

COVID-19 Resource Desk

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New Research

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Epidemiology & Public Health

- 1. Multistate Outbreak of SARS-CoV-2 Infections, Including Vaccine Breakthrough Infections, Associated with Large Public Gatherings, United States.** Gharpure R et al. *Emerg Infect Dis*. 2021 Nov 18;28(1). doi: 10.3201/eid2801.212220. https://wwwnc.cdc.gov/eid/article/28/1/21-2220_article
During July 2021, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.617.2 variant infections, including vaccine breakthrough infections, occurred after large public gatherings in Provincetown, Massachusetts, USA, prompting a multistate investigation. Public health departments identified primary and secondary cases by using coronavirus disease surveillance data, case investigations, and contact tracing. A primary case was defined as SARS-CoV-2 detected <14 days after travel to or residence in Provincetown during July 3-17. A secondary case was defined as SARS-CoV-2 detected <14 days after close contact with a person who had a primary case but without travel to or residence in Provincetown during July 3-August 10. We identified 1,098 primary cases and 30 secondary cases associated with 26 primary cases among fully and non-fully vaccinated persons. Large gatherings can have widespread effects on SARS-CoV-2 transmission, and fully vaccinated persons should take precautions, such as masking, to prevent SARS-CoV-2 transmission, particularly during substantial or high transmission.
- 2. Incidence of SARS-CoV-2 Infection, Emergency Department Visits, and Hospitalizations Because of COVID-19 Among Persons Aged ≥12 Years, by COVID-19 Vaccination Status - Oregon and Washington, July 4-September 25, 2021.** Naleway AL et al. *MMWR Morb Mortal Wkly Rep*. 2021 Nov 19;70(46):1608-1612. doi: 10.15585/mmwr.mm7046a4. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7046a4.htm>
During the July-September 2021 surveillance period, SARS-CoV-2 infection occurred among 4,146 of 137,616 unvaccinated persons (30.1 per 1,000 persons) and 3,009 of 344,848 fully vaccinated persons (8.7 per 1,000). Incidence was higher among unvaccinated persons than among vaccinated persons across all demographic strata. Unvaccinated persons with SARS-CoV-2 infection were more than twice as likely to receive ED care (18.5%) or to be hospitalized (9.0%) than were vaccinated persons with COVID-19 (8.1% and 3.9%, respectively). The crude mortality rate was also higher among unvaccinated patients (0.43 per 1,000) than in fully

vaccinated patients (0.06 per 1,000). These data support CDC recommendations for COVID-19 vaccination, including additional and booster doses, to protect individual persons and communities against COVID-19, including illness and hospitalization caused by the Delta variant.

3. **Impact of Hospital Strain on Excess Deaths during the COVID-19 Pandemic - United States, July 2020-July 2021.** French G, et al. *MMWR Morb Mortal Wkly Rep.* 2021 Nov 19;70(46):1613-1616. doi: 10.15585/mmwr.mm7046a5.

https://www.cdc.gov/mmwr/volumes/70/wr/mm7046a5.htm?s_cid=mm7046a5_x

The Cybersecurity & Infrastructure Security Agency (CISA) COVID Task Force* examined the relationship between hospital strain and excess deaths during July 4, 2020-July 10, 2021, to assess the impact of COVID-19 surges on hospital system operations and potential effects on other critical infrastructure sectors and national critical functions. The study period included the months during which the highly transmissible SARS-CoV-2 B.1.617.2 (Delta) variant became predominant in the United States. The negative binomial regression model used to calculate estimated deaths predicted that, if intensive care unit (ICU) bed use nationwide reached 75% capacity an estimated 12,000 additional excess deaths would occur nationally over the next 2 weeks. As hospitals exceed 100% ICU bed capacity, 80,000 excess deaths would be expected in the following 2 weeks. This analysis indicates the importance of controlling case growth and subsequent hospitalizations before severe strain. State, local, tribal, and territorial leaders could evaluate ways to reduce strain on public health and health care infrastructures, including implementing interventions to reduce overall disease prevalence such as vaccination and other prevention strategies, as well as ways to expand or enhance capacity during times of high disease prevalence.

