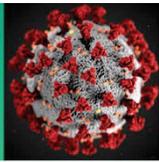


COVID-19 Science Update



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

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

Epidemiology

PEER-REVIEWED

[Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: A systematic review and meta-analysis.](#) Chu *et al.* Lancet (June 1, 2020).

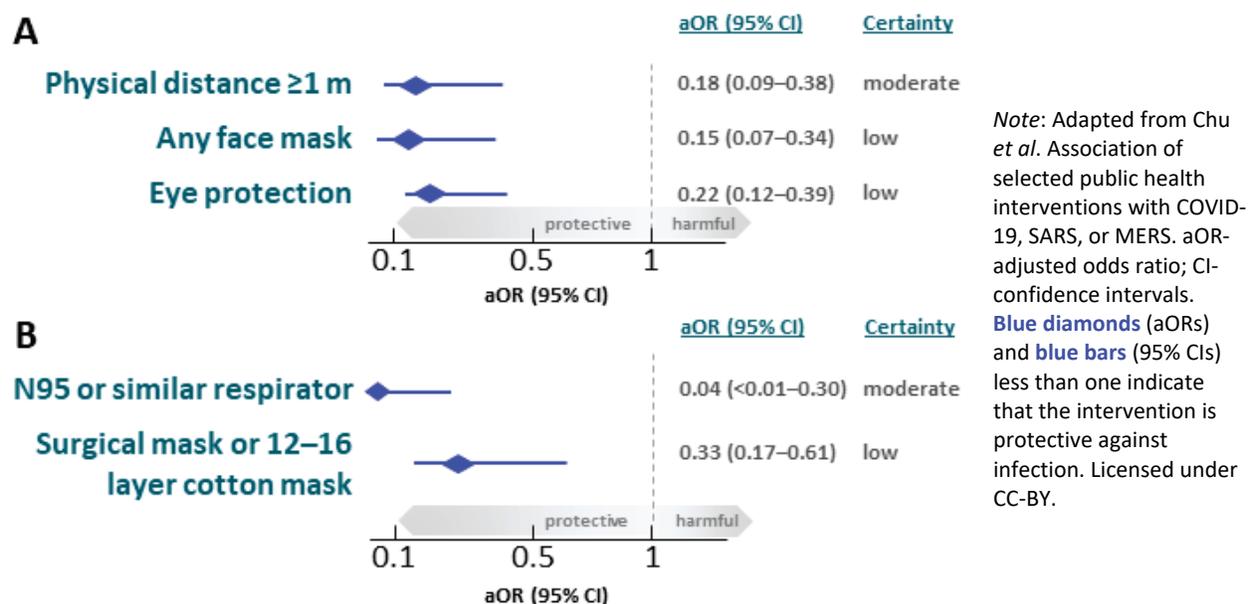
Key findings:

- Meta-analysis of data from observational studies indicated that physical distancing, face masks, and eye protection were protective against COVID-19, SARS, or MERS (Figure A).
 - Protective effect of distancing may double with additional meter added.
- Use of N95 or similar respirator was highly protective; use of 12–16-layer cotton masks demonstrated protection (Figure B). (Insufficient data to assess homemade face coverings.)

Methods: Systematic review and meta-analyses of data from 44 comparative studies (25,697 patients) in healthcare and non-healthcare settings from 10 countries, published 2003–May 3, 2020. Certainty of evidence rated according to Cochrane methods and GRADE approach. *Limitations:* Limited data from non-healthcare settings; only 2 studies with US-based COVID-19 data, results might not be generalizable to US.

Implications: Physical distance, face masks, and eye protection prevent person-to-person spread of coronaviruses. No single intervention is fully protective; combination use is recommended.

Figure:



COVID-19-related economic anxiety is as high as health anxiety: Findings from the USA, the UK, and Israel. Bareket-Bojmel *et al.* International Journal of Cognitive Therapy (May 29, 2020).

