Providence

COVID-19 Resource Desk

#37 | 12.30.2020 to 1.5.2020

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 Digital Commons

Clinical Syndrome

1. **Microvascular Injury in the Brains of Patients with Covid-19.** Lee MH, et al. *NEJM* December 30, 2020 DOI: 10.1056/NEJMc2033369 https://www.nejm.org/doi/10.1056/NEJMc2033369
Findings: Blood vessel damage has been observed in the brains of patients who died as a result of COVID-19, though no evidence of the virus was found in the brain tissue. It is unknown exactly what causes the vessel damage but the brains of infected patients might be sensitive to microvascular blood vessel harm that may be caused by the body's inflammatory response to the virus.

2. **Predictors of hospital-acquired bacterial and fungal superinfections in COVID-19: a prospective observational study.** Falcone M, Tiseo G, Giordano C, et al. *J Antimicrob Chemother*. 2020 Dec 29:dkaa530. doi: 10.1093/jac/dkaa530.
https://academic.oup.com/jac/advance-article/doi/10.1093/jac/dkaa530/6055075
Findings: Prospective, observational study including patients with COVID-19 consecutively admitted to the University Hospital of Pisa, Italy, between 4 March and 30 April 2020. A multivariate analysis was performed to identify factors independently associated with superinfections. Overall, 315 patients with COVID-19 were hospitalized and 109 episodes of superinfections were documented in 69 (21.9%) patients. The risk of bacterial and fungal superinfections in COVID-19 is consistent. Patients who need empiric broad-spectrum antibiotics and immunomodulant drugs should be carefully selected. Infection control rules must be reinforced.

3. **Relationship between SARS-CoV-2 infection and the incidence of ventilator-associated lower respiratory tract infections: a European multicenter cohort study.** Rouzé A, Martin-Loeches I, Povoa P, et al. *Intensive Care Med.* 2021 Jan 3. doi: 10.1007/s00134-020-06323-9.
https://link.springer.com/article/10.1007/s00134-020-06323-9
Findings: Multicenter retrospective European cohort performed in 36 ICUs. 1576 patients were included (568 in SARS-CoV-2, 482 in influenza, and 526 in no viral infection groups). VA-LRTI incidence was significantly higher in SARS-CoV-2 patients (287, 50.5%), as compared to influenza patients or patients with no viral infection. Gram-negative bacilli were responsible for

a large proportion (82% to 89.7%) of VA-LRTI, mainly Pseudomonas aeruginosa, Enterobacter spp., and Klebsiella spp. The incidence of VA-LRTI is significantly higher in patients with SARS-CoV-2 infection, as compared to patients with influenza pneumonia, or no viral infection after statistical adjustment, but residual confounding may still play a role in the effect estimates.

4. **Distinct disease severity between children and older adults with COVID-19: Impacts of ACE2 expression, distribution, and lung progenitor cells.** Zhang Z, Guo L, Huang L, et al. *Clin Infect Dis*. 2021 Jan 3:ciaa1911. doi: 10.1093/cid/ciaa1911. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1911/6059779
   Findings: We retrospectively analysed clinical features in a cohort of 299 patients with COVID-19. The expression and distribution of ACE2 and lung progenitor cells were systematically examined using a combination of public single-cell RNA-seq datasets, lung biopsies, and ex vivo infection of lung tissues with SARS-CoV-2 pseudovirus in children and older adults. Compared with children, older patients (> 50 yrs.) were more likely to develop into serious pneumonia with reduced lymphocytes and aberrant inflammatory response. The expression level of ACE2 and lung progenitor cell markers were generally decreased in older patients. Notably, ACE2 positive cells were mainly distributed in the alveolar region, including SFTPC positive cells, but rarely in airway regions in the older adults. The follow-up of discharged patients revealed a prolonged recovery from pneumonia in the older. Compared to children, ACE2 positive cells are generally decreased in older adults and mainly presented in the lower pulmonary tract. The lung progenitor cells are also decreased. These risk factors may impact disease severity and recovery from pneumonia caused by SARS-Cov-2 infection in older patients.