4. **Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis.** Talic S et al. *BMJ.* 2021 Nov 17;375:e068302. doi: 10.1136/bmj-2021-068302.

<https://www.bmj.com/content/375/bmj-2021-068302>

This systematic review and meta-analysis suggests that several personal protective and social measures, including handwashing, mask wearing, and physical distancing are associated with reductions in the incidence covid-19. Public health efforts to implement public health measures should consider community health and sociocultural needs, and future research is needed to better understand the effectiveness of public health measures in the context of covid-19 vaccination.

Healthcare Delivery & Healthcare Workers

5. **Which outcomes are most important to measure in patients with COVID-19 and how and when should these be measured? Development of an international standard set of outcomes measures for clinical use in patients with COVID-19: a report of the International Consortium for Health Outcomes Measurement (ICHOM) COVID-19 Working Group.** Seligman WH et al. *BMJ Open.* 2021 Nov 15;11(11):e051065. doi: 10.1136/bmjopen-2021-051065.

<https://adc.bmj.com/content/106/9/868>

The outcomes considered by the WG to be most important were selected and categorised into five domains: (1) functional status and quality of life, (2) mental functioning, (3) social functioning, (4) clinical outcomes and (5) symptoms. The WG identified demographic and clinical variables for use as case-mix risk adjusters. These included baseline demographics, clinical factors and treatment-related factors. Implementation of these consensus recommendations could help institutions to monitor, compare and improve the quality and delivery of care to patients with COVID-19. Their consistent definition and collection could also broaden the implementation of more patient-centric clinical outcomes research.

- 6. The Risk of Postoperative Complications following Major Elective Surgery in Active or Resolved COVID-19 in the United States.** Deng JZ, et al. *Ann Surg.* 2021 Nov 18. doi: 10.1097/SLA.0000000000005308.
https://journals.lww.com/annalsofsurgery/Abstract/9000/The_Risk_of_Postoperative_Complications_following.93177.aspx
Major, elective surgery 0-4 weeks after SARS-CoV-2 infection is associated with an increased risk of postoperative complications. Surgery performed 4-8 weeks after SARS-CoV-2 infection is still associated with an increased risk of pneumonia while surgery eight weeks after Covid-19 diagnosis is not associated with increased complications.

Prognosis

- 7. External validation of the QCovid risk prediction algorithm for risk of COVID-19 hospitalisation and mortality in adults: national validation cohort study in Scotland.** Simpson CR et al. *Thorax.* 2021 Nov 15:thoraxjnl-2021-217580. doi: 10.1136/thoraxjnl-2021-217580.
[https://www.thelancet.com/journals/landig/article/PIIS2589-7500\(21\)00080-7/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500(21)00080-7/fulltext)
Our dataset comprised 5 384 819 individuals, representing 99% of the estimated population (5 463 300) resident in Scotland in 2020. The algorithm showed good calibration in the first period, but systematic overestimation of risk in the second period, prior to temporal recalibration. Harrell's C for deaths in females and males in the first period was 0.95 (95% CI 0.94 to 0.95) and 0.93 (95% CI 0.92 to 0.93), respectively. Harrell's C for hospitalisations in females and males in the first period was 0.81 (95% CI 0.80 to 0.82) and 0.82 (95% CI 0.81 to 0.82), respectively. CONCLUSIONS: Version 1 of the QCovid algorithm showed high levels of discrimination in predicting the risk of COVID-19 hospitalisations and deaths in adults resident in Scotland for the original two time periods studied, but is likely to need ongoing recalibration prospectively.

Therapeutics

- 8. Intravenous immunoglobulins in patients with COVID-19-associated moderate-to-severe acute respiratory distress syndrome (ICAR): multicentre, double-blind, placebo-controlled, phase 3 trial.** Mazeraud A et al. *Lancet Respir Med.* 2021 Nov 11:S2213-2600(21)00440-9. doi: 10.1016/S2213-2600(21)00440-9. [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00440-9/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00440-9/fulltext)

In patients with COVID-19 who received invasive mechanical ventilation for moderate-to-severe ARDS, IVIG did not improve clinical outcomes at day 28 and tended to be associated with an increased frequency of serious adverse events, although not significant. The effect of IVIGs on earlier disease stages of COVID-19 should be assessed in future trials.