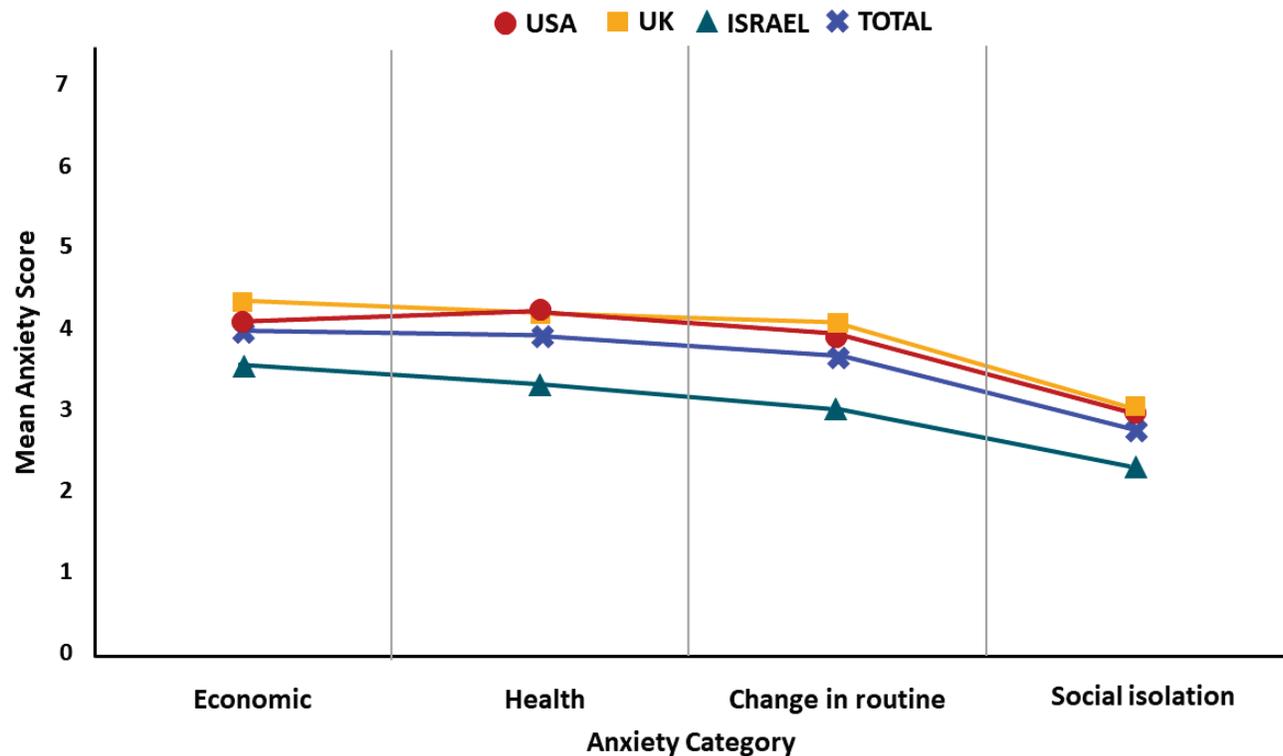
Key findings:

- Among residents of the US, UK, and Israel, health- and economic-related anxiety levels were higher than anxiety from changes in daily routines and social isolation (Figure).
- US residents reported moderate levels of health- and economic-related anxiety (~4 on 7-point scale) (Figure).

Methods: 1,200 participants (400 from US, UK and Israel each) completed an anxiety questionnaire (April 2020). Responses were provided on a 7-point Likert scale. **Limitations:** Used non-validated questionnaire; inability to compare scores to other populations or time points; convenience sample.

Implications: During the COVID-19 pandemic, US residents reported moderate health- and economic-related anxiety. Studies of mental health symptoms may identify populations that need emotional support and mental health services.

Figure:



Note: Adapted from Bareket-Bojmel *et al.* Mean scores for 4 anxiety categories among 1,200 residents of the US (400), UK (400), and Israel (400). Economic-related anxiety levels were comparable to those of health-related anxiety. Available via Nature Public Health Emergency Collection through PubMed Central.

