

COVID-19 Resource Desk

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New Research

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

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Clinical Syndrome

- 1. Cardiac performance in patients hospitalized with COVID-19: a 6 month follow-up study.** French COVID cohort study group. *ESC Heart Fail*. 2021 Mar 27. doi: 10.1002/ehf2.13315. <https://onlinelibrary.wiley.com/doi/full/10.1002/ehf2.13315>
We conducted a prospective echocardiographic evaluation of 48 patients (mean age 58) hospitalized 6 ± 1 month earlier for a laboratory-confirmed and symptomatic COVID-19. Six months after the acute COVID-19 phase, significant cardiac diastolic abnormalities are observed in patients who experienced myocardial injury but not in patients without cardiac involvement.
- 2. Right Ventricular Strain Is Common in Intubated COVID-19 Patients and Does Not Reflect Severity of Respiratory Illness.** Gibson LE, Fenza RD, Lang M, Capriles MI, Li MD, Kalpathy-Cramer J, Little BP, Arora P, Mueller AL, Ichinose F, Bittner EA, Berra L, G Chang M. *J Intensive Care Med*. 2021 Mar 30:8850666211006335. doi: 10.1177/08850666211006335. Online ahead of print. <https://journals.sagepub.com/doi/full/10.1177/08850666211006335>
Abnormal FWLS [free wall longitudinal strain] was present in 66% of mechanically ventilated COVID-19 patients and was associated with higher lung compliance (39.6 vs 29.4 mL/cmH₂O, P = 0.016), lower airway plateau pressures (21 vs 24 cmH₂O, P = 0.043), lower tidal volume ventilation (5.74 vs 6.17 cc/kg, P = 0.031), and reduced left ventricular function. FWLS correlated negatively with age (r = -0.414, P = 0.018) and with serum troponin (r = 0.402, P = 0.034). Patients with abnormal RV strain did not exhibit decreased oxygenation or increased disease severity based on inflammatory markers, vasopressor requirements, or chest imaging findings. RV dysfunction is common among critically ill COVID-19 patients and is not related to abnormal lung mechanics or ventilatory pressures. Instead, patients with abnormal FWLS had more favorable lung compliance. RV dysfunction may be secondary to diffuse intravascular micro- and macro-thrombosis or direct myocardial damage.

Diagnostics & Screening

- 3. Are saliva and deep throat sputum as reliable as common respiratory specimens for SARS-CoV-2 detection? A systematic review and meta-analysis.** Khiabani K, et al. *Am J Infect Control*. 2021 Mar 24:S0196-6553(21)00140-1.

<https://www.clinicalkey.com/#!/content/journal/1-s2.0-S0196655321001401>

The present review provides evidence for the diagnostic value of different respiratory specimens and supports saliva and DTS as promising diagnostic tools for first-line screening of SARS-CoV-2 infection. However, sampling, storing, and laboratory assay needs to be optimized and validated before introducing a definite diagnosis tool. Saliva, DTS, nasopharyngeal, and even double naso/oropharyngeal swabs showed approximately similar results, and sensitivity was directly related to the disease severity. This review revealed a relationship between viral load, disease severity, and test sensitivity. None of the specimens showed appropriate diagnostic sensitivity for asymptomatic patients.

- 4. A haemagglutination test for rapid detection of antibodies to SARS-CoV-2.** Townsend A et al. Nat Commun. 2021 Mar 29;12(1):1951. doi: 10.1038/s41467-021-22045-y.

<https://www.nature.com/articles/s41467-021-22045-y>

Here we describe a quantitative Haemagglutination test (HAT) for the detection of antibodies to the receptor binding domain of the SARS-CoV-2 spike protein. The HAT has a sensitivity of 90% and specificity of 99% for detection of antibodies after a PCR diagnosed infection. We will supply aliquots of the test reagent sufficient for ten thousand test wells free of charge to qualified research groups anywhere in the world.

- 5. Diagnosis of SARS-CoV-2 infection with LamPORE, a high-throughput platform combining loop-mediated isothermal amplification and nanopore sequencing.** Peto L et al. J Clin Microbiol. 2021 Mar 29;JCM.03271-20. doi: 10.1128/JCM.03271-20. Online ahead of print.

<https://jcm.asm.org/content/early/2021/03/26/JCM.03271-20>

The limit of detection of LamPORE was ten genome copies/ μ l of extracted RNA, which is above the limit achievable by RT-PCR but was not associated with a significant reduction of sensitivity in clinical samples. Positive clinical specimens came mostly from patients with acute symptomatic infection, and among these LamPORE had a diagnostic sensitivity of 99.1% (226/228 [95% CI 96.9-99.9%]). Among negative clinical specimens, including 153 with other respiratory pathogens detected, LamPORE had a diagnostic specificity of 99.6% (278/279 [98.0-100.0%]). Overall, 1.4% (7/514 [0.5-2.9%]) of samples produced an indeterminate result on first testing, and repeat LamPORE testing on the same RNA extract had a reproducibility of 96.8% (478/494 [94.8-98.1%]). Interpretation LamPORE has a similar performance to RT-PCR for the diagnosis of SARS-CoV-2 infection in symptomatic patients, and offers a promising approach to high-throughput testing.

