New Research

*note, PREPRINTS have not undergone formal peer review

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

Clinical Syndrome


   The findings revealed that concurrent infectious diseases rarely occurred despite the infrequent use of antimicrobial drugs during hospitalization among patients with COVID-19 infection, most of whom had noncritical cases. This finding supports the results of recent studies showing that concurrent bacterial infections were uncommon in patients with COVID-19 infection. Given that most patients with noncritical severity recovered without antimicrobial drugs, the use of most antimicrobial drugs to treat noncritical cases in many hospitals might be unnecessary. Antimicrobial drugs should be used cautiously to treat patients with COVID-19 infection.


   SARS-CoV-2 can cause acute testicular damage with subsequent chronic asymmetric testicular atrophy and associated hormonal changes despite a self-limiting pneumonia in hamsters. Awareness of possible hypogonadism and subfertility is important in managing convalescent COVID-19 males.


   Vaccines remain the best option for controlling the COVID-19 pandemic, but variants of concern such as Omicron continue to emerge that will probably decrease vaccine efficacy. COVID-19 has both acute manifestations and post-acute manifestations (sometimes called ‘long COVID’); given the unknown outcomes of endotheliopathies and coagulopathies in COVID-19, there may be ‘time bomb’ manifestations of COVID-19 whereby unforeseen clinical events such as increased incidences of cerebrovascular, myocardial, and kidney disease appear months after recovery from initial infection. Better, practical diagnostics and treatments for COVID-19 are desperately needed, and tissue-based...
pathology studies are vital for providing direct clues of how to understand the pathogenesis of the virus, and how to mitigate its impact.

**Diagnostics & Screening**


We conducted a multilaboratory evaluation of 21 commercial high-throughput SARS-CoV-2 serologic assays using blinded panels of 1,000 highly characterized specimens. Assays demonstrated a range of sensitivities (96%-63%), specificities (99%-96%), and precision (intraclass correlation coefficient 0.55-0.99). Durability of antibody detection was dependent on antigen and immunoglobulin targets; antispike and total Ig assays demonstrated more stable longitudinal reactivity than antinucleocapsid and IgG assays. Assays with high sensitivity, specificity, and durable antibody detection are ideal for serosurveillance, but assays demonstrating waning reactivity are appropriate for other applications, including correlation with neutralizing activity and detection of anamnestic boosting by reinfections. Assay performance must be evaluated in context of intended use, particularly in the context of widespread vaccination and circulation of SARS-CoV-2 variants.

**Epidemiology & Public Health**


Hospitalized patients with COVID-19 from socially vulnerable neighborhoods presented with greater illness severity and required more intensive treatment, but once hospitalized they did not experience differences in hospital mortality or discharge disposition. Policies that target socially vulnerable neighborhoods and access to COVID-19 care may help ameliorate health disparities.


Widespread underlying SARS-CoV-2 seropositivity was observed in Gauteng before the omicron-dominant wave of Covid-19. Epidemiologic data showed a decoupling of hospitalizations and deaths from infections while omicron was circulating. (Funded by the Bill and Melinda Gates Foundation.).


The B.1.1.529 (Omicron) variant, first detected in November 2021, was responsible for a surge in U.S. infections with SARS-CoV-2, the virus that causes COVID-19, during December 2021–January 2022 (1). To investigate the effectiveness of prevention strategies in household settings, CDC partnered with
four U.S. jurisdictions to describe Omicron household transmission during November 2021–February 2022. Persons with sequence-confirmed Omicron infection and their household contacts were interviewed. Omicron transmission occurred in 124 (67.8%) of 183 households. Among 431 household contacts, 227 were classified as having a case of COVID-19 (attack rate [AR] = 52.7%).† The ARs among household contacts of index patients who had received a COVID-19 booster dose, of fully vaccinated index patients who completed their COVID-19 primary series within the previous 5 months, and of unvaccinated index patients were 42.7% (47 of 110), 43.6% (17 of 39), and 63.9% (69 of 108), respectively. The AR was lower among household contacts of index patients who isolated (41.2%, 99 of 240) compared with those of index patients who did not isolate (67.5%, 112 of 166) (p-value <0.01). Similarly, the AR was lower among household contacts of index patients who ever wore a mask at home during their potentially infectious period (39.5%, 88 of 223) compared with those of index patients who never wore a mask at home (68.9%, 124 of 180) (p-value <0.01). Multicomponent COVID-19 prevention strategies, including up-to-date vaccination, isolation of infected persons, and mask use at home, are critical to reducing Omicron transmission in household settings.


