Heinstein C, MacDonald J, Pettipas J, Hatchette TF, Patriquin G.. J Clin Virol. 2020 Jul;128:104442. doi: 10.1016/j.jcv.2020.104442. Epub 2020 May 16.

Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard"

#### BLUF

In this cohort study of 190 patients in community centers in Canada, a group of researchers compare the efficacy of combined oropharyngeal/nares swabs (OP/Na) via the Aptima Multitest swab kit to that of traditional nasopharyngeal swabs (NP) in detecting SARS-CoV-2. They found that OP/Na swabs and NP swabs had sensitivities of 91.7% and 94.4%, respectively, suggesting that OP/Na sampling, which may be more readily available during the COVID-19 pandemic, is an effective alternative to NP swabs in ambulatory settings; however low viral loads were associated with discrepant results between the two swabs (Table 1).

## ABSTRACT

Given the global shortage of nasopharyngeal (NP) swabs typically used for respiratory virus detection, alternative collection methods were evaluated during the COVID-19 pandemic. This study showed that a combined oropharyngeal/nares swab is a suitable alternative to NP swabs for the detection of SARS-CoV-2, with sensitivities of 91.7% and 94.4%, respectively.

## FIGURES

Table 1  
Relevant characteristics among ambulatory patients in whom results of paired nasopharyngeal and oropharyngeal/nares swabs were discrepant for the detection of SARS-CoV-2.

| Patient | LDT       |        |        |           |        |        | 6800        |        |        |             |        |        | Xpert   |         |        | Comments                      |  |
|---------|-----------|--------|--------|-----------|--------|--------|-------------|--------|--------|-------------|--------|--------|---------|---------|--------|-------------------------------|--|
|         | NP        |        |        | OP/Na     |        |        | NP          |        |        | OP/Na       |        |        | NP      |         |        |                               |  |
|         | Ct (RdRp) | Ct (E) | Result | Ct (RdRp) | Ct (E) | Result | Ct (OrfLab) | Ct (E) | Result | Ct (OrfLab) | Ct (E) | Result | Ct (N2) | Ct (N2) | Result |                               |  |
| 1       | ND        | ND     | NEG    | ND        | 35.3   | POS    | ND          | 38.6   | POS    | 35.8        | 37.6   | POS    | ND      | 40.0    | POS    | Yes, but onset not recorded   |  |
| 2       | ND        | ND     | NEG    | 36.2      | 34.7   | POS    | ND          | 38.3   | POS    | 33.9        | 36.2   | POS    | 41.6    | 41.2    | POS    | No                            |  |
| 3       | 37.8      | 35.7   | POS    | ND        | 37.6   | POS    | 33.6        | 35.9   | POS    | ND          | ND     | NEG    | 35.2    | 37.5    | POS    | No                            |  |
| 4       | 27.3      | 26.8   | POS    | ND        | ND     | NEG    | 27.5        | 28.2   | POS    | ND          | ND     | NEG    | 25.4    | 28.2    | POS    | No                            |  |
| 5       | 33.7      | 33.1   | POS    | ND        | ND     | NEG    | 30.7        | 33.1   | POS    | ND          | ND     | NEG    | 30.5    | 33.5    | POS    | Yes, with onset 18 days prior |  |
| 6       | 33.6      | 33.4   | POS    | ND        | ND     | NEG    | 32.1        | 34.1   | POS    | ND          | ND     | NEG    | 34.2    | 37.4    | POS    | Yes, with onset 14 days prior |  |

\*Discrepant analysis using Xpert testing was only performed on nasopharyngeal swabs in UTM, as the OP/Na showed reduced sensitivity for this assay (Table S1). Abbreviations: Threshold cycle (Ct), envelope (E); laboratory-developed test (LDT); nucleoprotein (N2); not available (N/A); not detected (ND); negative (NEG); nasopharyngeal (NP); oropharyngeal/nares (OP/Na); positive (POS); RNA-dependent RNA polymerase (RdRp); ribonuclease P (RNaseP).

## DEVELOPMENTS IN TREATMENTS

### REPOSITIONING OF 8565 EXISTING DRUGS FOR COVID-19

Gao K, Nguyen DD, Chen J, Wang R, Wei G.. J Phys Chem Lett. 2020 Jun 16. doi: 10.1021/acs.jpclett.0c01579. Online ahead of print.

Level of Evidence: Other - Modeling

## BLUF

This study uses a computational method to predict the binding affinity of 1553 FDA-approved drugs and 7012 investigational/off-market drugs to SARS-CoV-2 main protease. The authors identify 20 FDA-approved drugs and 20 investigational/off-market drugs that may be effective against SARS-CoV-2 (Tables 1 and 2). The findings of this study provide preliminary evidence for future experimental studies investigating the efficacy of these medications against COVID-19.