PREPRINTS (NOT PEER-REVIEWED)

Cumulative incidence and diagnosis of SARS-CoV-2 infection in New York. Rosenberg *et al.* medRxiv (May 29, 2020). [Published](#) in Annals of Epidemiology (June 17, 2020).

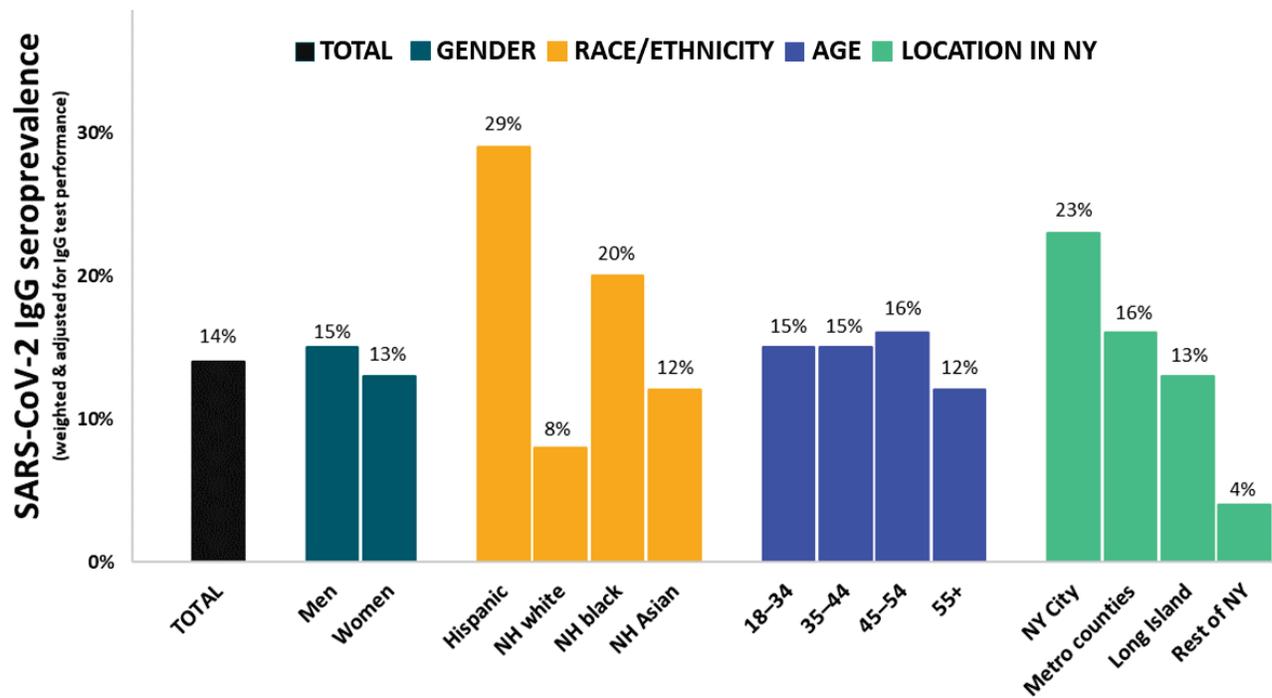
Key findings:

- After statistical weighting, SARS-CoV-2 IgG antibodies were detected in 14% of adult New York State residents as of March 29, 2020 corresponding to 2.1 million New Yorkers.
- Antibody prevalence was slightly higher in men than women, and highest among those of Hispanic/Latino ethnicity and those who live in New York City (Figure).
 - Racial/ethnic disparities were noted in New York City, Westchester & Rockland Counties, and Long Island but not in the rest of New York State.
- Only 9% (estimated) of SARS-CoV-2 infections had actually been diagnosed.

Methods: Cross-sectional seroprevalence study of >15,000 adults recruited at grocery stores across New York State (April 19–28, 2020). Seroprevalence weighted to underlying New York demographics and geographic distribution and adjusted for antibody test performance. Estimated number of SARS-CoV-2 infections (based on seroprevalence) was compared to number of diagnosed COVID-19 cases. **Limitations:** Likely under-sampling of vulnerable groups less likely to grocery shop, including those in long-term care facilities and hospitals or persons with disabilities.