To determine the extent of gaps in coronavirus disease (COVID-19) vaccine coverage among those in the United States with and without previous COVID-19 diagnoses, we used data from a large, nationally representative survey conducted during July 21-August 2, 2021. We analyzed vaccine receipt (≥1 dose and full vaccination) and intention to be vaccinated for 63,266 persons. Vaccination receipt was lower among those who had a prior diagnosis of COVID-19 compared to those without: >1 dose: 73% and 85%, respectively, p<0.001; full vaccination: 69% and 82%, respectively, p<0.001). Reluctance to be vaccinated was higher among those with a previous COVID-19 diagnosis (14%) than among those without (9%). These findings suggest the need to focus educational and confidence-building interventions on adults who receive a COVID-19 diagnosis during clinic visits, or at the time of discharge if hospitalized, and to better educate the public about the value of being vaccinated, regardless of previous COVID-19 infection.


On January 5, 2022, the Yukon-Kuskokwim Health Corporation (YKHC) recommended that persons with SARS-CoV-2 infection isolate for 10 days after symptom onset (or, for asymptomatic persons, 10 days after a positive nucleic acid amplification or antigen test result). However, isolation could end after 5-9 days if symptoms were resolving or absent, fever was absent for ≥24 hours without fever-reducing medications, and an Abbott BinaxNOW COVID-19 Ag (BinaxNOW) rapid antigen test result was negative. Antigen test results and associated individual characteristics were analyzed among 3,502 infections reported to YKHC during January 1-February 9, 2022. After 5-9 days, 396 of 729 persons evaluated (54.3%) had a positive antigen test result, with a declining percentage positive over time. In a multivariable model, a positive antigen test result was more likely after 5 days compared with 9 days (adjusted odds ratio [aOR] = 6.39) or after symptomatic infection (aOR = 9.63), and less likely after
previous infection (aOR = 0.30), receipt of a primary COVID-19 vaccination series (aOR = 0.60), or after both previous infection and receipt of a primary COVID-19 vaccination series (aOR = 0.17). Antigen tests might be a useful tool to guide recommendations for isolation after SARS-CoV-2 infection. During the 10 days after infection, persons might be infectious to others and are recommended to wear a well-fitting mask when around others, even if ending isolation after 5 days.

Prognosis


A model to predict clinical deterioration was developed rapidly in response to the covid-19 pandemic at a single hospital, was applied externally without the sharing of data, and performed well across multiple medical centers, patient subgroups, and time periods, showing its potential as a tool for use in optimizing healthcare resources.


The findings of this study of patients with active cancer suggest that recent SACT is not associated with inferior outcomes from COVID-19 infection. This has relevance for the care of patients with cancer requiring treatment, particularly in countries experiencing an increase in COVID-19 case numbers. Important differences in outcomes among patients with hematological and lung cancers were observed.

Therapeutics


Hypoxaemia in COVID-19 is primarily caused by disruption of the alveolocapillary barrier on inflammation and dysfunction of the endothelium. To date, antiviral or immune-modulatory treatment options have been thoroughly studied, yet there is no approved therapy targeting endothelial dysfunction. Imatinib is a tyrosine kinase inhibitor that attenuates vascular leakage under inflammatory conditions. In the CounterCOVID study, patients admitted to hospital with COVID-19 treated with imatinib had a shorter duration of invasive ventilation and shorter stay at the intensive care unit (ICU). Although a signal for reduced mortality was observed, a definite answer on mortality was precluded by correction for imbalances in patient characteristics at baseline and the short follow-up of 28 days. Here we report the 90-day outcomes of the CounterCOVID study and investigate the mechanisms underlying the clinical benefit of imatinib.

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.


ECMO facilitates salvage and survival of select critically ill patients with COVID-19. Survivors tend to be younger and have shorter time from diagnosis to intubation. Survival of patients supported with only veno-venous ECMO was 39.5%.

**Transmission / Infection Control**


In a study of household transmission in four U.S. jurisdictions, Omicron infection resulted in high transmission among household contacts, particularly among those who lived with index patients who were not vaccinated or who did not take measures to reduce the risk of transmission to household contacts. Multicomponent COVID-19 prevention strategies, including up-to-date vaccination, isolation of infected persons, and mask use at home, are important to reduce Omicron transmission in household settings.


