COVID-19 Evidence Bulletin

7th December 2022

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**clinical management**

**title:** Association of Remdesivir Treatment With Mortality Among Hospitalized Adults With COVID-19 in the United States

jama network open | 1st december 2022

Key Points

Question Is remdesivir treatment associated with reduced risk of inpatient mortality among US patients hospitalized with COVID-19?

Findings In this retrospective cohort study of 24 856 patients with COVID-19 and 24 856 propensity score–matched control patients using US-based health insurance claims and hospital chargemaster data, remdesivir treatment was associated with significant 17% lower risk of inpatient mortality among patients hospitalized with COVID-19.

Meaning Results of this study complement those from randomized clinical trials and suggest that remdesivir treatment was associated with significantly reduced inpatient mortality among patients hospitalized with COVID-19.

Abstract

Importance SARS-CoV-2, which causes COVID-19, poses considerable morbidity and mortality risks. Studies using data collected during routine clinical practice can supplement randomized clinical trials to provide needed evidence, especially during a global pandemic, and can yield markedly larger sample sizes to assess outcomes for important patient subgroups.

Objective To evaluate the association of remdesivir treatment with inpatient mortality among patients with COVID-19 outside of the clinical trial setting.

Design, Setting, and Participants A retrospective cohort study in US hospitals using health insurance claims data linked to hospital chargemaster data from December 1, 2018, to May 3, 2021, was conducted among 24 856 adults hospitalized between May 1, 2020, and May 3, 2021, with newly diagnosed COVID-19 who received remdesivir and 24 856 propensity score–matched control patients.

Exposure Remdesivir treatment.

Main Outcomes and Measures All-cause inpatient mortality within 28 days of the start of remdesivir treatment for the remdesivir-exposed group or the matched index date for the control group.

Results A total of 24 856 remdesivir-exposed patients (12 596 men [50.7%]; mean [SD] age, 66.8 [15.4] years) and 24 856 propensity score–matched control patients (12 621 men [50.8%]; mean [SD] age, 66.8 [15.4] years) were included in the study. Median follow-up was 6 days (IQR, 4-11 days) in the remdesivir group and 5 days (IQR, 2-10 days) in the control group. There were 3557 mortality events (14.3%) in the remdesivir group and 3775 mortality events (15.2%) in the control group. The 28-day mortality rate was 0.5 per person-month in the remdesivir group and 0.6 per person-month in the control group. Remdesivir treatment was associated with a statistically significant 17% reduction in inpatient mortality among patients hospitalized with COVID-19 compared with propensity score–matched control patients (hazard ratio, 0.83 [95% CI, 0.79-0.87]).

Conclusions and Relevance In this retrospective cohort study using health insurance claims and hospital chargemaster data, remdesivir treatment was associated with a significantly reduced inpatient mortality overall among patients hospitalized with COVID-19. Results of this analysis using data collected during routine clinical practice and state-of-the-art methods complement results from randomized clinical trials. Future areas of research include assessing the association of remdesivir treatment with inpatient mortality during the circulation of different variants and relative to time from symptom onset…

 <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799114>

**title:** Longitudinal Use of Telehealth During the COVID-19 Pandemic and Utility of Asynchronous Testing for Subspecialty-Level Ophthalmic Care

JAMA Ophthalmology | 1st December 2022

Key Points

Question How did telehealth use compare among clinical specialties during the COVID-19 pandemic, and was there utility for asynchronous testing in teleophthalmology at an academic institution?

Findings In this quality improvement study of 881 080 patient encounters over the first 18 months of the COVID-19 pandemic, use of telehealth increased across specialties before stabilizing, with the highest use in gastroenterology, urology, neurosurgery, and neurology and lowest use in ophthalmology. Asynchronous testing was used to augment teleophthalmology and, when used, was associated with change in management for 25.4% of encounters.

Meaning The COVID-19 pandemic was associated with increased telehealth use across specialties, with asynchronous testing appearing to be a feasible approach to expanding teleophthalmic subspecialty care.

Abstract

Importance Telehealth in ophthalmology has traditionally focused on preventive disease screening with limited use in outpatient evaluation. The unique conditions of the COVID-19 pandemic afforded the opportunity to evaluate different implementations of teleophthalmology at scale, providing insight into expanding teleophthalmology care.

Objective To compare telehealth use in ophthalmology with other specialties and assess the feasibility of augmenting ophthalmic telehealth encounters with asynchronous testing during the COVID-19 pandemic.

Design, Setting, and Participants This quality improvement study evaluated retrospective, longitudinal, observational data from the first 18 months of the COVID-19 pandemic (January 1, 2020, through July 31, 2021) for 881 080 patients receiving care from outpatient primary care, cardiology, neurology, gastroenterology, surgery, neurosurgery, urology, orthopedic surgery, otolaryngology, obstetrics/gynecology, and ophthalmology clinics of the University of California, San Francisco. Asynchronous testing was evaluated for teleophthalmology encounters.

Interventions A hybrid care model wherein ophthalmic testing data were acquired asynchronously and used to augment telehealth encounters.

Main Outcomes and Measures Telehealth as a percentage of total volume of ambulatory care and use of asynchronous testing for ophthalmic conditions.

Results The volume of in-person outpatient visits dropped by 83.3% (39 488 of 47 390) across the evaluated specialties at the onset of shelter-in-place orders for the COVID-19 pandemic, and the initial use of telehealth increased for these specialties before stabilizing over the 18-month study period. In ophthalmology, telehealth use peaked at 488 of 1575 encounters (31.0%) early in the pandemic and returned to mostly in-person visits as COVID-19 restrictions lifted. Elective use of telehealth was highest in gastroenterology, urology, neurology, and neurosurgery and lowest in ophthalmology. Asynchronous testing was combined with 126 teleophthalmology encounters, resulting in change of clinical management for 32 patients (25.4%) and no change for 91 (72.2%).

Conclusions and Relevance Telehealth increased across various specialties during the COVID-19 pandemic. Combining teleophthalmic visits with asynchronous testing suggested that this approach is feasible for subspecialty-level evaluation. Additional study is needed to evaluate whether asynchronous testing outside the same institution could provide an effective and lasting approach for expanding the reach of ophthalmic telehealth.

<https://jamanetwork.com/journals/jamaophthalmology/article-abstract/2799231>

**title:** In Vitro Efficacy of Antiviral Agents against Omicron Subvariant BA.4.6 [Correspondence]

nejm | 1st december 2022

As of September 2022, the BA.5 subvariant of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.1.529 (omicron) variant has become dominant in most countries around the world. However, the prevalence of the BA.4.6 subvariant is increasing in the United States… BA.4.6 and BA.5 share the same amino acid substitutions in the receptor-binding domain of the spike protein, which is the major target for vaccines and therapeutic monoclonal antibodies against SARS-CoV-2. BA.4.6 also has an additional mutation that is not found in BA.5 (i.e., R346T),…a finding that arouses concern that the effectiveness of current vaccines and therapeutic monoclonal antibodies against this subvariant will be greatly decreased.

Accordingly, we assessed the effectiveness of several therapeutic monoclonal antibodies that have been authorized for the treatment of coronavirus disease 2019 (Covid-19), individually and in combination, against two omicron BA.4.6 isolates — hCoV-19/USA/WI-UW-12757/2022 (UW-12757) and hCoV-19/USA/WI-UW-12767/2022 (UW-12767). Both isolates had been obtained from patients with Covid-19. The spike protein of these two isolates contained two additional amino acid changes (R346T and N658S) as compared with a BA.5 isolate (hCoV-19/Japan/TY41-702/2022)… In addition, one of the isolates (UW-12757) also had an N487D mutation in its receptor-binding domain.

