

COVID-19 Resource Desk

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Prepared by System Library Services

Retraction Watch

New Research

*note, **PREPRINTS** have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see <u>Digital Commons</u>

Clinical Syndrome

- 1. Secondary infections in critically ill patients with COVID-19. Grasselli G, et al. Crit Care. 2021 Aug 31;25(1):317. doi: 10.1186/s13054-021-03672-9. https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03672-9
 For a number of reasons, patients with COVID-19 admitted to the ICU are at high risk of developing infectious complications during their ICU stay. First, they frequently develop multiple organ failure with need for vasopressors, renal replacement therapy (RRT) and, in some cases, extracorporeal membrane oxygenation support. The duration of mechanical ventilation and the ICU lengths of stay of these patients are therefore usually prolonged (up to 19 days for mechanical ventilation and up to 49 days for ICU length of stay). Second, COVID-19 per se is associated with significant dysfunction of the patient's immune system. Multiple studies have shown the involvement of both innate and acquired immunity as a response to SARS-CoV-2 infection.
- 2. Association between COVID-19 and Myocarditis Using Hospital-Based Administrative Data -United States, March 2020-January 2021. Boehmer TK, et al. MMWR Morb Mortal Wkly Rep. 2021 Sep 3;70(35):1228-1232. doi: 10.15585/mmwr.mm7035e5. https://www.cdc.gov/mmwr/volumes/70/wr/mm7035e5.htm During March 2020-January 2021, the period that coincided with the COVID-19 pandemic, the risk for myocarditis was 0.146% among patients diagnosed with COVID-19 during an inpatient or hospital-based outpatient encounter and 0.009% among patients who were not diagnosed with COVID-19. After adjusting for patient and hospital characteristics, patients with COVID-19 during March 2020-January 2021 had, on average, 15.7 times the risk for myocarditis compared with those without COVID-19 (95% confidence interval [CI] = 14.1-17.2); by age, risk ratios ranged from approximately 7.0 for patients aged 16-39 years to >30.0 for patients aged <16 years or ≥75 years. Overall, myocarditis was uncommon among persons with and without COVID-19; however, COVID-19 was significantly associated with an increased risk for myocarditis, with risk varying by age group. These findings underscore the importance of implementing evidence-based COVID-19 prevention strategies, including vaccination, to reduce the public health impact of COVID-19 and its associated complications.

Diagnostics & Screening

3. Validation of an At-Home Direct Antigen Rapid Test for COVID-19. Harmon A, et al. JAMA Netw Open. 2021 Aug 2;4(8):e2126931. doi: 10.1001/jamanetworkopen.2021.26931 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783550
Rapid antigen tests that permit new cases to isolate immediately can be important surveillance tools. A longitudinal comparison between antigen tests performed at home and qRT-PCR has not previously been performed, to our knowledge. Here, we describe implementation of high-frequency testing using inexpensive, at-home, semiquantitative, direct antigen rapid tests (DARTs) and compare their performance with that of qRT-PCR on self-collected nasal specimens.

Epidemiology & Public Health

- 4. Factors Associated with Household Transmission of SARS-CoV-2: An Updated Systematic Review and Meta-analysis. Madewell ZJ, et al. JAMA Netw Open. 2021 Aug 2;4(8):e2122240. doi: 10.1001/jamanetworkopen.2021.22240. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783544
 The findings of this study suggest that the household remains an important site of SARS-CoV-2 transmission, and recent studies have higher household SAR estimates compared with the earliest reports. More transmissible variants and vaccines may be associated with further changes.
- 5. Outbreak Associated with SARS-CoV-2 B.1.617.2 (Delta) Variant in an Elementary School -Marin County, California, May-June 2021. Lam-Hine T, et al. MMWR Morb Mortal Wkly Rep. 2021 Sep 3;70(35):1214-1219. doi: 10.15585/mmwr.mm7035e2. https://www.cdc.gov/mmwr/volumes/70/wr/mm7035e2.htm On May 25, 2021, the Marin County Department of Public Health (MCPH) was notified by an elementary school that on May 23, an unvaccinated teacher had reported receiving a positive test result for SARS-CoV-2, the virus that causes COVID-19. The teacher reported becoming symptomatic on May 19, but continued to work for 2 days before receiving a test on May 21. On occasion during this time, the teacher read aloud unmasked to the class despite school requirements to mask while indoors. Beginning May 23, additional cases of COVID-19 were reported among other staff members, students, parents, and siblings connected to the school. To characterize the outbreak, on May 26, MCPH initiated case investigation and contact tracing that included whole genome sequencing (WGS) of available specimens. A total of 27 cases were identified, including that of the teacher. During May 23-26, among the teacher's 24 students, 22 students, all ineligible for vaccination because of age, received testing for SARS-CoV-2; 12 received positive test results. The attack rate in the two rows seated closest to the teacher's desk was 80% (eight of 10) and was 28% (four of 14) in the three back rows (Fisher's exact test; p = 0.036). During May 24-June 1, six of 18 students in a separate grade at the school, all also too young for vaccination, received positive SARS-CoV-2 test results. Eight additional cases were also identified, all in parents and siblings of students in these two grades. Among these

