New Research

*note, PREPRINTS have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see Digital Commons

Retracted Articles - see also Retraction Watch


On July 6, 2021, Open Forum Infectious Diseases published the article “Meta-analysis of Randomized Trials of Ivermectin to Treat SARS-CoV-2 Infection” by Hill, et al. Subsequently, we and the authors learned that one of the largest studies on which this analysis was based was withdrawn due to fraudulent data; additional problems have emerged regarding other studies included in the original paper. An editorial Expression of Concern was first published under this record as the authors revised their analysis for resubmission.

The authors submitted and published a corrected version of the analysis with commentary on assessing trial quality while creating meta-analyses, available to read in OFID: “Ivermectin for COVID-19: Addressing Potential Bias and Medical Fraud” by Hill et al., https://doi.org/10.1093/ofid/ofab645. The original analysis has been retracted.

Basic Science / Virology / Pre-clinical


The COVID-19 pandemic continues to pose substantial risks to public health, worsened by the emergence of SARS-CoV-2 variants which may have a higher transmissibility and reduce vaccine effectiveness. We conducted a systematic review and meta-analysis on reproduction numbers of SARS-CoV-2 variants and provided pooled estimates for each variant.

Clinical Syndrome

RESULTS: 51 studies were included. Among 3,297 COVID-19 patients in ICU cohort studies, 313 were diagnosed with CAPA (prevalence 10%, 95% confidence interval 8-13%). 277 patients had patient-level data allowing reclassification. Definitions had limited correlation with one another (ρ=0.268 to 0.447, p<0.001) with the exception of Koehler and Verweij (ρ=0.893, p<0.001). 33.9% of patients reported to have CAPA did not fulfill any research definitions. Patients were diagnosed after a median of 8 days (interquartile range 5-14) in ICUs. Tracheobronchitis occurred in 3% of patients examined with bronchoscopy. The mortality rate was high (59.2%). Applying CAPA research definitions did not strengthen the association between mould-active antifungals and survival. The reported prevalence of CAPA is significant, but may be exaggerated by non-standard definitions.


   Findings from this study indicate a high likelihood of acute COVID-19 among RT-PCR negative with typical signs/symptoms, but a common omission of COVID-19 therapies among these patients. Clinically diagnosed COVID-19, independent of RT-PCR positivity, thus has a potential vital role in guiding treatment decisions.

**Diagnostics & Screening**

   [https://www.journalofinfection.com/article/S0163-4453(22)00072-X/fulltext](https://www.journalofinfection.com/article/S0163-4453(22)00072-X/fulltext)

   The use of rapid antigen diagnostics tests (Ag-RDT) has gained widespread acceptance as an alternative method for diagnosis of COVID-19 outside of health care settings. Ag-RDT offer advantages as they can be deployed by members of the general public, which require the use of self-collected specimens. Various authors have reported that saliva is a reliable specimen, alternative to nasopharyngeal and mid-nasal swabs, to detect SARS-CoV-2 infections by RT-PCR. Regarding the use of Ag-RDTs with saliva samples, previous studies have mainly reported limitations on the ability of Ag-RDT for COVID-19 diagnosis in this specimen. These limitations could be derived on the viral load distribution or sample preparation protocols, which might need to be adapted to the rheological properties of saliva. Therefore, even if several commercialized Ag-RDT tests list saliva as a possible specimen, the European Centre for Disease Prevention and Control (ECDC) currently only validates tests based on nasal, oropharyngeal and/or nasopharyngeal specimens.

**Epidemiology & Public Health**

Data from this investigation reinforce the importance of COVID-19 booster doses and early notification in combination with other multicomponent prevention measures to limit transmission and prevent severe illness from Omicron and other SARS-CoV-2 variants.

**Healthcare Delivery & Healthcare Workers**


This analysis of US academic centers showed that 28.6% of COVID-19 adults who sought care at one of the hospitals reporting data to the Vizient clinical database required in-patient treatment. The rate of hospitalization in our study was lowest for the youngest age group of 18–30 years and highest for age group >75 years. Beside older age, other factors associated with outpatient management included female gender, white race, and having commercial insurance.


Characteristics significantly associated with hesitancy included Black race/ethnicity, younger age, not having a high-risk household member, and prior personal experience with COVID-19 illness. Hesitancy was also significantly associated with many vaccine-related perceptions, including concerns about short-term and long-term side-effects and a belief that the vaccines are not effective. Among acceptant participants, wanting to protect others and wanting to help end the pandemic were the most common reasons for getting vaccinated. Personal physicians were cited most frequently as trusted source of information about COVID-19 among both vaccine-hesitant and vaccine-acceptant respondents.


In our study cohort of HCP working in an academic healthcare system, <10% had evidence of SARS-CoV-2 infection over six months. No specific occupational activities were identified as increasing risk for SARS-CoV-2 infection.