Epidemiology & Public Health

- 6. Excess Deaths From COVID-19 and Other Causes in the US, March 1, 2020, to January 2, 2021.**

Woolf SH, Chapman DA, Sabo RT, Zimmerman EB. *JAMA*. Published online April 02, 2021.

doi:10.1001/jama.2021.5199 <https://jamanetwork.com/journals/jama/fullarticle/2778361>

Between March 1, 2020, and January 2, 2021, the US experienced 2 801 439 deaths, 22.9% more than expected, representing 522 368 excess deaths. The excess death rate was higher among non-Hispanic Black (208.4 deaths per 100 000) than non-Hispanic White or Hispanic populations (157.0 and 139.8 deaths per 100 000, respectively); these groups accounted for

16.9%, 61.1%, and 16.7% of excess deaths, respectively. The US experienced 4 surge patterns: in New England and the Northeast, excess deaths surged in the spring; in the Southeast and Southwest, in the summer and early winter; in the Plains, Rocky Mountain, and far West, primarily in early winter; and in the Great Lakes, bimodally, in the spring and early winter. Excess deaths were increasing in all regions at the end of 2020.

- 7. Risk Factors Associated With SARS-CoV-2 Infections, Hospitalization, and Mortality Among US Nursing Home Residents.** Mehta HB, Li S, Goodwin JS. *JAMA Netw Open*. 2021;4(3):e216315. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777972>

In this cohort study among 482 323 long-stay residents, risk of SARS-CoV-2 infections were associated with geographic area and the specific facility, not by characteristics of the residents. Among residents diagnosed with SARS-CoV-2 infections, the risk of hospitalization associated with individual resident characteristics differed from the risk of death.

- 8. Assessing asymptomatic, pre-symptomatic and symptomatic transmission risk of SARS-CoV-2.** Wu P, et al. *Clin Infect Dis*. 2021 Mar 27:ciab271. doi: 10.1093/cid/ciab271. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab271/6193430>

Asymptomatic and pre-symptomatic transmission play an important role in spreading infection, although asymptomatic cases pose a lower risk of transmission than symptomatic cases. Early case detection and effective test-and-trace measures are important to reduce transmission.

- 9. Assessing transmissibility of SARS-CoV-2 lineage B.1.1.7 in England.** Volz E et al. *Nature*. 2021 Mar 25. doi: 10.1038/s41586-021-03470-x. https://www.nature.com/articles/s41586-021-03470-x_reference.pdf

The SARS-CoV-2 lineage B.1.1.7 originated in the UK in late Summer to early Autumn 2020. Whole genome SARS-CoV-2 sequence data collected from community-based diagnostic testing shows an unprecedentedly rapid expansion of the B.1.1.7 lineage during Autumn 2020, suggesting a selective advantage. The best supported models did not indicate a substantial difference in VOC transmissibility among different age groups. There is a consensus among all analyses that the VOC has a substantial transmission advantage with a 50% to 100% higher reproduction number.

- 10. Symptoms of Anxiety or Depressive Disorder and Use of Mental Health Care Among Adults During the COVID-19 Pandemic — United States, August 2020–February 2021.** Vahratian A, Blumberg SJ, Terlizzi EP, Schiller JS. *MMWR Morb Mortal Wkly Rep*. ePub: 26 March 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7013e2>

During August 2020–February 2021, the percentage of adults with recent symptoms of an anxiety or a depressive disorder increased from 36.4% to 41.5%, and the percentage of those reporting an unmet mental health care need increased from 9.2% to 11.7%. Increases were largest among adults aged 18–29 years and those with less than a high school education.

- 11. Death Certificate–Based ICD-10 Diagnosis Codes for COVID-19 Mortality Surveillance — United States, January–December 2020.** Gundlapalli AV, Lavery AM, Boehmer TK, et al. *MMWR*

Morb Mortal Wkly Rep. ePub: 31 March 2021.

https://www.cdc.gov/mmwr/volumes/70/wr/mm7014e2.htm?s_cid=mm7014e2_x

Among 378,048 death certificates from 2020 listing COVID-19, 5.5% listed COVID-19 without codes for any other conditions. Among 357,133 death certificates with at least one other condition, 97% had a co-occurring diagnosis of a plausible chain-of-event condition (e.g., pneumonia or respiratory failure), or a significant contributing condition (e.g., hypertension or diabetes), or both.

12. Sudden rise in COVID-19 case fatality among young and middle-aged adults in the south of Brazil after identification of the novel B.1.1.28.1 (P.1) SARS-CoV-2 strain: analysis of data from the state of Parana.