Implications: >85% of the New York population may still be susceptible to COVID-19. Monitoring, testing, and contact tracing remain critical to limit spread of SARS-CoV-2 and address racial/ethnic disparities. Case counts based on current PCR-based testing approaches may substantially underestimate the number of SARS-CoV-2 infections.

Figure:



Note: Adapted from Rosenberg *et al.* Prevalence of SARS-CoV-2 IgG antibodies in New York as of March 29, 2020. NH - non-Hispanic/Latino, Metro counties - Westchester and Rockland Counties, NY - New York. Data used in figure is in the public domain per communication with author.

Clinical Treatment & Management

PEER-REVIEWED

[Famotidine use is associated with improved clinical outcomes in hospitalized COVID-19 patients: a propensity score matched retrospective cohort study](#). Freedberg *et al.* *Gastroenterology* (May 21, 2020).

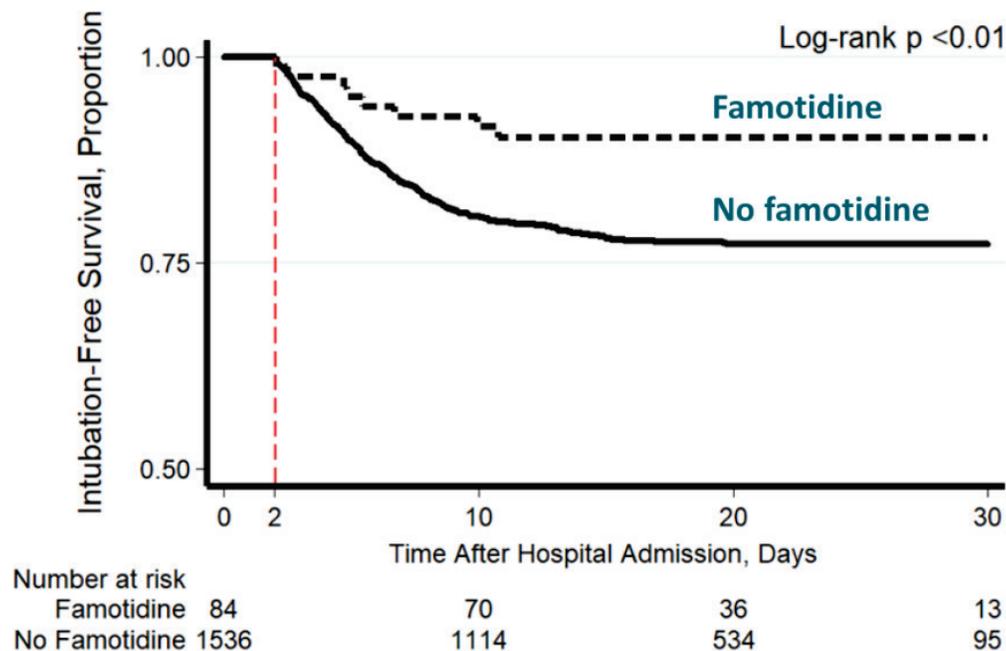
Key findings:

- Hospitalized patients with COVID-19 who received famotidine (a histamine-2 receptor agonist commonly used for heartburn) within 24 hours of admission were less likely to die or be intubated within 30 days (Figure).
 - Association remained after adjustment and propensity score matching (adjusted hazard ratio 0.4, 95% CI 0.2–0.9).

Methods: Single-center observational cohort study of 1,620 adults hospitalized for COVID-19 (February 25–April 13, 2020). Adjusted analysis and propensity score matching used to control for differences in baseline characteristics. **Limitations:** Observational, possible unmeasured confounding might account for findings; single center; methods for adjustment (including baseline characteristics used) and propensity score matching not described; biological explanation for observed association unclear.

Implications: Preliminary data that famotidine might have benefit in COVID-19 treatment. Randomized clinical trial data are needed; [one clinical trial](#) investigating famotidine and hydroxychloroquine is underway.

