COVID-19 weekly update

December 23rd 2021

clinical management

**Title:** Diagnostics for COVID-19: moving from pandemic response to control

The Lancet – 20th December, 2021

Diagnostics have proven to be crucial to the COVID-19 pandemic response. There are three major methods for the detection of SARS-CoV-2 infection and their role has evolved during the course of the pandemic. Molecular tests such as PCR are highly sensitive and specific at detecting viral RNA, and are recommended by WHO for confirming diagnosis in individuals who are symptomatic and for activating public health measures. Antigen rapid detection tests detect viral proteins and, although they are less sensitive than molecular tests, have the advantages of being easier to do, giving a faster time to result, of being lower cost, and able to detect infection in those who are most likely to be at risk of transmitting the virus to others. Antigen rapid detection tests can be used as a public health tool for screening individuals at enhanced risk of infection, to protect people who are clinically vulnerable, to ensure safe travel and the resumption of schooling and social activities, and to enable economic recovery. With vaccine roll-out, antibody tests (which detect the host's response to infection or vaccination) can be useful surveillance tools to inform public policy, but should not be used to provide proof of immunity, as the correlates of protection remain unclear. All three types of COVID-19 test continue to have a crucial role in the transition from pandemic response to pandemic control.

Full text: [Diagnostics for COVID-19: moving from pandemic response to control - The Lancet](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2821%2902346-1/fulltext)

**Title:** A clinical case definition of post-COVID-19 condition by a Delphi consensus

The Lancet Infectious Diseases – 21st December, 2021

People with COVID-19 might have sustained postinfection sequelae. Known by a variety of names, including long COVID or long-haul COVID, and listed in the ICD-10 classification as post-COVID-19 condition since September, 2020, this occurrence is variable in its expression and its impact. The absence of a globally standardised and agreed-upon definition hampers progress in characterisation of its epidemiology and the development of candidate treatments. In a WHO-led Delphi process, we engaged with an international panel of 265 patients, clinicians, researchers, and WHO staff to develop a consensus definition for this condition. 14 domains and 45 items were evaluated in two rounds of the Delphi process to create a final consensus definition for adults: post-COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include, but are not limited to, fatigue, shortness of breath, and cognitive dysfunction, and generally have an impact on everyday functioning. Symptoms might be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms might also fluctuate or relapse over time. A separate definition might be applicable for children. Although the consensus definition is likely to change as knowledge increases, this common framework provides a foundation for ongoing and future studies of epidemiology, risk factors, clinical characteristics, and therapy.

Full article: [A clinical case definition of post-COVID-19 condition by a Delphi consensus - The Lancet Infectious Diseases](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2821%2900703-9/fulltext)

**Title:** Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients

The New England Journal of Medicine – 22nd December, 2021

**BACKGROUND** Remdesivir improves clinical outcomes in patients hospitalized with moderate-to-severe coronavirus disease 2019 (Covid-19). Whether the use of remdesivir in symptomatic, nonhospitalized patients with Covid-19 who are at high risk for disease progression prevents hospitalization is uncertain.

**METHODS** We conducted a randomized, double-blind, placebo-controlled trial involving nonhospitalized patients with Covid-19 who had symptom onset within the previous 7 days and who had at least one risk factor for disease progression (age ≥60 years, obesity, or certain coexisting medical conditions). Patients were randomly assigned to receive intravenous remdesivir (200 mg on day 1 and 100 mg on days 2 and 3) or placebo. The primary efficacy end point was a composite of Covid-19–related hospitalization or death from any cause by day 28. The primary safety end point was any adverse event. A secondary end point was a composite of a Covid-19–related medically attended visit or death from any cause by day 28.

**RESULTS** A total of 562 patients who underwent randomization and received at least one dose of remdesivir or placebo were included in the analyses: 279 patients in the remdesivir group and 283 in the placebo group. The mean age was 50 years, 47.9% of the patients were women, and 41.8% were Hispanic or Latinx. The most common coexisting conditions were diabetes mellitus (61.6%), obesity (55.2%), and hypertension (47.7%). Covid-19–related hospitalization or death from any cause occurred in 2 patients (0.7%) in the remdesivir group and in 15 (5.3%) in the placebo group (hazard ratio, 0.13; 95% confidence interval [CI], 0.03 to 0.59; P=0.008). A total of 4 of 246 patients (1.6%) in the remdesivir group and 21 of 252 (8.3%) in the placebo group had a Covid-19–related medically attended visit by day 28 (hazard ratio, 0.19; 95% CI, 0.07 to 0.56). No patients had died by day 28. Adverse events occurred in 42.3% of the patients in the remdesivir group and in 46.3% of those in the placebo group.