5. **A Review of Pathophysiology, Clinical Features, and Management Options of COVID-19 Associated Coagulopathy.** Goswami J, MacArthur TA, Sridharan M, et al. *Shock*. 2020 Dec 29. doi: 10.1097/SHK.0000000000001680.
   https://journals.lww.com/shockjournal/Abstract/9000/A_Review_of_Pathophysiology,_Clinical_Features,.97330.aspx
   Findings: There is increasing evidence that novel coronavirus disease 2019 (COVID-19) leads to a significant coagulopathy, a phenomenon termed "COVID-19 associated coagulopathy". COVID-19 has been associated with increased rates of both venous and arterial thromboembolic events, a source of significant morbidity and mortality in this disease. Further evidence suggests a link between the inflammatory response and coagulopathy associated with COVID-19. This presents a unique set of challenges for diagnosis, prevention, and treatment of thrombotic complications. In this review, we summarize and discuss the current literature on laboratory coagulation disruptions associated with COVID-19 and the clinical effects of thromboembolic events including pulmonary embolism (PE), deep vein thrombosis (DVT), peripheral arterial thrombosis, and acute ischemic stroke in COVID-19. Endothelial injury and augmented innate immune response are implicated in the development of diffuse macro- and microvascular thrombosis in COVID-19. The pathophysiology of COVID-19 associated coagulopathy is an important determinant of appropriate treatment and monitoring of these complications. We highlight the importance of diagnosis and management of dysregulated coagulation in COVID-19 to improve outcomes in COVID-19 patients with thromboembolic complications.

Diagnostics & Screening

6. **Performance of an Antigen-Based Test for Asymptomatic and Symptomatic SARS-CoV-2 Testing at Two University Campuses — Wisconsin, September–October 2020.** Pray IW, Ford L, Cole D, et al. *MMWR Morb Mortal Wkly Rep* 2021;69:1642–1647. DOI: http://dx.doi.org/10.15585/mmwr.mm695152a3
   Findings: Antigen tests for SARS-CoV-2 are inexpensive and can return results within 15 minutes, but test performance data in asymptomatic and symptomatic persons are limited. Compared with real-time reverse transcription–polymerase chain reaction (RT-PCR) testing, the Sofia antigen test had a sensitivity of 80.0% and specificity of 98.9% among symptomatic persons; accuracy was lower (sensitivity 41.2% and specificity 98.4%) when used for screening of asymptomatic persons. To account for reduced antigen test accuracy, confirmatory testing with a nucleic acid amplification test (e.g., RT-PCR) should be considered after negative antigen test results in symptomatic persons and positive antigen test results in asymptomatic persons.

7. **Performance characteristics of a rapid SARS-CoV-2 antigen detection assay at a public plaza testing site in San Francisco.** Pilarowski G, Lebel P, Sunshine S, et al. *J Infect Dis*. 2021 Jan 4:jiaa802. doi: 10.1093/infdis/jiaa802. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa802/6061974
   Findings: We evaluated the performance of the Abbott BinaxNOW TM Covid-19 rapid antigen test (Binax-CoV2) to detect virus among persons, regardless of symptoms, at a public plaza site of ongoing community transmission. Titration with cultured SARS-CoV-2 yielded a human observable threshold between 1.6x10 4-4.3x10 4 viral RNA copies (cycle threshold (Ct) of 30.3-28.8). Among 878 subjects tested, 3% (26/878) were positive by RT-PCR, of which 15/26 had Ct<30, indicating high viral load. 40% (6/15) of Ct<30 were asymptomatic. Using this Ct<30 threshold for Binax-CoV2 evaluation, the sensitivity of Binax-CoV2 was 93.3% (14/15), 95% CI: 68.1-99.8%, and the specificity was 99.9% (855/856), 95% CI: 99.4-99.9%.

Epidemiology & Public Health

8. **Estimation of US SARS-CoV-2 Infections, Symptomatic Infections, Hospitalizations, and Deaths Using Seroprevalence Surveys.** Angulo FJ, Finelli L, Swerdlow DL. *JAMA Netw Open.* 2021;4(1):e2033706. Jan 5, 2021. doi:10.1001/jamanetworkopen.2020.33706 https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774584
   Findings: Accounting for underreporting, what is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease burden in the US? In this cross-sectional study using data from public health surveillance of reported coronavirus disease 2019 cases and seroprevalence surveys, an estimated 46 910 006 SARS-CoV-2 infections, 28 122 752 symptomatic infections, 956 174 hospitalizations, and 304 915 deaths occurred in the US through November 15, 2020. Findings of this study suggest that although more than 14% of the US population was infected with SARS-CoV-2 by mid-November, a substantial gap remains before herd immunity can be reached.