We used a live-virus 50% focus reduction neutralization test (FRNT50) to determine neutralization titers of monoclonal antibodies, including REGN10987 (marketed as imdevimab) and REGN10933 (marketed as casirivimab). REGN10987 retained some neutralizing activity against the two BA.4.6 isolates…, but REGN10933 did not retain such activity. REGN10987 in combination with REGN10933 (imdevimab–casirivimab) neutralized both BA.4.6 isolates; however, as compared with the ancestral strain, the effectiveness of this combination was lower by a factor of 52.9 against UW-12757 and by a factor of 87.3 against UW-12767. The monoclonal antibodies COV2-2196 (marketed as tixagevimab) and COV2-2130 (marketed as cilgavimab), individually and in combination, had reduced activity against the BA.4.6 isolates, as did S309, the precursor of sotrovimab. In contrast, LYCoV1404 (marketed as bebtelovimab) efficiently inhibited both UW-12757 and UW-12767 with a very low FRNT50 value (3.80 ng per milliliter and 2.26 ng per milliliter, respectively), results that were similar to those for the ancestral strain.

The Food and Drug Administration has approved the use of remdesivir (an RNA-dependent RNA polymerase [RdRp] inhibitor) for the treatment of Covid-19 and has issued Emergency Use Authorizations for two other antiviral drugs: molnupiravir (an RdRp inhibitor) and nirmatrelvir (a main protease inhibitor of SARS-CoV-2). We therefore tested the efficacy of these antiviral drugs against BA.4.6 by determining their in vitro 50% inhibitory concentration (IC50) values against this variant. Of note, these two BA.4.6 isolates had P314L and P3395H mutations in the RdRp and main protease, respectively (Fig. S1B). The two BA.4.6 isolates had susceptibilities to the three compounds that were similar to the susceptibility of the ancestral strain: for UW-12757, the IC50 value was higher by a factor of 1.6 with remdesivir, by a factor of 5.7 with molnupiravir, and by a factor of 4.1 with nirmatrelvir; for UW-12767, the IC50 values were higher by a factor of 0.4, 1.8, and 1.2, respectively. The clinical Cmax (i.e., the highest concentration of a drug in the blood) of the therapeutic agents is shown…

The neutralizing activity of plasma obtained from patients who had recovered from Covid-19 and from recipients of vaccines was lower against BA.4.6, BA.2, and BA.5 than it was against the ancestral strain. This reduction in neutralizing titers was larger for BA.4.6 and BA.5 than for BA.2…

Our data suggest that remdesivir, molnupiravir, and nirmatrelvir and the monoclonal antibodies bebtelovimab and imdevimab retain effectiveness against BA.4.6 in vitro... Our findings also indicate that monoclonal antibodies casirivimab, sotrovimab, tixagevimab, and cilgavimab may not be effective against BA.4.6.

<https://www.nejm.org/doi/full/10.1056/NEJMc2211845?query=featured_coronavirus>

**title:** Analysis of Clinical Outcomes of Pregnant Patients Treated With Nirmatrelvir and Ritonavir for Acute SARS-CoV-2 Infection

jama network open | 29th november 2022

Key Points

 Question What outcomes are associated with nirmatrelvir and ritonavir for treatment of SARS-CoV-2 infection in pregnant patients?

Findings In this case series of 47 pregnant patients who were treated with nirmatrelvir and ritonavir, the medication was well tolerated without evidence of an increase in complications affecting birthing parents or their offspring. Approximately half of deliveries after treatment with nirmatrelvir and ritonavir were via cesarean delivery.

Meaning Results of this study suggest that pregnant patients with SARS-CoV-2 infection can be safely treated with nirmatrelvir and ritonavir.

Abstract

Importance Pregnant people are at increased risk of poor outcomes due to infection with SARS-CoV-2, and there are limited therapeutic options available.

Objective To evaluate the clinical outcomes associated with nirmatrelvir and ritonavir used to treat SARS-CoV-2 infection in pregnant patients.

Design, Setting, and Participants This case series included pregnant patients who were diagnosed with SARS-CoV-2 infection, received nirmatrelvir and ritonavir, and delivered their offspring within the Johns Hopkins Health System between December 22, 2021, and August 20, 2022.

Results Forty-seven pregnant patients (median [range] age, 34 [22-43] years) were included in the study, and the median (range) gestational age of their offspring was 28.4 (4.3-39.6) weeks. Medication was initiated at a median (range) of 1 (0-5) day after symptom onset, and only 2 patients [4.3%] did not complete the course of therapy because of adverse effects.

Exposures Treatment with nirmatrelvir and ritonavir for SARS-CoV-2 infection during pregnancy.

Main Outcomes and Measures Clinical characteristics and outcomes were ascertained through manual record review.

Results Forty-seven pregnant patients (median [range] age, 34 [22-43] years) were included in the study, and the median (range) gestational age of their offspring was 28.4 (4.3-39.6) weeks. Medication was initiated at a median (range) of 1 (0-5) day after symptom onset, and only 2 patients [4.3%] did not complete the course of therapy because of adverse effects. Thirty patients (63.8%) treated with nirmatrelvir and ritonavir had a comorbidity in addition to pregnancy that could be a risk factor for developing severe COVID-19. Twenty-five patients [53.2%] delivered after treatment with nirmatrelvir and ritonavir. Twelve of these patients [48.0%] underwent cesarean delivery, 9 [75.0%] of which were scheduled. Two of 47 patients [4.3%] were hospitalized for conditions related to preexisting comorbidities.

Conclusions and Relevance In this case series, pregnant patients who were treated with nirmatrelvir and ritonavir tolerated treatment well, although there was an unexpectedly high rate of cesarean deliveries. The lack of an increase in serious adverse effects affecting pregnant patients or offspring suggests that clinicians can use this drug combination to treat pregnant patients with SARS-CoV-2 infection.

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799023>

**long-****term effects**

**title:** Association of Initial SARS-CoV-2 Test Positivity With Patient-Reported Well-being 3 Months After a Symptomatic Illness

jama network open | 1st december 2022

Key Points

Question How do patient-reported physical, mental, and social well-being compare at 3 months after symptomatic illness among those who tested positive vs negative for SARS-CoV-2 infection?

Findings In this cohort study of 1000 US adults with symptomatic illness, poor well-being scores at follow-up were common in both those who tested positive and negative for SARS-CoV-2 infection. Despite some improvements over time, 39.6% of COVID-19–positive and 53.5% of COVID-19–negative patients reported residual symptoms.

Meaning These findings emphasize the importance of including a concurrent control group when studying sequelae of COVID-19 illness.

Abstract

Importance Long-term sequelae after symptomatic SARS-CoV-2 infection may impact well-being, yet existing data primarily focus on discrete symptoms and/or health care use.

Objective To compare patient-reported outcomes of physical, mental, and social well-being among adults with symptomatic illness who received a positive vs negative test result for SARS-CoV-2 infection.

Design, Setting, and Participants This cohort study was a planned interim analysis of an ongoing multicenter prospective longitudinal registry study (the Innovative Support for Patients With SARS-CoV-2 Infections Registry [INSPIRE]). Participants were enrolled from December 11, 2020, to September 10, 2021, and comprised adults (aged ≥18 years) with acute symptoms suggestive of SARS-CoV-2 infection at the time of receipt of a SARS-CoV-2 test approved by the US Food and Drug Administration. The analysis included the first 1000 participants who completed baseline and 3-month follow-up surveys consisting of questions from the 29-item Patient-Reported Outcomes Measurement Information System (PROMIS-29; 7 subscales, including physical function, anxiety, depression, fatigue, social participation, sleep disturbance, and pain interference) and the PROMIS Short Form–Cognitive Function 8a scale, for which population-normed T scores were reported.

Exposures SARS-CoV-2 status (positive or negative test result) at enrollment.

Main Outcomes and Measures Mean PROMIS scores for participants with positive COVID-19 tests vs negative COVID-19 tests were compared descriptively and using multivariable regression analysis.