## ABSTRACT

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected over 5 million people and led to over 0.3 million deaths. Currently, there is no specific anti-SARS-CoV-2 medication. New drug discovery typically takes more than ten years. Drug repositioning becomes one of the most feasible approaches for combating COVID-19. This work curates the largest available experimental dataset for SARS-CoV-2 or SARS-CoV main protease inhibitors. Based on this dataset, we develop validated machine learning models with relatively low root mean square error to screen 1553 FDA-approved drugs as well as other 7012 investigational or off-market drugs in DrugBank. We found that many existing drugs might be potentially potent to SARS-CoV-2. The druggability of many potent SARS-CoV-2 main protease inhibitors is analyzed. This work offers a foundation for further experimental studies of COVID-19 drug repositioning.

## FIGURES

Table 1: A summary of the top 20 potential anti-SARS-CoV-2 drugs from 1553 FDA-approved drugs with their predicted binding affinities (unit: kcal/mol), IC<sub>50</sub> (μM), and corresponding brand names.

| DrugID  | Name            | Brand name                            | Predicted binding affinity | IC <sub>50</sub> |
|---------|-----------------|---------------------------------------|----------------------------|------------------|
| DB01123 | Proflavine      | Bayer Pessaries, Molca, Septicide     | -8.37                      | 0.72             |
| DB01243 | Chloroxine      | Capitol                               | -8.24                      | 0.89             |
| DB08994 | Demexiptiline   | Deparon, Tinoran                      | -8.14                      | 1.06             |
| DB00544 | Fluorouracil    | Adrucil                               | -8.11                      | 1.11             |
| DB03209 | Oteracil        | Teyuno                                | -8.09                      | 1.16             |
| DB13222 | Tilbroquinol    | Intetrix                              | -8.08                      | 1.18             |
| DB01136 | Carvedilol      | Coreg                                 | -8.06                      | 1.22             |
| DB01033 | Mercaptopurine  | Purinethol                            | -8.04                      | 1.26             |
| DB08903 | Bedaquiline     | Sirturo                               | -8.02                      | 1.29             |
| DB00257 | Clotrimazole    | Canesten                              | -8.00                      | 1.35             |
| DB00878 | Chlorhexidine   | Betasert, Biopatch                    | -8.00                      | 1.35             |
| DB00666 | Nafarelin       | Synarel                               | -8.00                      | 1.35             |
| DB01213 | Fomepizole      | Antizol                               | -7.98                      | 1.39             |
| DB01656 | Roflumilast     | Daxas, Daliresp                       | -7.97                      | 1.41             |
| DB00676 | Benzyl benzoate | Ascarbin, Ascabiol, Ascarbin, Temutex | -7.96                      | 1.45             |
| DB06663 | Pasirootide     | Signifor                              | -7.95                      | 1.47             |
| DB08983 | Etofibrate      | Lipo Merz Retard, Liposec             | -7.94                      | 1.48             |
| DB06791 | Lauroteotide    | Somatuline                            | -7.94                      | 1.48             |
| DB00027 | Gramicidin D    | Neosporin Ophthalmic                  | -7.94                      | 1.48             |
| DB00730 | Thiabendazole   | Mintezol, Tresaderm, and Arbotect     | -7.93                      | 1.51             |

**Table 2: A summary of top 20 potential anti-SARS-CoV-2 drugs from 7012 investigational or off-market drugs with predicted binding affinities (BAs) (unit: kcal/mol), IC<sub>50</sub> (μM), and corresponding trade names.**

| DrugID  | Name   | Predicted BA | IC <sub>50</sub> |
|---------|--|--------------|------------------|
| DB12903 | DEBIO-1347   | -9.02        | 0.24             |
| DB07959 | 3-(1H-BENZIMIDAZOL-2-YL)-1H-INDAZOLE   | -9.01        | 0.24             |
| DB07301 | 9H-CARBAZOLE   | -8.96        | 0.27             |
| DB07620 | 2-[(2,4-DICHLORO-5-METHYLPHENYL)SULFONYL]-1,3-DINITRO-5-(TRIFLUOROMETHYL)BENZENE       | -8.89        | 0.30             |
| DB08036 | 6,7,12,13-tetrahydro-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazol-5-one                      | -8.89        | 0.30             |
| DB08440 | N-1,10-phenanthrolin-5-ylacetamide   | -8.83        | 0.33             |
| DB01767 | Hemi-Babim   | -8.80        | 0.35             |
| DB06828 | 5-[2-(1H-pyrrol-1-yl)ethoxy]-1H-indole   | -8.73        | 0.39             |
| DB14914 | Flortaucipir F-18  | -8.69        | 0.42             |
| DB15033 | Flortaucipir   | -8.69        | 0.42             |
| DB13534 | Gedocarnil   | -8.67        | 0.44             |
| DB02365 | 1,10-Phenanthroline  | -8.64        | 0.45             |
| DB09473 | Indium In-111 oxyquinoline   | -8.64        | 0.45             |
| DB08512 | 6-amino-2-[(1-naphthylmethyl)amino]-3,7-dihydro-8H-imidazo[4,5-g]quinazolin-8-one      | -8.60        | 0.48             |
| DB01876 | Bis(5-Amidino-2-Benzimidazolyl)Methanone   | -8.60        | 0.49             |
| DB07919 | 7-METHOXY-1-METHYL-9H-BETA-CARBOLINE   | -8.59        | 0.49             |
| DB02089 | CP-526423  | -8.59        | 0.50             |
| DB07837 | [4-(5-naphthalen-2-yl-1H-pyrrolo[2,3-b]pyridin-3-yl)phenyl]acetic acid                 | -8.53        | 0.55             |
| DB08073 | (2S)-1-(1H-INDOL-3-YL)-3-{ 5-(3-METHYL-1H-INDAZOL-5-YL)PYRIDIN-3-YL OXY}PROPAN-2-AMINE | -8.53        | 0.55             |
| DB08267 | 6-amino-4-(2-phenylethyl)-1,7-dihydro-8H-imidazo[4,5-g]quinazolin-8-one                | -8.52        | 0.56             |