9. **Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis.** Langford BJ, So M, Raybardhan S, et al. *Clin Microbiol Infect.* January 04, 2021 DOI:https://doi.org/10.1016/j.cmi.2020.12.018 https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30778-3/fulltext
Findings: We screened 7469 studies, from which 154 were included in the final analysis. Antibiotic data were available from 30,623 patients. The prevalence of antibiotic prescribing was 74.6% (95% CI 68.3 to 80.0%). On univariable meta-regression, antibiotic prescribing was lower in children (prescribing prevalence odds ratio (OR) 0.10, 95%CI 0.03 to 0.33) compared to adults. Antibiotic prescribing was higher with increasing patient age (OR 1.45 per 10 year increase, 95%CI 1.18 to 1.77) and higher with increasing proportion of patients requiring mechanical ventilation (OR 1.33 per 10% increase, 95%CI 1.15 to 1.54). Estimated bacterial co-infection was 8.6% (95% CI 4.7-15.2%) from 31 studies. Three-quarters of patients with COVID-19 receive antibiotics, prescribing is significantly higher than the estimated prevalence of bacterial co-infection. Unnecessary antibiotic use is likely high in patients with COVID-19.

Laboratory Results

10. **Plasma Antithrombin Values Are Significantly Decreased in Coronavirus Disease 2019 (COVID-19) Patients with Severe Illness.** Lippi G, Henry BM, Sanchis-Gomar F. *Semin Thromb Hemost*. 2020 Dec 30. doi: 10.1055/s-0040-1716873. https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-0040-1716873
Findings: Antithrombin, a 432-aminoacid serpin produced by the liver, is now recognized as one of the most powerful endogenous anticoagulants, which functions by competitively inhibiting the activity of thrombin and activated factor X (FXa). Both inherited and acquired antithrombin deficiencies are associated with a magnified thrombotic risk, especially venous thromboembolism. Importantly, reduced antithrombin levels are also observed in patients with intravascular consumption coagulopathies, including those caused by bacteria, viruses, and other microorganisms. Since both venous and arterial thrombotic complications are commonly observed in patients with COVID-19 and appear to have a significant impact on patient prognosis, we performed a literature search to identify all clinical studies that measured antithrombin in COVID-19 patients and correlated the values of this endogenous inhibitor with disease severity.

11. **Peripheral Blood Immune Profiling of Convalescent Plasma Donors Reveals Alterations in Specific Immune Subpopulations Even at 2 Months Post SARS-CoV-2 Infection.** Orologas-Stavrou N, Politou M, Rousakis P, et al. *Viruses*. 2020 Dec 25;13(1):E26. doi: 10.3390/v13010026. https://www.mdpi.com/1999-4915/13/1/26/htm
Findings: Immune profiling of patients with COVID-19 has shown that SARS-CoV-2 causes severe lymphocyte deficiencies (e.g., lymphopenia, decreased numbers, and exhaustion of T cells) and increased levels of pro-inflammatory monocytes. Peripheral blood (PB) samples from convalescent plasma (CP) donors, COVID-19 patients, and control subjects were analyzed by multiparametric flow cytometry, allowing the identification of a wide panel of immune cells, comprising lymphocytes (T, B, natural killer (NK) and NKT cells), monocytes, granulocytes, and their subsets. Compared to active COVID-19 patients, our results revealed that the immune

profile of recovered donors was restored for most subpopulations. Nevertheless, even 2 months after recovery, CP donors still had reduced levels of CD4+ T and B cells, as well as granulocytes. CP donors with non-detectable levels of anti-SARS-CoV-2-specific antibodies in their serum were characterized by higher Th9 and Th17 cells, which were possibly expanded at the expense of Th2 humoral immunity. The most noticeable alterations were identified in previously hospitalized CP donors, who presented the lowest levels of CD8+ regulatory T cells, the highest levels of CD56+CD16- NKT cells, and a promotion of a Th17-type phenotype, which might be associated with a prolonged pro-inflammatory response. A longer follow-up of CP donors will eventually reveal the time needed for full recovery of their immune system competence.