Results Among 1000 participants, 722 (72.2%) received a positive COVID-19 result and 278 (27.8%) received a negative result; 406 of 998 participants (40.7%) were aged 18 to 34 years, 644 of 972 (66.3%) were female, 833 of 984 (84.7%) were non-Hispanic, and 685 of 974 (70.3%) were White. A total of 282 of 712 participants (39.6%) in the COVID-19–positive group and 147 of 275 participants (53.5%) in the COVID-19–negative group reported persistently poor physical, mental, or social well-being at 3-month follow-up. After adjustment, improvements in well-being were statistically and clinically greater for participants in the COVID-19–positive group vs the COVID-19–negative group only for social participation (β = 3.32; 95% CI, 1.84-4.80; P < .001); changes in other well-being domains were not clinically different between groups. Improvements in well-being in the COVID-19–positive group were concentrated among participants aged 18 to 34 years (eg, social participation: β = 3.90; 95% CI, 1.75-6.05; P < .001) and those who presented for COVID-19 testing in an ambulatory setting (eg, social participation: β = 4.16; 95% CI, 2.12-6.20; P < .001).

Conclusions and Relevance In this study, participants in both the COVID-19–positive and COVID-19–negative groups reported persistently poor physical, mental, or social well-being at 3-month follow-up. Although some individuals had clinically meaningful improvements over time, many reported moderate to severe impairments in well-being 3 months later. These results highlight the importance of including a control group of participants with negative COVID-19 results for comparison when examining the sequelae of COVID-19…

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799116>

**title:** Diabetes after SARS-CoV-2 infection [Comment]

The Lancet Diabetes & Endocrinology | 1st december 2022

The COVID-19 global pandemic represents a unique opportunity to better understand the post-viral and post-infectious condition. More than 2 years into the pandemic, a large body of evidence makes it clear that infection with SARS-CoV-2 can lead to post-acute sequelae in the pulmonary and broad array of extrapulmonary organ systems—collectively referred to by the umbrella term of long COVID… Evidence also suggests that the myriad clinical abnormalities of long COVID might extend to new onset diabetes.

A US Center of Disease Control (CDC) analysis of a large electronic health-care database of 353 164 adults with COVID-19 and 1 640 776 controls with no evidence of infection, suggested that people with COVID-19 had an increased risk of new onset type 1 diabetes and type 2 diabetes… Furthermore, a German cohort study of 35 865 people with COVID-19 showed higher risk of newly diagnosed type 2 diabetes than an equal number of matched controls with acute upper respiratory tract infections…

I also investigated whether there was an association between new-onset diabetes and COVID-19. Together with my colleague Yan Xie, we used data from the US Department of Veterans Affairs to characterise the risk and 12-month burden of diabetes in 181 280 people with SARS-CoV-2 infection versus two control groups: 4 118 441 contemporary controls who were enrolled during the same time but did not get infected with SARS-CoV-2 and 4 286 911 historical controls from before the pandemic… Our findings suggested that compared with both the contemporary and historical controls, people with SARS-CoV-2 had increased risk of incident diabetes and incident use of antihyperglycemic therapy in the post-acute phase… Interestingly, compared with non-infected controls, the increased risk of diabetes (>99% was type 2 diabetes) was evident even in people who had very low baseline (pre-COVID-19) risk of diabetes according to traditional risk factors including age, race, sex, body-mass index, hypertension, and hyperlipidaemia). Among people with COVID-19, the risk of diabetes increased in a graded fashion according to baseline risk of diabetes (ie, the traditional baseline characteristics that predict the risk of developing diabetes in an individual). The main limitation of our study was that the participants were mostly White males. Our findings, along with the findings of others, suggest the possible coexistence of two pathways that should be investigated in mechanistic studies: (1) COVID-19 leading to de novo disease in people who might have otherwise not developed diabetes, and (2) COVID-19 as an amplifier of baseline risks and accelerant of disease development.

Due to paucity of studies, the evidence base of new onset diabetes following COVID-19 in children is far less well developed. In an analysis of two large health-care databases, researchers from the US CDC suggested that, compared with non-infected controls, people younger than 18 years with SARS-CoV-2 infection had increased risk of a diabetes diagnosis in the post-acute phase of COVID-19; they also showed that COVID-19 was associated with higher risk of diabetes than pre-pandemic acute respiratory infections and that non–SARS-CoV-2 respiratory infection was not associated with an increased risk for diabetes… However, this study did not differentiate between type 1 and type 2 diabetes.

The evidence for increased risk of diabetes after SARS-CoV-2 infection is not universally consistent. A Scottish study in people younger than 35 years documented a 20% increase in the incidence of type 1 diabetes during the pandemic in general, and increased risk of type 1 diabetes within, but not beyond, the first 30 days of SARS-CoV-2 infection… Another study of 428 650 people (median age 35 years) with COVID-19 and matched controls showed a net increase in incidence of diabetes in the first 4 weeks after COVID-19, which remained elevated from 5 to 12 weeks but not from 13 to 52 weeks…

Most of these studies on COVID-19 and diabetes were conducted before vaccines were available and when reinfections were uncommon. However, recent evidence from a US Department of Veterans Affairs study involving more than 13 million individuals suggests that compared with non-infected controls, both unvaccinated and vaccinated individuals with SARS-CoV-2 infection are at increased risk of diabetes and that the risk of diabetes in the post-acute phase of COVID-19 was not significantly different in people who had a SARS-CoV-2 infection after vaccination than unvaccinated individuals… A new study of more than 5 million people (also from the US Department of Veterans Affairs) suggests that reinfections with SARS-CoV-2 (compared with no reinfection) could contribute additional risks of acute and post-acute sequelae including increased risk of diabetes in both phases of the disease… A major methodological challenge in studying the post-acute and long-term health effects of SARS-CoV-2 infection—and a main reason for the discordance in evidence—is how to best disentangle the causal effects of the infection itself from other changes that might relate to both exposure and outcomes. For example, increased health-care use following SARS-CoV-2 infection and changes due to the pandemic itself (without SARS-CoV-2 infection) including effects of lockdowns, social isolation, loss of employment, and other factors that might have differentially affected people with SARS-CoV-2 infection might influence the risk of health outcomes (including diabetes). Although, for obvious ethical reasons, randomly exposing people to SARS-CoV-2 versus placebo is not possible, leveraging large-scale observational data and advances in causal inference methodologies to emulate a target trial are indeed feasible and should be actively pursued. The target trial emulation approach might be especially helpful to approximate—by design—a matched comparison between people with COVID-19 and non-infected controls, and estimate the causal effects of COVID-19 exposure. A trial emulation approach would first specify the causal question and lay out the protocol components of the ideal randomised trial that—if conducted—would randomise exposure and answer the causal question. This step would be then followed by specification of the emulation strategy including specification of the target population, eligibility (inclusion and exclusion) criteria, follow up, outcome, causal estimate, and a detailed analysis plan to estimate the causal contrast of interest. Although conceptualisation of an infection as a treatment in a randomised controlled trial might be perceived as unusual, the target trial emulation approach will further elevate the scientific rigor of large epidemiological analyses and enhance the ability to infer the causal long-term health effects of SARS-CoV-2 infection. Additionally, prospective controlled studies with detailed assessment of pre-COVID-19 health status and protocolised longitudinal health assessments are also useful to characterise the health trajectories of people with SARS-CoV-2 infection. Although, these studies might be less powered because they generally include far fewer participants than large observational studies.

Robust research agendas to better understand long COVID (and all its components including the increased risk of diabetes), prevent it, and treat it are urgently needed. Several pressing strategic considerations and research questions will need to be answered in the near future…

The broad implications of SARS-CoV-2 infection on human health are becoming increasingly clear. Before the pandemic, the global burden of diabetes was high and rising; the possible increased incidence of diabetes due to the pandemic could further compound the already staggering pre-pandemic burden. In turn, this could lead to substantial ramifications on health systems, health-care costs, life expectancy and economic indicators such as employment and labour participation. More broadly, the multifaceted long-term consequences of SARS-CoV-2 infection (including the risk of diabetes) should be reflected in the global discussion about non-communicable diseases.