9. **Mortality Risk Among Patients With COVID-19 Prescribed Selective Serotonin Reuptake Inhibitor Antidepressants.** Oskotsky T, et al. *JAMA Netw Open.* 2021 Nov 1;4(11):e2133090. doi: 10.1001/jamanetworkopen.2021.33090.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2786136>

These results support evidence that SSRIs may be associated with reduced severity of COVID-19 reflected in the reduced RR of mortality. Further research and randomized clinical trials are needed to elucidate the effect of SSRIs generally, or more specifically of fluoxetine and fluvoxamine, on the severity of COVID-19 outcomes.

10. **Monoclonal Antibody Treatment of Breakthrough COVID-19 in Fully Vaccinated Individuals with High-Risk Comorbidities.** Bierle DM, et al. *J Infect Dis* 2021;; jiab570, <https://doi.org/10.1093/infdis/jiab570>

Breakthrough COVID-19 may occur in fully vaccinated persons. In this cohort of 1395 persons (mean age, 54.3 years; 60% female; median body mass index, 30.7) who developed breakthrough COVID-19, there were 107 (7.7%) who required hospitalization by day 28. Hospitalization was significantly associated with the number of medical comorbidities. Anti-spike monoclonal antibody treatment was significantly associated with a lower risk of hospitalization. The number needed to treat (NNT) to prevent one hospitalization was 225 among the lowest-risk patient group compared to NNT of 4 among those with highest numbers of medical comorbidity.

11. **Azithromycin in patients with COVID-19: a systematic review and meta-analysis.** Ayerbe L, et al. *J Antimicrob Chemother.* 2021 Nov 17;dkab404. doi: 10.1093/jac/dkab404.

<https://academic.oup.com/jac/advance-article/doi/10.1093/jac/dkab404/6430403>

16 studies, 5 RCTs and 11 with an observational design, with a total of 22 984 patients, were included. The meta-analysis showed no difference in mortality for those treated with or without azithromycin, in observational studies and also when both types of studies were pooled together. Different individual studies also reported no significant difference for those treated with or without azithromycin in need for hospital admission or time to admission from ambulatory settings, clinical severity, need for intensive care, or adverse effects. The results presented in this systematic review do not support the use of azithromycin in the management of COVID-19. Future research on treatment for patients with COVID-19 may need to focus on other drugs.

Transmission / Infection Control

12. **Infection control in the intensive care unit: expert consensus statements for SARS-CoV-2 using a Delphi method.** Nasa P et al. *Lancet Infect Dis.* 2021 Nov 10:S1473-3099(21)00626-5.

doi: 10.1016/S1473-3099(21)00626-5.

[https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099\(21\)00626-5.pdf](https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(21)00626-5.pdf)

In the absence of high-quality evidence on the transmission of SARS-CoV-2, clinical practice of infection control and prevention in ICUs varies widely. Using a Delphi process, international experts in intensive care, infectious diseases, and infection control developed consensus statements on infection control for SARS-CoV-2 in an ICU. Consensus was achieved for 31 (94%) of 33 statements, from which 25 clinical practice statements were issued. These statements include guidance on ICU design and engineering, health-care worker safety, visiting policy, personal protective equipment, patients and procedures, disinfection, and sterilisation. Consensus was not reached on optimal return to work criteria for health-care workers who were infected with SARS-CoV-2 or the acceptable disinfection strategy for heat-sensitive instruments used for airway management of patients with SARS-CoV-2 infection. Well designed studies are needed to assess the effects of these practice statements and address the remaining uncertainties.

