

COVID-19 Resource Desk

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New Research

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Clinical Syndrome

- 1. Brain injury in COVID-19 is associated with dysregulated innate and adaptive immune responses.** Needham EJ et al. *Brain*. 2022 Sep 6:awac321. doi: 10.1093/brain/awac321. <https://academic.oup.com/brain/advance-article/doi/10.1093/brain/awac321/6692467>

We investigated the dynamics of, and relationship between, serum markers of brain injury (neurofilament light [NfL], glial fibrillary acidic protein [GFAP] and total tau) and markers of dysregulated host response (autoantibody production and cytokine profiles) in 175 patients admitted with COVID-19 and 45 patients with influenza. During hospitalisation, sera from patients with COVID-19 demonstrated elevations of NfL and GFAP in a severity-dependent manner, with evidence of ongoing active brain injury at follow-up 4 months later. These biomarkers were associated with elevations of pro-inflammatory cytokines and the presence of autoantibodies to a large number of different antigens. Autoantibodies were commonly seen against lung surfactant proteins but also brain proteins such as myelin associated glycoprotein. Commensurate findings were seen in the influenza cohort. A distinct process characterised by elevation of serum total tau was seen in patients at follow-up, which appeared to be independent of initial disease severity and was not associated with dysregulated immune responses unlike NfL and GFAP. These results demonstrate that brain injury is a common consequence of both COVID-19 and influenza, and is therefore likely to be a feature of severe viral infection more broadly. The brain injury occurs in the context of dysregulation of both innate and adaptive immune responses, with no single pathogenic mechanism clearly responsible.

- 2. Gastrointestinal and sensory manifestations, nutrition management, and energy-protein intake in hospitalized patients with COVID-19.** Torrinhas RS et al. *Nutr Clin Pract*. 2022 Oct;37(5):1152-1161. doi: 10.1002/ncp.10906.

<https://aspenjournals.onlinelibrary.wiley.com/doi/10.1002/ncp.10906>

GSM were prevalent in COVID-19 and it impaired EER attendance and patient recovery. ONS was well-tolerated, aided EER attendance, and potentially facilitated hospital discharge.

Diagnostics & Screening

- 3. The impact of repeated rapid test strategies on the effectiveness of at-home antiviral treatments for SARS-CoV-2.** Menkir TF, Donnelly CA. *Nat Commun.* 2022 Sep 8;13(1):5283. doi: 10.1038/s41467-022-32640-2. <https://www.nature.com/articles/s41467-022-32640-2>

Regular rapid testing can provide twofold benefits: identifying infectious individuals and providing positive tests sufficiently early during infection that treatment with antivirals can effectively inhibit development of severe disease. Here, we provide a quantitative illustration of the extent of nirmatrelvir-associated treatment benefits that are accrued among high-risk populations when rapid tests are administered at various intervals. Strategies for which tests are administered more frequently are associated with greater reductions in the risk of hospitalization, with weighted risk ratios for testing every other day to once every 2 weeks ranging from 0.17 to 0.77 and correspondingly, higher proportions of the infected population benefiting from treatment, ranging from 0.26 to 0.92, respectively. Importantly, reduced treatment delays, coupled with increased test and treatment coverage, have a critical influence on average treatment benefits, confirming the significance of access.

Epidemiology & Public Health

- 4. Booster COVID-19 Vaccinations Among Persons Aged ≥ 5 Years and Second Booster COVID-19 Vaccinations Among Persons Aged ≥ 50 Years - United States, August 13, 2021-August 5, 2022.** Fast HE, et al. *MMWR Morb Mortal Wkly Rep.* 2022 Sep 2;71(35):1121-1125. doi: 10.15585/mmwr.mm7135a4. https://www.cdc.gov/mmwr/volumes/71/wr/mm7135a4.htm?s_cid=mm7135a4_w

Among 214 million eligible persons aged ≥ 5 years, approximately one half received a booster dose. Among 55 million eligible persons aged ≥ 50 years, approximately one third received a second booster dose. Booster and second booster dose coverage rates were lower among the youngest age groups; males; non-Hispanic Black or African American, Hispanic or Latino, and multiracial persons; residents of rural counties; and Janssen (Johnson & Johnson) primary series recipients.

- 5. COVID-19-Associated Hospitalizations Among Vaccinated and Unvaccinated Adults 18 Years or Older in 13 US States, January 2021 to April 2022.** Havers FP et al. *JAMA Intern Med.* 2022 Sep 8. doi: 10.1001/jamainternmed.2022.4299. <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2796235>

In this cross-sectional study of US adults hospitalized with COVID-19, unvaccinated adults were more likely to be hospitalized compared with vaccinated adults; hospitalization rates were lowest in those who had received a booster dose. Hospitalized vaccinated persons were older and more likely to have 3 or more underlying medical conditions and be long-term care facility residents compared with hospitalized unvaccinated persons. The study results suggest that clinicians and public health practitioners should continue to promote vaccination with all recommended doses for eligible persons.