Long after the pandemic ends (and we must admit that it has not yet ended), millions of people around the world will still bear its scars. Chronic conditions, including diabetes, require lifelong care and can affect people's lives, livelihood, the economy, and societal wellbeing. A silverlining of this pandemic is the opportunity to more broadly understand the post-viral condition, which has been marginalised and understudied for more than a century. Long COVID, including the possible burden of diabetes, must be further investigated, understood and considered in every health-care and health policy decision we make now and going forward…

[https://www.thelancet.com/journals/landia/article/PIIS2213-8587(22)00324-2/fulltext](https://www.thelancet.com/journals/landia/article/PIIS2213-8587%2822%2900324-2/fulltext)

**title:** Lung health after covid . . . and other stories

BMJ | 1st december 2022

Long term effects of covid-19 pneumonia

Persisting structural lung abnormalities after covid-19 pneumonia seem to be infrequent. Eighty four people who had survived covid-19 pneumonia severe enough to require hospitalisation, but not severe enough to need intubation or mechanical ventilation, were investigated using high resolution computed tomography scanning a year later. Lung abnormalities had completely resolved in 78 of the participants…

<https://www.bmj.com/content/379/bmj.o2826>

**infection control**

**title:** Effect of Wearing Glasses on Risk of Infection With SARS-CoV-2 in the Community: A Randomized Clinical Trial

jama network open | 1st december 2022

Key Points

Question What is the effect of wearing glasses on the risk of being infected with SARS-CoV-2 and other respiratory viruses?

Findings In this randomized clinical trial with 3717 participants, there was no statistically significant difference in the incidence of positive reported COVID-19 cases. There was a statistically significant lower self-reported incidence of respiratory infection in the intervention group.

Meaning This study does not conclude that recommending the use of glasses to prevent infection with SARS-CoV-2 and other respiratory viruses is beneficial, but the intervention is worth considering because it is simple, low cost, and has few negative consequences.

Abstract

Importance Observational studies have reported an association between the use of eye protection and reduced risk of infection with SARS-CoV-2 and other respiratory viruses, but, as with most infection control measures, no randomized clinical trials have been conducted.

Objectives To evaluate the effectiveness of wearing glasses in public as protection against being infected with SARS-CoV-2 and other respiratory viruses.

Design, Setting, and Participants A randomized clinical trial was conducted in Norway from February 2 to April 24, 2022; all adult members of the public who did not regularly wear glasses, had no symptoms of COVID-19, and did not have COVID-19 in the last 6 weeks were eligible.

Intervention Wearing glasses (eg, sunglasses) when close to others in public spaces for 2 weeks.

Main Outcomes and Measures The primary outcome was a positive COVID-19 test result reported to the Norwegian Surveillance System for Communicable Diseases. Secondary outcomes included a positive COVID-19 test result and respiratory infection based on self-report. All analyses adhered to the intention-to-treat principle.

Results A total of 3717 adults (2439 women [65.6%]; mean [SD] age, 46.9 [15.1] years) were randomized. All were identified and followed up in the registries, and 3231 (86.9%) responded to the end of study questionnaire. The proportions with a reported positive COVID-19 test result in the national registry were 3.7% (68 of 1852) in the intervention group and 3.5% (65 of 1865) in the control group (absolute risk difference, 0.2%; 95% CI, −1.0% to 1.4%; relative risk, 1.10; 95% CI, 0.75-1.50). The proportions with a positive COVID-19 test result based on self-report were 9.6% (177 of 1852) in the intervention group and 11.5% (214 of 1865) in the control group (absolute risk difference, –1.9%; 95% CI, −3.9% to 0.1%; relative risk, 0.83; 95% CI, 0.69-1.00). The risk of respiratory infections based on self-reported symptoms was lower in the intervention group (30.8% [571 of 1852]) than in the control group (34.1% [636 of 1865]; absolute risk difference, –3.3%; 95% CI, −6.3% to −0.3%; relative risk, 0.90; 95% CI, 0.82-0.99).

Conclusions and Relevance In this randomized clinical trial, wearing glasses in the community was not protective regarding the primary outcome of a reported positive COVID-19 test. However, results were limited by a small sample size and other issues. Glasses may be worth considering as one component in infection control, pending further studies…

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2799115>

**title:** Decline of RSV-specific antibodies during the COVID-19 pandemic [Correspondence]

The Lancet Infectious Diseases | 1st december 2022

Hospitalisations due to respiratory syncytial virus (RSV) infections largely decreased after social distancing measures were introduced to control the COVID-19 pandemic. Lifting these measures resulted in out-of-season RSV activity, sometimes exceeding the incidence of hospitalisations observed in regular seasons… Declining immunity due to reduced exposure to the virus may contribute to this altered epidemiology. Bardsley and colleagues…showed that the combination of laboratory, clinical, and syndromic data capture the impact of RSV activity, yet did not provide insight into the proposed decline in immunity. To investigate this effect, we analysed sera of 558 randomly selected participants of a prospective nationwide study in the Netherlands for changes in IgG antibody concentrations to the RSV post-fusion F protein... Participants were 1–89 years of age (mean age 48 years [SD 20·7]). 236 (42·3%) were male; 245 (43·9%) were female; and 77 (13·8%) were other, missed the question, or did not disclose this information. Samples of the same people were collected in June, 2020 (timepoint 1, several months after the introduction of social restrictions), February, 2021 (timepoint 2, approximately 1 year after the end of the last typical RSV season), and June, 2021 (timepoint 3, the month when social restrictive measures were lifted in the Netherlands and the out-of-season RSV epidemic started… Concentrations were log10 transformed for all statistical analyses. The repeated-measures general linear model (SPSS version 28; IBM, Armonk, NY, USA) was used to compare antibody concentrations between sampling timepoints of the same subjects and between age groups. p values, adjusted to Bonferroni and Benjamini-Hochberg procedures, are reported for timepoints and age-group differences respectively. Student's t test was used to compare the 2020 IgG concentrations of the people who showed at least a twofold increase in RSV-specific IgG from 2020 to 2021 (n=9) and those who did not (n=549)…

Post-fusion F IgG antibody concentrations declined from 2020 to 2021 (p<0·001) and increased with age (p<0·001…). The decrease was greatest for the 1-year interval between timepoints 1 and 3 (p<0·001) when compared with the decrease between timepoints 1 and 2 (p<0·001) and between timepoints 2 and 3 (p=0·182). The decrease in antibodies was significant in all age groups, except for participants aged 31–40 years. Across the 3 timepoints, the age group of 71 years and older had higher antibody concentrations than participants aged 1–10 years (p=0·019), 21–30 years (p<0·001), 31–40 years (p=0·021), 41–50 years (p<0·001), and 51–60 years (p=0·034). In our analysis, we did not find evidence of differences in decay rates between age groups. We found 9 individuals (1·6%) with antibody boosting of at least two-fold during this period, indicative of exposure to the virus... These individuals were all adults of at least 30 years of age, and since two adults showed elevated IgG before the increase in clinical reports of RSV infections, these findings might indicate that circulation initiated in the adult population. On average, these individuals had lower IgG concentrations in 2020 (p=0·028) than those not showing a rise in IgG concentrations...

These data support the assumption that RSV-specific antibody concentrations declined during the COVID-19 pandemic in all age groups and are in line with a previous report showing decay of antibodies to RS… We do not have data on RSV-specific antibody kinetics in our cohort before the pandemic and there are relatively large variations between individuals, so the effect on susceptibility to RSV is not clear yet. Antibodies to the F protein, especially in pre-fusion confirmation, have an important role in the neutralisation of RSV and were previously shown to correlate well with virus neutralisation… However, the degree to which virus neutralisation is affected and the exact correlation with immune protection are yet to be determined… Following this preliminary analysis, additional timepoints, including follow-up samples, are being investigated to support and extend these findings. In conclusion, monitoring changes in antibody concentrations could identify populations susceptible to RSV infection.