## MENTAL HEALTH & RESILIENCE NEEDS

### IMPACT ON PUBLIC MENTAL HEALTH

#### DID THE GENERAL POPULATION IN GERMANY DRINK MORE ALCOHOL DURING THE COVID-19 PANDEMIC LOCKDOWN?

32556079. Did the General Population in Germany Drink More Alcohol during the COVID-19 Pandemic Lockdown?

Level of Evidence: 3 - Local non-random sample

#### BLUF

Psychiatrists and addiction medicine experts from Germany conducted an anonymous online survey of 2,102 German citizens to understand how community lockdown measures during the COVID-19 pandemic have impacted alcohol consumption. Their survey revealed that 34.7% of respondents have consumed "more or much more" alcohol during the pandemic compared to their baseline, and indicated that increased alcohol consumption during this time is associated with lower educational status and increased stress. Given these findings, healthcare providers should be prepared to screen for and support patients with alcohol use disorders, especially patients with increased risk factors and in vulnerable populations.

#### SUMMARY

The COVID-19 pandemic has created unprecedented stress among the general population, which increases the risk of certain psychiatric conditions including alcohol and substance use disorders. Currently, not much is known about how the lockdown and self-isolation measures implemented to curb the spread of COVID-19 have influenced the rate of alcohol consumption, but data from the German Consumer Research Association revealed a 6.1% increase in alcohol revenue compared to pre-pandemic sales. In an anonymous online survey completed by 2,102 respondents, "8.2% reported to drink no alcohol, 37.7% reported no change in their alcohol drinking behavior, 19.4% reported to drink less or much less and 34.7% reported to drink more or much more alcohol since the begin of the lockdown [sic]." Further analysis of the results showed that the increased alcohol consumption category was correlated with lower educational status and increased feelings of stress during the pandemic. Overall, these responses support the notion that community stress due to lockdown measures increases alcohol consumption in vulnerable individuals and could predispose to a greater prevalence of alcohol use disorders in the future.

## RESOURCES

### MATERNAL MORTALITY FROM CORONAVIRUS DISEASE 2019 (COVID-19) IN THE UNITED STATES

Metz TD, Collier C, Hollier LM.. Obstet Gynecol. 2020 Jun 16. doi: 10.1097/AOG.0000000000004024. Online ahead of print.  
Level of Evidence: Other - Guidelines and Recommendations

#### BLUF

The authors – each of whom serves as a Chair of the Maternal Mortality Review Committee for one of three states: Utah, Mississippi, and Texas – highlight the scarcity of data regarding maternal deaths related to COVID-19 within the United States. While current literature suggests that 8% of pregnant women with COVID-19 have severe disease, data regarding maternal mortality and associated contextual information, including social determinants, are very limited. The authors recommend that all states report maternal deaths via the CDC Maternal Mortality Review Information Application form to allow for the national compilation of case series data. This information would help improve our understanding of the effects of COVID-19 on a variety of maternal morbidity and mortality measures and could ultimately guide recommendations to improve outcomes in the context of COVID-19.

#### ABSTRACT

Individual state maternal mortality review committees aim to comprehensively review all maternal deaths to not only evaluate the cause of death, but also to assess preventability and make recommendations for action to prevent future deaths. The maternal mortality review committee process remains critical during the coronavirus disease 2019 (COVID-19) pandemic. Maternal deaths due to COVID-19 have been reported in the United States. Some state maternal mortality review committees may choose to expedite review of these deaths in an effort to quickly provide clinicians with information intended to prevent other deaths during the ongoing pandemic. If states opt to pursue rapid review, entry of data into the Maternal Mortality Review Information Application system for submission to the Centers for Disease Control and Prevention will allow for aggregation nationally without duplication. It will be important to review not only deaths directly attributed to COVID-19, but also those that may be indirectly related to the COVID-19 pandemic, such as those influenced by changes in care practices or delays in seeking care during the pandemic. Therefore, regardless of the timing of the review, maternal deaths that occur during the time of the COVID-19 pandemic must be evaluated within that framework to ensure that all factors contributing to the death are considered to better understand the context of each of these tragic events.

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