Prognosis

12. **Mortality in hospitalized patients with cancer and coronavirus disease 2019: A systematic review and meta-analysis of cohort studies.** Desai A, Gupta R, Advani S, et al. *Cancer.* 2020 Dec 30. doi: 10.1002/cncr.33386.
https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cncr.33386
Findings: Among 2922 patients from 13 primarily inpatient studies of individuals with COVID-19 and cancer, the pooled 30-day mortality rate was 30%. The overall pooled 30-day mortality rate among 624 patients from 5 studies that included a mixture of inpatient and outpatient populations was 15%. Pooled mortality estimates for hospitalized patients with cancer and COVID-19 remain high at 30%, with significant heterogeneity across studies. Dedicated community-based studies are needed in the future to help assess overall COVID-19 mortality among the broader population of patients with cancer.

13. **Impact of arterial stiffness on all-cause mortality in patients hospitalized with COVID-19 in Spain.** Rodilla E, Lopez-Carmona MD, Cortes X, et al. *Hypertension.* 2020 Dec 30. doi: 10.1161/HYPERTENSIONAHA.120.16563.
https://www.ahajournals.org/doi/10.1161/HYPERTENSIONAHA.120.16563
Findings: Older age and cardiovascular comorbidities are well-known risk factors for all-cause mortality in COVID-19 patients. Hypertension and age are the two principal determinants of arterial stiffness (AS). This study aimed to estimate AS in COVID-19 patients requiring hospitalization and analyze its association with all-cause in-hospital mortality. This observational, retrospective, multicenter cohort-study analyzed 12,170 patients admitted to 150 Spanish centers included in the SEMI-COVID-19 Network. We compared AS, defined as pulse pressure {greater than or equal to} 60 mmHg, and clinical characteristics between survivors and nonsurvivors. Mean age was 67.5 years and 42.5% were women. Overall, 2,606 (21.4%) subjects died. Admission systolic blood pressure (SBP) < 120 and {greater than or equal to} 140 mmHg was a predictor of higher all-cause mortality (23.5% and 22.8%, respectively, p < .001), compared to BP =120-140 mmHg (18.6%). The 4,379 patients with AS (36.0%) were older and had higher systolic and lower diastolic BP. Our data show that AS and admission SBP < 120 mmHg had independent prognostic value for all-cause mortality in COVID-19 patients requiring hospitalization.

14. **Regular Use of VKA Prior to COVID-19 Associated with Lower 7-Day Survival in Hospitalized Frail Elderly COVID-19 Patients: The GERIA-COVID Cohort Study.** Ménager P, Brière O, Gautier J, et al. *Nutrients.* 2020 Dec 24;13(1):E39. doi: 10.3390/nu13010039. https://www.mdpi.com/2072-6643/13/1/39/htm
Findings: Eighty-two patients consecutively hospitalized for COVID-19 in a geriatric acute care unit were included. The association of the regular use of VKA prior to COVID-19 with survival after 7 days of COVID-19 was examined. Among 82 patients, 73 survived COVID-19 at day 7 while 9 died. Consistently, COVID-19 patients using VKA on a regular basis had shorter survival times than the others (p = 0.031). CONCLUSIONS: Regular use of VKA was associated with increased mortality at day 7 in hospitalized frail elderly patients with COVID-19.

15. **Shock index as a predictor of mortality among the Covid-19 patients.** Doğanay F, Elkonca F, Seyhan AU, Yılmaz E, Batırel A, Ak R. *Am J Emerg Med*. 2020 Dec 23;40:106-109. doi: 10.1016/j.ajem.2020.12.053. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7757345/
Findings: Our primary aim is to determine the power of SI at the time of ED presentation as a predictor of mortality in patients with COVID-19. Secondarily, we aimed to determine the relationship between mortality and vital signs and medical history data available at the time of ED triage in this patient population. In our study, the first classification by CHAID analysis was made by age, and in our sample, it was divided into 3 groups, ages 56 and 77 stand out as critical limits. The mortality rate was found to be the lowest in those younger than 56 years old, and those over 77 years old constitute the group with the highest mortality rate. In our study, advanced age was found to be directly related to mortality, and this is consistent with the literature. We concluded that an SI value above 0.93 showed a significant correlation with mortality rate. Using a 0.9 value of SI with age and SpO2 value may be helpful for clinicians to early identification of patients with high mortality expectation that it will also be important in terms of protecting the functionality of the health system.