The study was funded by the Dutch Ministry of Health, Welfare, and Sports. The funder had no role in the generation of the data or writing of the manuscript. ACT received funds from the Respiratory Syncytial Virus Consortium in Europe and Preparing for RSV Immunisation and Surveillance in Europe consortium for grants and travel costs. All other authors declare no competing interests. We thank all study participants, the Dutch Working Group on Clinical Virology from the Dutch Society for Clinical Microbiology, and all participating laboratories for providing the virological data from the weekly laboratory virological report…

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(22)00763-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2822%2900763-0/fulltext)

**title:** It Ain’t Over Till It’s Over…but It’s Never Over — Emerging and Reemerging Infectious Diseases [Perspective]

NEJM| 1st december 2022

As I (Anthony S. Fauci) prepare to step down from my dual positions at the National Institute of Allergy and Infectious Diseases (NIAID), where I have been a physician-scientist for 54 years and the director for 38 years, a bit of reflection is inevitable. As I think back over my career, what stands out most is the striking evolution of the field of infectious diseases and the changing perception of the importance and relevance of the field by both the academic community and the public…

An inevitable conclusion of my reflections on the evolution of the field of infectious diseases is that the pundits of years ago were incorrect and that the discipline is certainly not static; it is truly dynamic. In addition to the obvious need to continue to improve on our capabilities for dealing with established infectious diseases such as malaria and tuberculosis, among others, it is now clear that emerging infectious diseases are truly a perpetual challenge. As one of my favorite pundits, Yogi Berra, once said, “It ain’t over till it’s over.” Clearly, we can now extend that axiom: when it comes to emerging infectious diseases, it’s never over. As infectious-disease specialists, we must be perpetually prepared and able to respond to the perpetual challenge.

<https://www.nejm.org/doi/full/10.1056/NEJMp2213814?query=featured_coronavirus>

**title:** Mask Wars [Video]

NEJM | 1st december 2022

This documentary video explores the controversies surrounding masks and mask mandates throughout the centuries. The changing perceptions of masking leading up to the Covid-19 pandemic are discussed.

<https://www.nejm.org/doi/full/10.1056/NEJMp2214296?query=featured_coronavirus>

**title:** Effectiveness of mRNA-1273, BNT162b2, and BBIBP-CorV vaccines against infection and mortality in children in Argentina, during predominance of delta and omicron covid-19 variants: test negative, case-control study

bmj | 3oth november 2022

Abstract

Objective To estimate the effectiveness of a two dose vaccine schedule (mRNA-1273, BNT162b2, and BBIBP-CorV) against SARS-CoV-2 infection and covid-19 related death and short term waning of immunity in children (3-11 years old) and adolescents (12-17 years old) during periods of delta and omicron variant predominance in Argentina.

Design Test negative, case-control study.

Setting Database of the National Surveillance System and the Nominalized Federal Vaccination Registry of Argentina.

Participants 844 460 children and adolescents without previous SARS-CoV-2 infection eligible to receive primary vaccination schedule who were tested for SARS-CoV-2 by polymerase chain reaction or rapid antigen test from September 2021 to April 2022. After matching with their corresponding controls, 139 321 (60.3%) of 231 181 cases remained for analysis.

Exposures Two dose mRNA-1273, BNT162b2, and BBIBP-CorV vaccination schedule.

Main outcome measures SARS-CoV-2 infection and covid-19 related death. Conditional logistic regression was used to estimate the odds of SARS-CoV-2 infection among two dose vaccinated and unvaccinated participants. Vaccine effectiveness was estimated as (1–odds ratio)×100%.

Results Estimated vaccine effectiveness against SARS-CoV-2 infection was 61.2% (95% confidence interval 56.4% to 65.5%) in children and 66.8% (63.9% to 69.5%) in adolescents during the delta dominant period and 15.9% (13.2% to 18.6%) and 26.0% (23.2% to 28.8%), respectively, when omicron was dominant. Vaccine effectiveness declined over time, especially during the omicron period, from 37.6% (34.2% to 40.8%) at 15-30 days after vaccination to 2.0% (1.8% to 5.6%) after ≥60 days in children and from 55.8% (52.4% to 59.0%) to 12.4% (8.6% to 16.1%) in adolescents.

Vaccine effectiveness against death related to SARS-CoV-2 infection during omicron predominance was 66.9% (6.4% to 89.8%) in children and 97.6% (81.0% to 99.7%) in adolescents.

Conclusions Vaccine effectiveness in preventing mortality remained high in children and adolescents regardless of the circulating variant. Vaccine effectiveness in preventing SARS-CoV-2 infection in the short term after vaccination was lower during omicron predominance and decreasing sharply over time…

<https://www.bmj.com/content/379/bmj-2022-073070>

**title:** The Uncertain Effects of Surveillance Screening for COVID-19 for Individuals Entering Health Care Facilities

jama internal medicine | 28th november 2022

Entrance surveillance screenings have been widely implemented in health care settings during the COVID-19 pandemic. These measures, which are required by the US Department of Labor,…rely on self-reported factors such as symptoms or exposure history and are intended to reduce risk to patients and health care workers. In this issue of JAMA Internal Medicine, Roberts and colleagues…examine the usefulness of entrance surveillance screenings at a single academic medical center. They find that during the first wave of the pandemic, about 1 in every 38 people screened positive. However, during later periods, the catch rate was considerably lower, closer to 1 in every 3000 people. This lower rate was constant regardless of community incidence of disease. It cannot be known from their findings if the screening requirement itself acted as a deterrent to those who might have otherwise sought entry to the health care center. Awareness of the screening procedure or of the nature of COVID-19 symptoms may have increased over the course of time.

Surveillance screening is expensive for health care systems and a daily annoyance for those who work there. The authors suggest that screening may have maximum utility during the early phase of a public health crisis… Nonetheless, self-reported symptoms have a low sensitivity for true infection with COVID-19,…so it remains unclear the degree to which screening measures are truly effective in reducing the spread of COVID-19.

Certainly there is value in keeping all symptomatically ill workers and visitors out of the hospital—not merely those who are infected with COVID-19. It is known that some health care workers come to work under virtually any personal health circumstance due to tacit pressure… COVID-19 surveillance screening has enabled workers to appropriately stay home when they are ill.

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2798553>

**title:** Analysis of Failure Rates for COVID-19 Entrance Screening at a US Academic Medical Center [research letter]

jama internal medicine | 28th november 2022

Many health care facilities use entrance screening to prevent individuals with acute COVID-19 from entering. In ambulatory settings, 1 study found failures (defined as an exposure, sign, or symptom concerning for COVID-19) for an average 0.1% of persons that peaked at 1.5% during the first pandemic wave …Less is known about screening in inpatient facilities. The aim of this study was to evaluate hospital entrance screening failure rates for patients, visitors, and health care personnel at a large academic medical center.

Methods

In this quality improvement study, screening occurred at 10 entrances at Yale New Haven Hospital, a 1541-bed academic medical center with 2 campuses in New Haven, Connecticut, from March 17, 2020, to May 8, 2021. Criteria for a failed screening were temperature of 38 °C (100.4 °F) or greater, any exposure to or symptom suggestive of COVID-19 or positive SARS-CoV-2 test result in the preceding 2 weeks, or recent travel to high-risk areas. Entrance screeners also evaluated masking and provided masks to those who were unmasked or had unacceptable coverings, such as cloth masks or bandanas. Data on the incidence of COVID-19 in Connecticut were obtained…High incidence was defined as greater than and low incidence as fewer than 10 cases per 100 000 individuals averaged over a month… The Yale University Institutional Review Board deemed the study exempt from review and waived the informed consent requirement because it met all the criteria for a quality improvement study. We followed the STROBE reporting guideline.