Santos de Oliveira MH, Lippi G, Henry BM. medRxiv

2021.03.24.21254046; doi: <https://doi.org/10.1101/2021.03.24.21254046>

All age groups showed either decline or stabilization of the case fatality rates (CFRs) between September 2020 and January 2021. In February 2021, an increase in CFR for almost all age groups could be instead observed. All groups above 20 years of age showed statistically significant increases in CFR when diagnosed in February 2021 as opposed to January 2021. Patients aged 20-29 years experienced a tripling of their CFR, from 0.04% to 0.13%, while those aged 30-39, 40-49, 50-59 experienced approximate CFR doubling. Individuals between 20 and 29 years of age whose diagnosis was made in February 2021 had an over 3-fold higher risk of death compared to those diagnosed in January 2021 (Risk Ratio (RR): 3.15 [95%CI: 1.52-6.53], $p < 0.01$), while those aged 30-39, 40-49, 50-59 years experienced 93% (1.93 [95%CI:1.31-2.85], $p < 0.01$), 110% (RR: 2.10 [95%CI:1.62-2.72], $p < 0.01$), and 80% (RR: 1.80 [95%CI:1.50-2.16], $p < 0.01$) increases in risk of death, respectively. Notably, the observed CFR increase coincided with the second consecutive month of declining number of diagnosed SARS-CoV-2 cases. Taken together, these preliminary findings suggest significant increases in CFR in young and middle-aged adults after identification of a novel SARS-CoV-2 strain circulating in Brazil, and this should raise public health alarms, including the need for more aggressive local and regional public health interventions and faster vaccination.

13. Characterizing the disproportionate burden of SARS-CoV-2 variants of concern among essential workers in the Greater Toronto Area, Canada.

Chagla Z, Ma H, Sander B, Baral SD, Mishra S. medRxiv 2021.03.22.21254127; doi: <https://doi.org/10.1101/2021.03.22.21254127>

Results. During the study period, VOC cases emerged faster in groups with lowest income (growth rate 43.8%, 34.6% and 21.6% by income tertile from lowest to highest), and most essential work (growth rate 18.4%, 30.8% and 50.8% by tertile from lowest tertile of essential workers to highest tertile of essential workers). Recent introduction of VOC in the large urban area of Toronto has disproportionately affected neighbourhoods with the most essential workers and lowest income levels. Notably, this is consistent with the increased burden of non-VOC COVID-19 cases suggesting shared risk factors. To date, restrictive public health strategies have been of limited impact in these communities suggesting the need for complementary and well-specified supportive strategies including vaccine prioritization to address disparities and overall incidence of both VOC and non-VOC COVID-19.

14. SARS-CoV-2 infection risk among unvaccinated is negatively associated with community-level vaccination rates. Milman O, Yelin I, Aharony N, Katz R, Herzal E, Ben-Tov A, Kuint J, Gazit S, Chodick G, Patalon T, Kishony R. medRxiv 2021.03.26.21254394; doi:

<https://doi.org/10.1101/2021.03.26.21254394>

Mass vaccination has the potential to curb the current COVID-19 pandemic by protecting vaccinees from the disease and possibly lowering the chance of transmission to unvaccinated individuals. The high effectiveness of the widely-administered BNT162b vaccine in preventing not only the disease but also infection suggests a potential for a population-level effect, critical for disease eradication. However, this putative effect is difficult to observe, especially in light of highly fluctuating spatio-temporal epidemic dynamics. Here, analyzing vaccination records and test results collected during a rapid vaccine rollout for a large population from 223 geographically defined communities, we find that the rates of vaccination in each community are highly correlated with a later decline in infections among a cohort of under 16 years old which are unvaccinated. These results provide observational evidence that vaccination not only protects individual vaccinees but also provides cross-protection to unvaccinated individuals in the community.

15. Estimation of secondary household attack rates for emergent spike L452R SARS-CoV-2 variants detected by genomic surveillance at a community-based testing site in San Francisco.

Peng J et al. Clin Infect Dis. 2021 Mar 31:ciab283. doi: 10.1093/cid/ciab283. Online ahead of print.

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab283/6206738>

A total of 12,124 tests were performed yielding 1,099 positives. From these, 928 high quality genomes were generated. Certain viral lineages bearing spike mutations, defined in part by L452R, S13I, and W152C, comprised 54.4% of the total sequences from January, compared to 15.7% in November. Household contacts exposed to the "California" or "West Coast" variants (B.1.427 and B.1.429) were at higher risk of infection compared to household contacts exposed to lineages lacking these variants (0.36 vs 0.29, RR=1.28; 95% CI:1.00-1.64). The reproductive number was estimated to be modestly higher than other lineages spreading in California during the second half of 2020. Viral loads were similar among persons infected with West Coast versus non-West Coast strains, as was the proportion of individuals with symptoms (60.9% vs 64.3%). The increase in prevalence, relative household attack rates, and reproductive number are consistent with a modest transmissibility increase of the West Coast variants.

16. Risk Factors Associated With SARS-CoV-2 Infections, Hospitalization, and Mortality Among US Nursing Home Residents. Mehta HB, Li S, Goodwin JS. JAMA Netw Open. 2021 Mar

1;4(3):e216315. doi: 10.1001/jamanetworkopen.2021.6315.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777972>

These findings suggest that among long-stay nursing home residents, risk of SARS-CoV-2 infection was associated with county and facility of residence, while risk of hospitalization and death after SARS-CoV-2 infection was associated with facility and individual resident characteristics. For many resident characteristics, there were substantial differences in risk of

hospitalization vs mortality. This may represent resident preferences, triaging decisions, or inadequate recognition of risk of death.