Survivorship & Rehabilitation

- 6. Long-term cardiac pathology in individuals with mild initial COVID-19 illness.** Puntmann VO et al. *Nat Med.* 2022 Sep 5. doi: 10.1038/s41591-022-02000-0. <https://www.nature.com/articles/s41591-022-02000-0>

Cardiac symptoms are increasingly recognized as late complications of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in previously well individuals with mild initial illness, but the underlying pathophysiology leading to long-term cardiac symptoms remains unclear. In this study, we conducted serial cardiac assessments in a selected population of individuals with Coronavirus Disease 2019 (COVID-19) with no previous cardiac disease or notable comorbidities by measuring blood biomarkers of heart injury or dysfunction and by performing magnetic resonance imaging. Baseline measurements from 346 individuals with COVID-19 (52% females) were obtained at a median of 109 days (interquartile range (IQR), 77-177 days) after infection, when 73% of participants reported cardiac symptoms, such as exertional dyspnea (62%), palpitations (28%), atypical chest pain (27%) and syncope (3%). Symptomatic individuals had higher heart rates and higher imaging values or contrast agent accumulation, denoting inflammatory cardiac involvement, compared to asymptomatic individuals. Structural heart disease or high levels of biomarkers of cardiac injury or dysfunction were rare in symptomatic individuals. At follow-up (329 days (IQR, 274-383 days) after infection), 57% of participants had persistent cardiac symptoms. Diffuse myocardial edema was more pronounced in participants who remained symptomatic at follow-up as compared to those who improved. Female gender and diffuse myocardial involvement on baseline imaging independently predicted the presence of cardiac symptoms at follow-up. Ongoing inflammatory cardiac involvement may, at least in part, explain the lingering cardiac symptoms in previously well individuals with mild initial COVID-19 illness.

7. Cardiorespiratory Fitness and Neuromuscular Function of Mechanically Ventilated ICU COVID-19 Patients. Millet GY et al. *Crit Care Med.* 2022 Sep 2. doi: 10.1097/CCM.0000000000005641. https://journals.lww.com/ccmjournal/Fulltext/9900/Cardiorespiratory_Fitness_and_Neuromuscular.41.aspx

Vo2max was on average only slightly above the 18 mL·min⁻¹·kg⁻¹, that is, the cut-off value known to induce difficulty in performing daily tasks. Overall, although low physical capacities at admission in ICU COVID-19 patients cannot be ruled out to explain the association between Vo2max or neuromuscular function and ICU stay/MV duration, altered cardiorespiratory fitness and neuromuscular function observed in the present study may not be specific to COVID-19 disease but seem applicable to all ICU/MV patients of similar duration.

8. Understanding post-COVID-19 interstitial lung disease (ILD): a new fibroinflammatory disease entity. Mehta P, et al. *Intensive Care Med.* 2022 Sep 8. doi: 10.1007/s00134-022-06877-w. <https://link.springer.com/article/10.1007/s00134-022-06877-w>

Immunomodulation and immunity from vaccination and natural infection have reduced mortality from coronavirus disease 2019 (COVID-19). However, there are ongoing concerns regarding emerging variants and residual pulmonary sequelae in survivors, given that the lungs are the principal site for the triumvirate of infection, inflammation and injury. The initial waves of acute, severe COVID-19 were profoundly inflammatory, usually manifest as organising pneumonia ± acute respiratory distress syndrome (ARDS). The extent of the fibrogenic potential of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and the modifiability of the pathogenic processes and disease course are unclear. Interestingly patients can develop 'post-COVID interstitial lung disease' (PC-ILD) irrespective of having ARDS during the acute phase. Here, we describe our evolving understanding of PC-ILD and the critical need to identify risk factors, including within the critical care setting. We also discuss

immunopathomechanisms that may facilitate early intervention to prevent, slow or arrest progression of lung damage e.g. with immunomodulatory and/or anti-fibrotic agents.

Therapeutics

9. Helmet versus facemask CPAP in COVID-19 respiratory failure: a prospective cohort study.

Colaïanni-Alfonso N, et al. *Chest*. 2022 Aug 29:S0012-3692(22)03690-X. doi: 10.1016/j.chest.2022.08.2221. [https://journal.chestnet.org/article/S0012-3692\(22\)03690-X/pdf](https://journal.chestnet.org/article/S0012-3692(22)03690-X/pdf)

These findings suggest a possible clinical benefit of helmet over facemask CPAP in patients with COVID-19 respiratory failure. Further randomized studies systematically assessing the clinical effects of helmet CPAP in COVID19 and other hypoxemic patients appear warranted to foster its use in other intensive care units.