We aimed to evaluate this efficacy of masks used by SARS-CoV-2-infected individuals. Data, masks used, and nasopharyngeal swab samples were obtained from these patients. Forty-five paired samples of nasopharyngeal swabs and masks were obtained and processed; the majority of masks were woven. Viral RNAs were amplified using quantitative reverse-transcription polymerase chain reaction and detected only on the inner parts of masks. Median viral load (VL) values of swabs and masks were 1.954x10^6 and 2.51x10^3, respectively. Statistically, there was a difference of approximately 1000 RNA copies/mL between swabs and masks and no significant difference in VL values among different types of masks. There were statistically significant differences in VL values between men and women and between symptomatic and asymptomatic patients. Our findings suggest the blocking of virus transmission by different types of masks and reinforce the use of masks by both infected and non-infected individuals.
226 primary cases were followed by 198 (49%) secondary SARS-CoV-2 infections among 404 household contacts. Age group-specific SIR among contacts ranged from 36% to 53%, with no differences by age. SIR was lower in primary cases age 12 to 17 years than from primary cases 18 to 49 years. SIR was 55% and 45%, respectively, among primary case-contact pairs in the same versus different age group. SIR was highest among primary case-contact pairs age ≥65 years (76%) and 5 to 11 years (69%). Among secondary SARS-CoV-2 infections, 19% were asymptomatic; there was no difference in the frequency of asymptomatic infections by age group. Both children and adults can transmit and are susceptible to SARS-CoV-2 infection. SIR did not vary by age, but further research is needed to understand age-related differences in probability of transmission from primary cases by age.

**Vaccines / Immunology**


We conducted a test-negative case-control study to evaluate mRNA-1273 vaccine effectiveness (VE) against infection and hospitalization with Omicron or Delta. The large, diverse study population included 26,683 SARS-CoV-2 test-positive cases with variants determined by S-gene target failure status (16% Delta, 84% Omicron). The 2-dose VE against Omicron infection at 14-90 days was 44.0% (95% CI, 35.1-51.6%) but declined quickly. The 3-dose VE was 93.7% (92.2-94.9%) and 86.0% (78.1-91.1%) against Delta infection and 71.6% (69.7-73.4%) and 47.4% (40.5-53.5%) against Omicron infection at 14-60 days and >60 days, respectively. The 3-dose VE was 29.4% (0.3-50.0%) against Omicron infection in immunocompromised individuals. The 3-dose VE against hospitalization with Delta or Omicron was >99% across the entire study population. Our findings demonstrate high, durable 3-dose VE against Delta infection but lower effectiveness against Omicron infection, particularly among immunocompromised people. However, 3-dose VE of mRNA-1273 was high against hospitalization with Delta and Omicron variants.


Although preliminary evidence suggests booster doses might enhance protection against omicron, studies are underway to fully determine vaccine effectiveness. Given the natural lag between infection and severe outcomes, we await further data on omicron for effectiveness of vaccinations in preventing severe disease—the key intended outcome of vaccination. In the meantime, the South Africa National Institute for Communicable Diseases has shared preliminary data indicating a decoupling of infection rates from hospitalisations and deaths with omicron. These data suggest underlying immune responses following infection and that primary and booster vaccination might attenuate the course of illness.

In this systematic review and meta-analysis of case studies and case reports, the risk of immediate allergic reactions and severe immediate reactions or anaphylaxis associated with a second dose of an SARS-CoV-2 mRNA vaccine was low among persons who experienced an immediate allergic reaction to their first dose. These findings suggest that revaccination of individuals with an immediate allergic reaction to a first SARS-CoV-2 mRNA vaccine dose in a supervised setting equipped to manage severe allergic reactions can be safe.

21. **Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression.** Feikin DR et al. *Lancet.* 2022 Feb 21:S0140-6736(22)00152-0. doi: 10.1016/S0140-6736(22)00152-0. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00152-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00152-0/fulltext)

COVID-19 vaccine efficacy or effectiveness against severe disease remained high, although it did decrease somewhat by 6 months after full vaccination. By contrast, vaccine efficacy or effectiveness against infection and symptomatic disease decreased approximately 20-30 percentage points by 6 months. The decrease in vaccine efficacy or effectiveness is likely caused by, at least in part, waning immunity, although an effect of bias cannot be ruled out. Evaluating vaccine efficacy or effectiveness beyond 6 months will be crucial for updating COVID-19 vaccine policy.


We conducted a nationwide retrospective cohort study to estimate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) breakthrough infection among recipients of 4 different vaccines in South Korea. Age-adjusted breakthrough infection rate per month was highest for Janssen (42.6/100,000 population), followed by AstraZeneca (21.7/100,000 population), Pfizer-BioNTech (8.5/100,000 population), and Moderna (1.8/100,000 population).


Mutations in viral genome arise as a natural by-product of viral replication and their fate is determined by natural selection. Accordingly, in the context of ‘variants of concern’ (VOC), SARS-CoV-2 evolution has been characterized by wide variation, altering transmissibility, antigenicity, immune response and disease severity. The most recent Omicron variant (B.1.1.529) puts scientists on alert because of its Spike protein extended mutational pattern, which could challenge the effectiveness of the worldwide vaccinal campaign: the receptor binding domain (RBD) presents 15 amino acid changes, some of which have been associated with increased binding affinity to ACE2; in addition, three mutations close to S1/S2 furin cleavage site may increase transmissibility, while the presence of several deletions and insertions in the N-terminal domain (NTD) have been shown to compromise some established PCR assays.
Women & Children


Rapid increases in paediatric COVID-19 cases and hospitalisations mirror high community transmission of the SARS-CoV-2 omicron variant in Tshwane District, South Africa. Continued monitoring is needed to understand the long-term effect of the omicron variant on children and adolescents.