- 17. Provisional Mortality Data — United States, 2020.** Ahmad FB, Cisewski JA, Miniño A, Anderson RN. *MMWR Morb Mortal Wkly Rep.* ePub: 31 March 2021. DOI:

<http://dx.doi.org/10.15585/mmwr.mm7014e1>

The age-adjusted death rate increased by 15.9% in 2020. Overall death rates were highest among non-Hispanic Black persons and non-Hispanic American Indian or Alaska Native persons. COVID-19 was the third leading cause of death, and the COVID-19 death rate was highest among Hispanics.

Healthcare Delivery & Healthcare Workers

- 18. Association of Race/Ethnicity With Likelihood of COVID-19 Vaccine Uptake Among Health Workers and the General Population in the San Francisco Bay Area.** Grumbach K, Judson T, Desai M, Jain V, Lindan C, Doernberg SB, Holubar M. *JAMA Intern Med.* 2021 Mar 30. doi: 10.1001/jamainternmed.2021.1445. Online ahead of print.

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2778176>

Surveys have demonstrated racial differences in the public's willingness to receive a COVID-19 vaccine^{1,2} but have not directly compared vaccine intentions among health workers and the general public.³ We investigated COVID-19 vaccine intentions among racially and ethnically diverse samples of health workers and the general population.

Survivorship & Rehabilitation

- 19. Lung Function Deficits and Symptom Burden in Survivors of COVID-19 Requiring Mechanical Ventilation.** Finney LJ, et al. *Ann Am Thorac Soc.* 2021 Mar 26. doi: 10.1513/AnnalsATS.202102-099RL.

<https://www.atsjournals.org/doi/10.1513/AnnalsATS.202102-099RL>

Despite 80% and 90% of our cohort reporting interval symptom improvement and showing radiographic improvement respectively, there remained high prevalence of lung function deficits, functional impairment and significant symptomatology. The most prominent symptoms were fatigue and breathlessness in line with previous reports in COVID-19. Muscle weakness and joint pain were also frequently reported in our cohort, perhaps reflecting the effects of post-intensive care syndrome, as observed in nonCOVID-19 ARDS survivors. Half of our cohort complained of shoulder pain. This

warrants further investigation given that 60% of our cohort underwent prone positioning during their hospital admission.

- 20. Postintensive Care Syndrome in Survivors of Critical Illness Related to Coronavirus Disease 2019: Cohort Study from a New York City Critical Care Recovery Clinic.** Martillo M, et al. *Crit Care Med.* 2021 Mar 16. doi: 10.1097/CCM.0000000000005014.

<https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=ovft&AN=00003246-900000000-95305&PDF=y>

We included 45 patients with a mean age of 54 years, and 73% were male. Ninety-one percent of coronavirus disease 2019 ICU survivors fit diagnostic criteria for postintensive care syndrome. 86.7 % had impairments in the physical domain, 48% reported impairments in the psychiatric domain, and 8% had impairments on cognitive screening. We found that 58% had some degree of mobility impairment. In the psychiatric domain, 38% exhibited at least mild depression, and 18 % moderate to severe depression. Survivors of critical illness related to coronavirus disease 2019 are at high risk of developing postintensive care syndrome. These findings highlight the importance of planning for appropriate post-ICU care to diagnose and treat this population.

21. Toward Understanding COVID-19 Recovery: National Institutes of Health Workshop on Postacute COVID-19. Lerner AM, et al. *Ann Intern Med.* 2021 Mar 30. doi: 10.7326/M21-1043. <https://www.acpjournals.org/doi/10.7326/M21-1043>

Key gaps in the understanding of postacute COVID-19 exists including: characterization of epidemiology, description of clinical spectrum, risk factors, pathophysiology, therapeutics and prevention.

22. Pulmonary Rehabilitation in Patients Recovering from COVID-19. Zampogna E, Paneroni M, Belli S, Aliani M, Gandolfo A, Visca D, Bellanti MT, Ambrosino N, Vitacca M. *Respiration.* 2021 Mar 30:1-7. doi: 10.1159/000514387. Online ahead of print.

<https://www.karger.com/Article/Abstract/514387>

RESULTS: Data of 140 patients were analyzed. After rehabilitation, patients showed improvements in SPPB {from: (median [IQR]) 0.5 (0-7) to 7 (4-10), $p < 0.001$ } and BI (from 55 [30-90] to 95 [65-100], $p < 0.001$), as well as in other assessed outcome measures. The proportion of patients unable at admission to stand, rise from a chair and walk was significantly reduced ($p < 0.00$).

CONCLUSIONS: Pulmonary rehabilitation is possible and effective in patients recovering from COVID-19. Our findings may be useful to guide clinicians taking care of patients surviving COVID-19 infection.

23. Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study. Ayoubkhani D, Khunti K, Nafilyan V, Maddox T, Humberstone B, Diamond I, Banerjee A. *BMJ.* 2021 Mar 31;372:n693. doi: 10.1136/bmj.n693.