10. Favipiravir in patients with early mild-to-moderate COVID-19: a randomized controlled trial.

Golan Y, et al. *Clin Infect Dis*. 2022 Sep 6:ciac712. doi: 10.1093/cid/ciac712. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac712/6692456>

Favipiravir was well tolerated but lacked efficacy in TT-SCR, progression to severe COVID-19, or cessation of viral shedding and should not be used to treat patients with COVID-19.

11. Dipeptidyl peptidase-1 inhibition in patients hospitalised with COVID-19: a multicentre, double-blind, randomised, parallel-group, placebo-controlled trial.

Keir HR et al. *Lancet Respir Med*. 2022 Sep 2:S2213-2600(22)00261-2. doi: 10.1016/S2213-2600(22)00261-2.

<https://www.sciencedirect.com/science/article/pii/S2213260022002612>

Brensocatib treatment did not improve clinical status at day 29 in patients hospitalised with COVID-19. FUNDING: Sponsored by the University of Dundee and supported through an Investigator Initiated Research award from Insmed, Bridgewater, NJ; STOP-COVID19 trial.

12. Eligibility for Posthospitalization Venous Thromboembolism Prophylaxis in Hospitalized Patients With COVID-19: A Retrospective Cohort Study.

Vaughn VM, et al. *J Am Heart Assoc*. 2022 Sep 8:e025914. doi: 10.1161/JAHA.122.025914.

<https://www.ahajournals.org/doi/10.1161/JAHA.122.025914>

Across 35 hospitals in Michigan, ≈1 in 4 patients hospitalized with COVID-19 would qualify for posthospital thromboprophylaxis. With only 13% of patients actually receiving postdischarge prophylaxis, there is a potential opportunity for improvement in care.

Transmission / Infection Control

13. Detection of Higher Cycle Threshold Values in Culturable SARS-CoV-2 Omicron BA.1 Sublineage Compared with Pre-Omicron Variant Specimens - San Francisco Bay Area, California, July 2021-March 2022.

Tassetto M et al. *MMWR Morb Mortal Wkly Rep*. 2022 Sep 9;71(36):1151-1154. doi: 10.15585/mmwr.mm7136a3.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7136a3.htm?s_cid=mm7136a3_w

In the current analysis, nasal specimens collected from an ongoing longitudinal cohort of nonhospitalized participants with positive SARS-CoV-2 test results living in the San Francisco Bay Area were used to generate Ct values and assess for the presence of culturable SARS-CoV-2 virus; findings were compared between specimens from participants infected with pre-Omicron variants and those infected with the Omicron BA.1 sublineage. Among specimens with culturable virus detected, Ct values were higher (suggesting lower RNA levels) during Omicron BA.1 infections than during pre-Omicron infections, suggesting variant-specific differences in viral dynamics. Supporting CDC guidance, these data show that Ct values likely do not provide a consistent proxy for infectiousness across SARS-CoV-2 variants.

Vaccines / Immunology

14. Effectiveness of COVID-19 Vaccines against SARS-CoV-2 Variants of Concern in Real-world: a Literature Review and Meta-analysis. Shao W, et al. *Emerg Microbes Infect.* 2022 Sep 7:1-75. doi: 10.1080/22221751.2022.2122582.

<https://www.tandfonline.com/doi/full/10.1080/22221751.2022.2122582?src=>

We identified 113 studies meeting the eligibility criteria. We found full vaccination provided strong protection against each clinical outcome with summary VE ranging from 86.8% to 96.0% Alpha, moderate protection against infection caused by Beta, Gamma and Delta with summary VE ranging from 70.9% to 72.8%, strong protection against severe disease caused by Delta with summary VE ranging from 84.9% to 90.3%, limited protection with summary VE of 23.5% (95% CI, 17.0-29.5) against infection and moderate protection with summary VE ranging from 56.5% to 82.4% against severe diseases caused by Omicron. Booster vaccination can provide a substantial improvement in protection against Delta and Omicron, but not as much as the Delta. The meta-regression analysis showed that the VE against the Omicron waned over time, and the VE against hospitalization declined relatively slowly compared to against infection.

15. Immunogenicity and safety of an inactivated whole-virus COVID-19 vaccine (VLA2001) compared with the adenoviral vector vaccine ChAdOx1-S in adults in the UK (COV-COMPARE): interim analysis of a randomised, controlled, phase 3, immunobridging trial. Lazarus R et al. *Lancet Infect Dis.* 2022 Sep 5:S1473-3099(22)00502-3. doi: 10.1016/S1473-3099(22)00502-3.