For patients admitted to ICU during the pandemic, unprecedented levels of ICU capacity strain were significantly associated with higher acute hospital mortality, after accounting for differences in baseline characteristics. Further study into possible differences in the provision of care and outcome for COVID-19 and non-COVID-19 patients is needed.

Prognosis


Of 3766 adults hospitalized with COVID-19 to three hospitals in New York City from March to May 2020, 963 were relatively lower-risk based on absence of preexisting health conditions. In individuals ≥55 years old (n = 522), 33.3% experienced a life-threatening complication, 17.4% were intubated, and 22.6% died. Among those <55 years (n = 441), 15.0% experienced a life-threatening complication, 11.1% were intubated, and 5.9% died. In multivariable analyses among those ≥55 years, age (OR 1.03 [95%CI 1.01–1.06]), male sex (OR 1.72 [95%CI 1.14–2.64]), being publicly insured (versus commercial insurance: Medicare, OR 2.02 [95%CI 1.22–3.38], Medicaid, OR 1.87 [95%CI 1.10–3.20]) and living in areas with relatively high limited English proficiency (highest versus lowest quartile: OR 3.50 [95%CI 1.74–7.13]) predicted life-threatening complications. In those <55 years, no sociodemographic factors significantly predicted life-threatening complications. A substantial proportion of relatively lower-risk patients hospitalized with COVID-19 experienced life-threatening complications and more than 1 in 20 died. Public messaging needs to effectively convey that relatively lower-risk individuals are still at risk of serious complications.


Despite increased experience and evidence-based treatments, the risk of death for patients admitted to the ICU with coronavirus disease 2019 was highest during the fall and winter of 2020. Reasons for this increased mortality are not clear.


We found that crude rates of HFNC failure assumed a U-shape as a function of time to-date using HFNC; specifically, only 1 in every 3.5 patients receiving HFNC for at least 6 days experienced failure while rates were higher among patients receiving any (1 in every 2 patients) and at least 14 days (1 in every 2.5 patients) of HFNC. However, after adjustment for patient characteristics, the probability of HFNC failure did not vary with the duration of previous support
with HFNC. Together these findings suggest that higher failure rates among cohorts inclusive of short-duration HFNC users likely reflects the fact that sicker patients received IMV early on. And, while HFNC failure rates eventually increase after 10 days receiving HFNC, this association is likely driven more by disease course and patient characteristics rather than any intrinsic harm associated with longer HFNC use itself. Moreover, there is no subgroup in which HFNC use for any amount of time up to 2 weeks is associated with odds of failure of >50%.

Survivorship & Rehabilitation


In this exploratory study of patients in 11 Dutch hospitals who survived 1 year following ICU treatment for COVID-19, physical, mental, or cognitive symptoms were frequently reported.

Therapeutics


In critically ill hospitalised patients with COVID-19 who were receiving invasive mechanical ventilation or extracorporeal membrane oxygenation, treatment with baricitinib compared with placebo (in combination with standard of care, including corticosteroids) reduced mortality, which is consistent with the mortality reduction observed in less severely ill patients in the hospitalised primary COV-BARRIER study population. However, this was an exploratory trial with a relatively small sample size; therefore, further phase 3 trials are needed to confirm these findings.


In patients admitted to hospital with COVID-19, the monoclonal antibody combination of casirivimab and imdevimab reduced 28-day mortality in patients who were seronegative (and therefore had not mounted their own humoral immune response) at baseline but not in those who were seropositive at baseline.

Methylene blue-treated convalescent plasma did not prevent progression from mild to severe illness and did not reduce viral load in outpatients with COVID-19. Therefore, formal recommendations to support the use of convalescent plasma in outpatients with COVID-19 cannot be concluded.


Famotidine was safe and well tolerated in outpatients with mild to moderate COVID-19. Famotidine led to earlier resolution of symptoms and inflammation without reducing anti-SARS-CoV-2 immunity. Additional randomised trials are required.


Treatment of symptomatic Covid-19 with nirmatrelvir plus ritonavir resulted in a risk of progression to severe Covid-19 that was 89% lower than the risk with placebo, without evident safety concerns. (Supported by Pfizer; ClinicalTrials.gov number, NCT04960202.).


In this randomized clinical trial of high-risk patients with mild to moderate COVID-19, ivermectin treatment during early illness did not prevent progression to severe disease. The study findings do not support the use of ivermectin for patients with COVID-19.