<https://www.bmj.com/content/372/bmj.n693>

Over a mean follow-up of 140 days, nearly a third of individuals who were discharged from hospital after acute covid-19 were readmitted (14 060 of 47 780) and more than 1 in 10 (5875) died after discharge, with these events occurring at rates four and eight times greater, respectively, than in the matched control group. Rates of respiratory disease ($P < 0.001$), diabetes ($P < 0.001$), and cardiovascular disease ($P < 0.001$) were also significantly raised in patients with covid-19, with 770 (95% confidence interval 758 to 783), 127 (122 to 132), and 126 (121 to 131) diagnoses per 1000 person years, respectively. Rate ratios were greater for individuals aged less than 70 than for those aged 70 or older, and in ethnic minority groups compared with the white population, with the largest differences seen for respiratory disease

(10.5 (95% confidence interval 9.7 to 11.4) for age less than 70 years v 4.6 (4.3 to 4.8) for age \geq 70, and 11.4 (9.8 to 13.3) for non-white v 5.2 (5.0 to 5.5) for white individuals).

Individuals discharged from hospital after covid-19 had increased rates of multiorgan dysfunction compared with the expected risk in the general population. The increase in risk was not confined to the elderly and was not uniform across ethnicities. The diagnosis, treatment, and prevention of post-covid syndrome requires integrated rather than organ or disease specific approaches, and urgent research is needed to establish the risk factors.

24. Mortality and Readmission Rates Among Patients With COVID-19 After Discharge From Acute Care Setting With Supplemental Oxygen. Banerjee, J. et al. (2021). *JAMA network open*, 4(4), e213990. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2778078>

A total of 621 patients with COVID-19 pneumonia (404 male [65.1%] and 217 female [34.9%]) were discharged with home oxygen. Median age of these patients was 51 years (interquartile range, 45-61 years), with 149 (24.0%) discharged from the emergency department and 472 (76%) discharged from inpatient encounters. The all-cause mortality rate was 1.3% (95% CI, 0.6%-2.5%) and the 30-day return hospital admission rate was 8.5% (95% CI, 6.2%-10.7%) with a median follow-up time of 26 days (interquartile range, 15-55 days). No deaths occurred in the ambulatory setting. In this cohort study, patients with COVID-19 pneumonia discharged on home oxygen had low rates of mortality and return admission within 30 days of discharge. Ambulatory management of COVID-19 with home oxygen has an acceptable safety profile, and the expected practice approach may help optimize outcomes, by ensuring right care in the right place at the right time and preserving access to acute care during the COVID-19 pandemic.

Therapeutics

25. Bleeding Risk by Intensity of Anticoagulation in Critically Ill Patients with COVID-19: A Retrospective Cohort Study. Halaby R, et al. *J Thromb Haemost.* 2021 Mar 28. doi: 10.1111/jth.15310. <https://onlinelibrary.wiley.com/doi/10.1111/jth.15310>

Critically ill patients with COVID-19 had a similar bleeding risk as other respiratory viral infection patients. When accounting for changes in anticoagulation that occurred in COVID-19 patients, therapeutic-intensity anticoagulation was associated with a greater risk of major bleeding compared with standard thromboprophylaxis.

26. Effect of Helmet Noninvasive Ventilation vs High-Flow Nasal Oxygen on Days Free of Respiratory Support in Patients With COVID-19 and Moderate to Severe Hypoxemic Respiratory Failure: The HENIVOT Randomized Clinical Trial. Grieco DL et al. *JAMA.* 2021 Mar 25. doi: 10.1001/jama.2021.4682. <https://jamanetwork.com/journals/jama/fullarticle/2778088>

Among patients with COVID-19 and moderate to severe hypoxemia, treatment with helmet noninvasive ventilation, compared with high-flow nasal oxygen, resulted in no significant difference in the number of days free of respiratory support within 28 days. Further research is warranted to determine effects on other outcomes, including the need for endotracheal intubation.

27. Assessment of Simulated SARS-CoV-2 Infection and Mortality Risk Associated with Radiation Therapy Among Patients in 8 Randomized Clinical Trials. Tabrizi S, et al. *JAMA Netw Open*. 2021 Mar 1;4(3):e213304. doi: 10.1001/jamanetworkopen.2021.3304.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777836>

In this comparative effectiveness study of data from 8 clinical trials of patients receiving radiation therapy to simulate COVID-19 risk and mortality rates, treatment modification was not associated with altered risk from COVID-19 in lower-risk scenarios and was only associated with decreased mortality in very high COVID-19-risk scenarios. This model, which can be adapted to dynamic changes in COVID-19 risk, provides a flexible, quantitative approach to assess the potential impact of treatment modifications and supports the continued delivery of standard evidence-based care with appropriate precautions against COVID-19.

28. Peginterferon Lambda-1a for treatment of outpatients with uncomplicated COVID-19: a randomized placebo-controlled trial. Jagannathan P et al. *Nat Commun*. 2021 Mar 30;12(1):1967. doi: 10.1038/s41467-021-22177-1.