additional cases, three were in persons fully vaccinated in accordance with CDC recommendations. Among the 27 total cases, 22 (81%) persons reported symptoms; the most frequently reported symptoms were fever (41%), cough (33%), headache (26%), and sore throat (26%). WGS of all 18 available specimens identified the B.1.617.2 (Delta) variant. Vaccines are effective against the Delta variant, but risk of transmission remains elevated among unvaccinated persons in schools without strict adherence to prevention strategies. In addition to vaccination for eligible persons, strict adherence to nonpharmaceutical prevention strategies, including masking, routine testing, facility ventilation, and staying home when symptomatic, are important to ensure safe in-person learning in schools.

- 6. Estimated US Infection- and Vaccine-Induced SARS-CoV-2 Seroprevalence Based on Blood Donations, July 2020-May 2021. Jones JM et al. JAMA. 2021 Sep 2. doi: 10.1001/jama.2021.15161. https://jamanetwork.com/journals/jama/fullarticle/2784013 Among 1 443 519 specimens included, 733 052 (50.8%) were from women, 174 842 (12.1%) were from persons aged 16 to 29 years, 292 258 (20.2%) were from persons aged 65 years and older, 36 654 (2.5%) were from non-Hispanic Black persons, and 88 773 (6.1%) were from Hispanic persons. The overall infection-induced SARS-CoV-2 seroprevalence estimate increased from 3.5% (95% CI, 3.2%-3.8%) in July 2020 to 20.2% (95% CI, 19.9%-20.6%) in May 2021; the combined infection- and vaccination-induced seroprevalence estimate in May 2021 was 83.3%. By May 2021, 2.1 SARS-CoV-2 infections per reported COVID-19 case were estimated to have occurred. Based on a sample of blood donations in the US from July 2020 through May 2021, vaccine- and infection-induced SARS-CoV-2 seroprevalence increased over time and varied by age, race and ethnicity, and geographic region. Despite weighting to adjust for demographic differences, these findings from a national sample of blood donors may not be representative of the entire US population.
- 7. The impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections in 2020: A summary of data reported to the National Healthcare Safety Network. Weiner-Lastinger LM, et al. Infect Control Hosp Epidemiol. 2021 Sep 3:1-14. doi: 10.1017/ice.2021.362.https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/impact-of-coronavirus-disease-2019-covid19-on-healthcare-associated-infections-in-2020-a-summary-of-data-reported-to-the-national-healthcare-safety-network/8197F323F4840D233A0C62F4726287E1

 Significant increases in the national SIRs for CLABSI, CAUTI, VAE, and MRSA bacteremia were observed in 2020. Changes in the SIR varied by quarter and state. The largest increase was observed for CLABSI, and significant increases in VAE incidence and ventilator utilization were seen across all 4 quarters of 2020. This report provides a national view of the increases in HAI incidence in 2020. These data highlight the need to return to conventional infection prevention and control practices and build resiliency in these programs to withstand future pandemics.