**CONCLUSIONS** Among nonhospitalized patients who were at high risk for Covid-19 progression, a 3-day course of remdesivir had an acceptable safety profile and resulted in an 87% lower risk of hospitalization or death than placebo. (Funded by Gilead Sciences; PINETREE ClinicalTrials.gov number, [**NCT04501952. opens in new tab**](http://clinicaltrials.gov/show/NCT04501952); EudraCT number, [**2020-003510-12. opens in new tab**](https://www.clinicaltrialsregister.eu/ctr-search/search?query=2020-003510-12).)

Full paper: [Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients | NEJM](https://www.nejm.org/doi/full/10.1056/NEJMoa2116846?query=featured_coronavirus)

**Title:** Multisystem Inflammatory Syndrome in Children by COVID-19 Vaccination Status of Adolescents in France

*JAMA.*Published online 20th December, 2021.

COVID-19 mRNA vaccine immunogenicity and effectiveness are well established in adolescents.[1](https://jamanetwork.com/journals/jama/fullarticle/2787495#jld210084r1) However, the effect of vaccination on multisystem inflammatory syndrome in children (MIS-C),[2](https://jamanetwork.com/journals/jama/fullarticle/2787495#jld210084r2) a severe complication associated with SARS-CoV-2,[3](https://jamanetwork.com/journals/jama/fullarticle/2787495#jld210084r3) has not yet been described. Summer 2021 in France was marked by both a fourth wave of COVID-19 cases due to the Delta variant, with a peak in August 2021, and by the recommendation of the French Public Health Agency to vaccinate children 12 years and older. We estimated the risk of MIS-C among adolescents by COVID-19 vaccination status during September 2021 and October 2021

Full article: [Multisystem Inflammatory Syndrome in Children by COVID-19 Vaccination Status of Adolescents in France | Adolescent Medicine | JAMA | JAMA Network](https://jamanetwork.com/journals/jama/fullarticle/2787495)

**Title:** Analysis of COVID-19 Vaccine Type and Adverse Effects Following Vaccination

JAMA Netw Open – 22nd December 2021.

**Question**  What factors are associated with adverse effects after COVID-19 vaccination?

**Findings**  In an online cohort study including 19 586 adults who received a COVID-19 vaccination, the factors most strongly associated with adverse effects were full vaccination dose, brand of vaccine, younger age, female sex, and having had COVID-19 before vaccination. Allergic reaction or anaphylaxis was reported in 0.3% of participants after partial vaccination and 0.2% of participants after full vaccination.

**Meaning**  These findings suggest that some individuals experience more adverse effects after COVID-19 vaccination, but serious adverse effects are rare.

Full paper: [Analysis of COVID-19 Vaccine Type and Adverse Effects Following Vaccination | Clinical Pharmacy and Pharmacology | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2787361)

**Title:** Metabolic Syndrome and Acute Respiratory Distress Syndrome in Hospitalized Patients With COVID-19

JAMA Netw Open - 22nd December 2021

**Question**  What is the risk of acute respiratory distress syndrome (ARDS) and death in patients with COVID-19 with metabolic syndrome?

**Findings**  In this cohort study including 46 441 patients hospitalized for COVID-19, metabolic syndrome was associated with significantly increased odds of ARDS and death. With each metabolic syndrome criterion added from 1 to 4 criteria, the risk of ARDS significantly increased in an additive fashion.

**Meaning**  These findings suggest that metabolic syndrome and its associated comorbidities were critical risk factors associated with COVID-19–related ARDS and death.

Full paper: [Metabolic Syndrome and Acute Respiratory Distress Syndrome in Hospitalized Patients With COVID-19 | Critical Care Medicine | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2787394)

**Title:** Severity of Illness in Persons Infected With the SARS-CoV-2 Delta Variant vs Beta Variant in Qatar

*JAMA Intern Med.*Published online 22nd December, 2021

**Question**  Do patients infected with the SARS-CoV-2 Delta variant experience more severe disease outcomes compared with those infected with the Beta variant?

**Findings**  In this cohort study of 1427 persons infected with the Delta variant and 5353 persons infected with the Beta variant in Qatar, among 451 propensity score–matched pairs identified, persons infected with the Delta variant were more likely to be hospitalized (27.3% vs 20.0%) or to experience more severe disease outcomes. Infection with the Delta variant was independently associated with higher odds of experiencing any adverse outcome, and vaccination was associated with significantly reduced odds of severe disease outcomes.