- 13. Post-exposure Lopinavir-Ritonavir Prophylaxis versus Surveillance for Individuals Exposed to SARS-CoV-2: The COPEP Pragmatic Open-Label, Cluster Randomized Trial.** Labhardt ND et al. *EClinicalMedicine*. 2021 Dec;42:101188. doi: 10.1016/j.eclinm.2021.101188. Epub 2021 Nov 6. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2786136>

The role of LPV/r as PEP for COVID-19 remains unanswered. Although LPV/r over 5 days did not significantly reduce the incidence of COVID-19 in exposed individuals, we observed a change in the directionality of the effect in favour of LPV/r after adjusting for baseline imbalance. LPV/r for this indication merits further testing against SARS-CoV-2 in clinical trials.

Vaccines / Immunology

- 14. Safety and immunogenicity of concomitant administration of COVID-19 vaccines (ChAdOx1 or BNT162b2) with seasonal influenza vaccines in adults in the UK (ComFluCOV): a multicentre, randomised, controlled, phase 4 trial.** Lazarus R et al. *Lancet*. 2021 Nov 11:S0140-6736(21)02329-1. doi: 10.1016/S0140-6736(21)02329-1.

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02329-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02329-1/fulltext)

Concomitant vaccination with ChAdOx1 or BNT162b2 plus an age-appropriate influenza vaccine raises no safety concerns and preserves antibody responses to both vaccines. Concomitant vaccination with both COVID-19 and influenza vaccines over the next immunisation season should reduce the burden on health-care services for vaccine delivery, allowing for timely vaccine administration and protection from COVID-19 and influenza for those in need.

- 15. Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): interim results of a randomised, double-blind, controlled, phase 3 trial.** Ella R et al. *Lancet*. 2021 Nov 11:S0140-6736(21)02000-6. doi: 10.1016/S0140-6736(21)02000-6. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02000-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02000-6/fulltext)

BBV152 was highly efficacious against laboratory-confirmed symptomatic COVID-19 disease in adults. Vaccination was well tolerated with no safety concerns raised in this interim analysis.

16. **Promoting COVID-19 vaccine acceptance: recommendations from the Lancet Commission on Vaccine Refusal, Acceptance, and Demand in the USA.** Omer SB et al. *Lancet*. 2021 Nov 15:S0140-6736(21)02507-1. doi: 10.1016/S0140-6736(21)02507-1.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02507-1/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02507-1/fulltext)
When paired with masking, physical distancing, and ventilation, COVID-19 vaccines are the best intervention to sustainably control the pandemic. However, surveys have consistently found that a sizeable minority of US residents do not plan to get a COVID-19 vaccine. The most severe consequence of an inadequate uptake of COVID-19 vaccines has been sustained community transmission (including of the delta [B.1.617.2] variant, a surge of which began in July, 2021). Exacerbating the direct impact of the virus, a low uptake of COVID-19 vaccines will prolong the social and economic repercussions of the pandemic on families and communities, especially low-income and minority ethnic groups, into 2022, or even longer. The scale and challenges of the COVID-19 vaccination campaign are unprecedented. Therefore, through a series of recommendations, we present a coordinated, evidence-based education, communication, and behavioural intervention strategy that is likely to improve the success of COVID-19 vaccine programmes across the USA.
17. **COVID-19 mRNA Vaccine Immunogenicity in Immunosuppressed Individuals.** Collier AY et al. *J Infect Dis*. 2021 Nov 18:jiab569. doi: 10.1093/infdis/jiab569.
<https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab569/6430790?searchresult=1>
Individuals on immunosuppressive therapy have increased mortality from SARS-CoV-2 infection, and delayed viral clearance may lead to new viral variants. IS therapy reduces antibody responses following COVID-19 messenger RNA (mRNA) vaccination; however, a comprehensive assessment of vaccine immunogenicity is lacking. Here we show that IS therapy reduced neutralizing, binding, and non-neutralizing antibody functions in addition to CD4 and CD8 T cell IFN- γ responses following COVID-19 mRNA vaccination compared to immunocompetent individuals. Moreover, IS therapy reduced cross-reactivity against SARS-CoV-2 variants. These data suggest that the current COVID-19 mRNA vaccine regimens will likely not provide optimal protection in immunocompromised individuals.