Healthcare Delivery & Healthcare Workers

8. Hospital admission and emergency care attendance risk for SARS-CoV-2 delta (B.1.617.2) compared with alpha (B.1.1.7) variants of concern: a cohort study. Twohig KA et al. Lancet Infect Dis. 2021 Aug 27:S1473-3099(21)00475-8. doi: 10.1016/S1473-3099(21)00475-8. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00475-8/fulltext
This large national study found a higher hospital admission or emergency care attendance risk for patients with COVID-19 infected with the delta variant compared with the alpha variant. Results suggest that outbreaks of the delta variant in unvaccinated populations might lead to a greater burden on health-care services than the alpha variant.

See also: Importance of epidemiological factors in the evaluation of transmissibility and clinical severity of SARS-CoV-2 variants. Lechien JR, Saussez S. Lancet Infect Dis. 2021 Aug 27:S1473-3099(21)00474-6. doi: 10.1016/S1473-3099(21)00474-6.

- 9. Durability of Spike Immunoglobin G Antibodies to SARS-CoV-2 among Health Care Workers with Prior Infection. Egbert ER, et al. JAMA Netw Open. 2021 Aug 2;4(8):e2123256. doi: 10.1001/jamanetworkopen.2021.23256. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783618
 Herd immunity is needed to reduce deaths, prevent transmission, and minimize the emergence of SARS-CoV-2 variants. The durability of serum antibodies against the spike protein of this virus provides insights into immunologic memory following natural infection. Recent literature supports that the levels of spike antibodies induced by natural infection correlate with neutralization and protect against subsequent infection. We evaluated the durability of naturally acquired spike immunoglobin (Ig) G antibodies to SARS-CoV-2 among a cohort of health care workers.
- 10. Choosing Wisely for COVID-19: ten evidence-based recommendations for patients and physicians. Pramesh CS et al. *Nat Med.* 2021 Aug;27(8):1324-1327. doi: 10.1038/s41591-021-01439-x. https://www.nature.com/articles/s41591-021-01439-x
 The Choosing Wisely initiative was begun to promote conversations between patients and physicians about avoiding unnecessary medical interventions. The mission of Choosing Wisely is to help patients and physicians choose care that is evidence based, not duplicative, free from harm, and truly necessary. It works by creating lists of 'things clinicians and patients should question', something that is particularly appropriate to public-health responses and management decisions in the current pandemic. In response to the widespread use of non–evidence-based practices, we initiated Choosing Wisely for COVID-19 to identify 'best buys' for the general public, patients and physicians.
- 11. Resurgence of SARS-CoV-2 Infection in a Highly Vaccinated Health System Workforce. Keehner J, et al. N Engl J Med. 2021 Sep 1. doi: 10.1056/NEJMc2112981. https://www.nejm.org/doi/10.1056/NEJMc2112981
 In December 2020, the University of California San Diego Health (UCSDH) workforce experienced a dramatic increase in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. Vaccination with mRNA vaccines began in mid-December 2020; by March,

76% of the workforce had been fully vaccinated, and by July, the percentage had risen to 83%. Infections had decreased dramatically by early February 2021. Between March and June, fewer than 30 health care workers tested positive each month. However, coincident with the end of California's mask mandate on June 15 and the rapid dominance of the B.1.617.2 (delta) variant that first emerged in mid-April and accounted for over 95% of UCSDH isolates by the end of July, infections increased rapidly, including cases among fully vaccinated persons.

Prognosis

12. Risk factors and outcome of pulmonary aspergillosis in critically ill coronavirus disease 2019 patients- a multinational observational study by the European Confederation of Medical Mycology. Prattes J et al. *Clin Microbiol Infect*. 2021 Aug 25:S1198-743X(21)00474-2. doi: 10.1016/j.cmi.2021.08.014. https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00474-2/fulltext

Prevalence of CAPA varied between centers. CAPA was significantly more prevalent among older patients, patients receiving invasive ventilation and patients receiving tocilizumab, and was an independent strong predictor of ICU mortality.