Results

A total of 951 033 screenings were performed with 631 (0.07%) failures, which totaled 0.66 per 1000 individuals screened. The rate of individuals who failed entrance screening varied substantially, peaking in March 2020 with 2.64% failed screenings (26.40 failures per 1000 individuals screened) before decreasing in subsequent months... During the first wave of the pandemic, 0.69% individuals had a failed screening (6.94 failures per 1000 individuals screened... After the first wave, screening failure rates were consistent across times of high (0.36 failures per 1000 individuals screened) and low (0.34 failures per 1000 individuals screened) community SARS-CoV-2 incidence. A total of 62 009 patients and visitors (6.84% of entrance encounters) and 7742 health care personnel were provided a mask due to inadequate or absent masking.

A total of 29.5 full-time equivalent staff were required to maintain 24-hour screening, which equates to $1 288 560 in total annual compensation (using an hourly minimum wage of $15 for Connecticut as an example) plus benefits (estimated at 40%); this estimate excludes managerial staff and supplies, such as gloves, masks, and thermometers. This total estimates the minimum cost to identify 1 screening failure as $223.58 during the first wave and $2350.96 across the entire study.

Discussion

We found limited benefit in maintaining hospital entrance screening for COVID-19 symptoms, exposures, or travel. Of the nearly 1 million persons screened, less than 0.1% had a failed screening. The failure rate was substantially higher in the beginning of the pandemic, possibly because of greater adherence to screening protocols and enhanced symptom and exposure vigilance. It is also possible that patient education and increased communication may have meant patients and visitors stayed home with exposures or symptoms or that people were not truthful on subsequent visits. We do not know whether having an entrance screener served as a deterrent, keeping sick persons from attempting to enter the hospital.

A high proportion of patients and visitors arrived with inadequate face masks. Given the effectiveness of masks and need for source control of asymptomatic contagious persons, this service represents an additional value of screeners in mitigating COVID-19 spread. A limitation of this study was that the true incidence of COVID-19 in those screened was unknown; thus, we were unable to ascertain the effectiveness of our screening strategy.

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2798551?resultClick=1>

**pub****lic health & health inequalities**

**title:** Technical report on the COVID-19 pandemic in the UK

department of health and social care | 1st december 2022

A technical report for future UK Chief Medical Officers, Government Chief Scientific Advisers, National Medical Directors and public health leaders in a pandemic.

Chapters include: Understanding the pathogen; Disparities; Research, situational awareness, analysis and assessment; Modelling; Testing; Contact tracing and isolation; Non-pharmaceutical interventions; NPIs in educational settings; Care homes; Pharmaceutical interventions: therapeutics and vaccines; Improvements in care of COVID-19; and Communications.

<https://www.gov.uk/government/publications/technical-report-on-the-covid-19-pandemic-in-the-uk>

**title:** Global impact of COVID-19 on childhood tuberculosis: an analysis of notification data

the lancet global health | december 2022

Summary

Background

There is concern that the COVID-19 pandemic has damaged global childhood tuberculosis management. Quantifying changes in childhood tuberculosis notifications could support more targeted interventions to restore childhood tuberculosis services. We aimed to use time-series modelling to evaluate the impact of COVID-19 on child tuberculosis notifications.

Methods

Annual tuberculosis case notification data reported to WHO by 215 countries were used to calculate annual notification counts for the years 2014–20, stratified by age groups (0–4, 5–14, and ≥15 years) and sex. We used time-series modelling to predict notification counts for 2020, and calculated differences between these predictions and observed notifications in 2020 for each of the six WHO regions and at the country level for 30 countries with high tuberculosis burden. We assessed associations between these differences and the COVID-19 stringency index, a measure of COVID-19 social impact.

Findings

From 2014 to 2019, annual tuberculosis notification counts increased across all age groups and WHO regions. More males than females in the 0–4 years age group and ≥15 years age group had notifications in all years from 2014 to 2020 and in all WHO regions. In the 5–14 years age group, more females than males were notified globally in all years, although some WHO regions had higher notifications from males than females. In 2020, global notifications were 35·4% lower than predicted (95% prediction interval –30·3 to –39·9; 142 525 observed vs 220 794 predicted notifications [95% prediction interval 204 509 to 237 078]) for children aged 0–4 years, 27·7% lower (–23·4 to –31·5; 256 398 vs 354 578 [334 724 to 374 431]) in children aged 5–14 years, and 18·8% lower (–15·4 to –21·9; 5 391 753 vs 6 639 547 [6 375 086 to 6 904 007]) for people aged 15 years or older. Among those aged 5–14 years, the reduction in observed relative to predicted notifications for 2020 was greater in males (–30·9% [–24·8 to –36·1]) than females (–24·5% [–18·1 to –29·9]). Among 28 countries with high tuberculosis burden, no association was observed between the stringency of COVID-19 restrictions and the relative difference in observed versus predicted notifications.

Interpretation

Our findings suggest that COVID-19 has substantially affected childhood tuberculosis services, with the youngest children most affected. Although children have mostly had fewer severe health consequences from COVID-19 than have adults, they have been disproportionately affected by the effects of the pandemic on tuberculosis care. Observed sex differences suggest that targeted interventions might be required. As countries rebuild health systems following the COVID-19 pandemic, it is crucial that childhood tuberculosis services are placed centrally within national strategic plans…

 [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00414-4/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2822%2900414-4/fulltext)

**title:** COVID-19 and global childhood tuberculosis notifications [Comment]

the lancet global health | december 2022

Globally, an estimated 1·2 million cases of tuberculosis disease each year occur in children younger than 15 years, and around 67 million children have tuberculosis infection, putting them at the risk of developing tuberculosis disease…Tuberculosis in childhood was historically neglected in surveillance efforts, with national tuberculosis programmes focusing primarily on cases of microscopically smear-positive tuberculosis, which is more common among older adolescents or adults. The diagnosis of tuberculosis in children is made challenging by low suspicion among health-care providers, reliance on sputum microscopy, which has very low sensitivity (ranging from 1–14%), children's difficulty in producing sputum, or disease with low bacillary load… In The Lancet Global Health, Lasith Ranasinghe and colleagues provide a retrospective analysis of childhood tuberculosis notifications and how the number of notifications changed in 2020 during the COVID-19 pandemic…The authors primarily focus on the 30 countries with high tuberculosis burden, using time-series prediction modelling to quantify the effect of the COVID-19 pandemic on observed tuberculosis notifications compared with the predicted number. This study offers an overview of regional trends in notifications before and during the COVID-19 pandemic. 24 of the 30 countries with high tuberculosis burden showed a decrease in tuberculosis notifications among children aged 0–4 years, and the global mean decrease in notifications in this age group was 35·4% (95% PI –30·3 to –39·9). These results can inform the allocation and management of human, technological, and financial resources for childhood tuberculosis care. The study also examines sex differences in childhood tuberculosis across all WHO regions, showing that substantially more boys aged 0–4 years than girls were notified annually from 2014 to 2020.

Although the authors attempt to explain the observed change in notifications and most notably emphasise the most concerning explanation that tuberculosis cases might have been missed or undiagnosed, there remain several questions that warrant further in-depth inquiry. One question pertains to whether the decline in notifications might represent an actual decline in tuberculosis incidence in any region. The authors do not directly measure access to care, diagnostic test use, delays in care, or patient outcomes. It is plausible that infection control measures (such as the use of masks or bans on social gatherings) or accelerated treatment for latent tuberculosis in children…in previous years contributed to the decline in notifications. In some countries with a high tuberculosis burden, such as South Africa, notifications among children increased in 2020. This country was the main driver behind the lack of major decline seen in paediatric tuberculosis notifications in the WHO African region. This finding emphasises the complexity of the notification metric and the heterogeneity of these trends across settings of high tuberculosis burden. Another open question regards the extent of under-reporting. Although tuberculosis diagnosis rates might have decreased because of reallocation of resources to COVID-19 and reduction of access to care, it is equally plausible that resource reallocation could have affected notifications independently of tuberculosis care in children. This question requires dedicated inquiry, including surveying care records independently of notifications, which was not a component of this study.