Women & Children

18. **Risk for Stillbirth Among Women with and Without COVID-19 at Delivery Hospitalization — United States, March 2020–September 2021.** DeSisto CL, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 19 November 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7047e1>
Among 1,249,634 delivery hospitalizations during March 2020–September 2021, U.S. women with COVID-19 were at increased risk for stillbirth compared with women without COVID-19 (adjusted relative risk [aRR] = 1.90; 95% CI = 1.69–2.15). The magnitude of association was higher during the period of SARS-CoV-2 B.1.617.2 (Delta) variant predominance than during the pre-Delta period. Implementing evidence-based COVID-19 prevention strategies, including vaccination before or during pregnancy, is critical to reduce the impact of COVID-19 on stillbirths.

19. **COVID-19–Associated Deaths after SARS-CoV-2 Infection during Pregnancy — Mississippi, March 1, 2020–October 6, 2021.** Kasehagen L, et al. *MMWR Morb Mortal Wkly Rep.* ePub: 19 November 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7047e2>
This study found 15 COVID-19–associated deaths after SARS-CoV-2 infection during pregnancy (nine deaths per 1,000 SARS-CoV-2 infections); during the same period, 413 COVID-19–associated deaths were reported among females of reproductive age (2.5 deaths per 1,000 SARS-CoV-2 infections). In addition, this study found an apparent increase in the ratio of COVID-19–associated deaths per 1,000 cases among pregnant women as the Delta variant became predominant (pre-Delta period: five deaths per 1,000 SARS-CoV-2 infections during pregnancy; Delta predominance period: 25 deaths per 1,000 SARS-CoV-2 infections during pregnancy). A similar increase in the ratio of deaths per 1,000 cases was observed for females of reproductive age in Mississippi, although the magnitude of the ratios was lower overall and by period.
20. **Pregnant/Peripartum Women with COVID-19 High Survival with ECMO: An ELSO Registry Analysis.** O'Neil ER, et al. *Am J Respir Crit Care Med.* 2021 Nov 12. doi: 10.1164/rccm.202109-2096LE. <https://www.atsjournals.org/doi/pdf/10.1164/rccm.202109-2096LE>
In the US, 131,512 pregnant/peripartum women have been affected by Coronavirus Disease 2019 (COVID-19), with 200 associated deaths (0.15%). The hormonal, physiological, and immunomodulatory changes during pregnancy increase susceptibility to respiratory infections and may predispose women to more severe presentations of COVID-19. COVID-19 in pregnant/peripartum This vulnerable population should be considered for V-V ECMO support for COVID-19. women is associated with higher risk for preterm birth, preeclampsia, cesarean delivery, perinatal death, and higher rates of intensive care admission, mechanical ventilation, and extracorporeal membrane oxygenation (ECMO) when compared to pregnant/peripartum women without COVID-19 or when compared to non-pregnant women with COVID-19. Venovenous (V-V) ECMO is an invasive strategy to support oxygenation and ventilation for respiratory failure when conventional therapies have failed. We investigated the survival and complications of pregnant/peripartum women with COVID19 supported with V-V ECMO reported to the Extracorporeal Life Support Organization (ELSO) Registry.

GUIDELINES & CONSENSUS STATEMENTS

[Infectious Diseases Society of America Guidelines on Infection Prevention for Healthcare Personnel Caring for Patients with Suspected or Known COVID-19.](#) Lynch JB et al. *Clin Infect Dis.* 2021 Nov 15:ciab953. doi: 10.1093/cid/ciab953.

[Maternal vaccination: A review of current evidence and recommendations.](#) Etti M, et al. *Am J Obstet Gynecol.* 2021 Nov 11:S0002-9378(21)01228-X. doi: 10.1016/j.ajog.2021.10.041.

FDA / CDC / NIH / WHO Updates

[FDA Expands Eligibility for COVID-19 Vaccine Boosters,](#) November 19, 2021

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