Survivorship & Rehabilitation

- 13. 1-year outcomes in hospital survivors with COVID-19: a longitudinal cohort study. Huang L et al. Lancet. 2021 Aug 28;398(10302):747-758. doi: 10.1016/S0140-6736(21)01755-4. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01755-4/fulltext Most COVID-19 survivors had a good physical and functional recovery during 1-year follow-up, and had returned to their original work and life. The health status in our cohort of COVID-19 survivors at 12 months was still lower than that in the control population.
- 14. One-Year Outcomes of Critical Care Patients Post-COVID-19 Multisystem Inflammatory Syndrome in Children. Davies P, et al. *JAMA Pediatr.* 2021 Aug 30. doi: 10.1001/jamapediatrics.2021.2993.

https://jamanetwork.com/journals/jamapediatrics/fullarticle/2783539

Medium- to long-term outcomes of the novel pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS)1 or multisystem inflammatory syndrome in children (MIS-C) are unknown. Short-term, 40-day, and 6-month outcomes have been published previously.

15. Evolution of COVID-19 symptoms during the first 12 months after illness onset. Wynberg E et al. *Clin Infect Dis.* 2021 Sep 2:ciab759. doi: 10.1093/cid/ciab759. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab408/6276644

The proportion of participants who reported at least one persistent symptom at 12 weeks after illness onset was greater in those with severe/critical disease (86.7%) compared to those with mild or moderate disease (30.7% and 63.8%). At twelve months after illness onset, two-fifths of participants continued to report ≥ 1 symptom. Recovery was slower in female compared to male participants and those with a BMI ≥ 30 kg/m 2 compared to BMI< 25kg/m 2.

Therapeutics

- 16. First in Human Study of Bamlanivimab in a Randomized Trial of Hospitalized Patients with COVID-19. Chen P et al. *Clin Pharmacol Ther.* 2021 Aug 28. doi: 10.1002/cpt.2405. https://ascpt.onlinelibrary.wiley.com/doi/abs/10.1002/cpt.2405
 - A total of 24 patients received either placebo or a single dose of bamlanivimab (700mg, 2800mg, 7000mg). The primary objective was assessment of safety and tolerability, including adverse events and serious adverse events, with secondary objectives of pharmacokinetic (PK) and pharmacodynamic (PD) analyses. Treatment-emergent adverse event (TEAE) rates were identical in the placebo and pooled bamlanivimab groups (66.7%). There were no apparent dose-related increases in the number or severity of TEAEs. There were no serious adverse events or deaths during the study, and no discontinuations due to adverse events. PK of bamlanivimab is linear and exposure increased proportionally with dose following single IV administration. The half-life was approximately 17 days. These results demonstrate the favourable safety profile of bamlanivimab, and provided the initial critical evaluation of safety, tolerability and PK in support of the development of bamlanivimab in several ongoing clinical trials.
- 17. Optimal dose and safety of molnupiravir in patients with early SARS-CoV-2: a Phase I, open-label, dose-escalating, randomized controlled study. Khoo SH et al. *J Antimicrob Chemother*. 2021 Aug 27:dkab318. doi: 10.1093/jac/dkab318. https://academic.oup.com/jac/advance-article/doi/10.1093/jac/dkab318/6358705
 - Of 103 participants screened, 18 participants were enrolled between 17 July and 30 October 2020. Molnupiravir was well tolerated at 300, 600 and 800 mg doses with no serious or severe adverse events. Overall, 4 of 4 (100%), 4 of 4 (100%) and 1 of 4 (25%) of the participants receiving 300, 600 and 800 mg molnupiravir, respectively, and 5 of 6 (83%) controls, had at least one adverse event, all of which were mild (\leq grade 2). The probability of \geq 30% excess toxicity over controls at 800 mg was estimated at 0.9%. Molnupiravir was safe and well tolerated; a dose of 800 mg twice daily for 5 days was recommended for Phase II evaluation.
- 18. **Tracheostomy for COVID-19: evolving best practice.** Williams T, McGrath BA. *Crit Care.* 2021 Aug 31;25(1):316. doi: 10.1186/s13054-021-03674-7. https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03674-7

As with many aspects of management, our understanding of how best to employ tracheostomy during the pandemic has evolved. There are many potential benefits of tracheostomy for the patient and for stressed healthcare systems, which have led some institutions to employ tracheostomy relatively early in the patient's ICU stay, but detailed outcome data from large case series are not available. Importantly, in non-COVID-19 patients, only around 20% of tracheostomy patients survive beyond ICU discharge to 1 year, repeatedly raising questions about patient selection, which are relevant as hospitals around the world struggle to manage large volumes of critically ill patients. These problems are compounded in the pandemic with patients frequently managed in makeshift or unfamiliar settings, often by non-CU trained medical, nursing and allied healthcare professional staff.