<https://www.sciencedirect.com/science/article/pii/S1473309922005023>

VLA2001 has a favourable tolerability profile and met superiority criteria for neutralising antibodies and non-inferiority criterion for seroconversion rates compared with ChAdOx1-S. The data presented here formed the basis of successful marketing approval for use of VLA2001 in primary vaccination in the EU, the UK, Bahrain, and United Arab Emirates.

16. Comparison of Semen Quality Before and After Inactivated SARS-CoV-2 Vaccination Among Men in China. Huang J, et al. *JAMA Netw Open.* 2022 Sep 1;5(9):e2230631. doi: 10.1001/jamanetworkopen.2022.30631.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2796001>

Mass vaccination campaigns have been conducted worldwide to control the COVID-19 pandemic. Despite reassuring safety profiles in clinical trials, vaccine hesitancy remains high among individuals of reproductive age, partially because of fertility concerns. Recent studies have shown that messenger

RNA and viral-vector SARS-CoV-2 vaccinations do not impair sperm parameters among participants. However, the effects of inactivated SARS-CoV-2 vaccines—the most widely used vaccine type in mainland China—on semen quality have not been assessed. We evaluated changes in semen quality before and after inactivated SARS-CoV-2 vaccination among men in China.

17. Evaluation of Risk Factors for Postbooster Omicron COVID-19 Deaths in England. National Core Studies—Immunology Breakthrough Consortium. *JAMA Netw Open*. 2022 Sep 1;5(9):e2233446. doi: 10.1001/jamanetworkopen.2022.33446.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2796000>

With the emergence of the Omicron variant, it has become critical to identify risk factors associated with COVID-19 death in individuals who have completed primary vaccination and received a messenger RNA (mRNA) booster dose. Existing evidence is based on people who have received 1 or 2 doses of a COVID-19 vaccine and were infected by the Alpha or Delta variant. Understanding which groups are at increased risk of COVID-19 death after receiving a booster is crucial for the prioritization of further booster doses and access to COVID-19 therapeutics.

18. Analysis of Vaccine Reactions After COVID-19 Vaccine Booster Doses Among Pregnant and Lactating Individuals. Kachikis A, et al. *JAMA Netw Open*. 2022 Sep 1;5(9):e2230495. doi: 10.1001/jamanetworkopen.2022.30495.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2795998>

This study suggests that COVID-19 vaccine boosters or third doses were well tolerated among pregnant and lactating individuals. Data to evaluate tolerability of boosters or additional doses among pregnant and lactating individuals will be important as they are considered for these populations.

Women & Children

19. COVID-19 mRNA Vaccine Safety Among Children Aged 6 Months-5 Years - United States, June 18, 2022-August 21, 2022. Hause AM, et al. *MMWR Morb Mortal Wkly Rep*. 2022 Sep 2;71(35):1115-1120. doi: 10.15585/mmwr.mm7135a3.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7135a3.htm?s_cid=mm7135a3_w

Initial vaccine safety data indicate that among young children, local and systemic reactions are expected after COVID-19 vaccination and serious adverse events are rare.

20. Parental Intentions and Perceptions Toward COVID-19 Vaccination Among Children Aged 4 Months to 4 Years - PROTECT Cohort, Four States, July 2021-May 2022. Lutrick K et al. *MMWR Morb Mortal Wkly Rep*. 2022 Sep 2;71(35):1109-1114. doi: 10.15585/mmwr.mm7135a2.

https://www.cdc.gov/mmwr/volumes/71/wr/mm7135a2.htm?s_cid=mm7135a2_w

During July 2021–May 2022, in a longitudinal cohort of 393 children aged <5 years in four states, parental intent to vaccinate children against COVID-19 and perception of COVID-19 vaccine safety and effectiveness declined over a 3-month period, but intent to vaccinate and perceptions of vaccine safety returned to baseline after 6 months.

21. Epidemiology of respiratory syncytial virus in children younger than 5 years in England during the COVID-19 pandemic, measured by laboratory, clinical, and syndromic surveillance: a

retrospective observational study. Bardsley M, et al. *Lancet Infect Dis.* 2022 Sep 2:S1473-3099(22)00525-4. doi: 10.1016/S1473-3099(22)00525-4.

<https://www.sciencedirect.com/science/article/pii/S1473309922005254>

The extraordinary absence of RSV during winter 2020-21 probably resulted in a cohort of young children without natural immunity to RSV, thereby raising the potential for increased RSV incidence, out-of-season activity, and health-service pressures when measures to restrict SARS-CoV-2 transmission were relaxed.

GUIDELINES & CONSENSUS STATEMENTS

[Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19.](#) Bhimraj A et al. *Clin Infect Dis.* 2022 Sep 5:ciac724. doi: 10.1093/cid/ciac724.

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