In October 2021, the US Food and Drug Administration granted emergency use authorization for the BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine to be used in children aged 5 to 11 years to reduce costly hospitalizations. By that time, for children in this age group, there had been 1.8 million people diagnosed with SARS-CoV-2 infection and 143 deaths, with more than 8000 hospitalizations. However, very little is known about the severity of these hospitalizations relative to the 2 most common childhood viruses, the influenza virus and respiratory syncytial virus (RSV), which resemble the SARS-CoV-2 virus. In this study, we compared the January through March 2021 hospitalizations of children aged 5 to 11 years who were diagnosed with SARS-CoV-2 infection and multisystem inflammatory syndrome in children (MIS-C; a sequela of COVID-19 disease) with those hospitalizations of children aged 5 to 11 years infected with influenza and RSV.

26. **Pediatric Emergency Department Visits Associated with Mental Health Conditions Before and During the COVID-19 Pandemic - United States, January 2019-January 2022.** Radhakrishnan L et al. *MMWR Morb Mortal Wkly Rep.* 2022 Feb 25;71(8):319-324. doi: 10.15585/mmwr.mm7108e2. [https://www.cdc.gov/mmwr/volumes/71/wr/mm7108e2.htm?s_cid=mm7108e2_w](https://www.cdc.gov/mmwr/volumes/71/wr/mm7108e2.htm?s_cid=mm7108e2_w)

In 2021, a national emergency* for children's mental health was declared by several pediatric health organizations, and the U.S. Surgeon General released an advisory† on mental health among youths. These actions resulted from ongoing concerns about children's mental health in the United States, which was exacerbated by the COVID-19 pandemic. During March-October 2020, among all emergency department (ED) visits, the proportion of mental health-related visits increased by 24% among U.S. children aged 5-11 years and 31% among adolescents aged 12-17 years, compared with 2019 (2). CDC examined changes in U.S. pediatric ED visits for overall mental health conditions (MHCs) and ED visits associated with specific MHCs (depression; anxiety; disruptive behavioral and impulse-control disorders; attention-deficit/hyperactivity disorder; trauma and stressor-related disorders; bipolar disorders; eating disorders; tic disorders; and obsessive-compulsive disorders [OCD]) during 2019 through January 2022 among children and adolescents aged 0-17 years, overall and by sex and age. After declines in weekly visits associated with MHCs among those aged 0-17 years during 2020, weekly numbers of ED visits for MHCs overall and for specific MHCs varied by age and sex during 2021 and January 2022, when compared with corresponding weeks in 2019. Among adolescent females aged 12-
17 years, weekly visits increased for two of nine MHCs during 2020 (eating disorders and tic disorders), for four of nine MHCs during 2021 (depression, eating disorders, tic disorders, and OCD), and for five of nine MHCs during January 2022 (anxiety, trauma and stressor-related disorders, eating disorders, tic disorders, and OCD), and overall MHC visits during January 2022, compared with 2019. Early identification and expanded evidence-based prevention and intervention strategies are critical to improving children's and adolescents' mental health, especially among adolescent females, who might have increased need.


CDC examined changes in U.S. ED visit trends to assess the continued impact of the pandemic on visits among children and adolescents aged 0-17 years (pediatric ED visits). Compared with 2019, pediatric ED visits declined by 51% during 2020, 22% during 2021, and 23% during January 2022. Although visits for non-COVID-19 respiratory illnesses mostly declined, the proportion of visits for some respiratory conditions increased during January 2022 compared with 2019. Weekly number and proportion of ED visits increased for certain types of injuries (e.g., drug poisonings, self-harm, and firearm injuries) and some chronic diseases, with variation by pandemic year and age group. Visits related to behavioral concerns increased across pandemic years, particularly among older children and adolescents. Health care providers and families should remain vigilant for potential indirect impacts of the COVID-19 pandemic, including health conditions resulting from delayed care, and increasing emotional distress and behavioral health concerns among children and adolescents.

GUIDELINES & CONSENSUS STATEMENTS


FDA / CDC / NIH / WHO Updates

CDC – Mask guidance based on COVID-19 Community Level

CDC - Added considerations for an 8-week interval between the first and second doses of a primary mRNA vaccine schedule
Commentary & News


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