<https://www.nature.com/articles/s41467-021-22177-1>

Type III interferons have been touted as promising therapeutics in outpatients with coronavirus disease 2019 (COVID-19). We conducted a randomized, single-blind, placebo-controlled trial (NCT04331899) in 120 outpatients with mild to moderate COVID-19 to determine whether a single, 180 mcg subcutaneous dose of Peginterferon Lambda-1a (Lambda) within 72 hours of diagnosis could shorten the duration of viral shedding (primary endpoint) or symptoms (secondary endpoint). In both the 60 patients receiving Lambda and 60 receiving placebo, the median time to cessation of viral shedding was 7 days (hazard ratio [HR] = 0.81; 95% confidence interval [CI] 0.56 to 1.19). Symptoms resolved in 8 and 9 days in Lambda and placebo, respectively, and symptom duration did not differ significantly between groups (HR 0.94; 95% CI 0.64 to 1.39). Both Lambda and placebo were well-tolerated, though liver transaminase elevations were more common in the Lambda vs. placebo arm (15/60 vs 5/60; $p = 0.027$). In this study, a single dose of subcutaneous Peginterferon Lambda-1a neither shortened the duration of SARS-CoV-2 viral shedding nor improved symptoms in outpatients with uncomplicated COVID-19.

Transmission / Infection Control

29. SARS-CoV-2 infection of the oral cavity and saliva. Huang N et al. *Nat Med*. 2021 Mar 25. doi: 10.1038/s41591-021-01296-8. <https://www.nature.com/articles/s41591-021-01296-8>

Signs of COVID-19 infection including taste loss, dry mouth and mucosal lesions such as ulcerations, enanthema and macules-the involvement of the oral cavity is poorly understood. Saliva from SARS-CoV-2-infected individuals harbored epithelial cells exhibiting ACE2 and TMPRSS expression and sustained SARS-CoV-2 infection. Matched nasopharyngeal and saliva samples displayed distinct viral shedding dynamics, and salivary viral burden correlated with COVID-19 symptoms, including taste loss. Upon recovery, this asymptomatic cohort exhibited sustained salivary IgG antibodies against SARS-CoV-2. Collectively, these data show that the oral cavity is an important site for SARS-CoV-2 infection and implicate saliva as a potential route of SARS-CoV-2 transmission.

30. The effect of respiratory activity, non-invasive respiratory support and facemasks on aerosol generation and its relevance to COVID-19. Wilson NM, Marks GB, Eckhardt A, Clarke AM, Young FP, Garden FL, Stewart W, Cook TM, Tovey ER. *Anaesthesia*. 2021 Mar 30. doi: 10.1111/anae.15475. Online ahead of print.

<https://associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/10.1111/anae.15475>

Authors compared emissions from ten healthy subjects during six respiratory activities (quiet breathing; talking; shouting; forced expiratory manoeuvres; exercise; and coughing) with three respiratory therapies (high-flow nasal oxygen and single or dual circuit non-invasive positive pressure ventilation). Activities were repeated while wearing facemasks. When compared with quiet breathing, exertional respiratory activities increased particle counts 34.6-fold during talking and 370.8-fold during coughing ($p < 0.001$). High-flow nasal oxygen 60 at l.min⁻¹ increased particle counts 2.3-fold ($p = 0.031$) during quiet breathing. Single and dual circuit non-invasive respiratory therapy at 25/10 cm.H₂O with quiet breathing increased counts by 2.6-fold and 7.8-fold, respectively (both $p < 0.001$). During exertional activities, respiratory therapies and facemasks reduced emissions compared with activities alone. Respiratory activities (including exertional breathing and coughing) which mimic respiratory patterns during illness generate substantially more aerosols than non-invasive respiratory therapies, which conversely can reduce total emissions. We argue the risk of aerosol exposure is underappreciated and warrants widespread, targeted interventions.

Vaccines / Immunology

31. Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021.

Thompson MG, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 29 March 2021. DOI:

<http://dx.doi.org/10.15585/mmwr.mm7013e3>

Prospective cohorts of 3,950 health care personnel, first responders, and other essential and frontline workers completed weekly SARS-CoV-2 testing for 13 consecutive weeks. Under real-world conditions, mRNA vaccine effectiveness of full immunization (≥ 14 days after second dose) was 90% against SARS-CoV-2 infections regardless of symptom status; vaccine effectiveness of partial immunization (≥ 14 days after first dose but before second dose) was 80%.

32. Sensitivity of infectious SARS-CoV-2 B.1.1.7 and B.1.351 variants to neutralizing antibodies.

Planas D et al. *Nat Med*. 2021 Mar 26. doi: 10.1038/s41591-021-01318-5.

<https://www.nature.com/articles/s41591-021-01318-5>

We examined sensitivity of the two variants to SARS-CoV-2 antibodies present in sera and nasal swabs from individuals infected with previously circulating strains or who were recently vaccinated. Sera from 58 convalescent individuals collected up to 9 months after symptoms, similarly neutralized B.1.1.7. In contrast, after 9 months, 40% of the samples lacked any activity against B.1.351. Sera from 19 individuals vaccinated twice with Pfizer were similarly potent

against B.1.1.7 but less efficacious against B.1.351. Our results indicate that B.1.351, but not B.1.1.7, may increase the risk of infection in immunized individuals.