Figure:



Note: Adapted from Freedberg *et al.* Kaplan-Meier plot showing that patients with COVID-19 who received famotidine (dashed black line) were less likely to die or be intubated during hospitalization than patients with COVID-19 who did not receive famotidine (solid black line). Patients were included in the analysis if they were alive and not intubated during first 48 hours of hospitalization (indicated by red dashed line). This article was published in *Gastroenterology*, Vol 159, Freedberg *et al.*, Famotidine use is associated with improved clinical outcomes in hospitalized COVID-19 patients: a propensity score matched retrospective cohort study, Page 1129-1131, Copyright the AGA Institute 2020. This article is currently available at the Elsevier COVID-19 resource center: <https://www.elsevier.com/connect/coronavirus-information-center>.

[A randomized trial of hydroxychloroquine as postexposure prophylaxis for COVID-19](#). Boulware *et al.* NEJM (June 3, 2020).

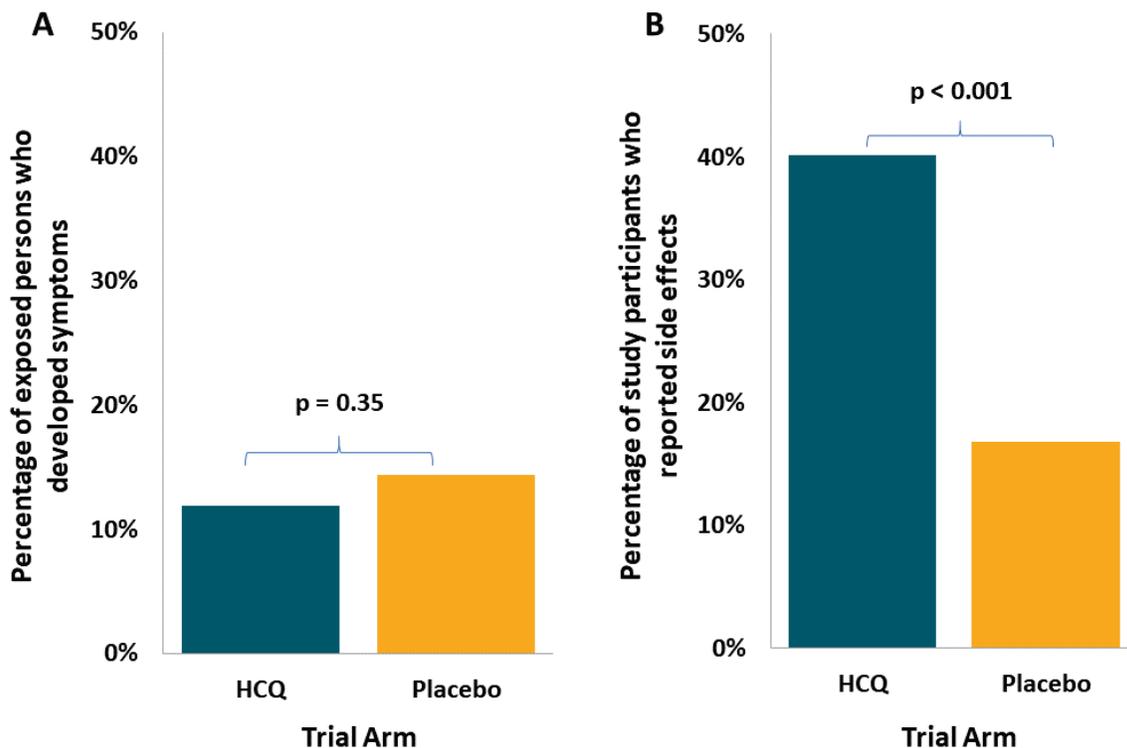
Key findings:

- After high- or moderate-risk exposure to SARS-CoV-2, incidence of COVID-19 symptoms did not differ between participants assigned to receive 5 days of hydroxychloroquine (HCQ) post-exposure prophylaxis (49/414 [11.8%]) versus placebo (58/407 [14.3%]; $p = 0.35$) (Figure A).
 - 66% of participants were healthcare workers, of whom 77% were exposed to infected patients or coworkers.
- Side effects were more common among participants who received HCQ (140/349 [40.1%]) versus placebo (59/351 [16.8%]; $p < 0.001$) (Figure B) and were predominantly gastrointestinal.
 - No arrhythmias were observed during the short course of HCQ used in this study.