16. **Risk Factors Associated with All-Cause 30-Day Mortality in Nursing Home Residents With COVID-19.** Panagiotou OA, Kosar CM, White EM, et al. *JAMA Intern Med*. January 04, 2021. doi:10.1001/jamainternmed.2020.7968
https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2774729
Findings: The study included 5256 nursing home residents (3185 women [61%]; median age, 79 years; and 3741 White residents [71%], 909 Black residents [17%], and 586 individuals of other races/ethnicities [11%]) with COVID-19. Compared with residents aged 75 to 79 years, the odds of death were 1.46 times higher for residents aged 80 to 84 years, 1.59 times higher for residents aged 85 to 89 years, and 2.14 times higher for residents aged 90 years or older. Women had lower risk for 30-day mortality than men. Two comorbidities were associated with mortality: diabetes and chronic kidney disease. In this cohort study of US nursing home residents with COVID-19, increased age, male sex, and impaired cognitive and physical function were independently associated with mortality. Understanding these risk factors can aid in the development of clinical prediction models of mortality in this population.

Survivorship & Rehabilitation

17. **Functional outcome after inpatient rehabilitation in post-intensive care unit COVID-19 patients: findings and clinical implications from a real-practice retrospective study.** Curci C, Negrini F, Ferrillo M, et al. *Eur J Phys Rehabil Med.* 2021 Jan 4. doi: 10.23736/S1973-9087.20.06660-5. https://www.minervamedica.it/en/journals/europa-medicophysica/article.php?cod=R33Y9999N00A21010402
Findings: COVID-19 survivors suffer functional impairments with a consequent key role of rehabilitation in this context. To date, there is a lack of findings on the role of rehabilitation in post-acute COVID-19 patients. We aimed at describing the role of a patient-tailored rehabilitation plan on functional outcome in hospitalized COVID-19 patients. We included 41 post-acute COVID-19 patients (25 male and 19 female), mean aged 72.15±11.07 years. Their mean LOS in the Rehabilitation Unit was 31.97±9.06 days, as 39 successfully completed the rehabilitation treatment and 2 deceased. We found statistically significant improvement in BI (84.87±15.56 vs 43.37±26.00; p<0.0001), 6-MWT (303.37±112.18 vs 240.0±81.31 meters; p=0.028), Borg RPE scale (12.23±2.51 vs 16.03±2.28; p<0.0001). These findings suggest that post-acute COVID-19 patients might beneficiate of a motor and respiratory rehabilitation treatment. However, further studies are advised to better understand long-term sequelae of the disease.

Therapeutics

18. **Noninvasive Ventilatory Support of COVID-19 Patients Outside the Intensive Care Units (WARd-COVID).** Bellani G, Grasselli G, Cecconi M, et al. *Ann Am Thorac Soc*. 2021 Jan 4. doi: 10.1513/AnnalsATS.202008-1080OC.
https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.202008-1080OC
Findings: In this prospective single day observational study, we enrolled adult COVID-19 patients, treated with NIV outside the ICU from thirty-one hospitals in Lombardy, Italy. We collected data on demographic, clinical characteristics, ventilatory management and patients' outcome. Of 8753 COVID-19 patients present in the hospitals on the study day, 909 (10%) were receiving NIV outside the ICU. 778/909 (85%) patients were treated with Continuous Positive Airway Pressure (CPAP), delivered by helmet in 617 (68%). NIV failed in 300 patients (37.6%), while 498 (62.4%) were discharged alive without intubation. Overall mortality was 25%. NIV failure occurred in 152/284 (53%) patients with a PaO2/FiO2 ratio < 150 mmHg. The use of NIV outside the ICUs, in COVID-19 was common, with a predominant use of helmet CPAP, with a rate of success greater than 60% and close to 75% in full treatment patients. C-reactive protein, PaO2/FiO2, platelet counts were independently associated with increased risk of NIV failure.