- 19. Comparative therapeutic efficacy of interferon alfa-2b and combination lopinavir/ritonavir plus interferon alfa-2b against SARS-CoV-2. Liu J, et al. BMC Infect Dis. 2021 Aug 30;21(1):885. doi: 10.1186/s12879-021-06595-6. https://pubmed.ncbi.nlm.nih.gov/34461841/ In patients with confirmed SARS-CoV-2 infection, no benefit was observed from interferon alfa-2b or LPV/r plus interferon alfa-2b treatment. The findings may provide references for treatment guidelines of patients with SARS-CoV-2 infection.
- 20. Association of Pre-Hospital Antiplatelet Therapy with Survival in Patients Hospitalized with COVID-19: A Propensity Score-Matched Analysis. Chow JH et al. *J Thromb Haemost*. 2021 Aug 29. doi: 10.1111/jth.15517. https://onlinelibrary.wiley.com/doi/10.1111/jth.15517
 In the largest observational study to date of pre-hospital antiplatelet therapy in patients with COVID-19, there was an association with significantly lower in-hospital mortality. Randomized controlled trials in diverse patient populations with high rates of baseline comorbidities are needed to determine the ultimate utility of antiplatelet therapy in COVID-19.
- 21. Fostamatinib for the treatment of hospitalized adults with COVD-19 A randomized trial. Strich JR et al. Clin Infect Dis. 2021 Sep 1:ciab732. doi: 10.1093/cid/ciab732. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab732/6358811
 For COVID-19 requiring hospitalization, the addition of fostamatinib to standard of care was safe and patients were observed to have improved clinical outcomes compared to placebo. These results warrant further validation in larger confirmatory trials.

Transmission / Infection Control

22. Risk of SARS-CoV-2 transmission from universally masked healthcare workers to patients or residents: A prospective cohort study. Williams VR, et al. Am J Infect Control. 2021 Aug 26:S0196-6553(21)00556-3. doi: 10.1016/j.ajic.2021.08.024. https://www.ajicjournal.org/article/S0196-6553(21)00556-3/fulltext
In a multi-facility prospective cohort study, we identified 116 acute care, 26 long-term care, and 67 rehabilitation patients who received direct care from a universally masked healthcare worker while communicable with COVID-19. Among 133(64%) patients with at least 14-day follow-up, three (2.3%, 95% CI, 0.77-6.4) became positive for SARS-CoV-2. Universal masking, embedded with other infection control practices, is associated with low risk of transmission of SARS-CoV-2 from healthcare workers to patients and residents.

Vaccines / Immunology

23. Association between Exposure Characteristics and the Risk for COVID-19 Infection among Health Care Workers with and Without BNT162b2 Vaccination. Oster Y, et al. JAMA Netw Open. 2021 Sep 1;4(9):e2125394. doi: 10.1001/jamanetworkopen.2021.25394. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783675
Mass vaccination of Israeli adults with the BNT162b2 vaccine has been associated with a substantially lower rate of SARS-CoV-2 infection. After the vaccination program, the Centers for

Disease Control and Prevention eliminated the need for quarantine after exposure. However, there are still cases of SARS-CoV-2 infection among fully vaccinated individuals. We studied the possible association between exposure characteristics and infection risk among vaccinated and nonvaccinated health care workers (HCWs) in Israel.

24. Evolution of antibody responses up to 13 months after SARS-CoV-2 infection and risk of reinfection. Gallais F et al. *EBioMedicine*. 2021 Aug 26;71:103561. doi: 10.1016/j.ebiom.2021.103561. https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964(21)00354-6/fulltext

Our study demonstrates a long-term persistence of anti-RBD antibodies that may reduce risk of reinfection. By significantly increasing cross-neutralizing antibody titers, a single-dose vaccination strengthens protection against variants.