**Transmission / Infection Control**


Our study emphasizes how the built environment can be relevant during PPE doffing in the context of COVID-19 care in inpatient settings, where the design of doffing spaces around patient room doors may help reduce risks of cross-contamination and occupational stress. To increase the strength of our findings, future research should operationalize and test our suggested design guidelines and strategies using an interdisciplinary approach that focuses on measuring actual improvements in PPE doffing, especially in terms of perceived HCW workload.
Vaccines / Immunology

https://jamanetwork.com/journals/jama/fullarticle/2789151
Reports of waning antibody levels and breakthrough infections among vaccinated individuals have prompted the recommendation for vaccine boosters to prevent SARS-CoV-2 infections. Despite more than 80% of the population in Singapore having received 2 doses of a COVID-19 vaccine, cases surged in September 2021 with the relaxation of social distancing and quarantine measures. In response, adults 60 years and older who completed their primary vaccination series at least 6 months prior were invited to receive a booster injection and given a choice of either 30-μg BNT162b2 (Pfizer-BioNTech) or 50-μg mRNA-1273 (Moderna). We estimated SARS-CoV-2 infections and disease severity with the receipt of a booster and by type of booster.

https://www.acpjournals.org/doi/10.7326/M21-4130
Persons previously infected with SARS-CoV-2 gained additional protection against reinfection and COVID-19 from a subsequent single dose of the BNT162b2 vaccine. Nonetheless, even without a subsequent vaccination, reinfection appeared relatively rare.

A total of 149,032 patients who had recovered from SARS-CoV-2 infection met the eligibility criteria. Of these patients, 83,356 (56%) received subsequent vaccination during the 270-day study period. Reinfection occurred in 354 of the vaccinated patients (2.46 cases per 100,000 persons per day) and in 2168 of 65,676 unvaccinated patients (10.21 cases per 100,000 persons per day). Vaccine effectiveness was estimated at 82% (95% confidence interval [CI], 80 to 84) among patients who were 16 to 64 years of age and 60% (95% CI, 36 to 76) among those 65 years of age or older. No significant difference in vaccine effectiveness was found for one dose as compared with two doses.
CONCLUSIONS: Among patients who had recovered from Covid-19, the receipt of at least one dose of the BNT162b2 vaccine was associated with a significantly lower risk of recurrent infection.

Two doses of BNT162b2 vaccine were associated with high short-term protection against SARS-CoV-2 infection; this protection waned considerably after 6 months. Infection-acquired immunity boosted with vaccination remained high more than 1 year after infection.
https://doi.org/10.15585/mmwr.mm7107e3

The Overcoming COVID-19 network conducted a test-negative, case-control study at 20 pediatric hospitals in 17 states during July 1, 2021-January 17, 2022, to assess effectiveness of maternal completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy against COVID-19 hospitalization in infants. Among 379 hospitalized infants aged <6 months (176 with COVID-19 [case-infants] and 203 without COVID-19 [control-infants]), the median age was 2 months, 21% had at least one underlying medical condition, and 22% of case- and control-infants were born premature (<37 weeks gestation). Effectiveness of maternal vaccination during pregnancy against COVID-19 hospitalization in infants aged <6 months was 61% (95% CI = 31%-78%). Completion of a 2-dose mRNA COVID-19 vaccination series during pregnancy might help prevent COVID-19 hospitalization among infants aged <6 months.

https://academic.oup.com/cid/article/74/3/467/6430942

We did not find an increased risk of severe COVID-19 or mortality in pregnancy. Hospitalization does not necessarily indicate severe COVID-19 in pregnancy, as half of pregnant patients with COVID-19 were admitted for L&D encounters in this study.


We found a decrease in planned antenatal and delivery care use due to COVID-19 concerns. The clinical implications of potential decreases in care are unclear, but decline in essential healthcare utilization during pregnancy and delivery could pose challenges for maternal and newborn health. More research is needed to address the impact of COVID-19 on routine pregnancy and delivery care.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788844

In this cohort study of US children with SARS-CoV-2, there were observed differences in demographic characteristics, preexisting comorbidities, and initial vital sign and laboratory values between severity subgroups. Taken together, these results suggest that early identification of children likely to progress to severe disease could be achieved using readily available data elements from the day of admission. Further work is needed to translate this knowledge into improved outcomes.

The Omicron variant peak (7.1 per 100,000) was four times that of the Delta variant peak (1.8), with the largest increase observed among children aged 0-4 years. During December 2021, the monthly hospitalization rate among unvaccinated adolescents aged 12-17 years (23.5) was six times that among fully vaccinated adolescents (3.8). Strategies to prevent COVID-19 among children and adolescents, including vaccination of eligible persons, are critical.

GUIDELINES & CONSENSUS STATEMENTS


UK Health Security Agency: The effectiveness of vaccination against long COVID: A rapid evidence briefing

Commentary


If you would like to receive a customized COVID-19 Topic Alert related to your specialty or area of interest, would like a literature search conducted, or have difficulty accessing any of the above articles please contact us at librarian@providence.org

Find previous weeks here.