Methods: Randomized, double-blind, placebo-controlled trial of HCQ among 821 asymptomatic adult participants exposed to SARS-CoV-2, March 13–May 6, 2020. Participants received 5 days of HCQ administered within 4 days of their exposure to SARS-CoV-2. Primary outcome was either PCR-confirmed infection (15%) or self-reported COVID-19-related symptoms consistent with infection within 14 days after enrollment (85%). **Limitations:** Participants not systematically tested for SARS-CoV-2 and asymptomatic infections were likely missed; relied on self-reported testing, illness, and hospitalization; no systematic monitoring for cardiac arrhythmias.

Implications: Evidence from this trial does not support use of HCQ for postexposure prophylaxis to prevent COVID-19.

Figure:



Note: Adapted from Boulware *et al.* Proportion of participants in each trial arm comparing hydroxychloroquine (HCQ) to placebo with (A) self-reported COVID-19-related symptoms and (B) side effects. From NEJM. 383:517-525; DOI: 10.1056/NEJMoa2016638. Copyright ©2020 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

Laboratory Science

PEER-REVIEWED

[Implication of SARS-CoV-2 evolution in the sensitivity of RT-qPCR diagnostic assays.](#) Osorio *et al.*
Lancet Infectious Diseases (May 28, 2020).

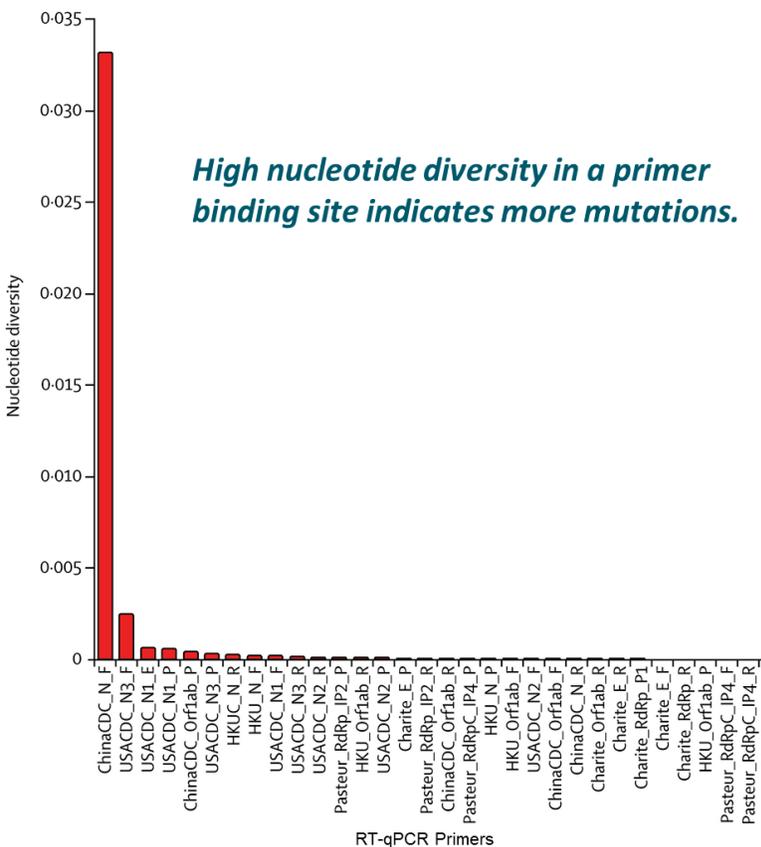
Key findings:

- SARS-CoV-2 is evolving. Phylogenetic sequencing of a selection of SARS-CoV-2 samples found that 79% of the viral genomic RNA sequences targeted by the primers used in current RT-qPCR diagnostic assays had undergone some extent of mutation in at least one viral sample.
 - The RNA sequence to which one such primer (China CDC_N_F) binds had undergone mutation in a substantial number of viral genome isolates (Figure, bar farthest left).
 - Mutations of RNA sequences targeted by the other primers were infrequent in the viruses that were examined (Figure).