19. **Corticosteroid therapy in critically ill patients with COVID-19: a multicenter, retrospective study.** Li Y, Meng Q, Rao X, et al. *Crit Care*. 2020 Dec 18;24(1):698. doi: 10.1186/s13054-020-03429-w. https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03429-w
Findings: 294 critically ill patients with COVID-19 were recruited between December 30, 2019 and February 19, 2020. Out of the 294 critically ill patients affected by COVID-19, 183 (62.2%) received corticosteroids, with methylprednisolone as the most frequently administered

corticosteroid (175 accounting for 96%). Of those treated with corticosteroids, 69.4% received corticosteroid prior to ICU admission. Early initiation of corticosteroid use (≤ 3 days after ICU admission) was associated with an increased 90-day mortality. Early use of methylprednisolone in the ICU is therefore not recommended in patients with severe COVID-19.

20. **Pharmacologic Thromboprophylaxis and Thrombosis in Hospitalized Patients with COVID-19: A Pooled Analysis.** Patell R, Chiasakul T, Bauer E, Zwicker JI. *Thromb Haemost*. 2020 Dec 30. doi: 10.1055/s-0040-1721664. https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-0040-1721664
Findings: Thirty-five observational studies were included. The pooled incidence rates of total venous thromboembolism (N = 4,685) were: no prophylaxis 41.9%, standard-dose prophylaxis 19.8%, intermediate-dose prophylaxis 11.9%, and therapeutic-dose anticoagulants 10.5%. The pooled incidence rates of arterial thrombosis were: no prophylaxis 11.3%, standard-dose prophylaxis 2.5%, intermediate-dose prophylaxis 2.1%, and therapeutic-dose anticoagulants 1.3%. Thrombosis rates were lower in hospitalized COVID-19 patients who received pharmacologic thromboprophylaxis. Thrombosis and bleeding rates for patients receiving intermediate-dose thromboprophylaxis or therapeutic anticoagulation were similar to those who received standard-dose pharmacologic thromboprophylaxis.

21. **Extracorporeal Membrane Oxygenation for Coronavirus Disease 2019: Crisis Standards of Care.** Agerstrand C, Dubois R, Takeda K, et al. *ASAIO J*. 2020 Dec 28. doi: 10.1097/MAT.0000000000001376.
https://journals.lww.com/asaiojournal/Abstract/9000/Extracorporeal_Membrane_Oxygenation_for.98384.aspx
Findings: We retrospectively investigated adult patients supported with ECMO for COVID-19 at our institution during the first 80 days following New York City's declaration of a state of emergency. The primary objective was to evaluate survival outcomes in patients supported with ECMO for COVID-19 and describe the programmatic adaptations made in response to pandemic-related crisis conditions. Twenty-two patients with COVID-19 were placed on ECMO during the study period. Median age was 52 years and 18 (81.8%) were male. Twenty-one patients (95.4%) had severe ARDS and 7 (31.8%) had cardiac failure. Fifteen patients (68.1%) were managed with venovenous ECMO while 7 (31.8%) required arterial support. Twelve patients (54.5%) were transported on ECMO from external institutions. Twelve patients were discharged alive from the hospital (54.5%). ECMO was used successfully in patients with respiratory and cardiac failure due to COVID-19. The continued use of ECMO, including ECMO transport, during crisis conditions was possible even at the height of the COVID-19 pandemic.

Transmission / Infection Control

22. **Implications of Shortened Quarantine among Household Contacts of Index Patients with Confirmed SARS-CoV-2 Infection — Tennessee and Wisconsin, April–September 2020.** Rolfes MA, Grijalva CG, Zhu Y, et al. *MMWR Morb Mortal Wkly Rep* 2021;69:1633–1637. DOI: http://dx.doi.org/10.15585/mmwr.mm695152a1

Findings: After exposure to COVID-19, a 14-day quarantine period can prevent further spread but might be challenging to maintain. Among persons exposed to COVID-19 in the household who were asymptomatic and had negative laboratory test results through 7 days after symptom onset in the index patient, 19% experienced symptoms or received positive test results in the following week. A shorter quarantine after household exposure to COVID-19 might be easier to adhere to but poses some risk for onward transmission. Persons released from quarantine before 14 days should continue to avoid close contact and wear masks when around others until 14 days after their last exposure.