- 25. Neutralization of SARS-CoV-2 variants by convalescent and BNT162b2 vaccinated serum.

 Bates TA et al. Nat Commun. 2021 Aug 26;12(1):5135. doi: 10.1038/s41467-021-25479-6.

 https://www.nature.com/articles/s41467-021-25479-6

 SARS CoV 2 and its variants continue to infect handwards of the average decreased as a first three decreas
 - SARS-CoV-2 and its variants continue to infect hundreds of thousands every day despite the rollout of effective vaccines. Therefore, it is essential to understand the levels of protection that these vaccines provide in the face of emerging variants. Here, we report two demographically balanced cohorts of BNT162b2 vaccine recipients and COVID-19 patients, from which we evaluate neutralizing antibody titers against SARS-CoV-2 as well as the B.1.1.7 (alpha) and B.1.351 (beta) variants. We show that both B.1.1.7 and B.1.351 are less well neutralized by serum from vaccinated individuals, and that B.1.351, but not B.1.1.7, is less well neutralized by convalescent serum. We also find that the levels of variant-specific anti-spike antibodies are proportional to neutralizing activities. Together, our results demonstrate the escape of the emerging SARS-CoV-2 variants from neutralization by serum antibodies, which may lead to reduced protection from re-infection or increased risk of vaccine breakthrough.
- 26. Effect of Immunosuppression on the Immunogenicity of mRNA Vaccines to SARS-CoV-2: A Prospective Cohort Study. Deepak P et al. Ann Intern Med. 2021 Aug 31. doi: 10.7326/M21-1757. https://www.acpjournals.org/doi/10.7326/M21-1757
 Compared with nonusers, patients with CID treated with glucocorticoids and BCDT seem to have lower SARS-CoV-2 vaccine-induced antibody responses. These preliminary findings require confirmation in a larger study.
- 27. Single-dose mRNA vaccine effectiveness against SARS-CoV-2 in healthcare workers extending 16 weeks post-vaccination: a test-negative design from Quebec, Canada. Carazo S et al. Clin Infect Dis. 2021 Aug 30:ciab739. doi: 10.1093/cid/ciab739. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab739/6359881
 One mRNA vaccine dose provided substantial and sustained protection to HCWs extending at least four months post-vaccination. In circumstances of vaccine shortage, delaying the second dose may be a pertinent public health strategy to consider.

- 28. Comparison of SARS-CoV-2 Antibody Response Following Vaccination with BNT162b2 and mRNA-1273. Steensels D, et al. *JAMA*. 2021 Aug 30. doi: 10.1001/jama.2021.15125. https://jamanetwork.com/journals/jama/fullarticle/2783797
 The SARS-CoV-2 messenger RNA (mRNA) vaccines BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) have each shown more than 90% efficacy in preventing COVID-19 illness but, to our knowledge, humoral immune responses have not been compared directly. This study demonstrated a significantly higher humoral immunogenicity of the SARS-CoV-2 mRNA-1273 vaccine (Moderna) compared with the BNT162b2 vaccine (Pfizer-BioNTech), in infected as well as uninfected participants, and across age categories. The higher mRNA content in mRNA-1273 compared with BNT162b2 and the longer interval between priming and boosting for mRNA-12733 (4 weeks vs 3 weeks for BNT162b2) might explain this difference.
- 29. Effectiveness of the CoronaVac vaccine in older adults during a gamma variant associated epidemic of covid-19 in Brazil: test negative case-control study. Ranzani OT et al. BMJ. 2021 Aug 20;374:n2015. doi: 10.1136/bmj.n2015. https://www.bmj.com/content/374/bmj.n2015
 Vaccination with CoronaVac was associated with a reduction in symptomatic covid-19, hospital admissions, and deaths in adults aged ≥70 years in a setting with extensive transmission of the gamma variant. Vaccine protection was, however, low until completion of the two dose regimen, and vaccine effectiveness was observe to decline with increasing age among this elderly population.
- 30. Effectiveness of BNT162b2 and mRNA-1273 covid-19 vaccines against symptomatic SARS-CoV-2 infection and severe covid-19 outcomes in Ontario, Canada: test negative design study. Chung H et al. BMJ. 2021 Aug 20;374:n1943. doi: 10.1136/bmj.n1943. https://www.bmj.com/content/374/bmj.n1943. Two doses of mRNA covid-19 vaccines were observed to be highly effective against symptomatic infection and severe outcomes. Vaccine effectiveness of one dose was observed to be lower, particularly for older adults shortly after the first dose.
- 31. Prevalence of Allergic Reactions after Pfizer-BioNTech COVID-19 Vaccination among Adults with High Allergy Risk. Shavit R et al. JAMA Netw Open. 2021 Aug 2;4(8):e2122255. doi: 10.1001/jamanetworkopen.2021.22255. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783626