Methods: Genomic analyses of 1,825 SARS-CoV-2 sequences collected from 24 countries and deposited in the Global Initiative on Sharing All Influenza Data (GISAID) database (as of March 31, 2020). Sequences were aligned to the SARS-CoV-2 Wuhan reference strain. Genetic mutations were determined for 33 primer binding sites along the SARS-CoV-2 genome used in RT-qPCR assays. **Limitations:** Potential errors in sequences submitted to GISAID.

Implications: Emerging viral mutations may render the primers used in some diagnostic assays ineffective and cause false-negative test results. Careful genomic surveillance and continued optimization of RT-qPCR primers are necessary to maintain high quality SARS-CoV-2 detection in the United States and worldwide.

Figure:



Note: Adapted from Osorio *et al.* Viral genetic diversity (amount of mutation) in 33 primer binding sites used in RT-qPCR diagnostic assays across 1,825 SARS-CoV-2 genomes isolated from humans in 24 countries. Each bar represents the extent of mutation of a primer binding site. This article was published in Lancet Infectious Diseases, Osorio *et al.*, Implication of SARS-CoV-2 evolution in the sensitivity of RT-qPCR diagnostic assays, Copyright Elsevier 2020. This article is currently available at the Elsevier COVID-19 resource center: <https://www.elsevier.com/connect/coronavirus-information-center>.

In Brief

- Cardone *et al.* [Lessons learned to date on COVID-19 hyperinflammatory syndrome: Considerations for interventions to mitigate SARS-CoV-2 viral infection and detrimental hyperinflammation](#). *Frontiers in Immunology*. Review article from FDA investigators that describes key immunological factors underlying COVID-19 disease progression and respective therapeutic options.
- Lester *et al.* [Absence of skin colour images in publications of COVID-19 skin manifestations](#). *British Journal of Dermatology*. Systematic review demonstrates a lack of published clinical images of COVID-19 dermatologic manifestations from patients with darker skin, which might reinforce existing health disparities.
- Lurie *et al.* [Developing COVID-19 vaccines at pandemic speed](#). *NEJM*. Overview of accelerated SARS-CoV-2 vaccine development and the status of specific vaccine candidates.
- Owens *et al.* [NASA's isolation experts: lockdown lessons from space](#). *Nature*. NASA astronauts confer their strategies for coping with social isolation.
- Schwartz *et al.* [Lack of COVID-19 transmission on an international flight](#). *Canadian Medical Association Journal*. Investigation of 2 confirmed COVID-19 patients who flew on a 15-hour flight; no secondary cases were identified.
- Smith *et al.* [Shielding from COVID-19 should be stratified by risk](#). *BMJ*. As countries re-open, this editorial discusses a strategy (“stratify and shield”) for identifying and targeting enhanced prevention measures at groups at high risk of dying from COVID-19.
- Haddout *et al.* [Water scarcity: A big challenge to slums in Africa to fight against COVID-19](#). *Science and Technology Libraries*. Discusses specific challenges for combating the spread of SARS-CoV-2 in areas of Africa that lack adequate water supply and proposes simple strategies to help.
- Rubin, E. [Expression of Concern: Mehra MR *et al.* Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. N Engl J Med. DOI: 10.1056/NEJMoa2007621](#). *NEJM*. Editors disclose that substantive concerns have been raised about data validity in this study. On June 4, 2020, the authors [retracted the article](#).
- Editors. [Expression of concern: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis](#). *Lancet*. Expression of Concern to notify readers of questions about data validity in this study. On June 5, 2020, the article was [retracted](#).

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