- 33. Safety and immunogenicity of a recombinant tandem-repeat dimeric RBD-based protein subunit vaccine (ZF2001) against COVID-19 in adults: two randomised, double-blind, placebo-controlled, phase 1 and 2 trials.** Yang S, et al. *Lancet Infect Dis.* 2021 Mar 24:S1473-3099(21)00127-4. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00127-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00127-4/fulltext)

The protein subunit vaccine ZF2001 appears to be well tolerated and immunogenic. The safety and immunogenicity data from the phase 1 and 2 trials support the use of the 25 µg dose in a three-dose schedule in an ongoing phase 3 trial for large-scale evaluation of ZF2001's safety and efficacy.

- 34. WHO International Standard for anti-SARS-CoV-2 immunoglobulin.** Kristiansen PA, et al. *Lancet.* 2021 Mar 23:S0140-6736(21)00527-4. doi: 10.1016/S0140-6736(21)00527-4. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00527-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00527-4/fulltext)

Although the correlate of protection against SARS-2-CoV has not yet been unequivocally defined, antibodies are likely to be at least part of the protective response. The effect of new variants on the evaluation of antibodies is obvious and unequivocal comparisons are required. Reporting the immunological responses from vaccine clinical trials against the International Standard is essential for the evaluation of clinical data submitted to national regulatory authorities as well as to WHO for emergency use listing, especially as placebo-controlled efficacy studies become operationally unfeasible.

- 35. Robust antibody responses in 70-80-year-olds 3 weeks after the first or second doses of Pfizer/BioNTech COVID-19 vaccine, United Kingdom, January to February 2021.** Subbarao S, et al. *Euro Surveill.* 2021 Mar;26(12). doi: 10.2807/1560-7917.ES.2021.26.12.2100329. <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.12.2100329>

Sera were collected from 185 adults aged ≥ 70 years in London to evaluate the immune response to COVID-19 vaccines. A single dose of Pfizer/BioNtech vaccine resulted in > 94% seropositivity after 3 weeks in naïve individuals using the Roche Spike antibody assay, while two doses produced very high spike antibody levels, significantly higher than convalescent sera from mild-to-moderate PCR-confirmed adult cases. Our findings support the United Kingdom's approach of prioritising the first dose and delaying the second dose of COVID-19 vaccine.

- 36. Single dose of a mRNA SARS-CoV-2 vaccine is associated with lower nasopharyngeal viral load among nursing home residents with asymptomatic COVID-19.** McEllistrem MC, et al. *Clin Infect Dis.* 2021 Mar 26:ciab263. doi: 10.1093/cid/ciab263. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab263/6188727>

In nursing home residents with asymptomatic COVID-19 diagnosed through twice-weekly surveillance testing, single dose BNT162b2 vaccination (Pfizer-BioNTech) was associated with lower nasopharyngeal viral load than detected in absence of vaccination. Since viral load is linked to transmission, single dose mRNA SARS-CoV-2 vaccination may help control outbreaks.

37. Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine.

Levine-Tiefenbrun M, Yelin I, Katz R, Herzel E, Golan Z, Schreiber L, Wolf T, Nadler V, Ben-Tov A, Kuint J, Gazit S, Patalon T, Chodick G, Kishony R. *Nat Med*. 2021 Mar 29. doi: 10.1038/s41591-021-01316-7. Online ahead of print.

<https://www.nature.com/articles/s41591-021-01316-7>

Beyond their substantial protection of individual vaccinees, coronavirus disease 2019 (COVID-19) vaccines might reduce viral load in breakthrough infection and thereby further suppress onward transmission. In this analysis of a real-world dataset of positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test results after inoculation with the BNT162b2 messenger RNA vaccine, we found that the viral load was substantially reduced for infections occurring 12-37 d after the first dose of vaccine. These reduced viral loads hint at a potentially lower infectiousness, further contributing to vaccine effect on virus spread.

38. Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial. Emary KRW et al. *Lancet* 2021 Mar 30. DOI:[https://doi.org/10.1016/S0140-6736\(21\)00628-0](https://doi.org/10.1016/S0140-6736(21)00628-0)

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00628-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00628-0/fulltext)

Participants in efficacy cohorts were recruited between May 31 and Nov 13, 2020, and received booster doses between Aug 3 and Dec 30, 2020. Of 8534 participants in the primary efficacy cohort, 6636 (78%) were aged 18–55 years and 5065 (59%) were female. Between Oct 1, 2020, and Jan 14, 2021, 520 participants developed SARS-CoV-2 infection. 1466 NAAT positive nose and throat swabs were collected from these participants during the trial. Of these, 401 swabs from 311 participants were successfully sequenced. Laboratory virus neutralisation activity by vaccine-induced antibodies was lower against the B.1.1.7 variant than against the Victoria lineage (geometric mean ratio 8·9, 95% CI 7·2–11·0). Clinical vaccine efficacy against symptomatic NAAT positive infection was 70·4% (95% CI 43·6–84·5) for B.1.1.7 and 81·5% (67·9–89·4) for non-B.1.1.7 lineages.

Interpretation. ChAdOx1 nCoV-19 showed reduced neutralisation activity against the B.1.1.7 variant compared with a non-B.1.1.7 variant in vitro, but the vaccine showed efficacy against the B.1.1.7 variant of SARS-CoV-2.