Vaccine

23. **National Trends in the US Public's Likelihood of Getting a COVID-19 Vaccine—April 1 to December 8, 2020.** Szilagyi PG, Thomas K, Shah MD, et al. *JAMA*. December 29, 2020. doi:10.1001/jama.2020.26419
https://jamanetwork.com/journals/jama/fullarticle/2774711?resultClick=1
Findings: We analyzed biweekly survey data from a nationally representative longitudinal study to describe changes over time in the public's likelihood of getting a COVID-19 vaccine and across demographic subgroups. In this nationally representative survey, self-reported likelihood of getting a COVID-19 vaccine declined from 74% in early April to 56% in early December 2020, despite the early November press releases of high vaccine efficacy for 2 vaccines in phase 3 trials, although prior to Emergency Use Authorization. Low likelihood of getting a COVID-19 vaccine among Black individuals and those with lower educational backgrounds is especially concerning because of their disproportionately higher burden from COVID-19 disease.

24. **Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine.** Baden LR, El Sahly HM, Essink B; COVE Study Group, et al. *N Engl J Med*. 2020 Dec 30. doi: 10.1056/NEJMoa2035389.
https://www.nejm.org/doi/full/10.1056/NEJMoa2035389
Findings: This phase 3 randomized, observer-blinded, placebo-controlled trial was conducted at 99 centers across the United States. Persons at high risk for SARS-CoV-2 infection or its complications were randomly assigned in a 1:1 ratio to receive two intramuscular injections of mRNA-1273 (100 µg) or placebo 28 days apart. The primary end point was prevention of Covid-19 illness with onset at least 14 days after the second injection in participants who had not previously been infected with SARS-CoV-2. The trial enrolled 30,420 volunteers who were randomly assigned in a 1:1 ratio to receive either vaccine or placebo (15,210 participants in each group). More than 96% of participants received both injections, and 2.2% had evidence (serologic, virologic, or both) of SARS-CoV-2 infection at baseline. Symptomatic Covid-19 illness was confirmed in 185 participants in the placebo group (56.5 per 1000 person-years; 95% confidence interval [CI], 48.7 to 65.3) and in 11 participants in the mRNA-1273 group (3.3 per 1000 person-years; 95% CI, 1.7 to 6.0); vaccine efficacy was 94.1% (95% CI, 89.3 to 96.8%; P<0.001). Efficacy was similar across key secondary analyses, including assessment 14 days after the first dose, analyses that included participants who had evidence of SARS-CoV-2 infection at baseline, and analyses in participants 65 years of age or older. Severe Covid-19 occurred in 30 participants, with one fatality; all 30 were in the placebo group. Moderate, transient reactogenicity after vaccination occurred more frequently in the mRNA-1273 group. Serious

adverse events were rare, and the incidence was similar in the two groups. CONCLUSIONS: The mRNA-1273 vaccine showed 94.1% efficacy at preventing Covid-19 illness, including severe disease. Aside from transient local and systemic reactions, no safety concerns were identified.

25. **mRNA Vaccines to Prevent COVID-19 Disease and Reported Allergic Reactions: Current Evidence and Approach.** Banerji A, Wickner PG, Saff R, et al. *J Allergy Clin Immunol Pract.* 2020 Dec 31;S2213-2198(20)31411-2. doi: 10.1016/j.jaip.2020.12.047. https://www.sciencedirect.com/science/article/pii/S2213219820314112?via%3Dihub
Findings: Allergic reactions to vaccines occur and can be attributed to various vaccine components. In support of the COVID-19 vaccine rollout programs, allergists must offer clear recommendations based on the best available information to date, which includes the comprehensive ingredients in the vaccines, allergy contraindications from the FDA, and guidance on administration from the CDC. As the US prepares for massive COVID-19 vaccination, allergists must prepare for two main population health challenges: (1) ensuring that highly allergic individuals feel appropriately informed and supported to receive the vaccine and (2) ensuring that rare patients who suffer from a potentially allergic reaction to the first dose of a SARS-CoV-2 vaccine have the requisite information and support needed to decide if and how to receive the second dose. While these challenges require attention immediately during the current vaccination process, it is of equal importance that we must also design and conduct adequately powered studies to investigate the potential mechanistic etiology of these reactions.