 The rate of allergic reactions to BNT162b2 vaccine, is higher among patients with allergies, particularly among a subgroup with a history of high-risk allergies. This study suggests that most patients with a history of allergic diseases and, particularly, highly allergic patients can be safely immunized by using an algorithm that can be implemented in different medical facilities and includes a referral center, a risk assessment questionnaire, and a setting for immunization under medical supervision of highly allergic patients. Further studies are required to define more specific risk factors for allergic reactions to the BNT162b2 vaccine.
- 32. Comparison of SARS-CoV-2 Antibody Response by Age among Recipients of the BNT162b2 vs the mRNA-1273 Vaccine. Richards NE, et al. *JAMA Netw Open.* 2021 Sep 1;4(9):e2124331. doi:

10.1001/jamanetworkopen.2021.24331.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2783685

In this cohort study, we used a quantitative assay for IgG to SARS-CoV-2 spike-receptor binding protein to compare antibody responses in an employee cohort in which both BNT162b2 and mRNA-1273 were administered. We hypothesized that there could be differences in antibody levels elicited by the 2 vaccines and explored the effect of age on immunogenicity. BNT162b2 elicited relatively lower antibody levels in older adults vs younger adults, which is consistent with emerging reports. By contrast, there was no difference in postboost antibody levels in older adults vs younger adults who received mRNA-1273. One explanation for the difference in immunogenicity observed in older adults could relate to the amount of mRNA used in the respective vaccines, with 30 μ g contained in BNT162b2 and 100 μ g in mRNA-1273.1,2 A limitation of this study is that the neutralizing antibodies were not measured; however, several groups have reported a strong correlation between SARS-CoV-2 binding and neutralizing antibodies.

33. Association of E484K spike protein mutation with SARS-CoV-2 infection in vaccinated persons---Maryland, January - May 2021. Feder KA et al. *Clin Infect Dis.* 2021 Sep 2:ciab762. doi: 10.1093/cid/ciab762. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab762/6362726

Among 9,048 people infected with SARS-CoV-2 between January-May, 2021 in Maryland, in regression-adjusted analysis, SARS-CoV-2 viruses carrying the spike protein mutation E484K were disproportionately prevalent among persons infected after full vaccination against COVID-19 as compared to infected persons who were not fully vaccinated.

Women & Children

34. SARS-COV-2 and the subsequent development of preeclampsia and preterm birth: evidence of a dose response relationship supporting causality. Lai J et al. *Am J Obstet Gynecol.* 2021 Aug 26:S0002-9378(21)00947-9. doi: 10.1016/j.ajog.2021.08.020. https://www.ajog.org/article/S0002-9378(21)00947-9/fulltext

The principal finding is that there is a dose response relationship between the severity of SARS-CoV-2 infection and the risk of subsequent development of preeclampsia and preterm birth. This conclusion is based on a large number of pregnant patients who tested positive for SARS-CoV-2 and a calculation of the individualized risk of preeclampsia and preterm birth for each patient based on maternal characteristics and obstetrical history. Patients with severe COVID-19 have a five-fold greater risk of preeclampsia than asymptomatic patients. Moreover, the relative risk of developing preeclampsia in women with moderate or severe COVID-19 was 3.3 fold higher than in those with asymptomatic/mild infection.

FDA / CDC / NIH / WHO Updates

CDC – American College of Emergency Physicians - Why You Should Not Use Ivermectin to Treat or Prevent COVID-19.

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