Whole Person Care

39. cAIR: Implementation of peer response support for frontline health care workers facing the COVID-19 pandemic. Rubin EW, Rassman A. [Providence authors]. *Soc Work Health Care*. 2021 Mar 24:1-10. doi: 10.1080/00981389.2021.1904321.

This paper presents the findings of a social work led peer support model, COVID-19 Am I Resilient (cAIR), developed and deployed during the first wave of the COVID-19 pandemic. This quality improvement initiative was developed and piloted within the Clinical Education and Practice department at a large urban health care system. The pilot included provision of peer support through synchronous video presentations, one-on-one peer support, and resourcing and referral. Pilot outcomes of feasibility and staff engagement were evaluated using participant responses to an online survey as well as attendance records at project activities. Developed to help frontline health care workers thrive in the midst, and wake, of the COVID-19

pandemic, the pilot study of the cAIR peer support model has implications for further development and implementation of peer support for typically underrepresented health care disciplines working during the COVID-19 pandemic as well as future public health emergencies.

40. Symptoms of Anxiety or Depressive Disorder and Use of Mental Health Care Among Adults During the COVID-19 Pandemic - United States, August 2020-February 2021. Vahratian, A., Blumberg, S. J., Terlizzi, E. P., & Schiller, J. S. *MMWR. Morbidity and mortality weekly report*, 70(13), 490–494. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7013e2.htm>

During August 2020–February 2021, the percentage of adults with recent symptoms of an anxiety or a depressive disorder increased from 36.4% to 41.5%, and the percentage of those reporting an unmet mental health care need increased from 9.2% to 11.7%. Increases were largest among adults aged 18–29 years and those with less than a high school education.

Women & Children

41. Continued proportional age shift of confirmed positive COVID-19 incidence over time to children and young adults: Washington State March-August 2020. Malmgren J, Guo B, Kaplan HG [Providence author]. *PLoS One*. 2021 Mar 24;16(3):e0243042. doi: 10.1371/journal.pone.0243042.

From March 1st to April 19, 2020 COVID-19 age distribution shifted with a 10% decline in cases age 60 years and older and a 20% increase in age 0-19/20-39 years. After the peak (March 22, 2020), incidence declined in older age groups and increased among age 0-19 and 20-39 age groups from 20% to 40% of total cases by April 19 and 50% by May 3. Percent positive cases age 0-19/20-39 years through August 2020 increased to a consistent average of 60%. An increased sustained proportion of COVID-19 incidence is present among children (age 0-19) and young adults (age 20-39) indicating an elevated role in disease spread during the epidemic creating a possible reservoir of disease with spillover risk to more vulnerable older persons and those with comorbid conditions.

42. [Children and COVID-19: State Data Report A joint report from the American Academy of Pediatrics and the Children’s Hospital Association Summary of publicly reported data from 49 states, NYC, DC, PR, and GU.](#) March 25, 2021.

As increasing numbers of older adults get vaccinated against COVID-19, the United States faces another surge of infections catalyzed by infections in children and teens. According to a Mar 25 American Academy of Pediatrics and Children's Hospital Association joint report, 64,029 children across the country were diagnosed as having COVID-19 in the week before the report, representing 19.2% of new weekly cases. Likewise, infections in 10- to 19-year-olds have climbed 227%, and 40% of recent outbreaks have been tied to the reopening of in-person K-12 schools, youth sports, or group gatherings after games.

[Update Alert 8: Epidemiology of and Risk Factors for Coronavirus Infection in Health Care Workers.](#)

Chou R, et al. *Ann Intern Med.* 2021 Mar 30. doi: 10.7326/L21-0143.

FDA / CDC / NIH / WHO Updates

CDC - [Variant Proportions in the U.S.](#)

CDC - [CDC Issues Updated Guidance on Travel for Fully Vaccinated People](#)

FDA - [Coronavirus \(COVID-19\) Update: FDA Makes Two Revisions to Moderna COVID-19 Vaccine Emergency Use Authorization to Help Increase the Number of Vaccine Doses Available](#)

WHO - [Joint Statement on prioritization of COVID-19 vaccination for seafarers and aircrew](#)

WHO - [WHO-convened global study of origins of SARS-CoV-2: China Part](#)

WHO - [Therapeutics and COVID-19: living guideline](#) – updated March 31, 2021

HHS - [March 24, 2021: Update on COVID-19 variants and impact on bamlanivimab distribution](#)

Commentary & News

[GSK and Vir Biotechnology announce submission of Emergency Use Authorization request to FDA for VIR-7831 for the early treatment of COVID-19](#)

[Press Briefing by White House COVID-19 Response Team and Public Health Officials](#)

[Pfizer and biontech confirm high efficacy and no serious safety concerns through up to six months following second dose in updated topline analysis of landmark covid-19 vaccine study](#)

[Pfizer-biontech announce positive topline results of pivotal covid-19 vaccine study in adolescents](#)

Perspective

[Breathless.](#) Sarah Carter, MD from Providence St. Mary Medical Center Walla Walla, WA. *N Engl J Med.* 2021 Mar 11;384(10):891-893. doi: 10.1056/NEJMp2032522.

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