26. **Alternative Dose Allocation Strategies to Increase Benefits from Constrained COVID-19 Vaccine Supply.** Tuite AR, Zhu L, Fisman DN, Salomon JA. *Ann Intern Med.* 2021 Jan 5. doi: 10.7326/M20-8137. https://www.acpjournals.org/doi/10.7326/M20-8137?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed
Findings: In this analysis, we demonstrated the potential to improve upon current policies for deploying tightly constrained early supply of highly efficacious COVID-19 vaccines in order to maximize population health benefits. Current policies place a premium on eliminating any possible delays to delivering second doses using an allocation scheme that maintains large reserves of vaccine to guard against complete collapse of supply. The cost of this conservative approach, however, is to delay receipt of first doses in many people who could gain substantial health benefits from earlier vaccination. We find that under most plausible scenarios, a more balanced approach that withholds fewer doses during early distribution in order to vaccinate more people as soon as possible could substantially increase the benefits of vaccines, while enabling most recipients to receive second doses on schedule. Our analysis is limited by focusing only on direct benefits to vaccine recipients rather than including potential secondary benefits from avoiding transmission. Key uncertainties remain around the time course of protection afforded by the first dose of vaccine and loss of protection with extended time to the second dose. Nevertheless, we suggest a simple modification to current policy that has potential to significantly amplify urgently needed benefits from limited vaccine supply.

27. **Speed Versus Efficacy: Quantifying Potential Tradeoffs in COVID-19 Vaccine Deployment.** Paltiel D, et al. *Ann Int Med*, Jan 5, 2021. https://doi.org/10.7326/M20-7866

Findings: Prior work has shown that the success of a COVID-19 vaccination program will depend more on the speed and reach of its implementation than on the efficacy of the vaccine itself. The analysis presented here highlights the steep clinical and epidemiologic costs imposed by a 2-dose vaccination series in the context of ongoing pandemic response. Depending on the duration of protection conferred—and, of note, considering only a 6-month time horizon—a single-dose vaccine with 55% effectiveness may confer greater population benefit than a 95%-effective vaccine requiring 2 doses. This suggests that now that a highly effective, 2-dose vaccine for COVID-19 has been authorized and vaccination programs have begun, sustained and aggressive investment in pursuit of faster-acting, more convenient, 1-dose vaccine candidates remains justified.

Women & Children

28. **Initial Guidance on Use of Monoclonal Antibody Therapy for Treatment of COVID-19 in Children and Adolescents.** Wolf J, Abzug MJ, Wattier RL, et al. *J Pediatric Infect Dis Soc*. 2021 Jan 3:piaa175. doi: 10.1093/jpids/piaa175. https://academic.oup.com/jpids/advance-article/doi/10.1093/jpids/piaa175/6060076?
Findings: The course of COVID-19 in children and adolescents is typically mild and there is no high-quality evidence supporting any high risk groups. There is no evidence for safety and efficacy of monoclonal antibody therapy for treatment of COVID-19 in children or adolescents, limited evidence of modest benefit in adults, and evidence for potential harm associated with infusion reactions or anaphylaxis. Based on evidence available as of December 20, 2020, the panel suggests against routine administration of monoclonal antibody therapy (bamlanivimab, or casirivimab and imdevimab), for treatment of COVID-19 in children or adolescents, including those designated by the FDA as at high risk of progression to hospitalization or severe disease. Clinicians and health systems choosing to use these agents on an individualized basis should consider risk factors supported by pediatric-specific evidence, and ensure implementation of a system for safe and timely administration that does not exacerbate existing healthcare disparities.

GUIDELINES & CONSENSUS STATEMENTS

Considerations for COVID-19 Vaccination in Lactation. Stuebe A. *Breastfeed Med*. 2020 Dec 23. doi: 10.1089/bfm.2020.29172.abm.

ARIA-EAACI statement on severe allergic reactions to COVID-19 vaccines - an EAACI-ARIA position paper. Klimek L, Jutel M, Akdis CA, et al. *Allergy.* 2020 Dec 30. doi: 10.1111/all.14726.

Update Alert 7: Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection in Adults. Mackey K, Kansagara D, Vela K. *Ann Intern Med*. 2021 Jan 5. doi: 10.7326/L20-1446.

FDA / CDC / NIH / WHO Updates

CDC - Emerging SARS-CoV-2 Variants. Jan 3, 2021

CDC - Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States

FDA - Statement on Following the Authorized Dosing Schedules for COVID-19 Vaccines. Jan 4, 2021

Commentary & News

UK becomes world's first to roll out Oxford/AstraZeneca vaccine as cases surge

New variant of SARS-CoV-2 in UK causes surge of COVID-19. *Lancet Resp Med*, January 05, 2021. DOI:https://doi.org/10.1016/S2213-2600(21)00005-9

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.**