Despite these open questions, we agree with the authors that the possibility of missed tuberculosis to this magnitude among children is highly alarming. In India, notifications were found to have some of the largest declines observed in Ranasinghe and colleagues’ study…Tuberculosis circulates predominantly in crowded localities… Lockdowns would have confined some residents to such localities, which seldom have stable structure or adequate infection control, and might thus have exacerbated transmission of tuberculosis between household members and neighbours. Children who develop tuberculosis represent sentinel cases that can be a barometer of the extent of community transmission; therefore, missed cases of tuberculosis among both adults and children will predominantly affect the vulnerable paediatric population. India's National Tuberculosis Elimination Program (NTEP) was affected by understaffing at the local level because of transfer of health-care staff to COVID-19 management. Although the NTEP in India provides the highest proportion of tuberculosis notifications, the private sector is usually the first and the main source of care sought for both adult and paediatric tuberculosis, and notifications from the private sector remain challenging… A closer look at trends in available private sector notifications might further inform our interpretation of changes in notifications overall and their main drivers. Lastly, worth mentioning is the potential complicating factor of delays in tuberculosis reporting relative to diagnosis and treatment initiation, highlighting the multifactorial nature of notification declines. Analysing data on the timing of local and regional notifications and notification to WHO might help resolve these discrepancies.

Although the above observations from India in part support the concerns raised by Ranasinghe and colleagues regarding the decline in notifications, we believe that all epidemiology is local, and that the same factors might not have influenced every country or tuberculosis programme to the same extent. Thus, generalisation to all countries would be inappropriate. The next 2 years of data including not only tuberculosis notifications but also treatment initiation rates, treatment outcomes, and antibiotic resistance rates will better quantify how the COVID-19 pandemic affected tuberculosis and childhood tuberculosis care in each country. In our opinion, as a next step, supporting qualitative data would add value to the current analysis by probing the programmatic circumstances in different countries and allow for a better interpretation of trends seen in the ecological quantitative data. Such qualitative data could be collected through interviews with key informants, such as national programme managers involved with notification procedures, state-level officials, and care providers. These suggested next steps could help to advance the goal of achieving zero tuberculosis deaths among children, as set out in WHO's road map for childhood tuberculosis…

[https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(22)00453-3/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2822%2900453-3/fulltext)

**recovery**

**title:** Integrated respiratory surveillance after the COVID-19 pandemic [Correspondence]

the lancet | 3rd december 2022

We welcome Thedi Ziegler and colleagues’ Comment on the WHO Global Influenza Surveillance and Response System and believe its proposals could strengthen global sentinel surveillance…

We respond to this Comment from the Oxford-Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC), one of Europe's oldest sentinel networks…The RSC is a collaboration between the University of Oxford, RCGP, and the UK Health Security Agency. The UK Health Security Agency's respiratory virus reference laboratory has provided data to the Global Influenza Surveillance and Response System and its predecessors since 1950. The RSC has grown substantially throughout the pandemic and, therefore, we are well placed to comment on the strategic and operational implications of the proposals…

We support the principle of year-round integrated respiratory surveillance and the broadening of laboratory testing to other respiratory viruses. Furthermore, we agree that measuring disease severity will support effective public health decision making. However, we should not overlook the importance of quality clinical data reporting and sufficient representative sampling to evaluate performance of diverse influenza and COVID-19 vaccine types across primary and secondary care networks. Additionally, longitudinal data enable prompt detection of changes in disease incidence, and routine surveillance with serology can also provide insights into heterogeneous population immunity…

The RSC's rapid expansion and improved digital maturity through the pandemic have shown that surveillance systems can be a test bed for innovation…The integration of data from near-patient diagnostics into the RSC surveillance system's dataset and the evaluation of interventions (eg, antiviral therapies and new vaccines) are examples of such innovation… Growth, however, comes at a cost, and if improvements are to be sustained and built upon, necessary investment in personnel and resources is essential…

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)02325-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2822%2902325-X/fulltext)

**title:** Patient collaboration in COVID-19 research: translating ideas to reality

the lancet respiratory medicine | 1st  december 2022

Involving patients in all stages of health data research is a noble aim; however, there are not too many examples of it being successfully put into practice—particularly not in real-time pandemic surveillance. In November, 2020, the Early Pandemic Evaluation and Enhanced Surveillance of COVID-19 (EAVE II) team created a unique collaboration, inviting a Public Advisory Group (PAG) of 15 patient and public contributors to work alongside university and Public Health Scotland staff to provide vital perspectives of the public on all areas of their COVID-19 research.

“Our PAG has played a crucial role in shaping key aspects of our research into COVID-19, asking questions, and often providing answers to issues that our researchers or analysts might never have thought of”, explains Dr Lana Woolford of the University of Edinburgh, Patient and Public Involvement (PPI) Coordinator for EAVE II…, to The Lancet Respiratory Medicine. “The relevance of research to the public and how it is communicated is absolutely essential. Some members of the advisory group have had COVID-19, some are shielding, some live with multiple health conditions or disabilities—and their unique insights have helped develop EAVE II and subsequent studies in a way that would not have been possible otherwise.”

…EAVE II has massively scaled up this research to track COVID-19 outcomes in almost the entire Scottish population (5·4 million people). The project has identified population groups most at risk from SARS-CoV-2 infection and COVID-19 hospital admission and death, and monitors the effectiveness and safety of population-wide vaccination…

The PAG subsequently moved into the other parts of the research cycle, including grant development (including shaping the project design and writing the lay research summary); analysis design, including protocols for research on COVID-19 vaccines in children and young people, and new COVID-19 treatments; and assistance throughout the actual project or study. This has included project steering, involving networks of contributors with relevant lived experience, and providing public perspectives throughout the research cycle…

The group also provides analysis and reflection on EAVE II's projects, in lay terms. For one study, PAG member Eve Smyth gave her perspective in a profile in The Lancet Respiratory Medicine, commenting that children with asthma should be prioritised for COVID-19 vaccination, including younger children aged 5–11 years who had just become eligible for vaccination.

Data access and quality have also been improved as a direct result of the PAG's work. After they raised concerns about the availability and quality of ethnicity data in Scottish health records, they successfully lobbied the Scottish Government and Public Health Scotland alongside researchers, enabling the EAVE II team to gain access to a wider repository of ethnicity records, which were not previously available to them. This also led to PPI representation from EAVE II on a collaboration study led by the University of Glasgow, looking at the impact of ethnicity and socioeconomic status on COVID-19 outcomes in Scotland…

 [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(22)00495-7/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600%2822%2900495-7/fulltext)

**title:** Covid-19: High rates in hospitals have hampered elective care recovery, says NHS chief [News]

bmj| 1st december 2022

The NHS in England significantly underestimated the continuing impact of covid-19 on hospital bed capacity this year, its chief executive has said. Amanda Pritchard said that the ongoing high numbers of patients with covid in hospitals had hindered efforts to tackle the backlog of elective care that had built up during the pandemic.

“We’ve been completely wrong on the assumptions about covid,” Pritchard told MPs on the House of Commons Public Accounts Committee on 28 November. “Having made, I think, some ambitious assumptions that the level of covid would be low . . . across the UK, we’ve never had less than 5000 patients in hospitals at any one time this year. Covid has been much higher than expected, and the consequences of that are not just beds with patients in, it’s the impact on sickness of staff.”

Pritchard conceded that the NHS was currently behind trajectory on its commitment to increase elective activity to 129% of pre-covid levels by 2025. “We are still absolutely aiming for 129% at the end of that period of time. What we do recognise is that we are going to need to reprofile the trajectories to get there,” she said.

She added that this reflected the squeeze on capacity this year, with inpatient activity particularly affected. “As a rule of thumb, we have about 10 000 beds in the NHS used for elective care. It has been about 8500 all year, so we’ve lost a significant amount of capacity,” she said.

James Mackey, national director of elective recovery at NHS England, told the committee that patients were being offered remote consultations with doctors elsewhere in the country to try to reduce long waits. “If you are a patient in the south west, it is technically possible to have a consultation with somebody in the north east,” he told MPs. “We are trying to do that, and it is starting to happen around the country.”

Cancer care backlog

During the session Pritchard also admitted that the NHS would not meet its target to ensure that by March 2023 no more than 85% of people waited longer than 62 days to start treatment for cancer after an urgent referral by their GP, as was the case before the pandemic. She said this was largely because the number of referrals to secondary care had risen substantially, by 20%, in the past year. “At the moment, roughly one in four referrals from a GP is for suspected cancer,” she said. “Clearly, that has put very significant pressure on the cancer treatment capacity, because it’s difficult to grow oncology services or specialist cancer services by 20% per year.”

But she emphasised the bigger picture in terms of patients getting an early diagnosis. “This is a classic example where you could meet the target and miss the point,” she said. “You could try and suppress referrals to get the backlog down, but that would be entirely the wrong thing to do because we want to encourage people if they are worried to come forward [and] get diagnosed as quickly as possible.”

Pritchard also sounded a cautious note on whether the NHS was on course to hit its target to clear all 78 week breaches from the waiting list from March 2023. She said, “We are supporting the NHS to try and do this, but within that, there are risks . . . what happens with covid, what happens with flu . . . what happens with the workforce. Realistically, this is a very challenging milestone.”

<https://www.bmj.com/content/379/bmj.o2909>

**title:** Co-design of new post-covid oncology rehabilitation services offers a model for the future [Opinion]

bmj| 29th december 2022

During the covid-19 pandemic the therapies department at the Royal Marsden NHS Foundation Trust, a tertiary cancer hospital in London, had to change the way it delivered cancer prehabilitation and rehabilitation services and move to remote methods. JustinRoe, Grainne Brady, and colleagues, and patient partner Dianne Mowbray-Pape, describe how the department adopted an experience based co-design approach to deliver a new model of service provision which includes telemedicine as well as face-to-face appointments and how their approach is influencing new digital developments in the trust…

Using experience based co-design methodology we were able to obtain an in-depth understanding of patient and staff members’ views and concerns regarding the use of telemedicine. Positive aspects included reduced financial and time burden on patients and increased flexibility for staff and patients. Key concerns included digital exclusion, safety, communication, and patient choice. Patients and staff members worked together to ensure that the positive aspects of telemedicine were maintained, including increased access to services for patients who did not wish to attend and the provision of face-to-face appointments when clinically indicated or requested by patients…

We also recognised that for patients who travel significant distances to reach us, and may have a very onerous burden of medical appointments with variable treatment regimens, additional trips to the hospital for an exercise appointment or prehabilitation advice, for example, would often be a low priority. Our perception when we first switched to virtual appointments was that this opened up the opportunity of accessing this area of healthcare to a larger cohort of patients who were able to access the care from their home a long distance away, or even while on holiday. There is no doubt that in the long term a hybrid solution offering all modes of treatment to account for all preferences will be the most likely solution…

Learning points:

The collective voice of patient partners and those who deliver clinical services are our greatest resource in improving care provision

For staff who do not see patients face-to-face but are involved in service delivery, experience based co-design provides a stronger sense of meaning in their work

Employing co-design and co-production methodology can impact more widely both for those participating in projects and organisational culture

Future directions

Using experience based co-design is now a core component of how we design and deliver services within the therapies department at Royal Marsden Hospital. Through the involvement of a broader stakeholder group, the methodology is being adopted more widely in our organisation. Patient partners are well placed to influence and guide service design and delivery alongside clinical and non-clinical staff within organisations.

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**international perspectives**

**title:** Covid-19: Protests against lockdowns in China reignite amid crackdown [News]

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The Chinese government has been struggling to quell protests against lockdowns throughout the country that have exposed the growing strain on its “zero covid” policy in the face of increasingly contagious variants…

“Unsustainable” approach

Earlier this month China’s government announced “20 measures” aimed at softening its zero covid approach. The quarantine period for suspected disease contacts was cut, and the dependence on centralised quarantine was reduced in favour of isolating at home. Authorities’ insistence on transporting contacts to quarantine centres, often over long distances at night, came under fire in September after a bus crash killed 27 people bound for such a centre.

Instead of the planned relaxation, however, many local authorities have tightened restrictions over the past fortnight as cases have surged in what is effectively China’s third wave. From about 500 new cases a day at the beginning of November, new daily cases passed 40 000 for the first time on 27 September, reaching 40 347. On 30 November authorities reported 37 828 new cases, down slightly for the second day in a row, although cases in Beijing continued to climb.

Few experts believe that China can hold off mass infection indefinitely. The zero covid approach has been extraordinarily effective at keeping case numbers down in comparison with the rest of the world. China’s 9.6 million total cases to date equate to a per capita infection rate just one 50th that of the United States. But, as a result, China’s population has almost no natural immunity…

China has refused to import foreign mRNA vaccines, preferring domestically produced but less effective shots. It prioritised vaccinating people of working age and has since struggled to achieve strong coverage among elderly people.

Amid a renewed booster campaign relying partly on a new inhaled vaccine, the government announced on 29 November that 66% of people aged over 80 have received a third vaccine dose, up from 40% on 11 November. But many of those 40% received their booster more than six months ago, and the protective effect by now will be negligible.

China is developing its own mRNA vaccines, with 10 candidates in the pipeline, but the earliest phase 3 trial results are not expected until next May.

“One option for China is to embark on an energetic supplementary vaccination programme using more effective, imported vaccines,” said Mark Woolhouse, a professor of infectious disease epidemiology at the University of Edinburgh. “But there is inevitably a political dimension to any country’s covid response, so this may not happen. If it doesn’t happen then it is hard to see how the cycle of virus incursions and lockdowns will end for many months and quite possibly years.”

Few ICU beds

Another worry is the shortage of intensive care beds, which number only four per 100 000 population. China is belatedly scrambling to add capacity, but official anxiety was palpable in a recent frontpage editorial in the People’s Daily, which acknowledged that China’s health system “currently has far fewer ICU beds than those of other developed countries.”

The editorial page, widely considered to be the direct voice of the government, cited a Bloomberg analysis that had found that a full reopening could lead to 5.8 million Chinese people needing intensive care, in a country with only 57 000 intensive care beds… The party newspaper relayed a warning from the pharmaceuticals analyst Sam Fazeli that “there’s no way an uncontrolled wave of infections can be managed.”

China watchers continue to scan state media for signs of a shift to a middle course that would seek to keep infections at a manageable level while allowing natural immunity to build. The government is acutely aware of the public anger at lockdowns—this week it was censoring footage of unmasked football fans in Qatar—and is also facing a record slump in economic growth this year.

On the ground, there are signs of a looser approach. Residents in several cities said on social media that local governments had ended lockdowns early after the weekend’s protests. The People’s Daily reminded overzealous local officials that only counties and higher authorities may impose controls. Beijing city authorities ordered an end to the barricading of residents in apartment blocks, a practice blamed by some for the deaths in the Urumqi fire.

But on 29 November the newspaper said that recent adjustments should be seen only as fine tuning. The zero covid policy, it said, was the work of President Xi, had “withstood the test of practice,” and would be “unswervingly implemented.”

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