**Meaning**  In this cohort study, infection with the Delta variant was more severe than infection with the Beta variant in persons in Qatar, although vaccination was highly protective against severe outcomes for both variants.

Full paper: [Severity of Illness in Persons Infected With the SARS-CoV-2 Delta Variant vs Beta Variant in Qatar | Global Health | JAMA Internal Medicine | JAMA Network](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2787492)

**Title:** Maternal and Neonatal SARS-CoV-2 Immunoglobulin G Antibody Levels at Delivery After Receipt of the BNT162b2 Messenger RNA COVID-19 Vaccine During the Second Trimester of Pregnancy

*JAMA Pediatr.*Published online December 21, 2021.

**Question**  What were the maternal and neonatal SARS-CoV-2 immunoglobulin G antibody levels at birth after messenger RNA (mRNA) COVID-19 vaccination during the second trimester of pregnancy?

**Findings**  In this cohort study of 130 pregnant women who received the BNT162b2 mRNA vaccine during their second trimester, antibody titers were positive for all women during delivery, and neonatal titers were higher than maternal titers, representing 100% placental antibody transfer.

**Meaning**  The findings suggest that administration of the mRNA COVID-19 vaccine during the second trimester is associated with a maternal humoral response that is sustained during labor and transfers antibodies to the neonate, supporting early vaccination of pregnant women.

Full paper: [Maternal and Neonatal SARS-CoV-2 Immunoglobulin G Antibody Levels at Delivery After Receipt of the BNT162b2 Messenger RNA COVID-19 Vaccine During the Second Trimester of Pregnancy | Neonatology | JAMA Pediatrics | JAMA Network](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2787270)

**Title:** Factors Associated With Severe Gastrointestinal Diagnoses in Children With SARS-CoV-2 Infection or Multisystem Inflammatory Syndrome

*JAMA Netw Open.*Published 20th December 2021.

**Question**  Is COVID-19 associated with severe gastrointestinal manifestations in children?

**Findings**  In this multicenter cohort study of 685 Italian children with COVID-19, 10% showed severe gastrointestinal involvement characterized by diffuse adeno-mesenteritis, appendicitis, abdominal fluid collection, ileal intussusception, or pancreatitis. Children older than 5 years and those presenting with abdominal pain, leukopenia, or receiving a diagnosis of multisystem inflammatory syndrome were more likely to have severe gastrointestinal manifestations.

**Meaning**  Severe gastrointestinal involvement is not uncommon in children with COVID-19, and awareness about its frequency and presentation may help practitioners to appropriately manage children at risk of severe outcomes.

Full article: [Factors Associated With Severe Gastrointestinal Diagnoses in Children With SARS-CoV-2 Infection or Multisystem Inflammatory Syndrome | Gastroenterology | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2787258)

**Title:** Comparison of SARS-CoV-2 Antibody Response 4 Weeks After Homologous vs Heterologous Third Vaccine Dose in Kidney Transplant Recipients

JAMA Intern Med. Published online December 20, 2021

**Question**  Does a heterologous SARS-CoV-2 vaccination strategy with the vector vaccine Ad26COVS1 result in a higher rate of antibody response compared with a homologous third dose of mRNA vaccine (mRNA-1273 or BNT162b2) in kidney transplant recipients who did not develop SARS-CoV-2 antibodies after 2 doses of an mRNA vaccine?

**Findings**  This randomized clinical trial found that a third dose of SARS-CoV-2 vaccine in 197 kidney transplant recipients without antibodies after 2 doses of an mRNA vaccine induced an antibody response in 35% of the homologous (mRNA) group vs 42% of the heterologous (vector) group, with no statistically significant difference.

**Meaning**  The findings of this randomized clinical trial show that homologous and heterologous vaccination strategies for a third SARS-CoV-2 vaccine dose in kidney transplant recipients are comparable, with both mRNA and vector vaccines achieving seroconversion in more than one-third of kidney transplant recipients. However, given the high rate of nonresponders after the third dose, additional strategies to induce an immune response in kidney transplant recipients are urgently needed.

Full paper: [Comparison of SARS-CoV-2 Antibody Response 4 Weeks After Homologous vs Heterologous Third Vaccine Dose in Kidney Transplant Recipients: A Randomized Clinical Trial | Nephrology | JAMA Internal Medicine | JAMA Network](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2787200)

**Title:** Emergency Use Authorizations of COVID-19–Related Medical Products

JAMA Internal Medicine 20th December 2021

Emergency use authorization (EUA) enables the US Food and Drug Administration (FDA) to facilitate the availability of medical countermeasures when public health emergencies are declared by the secretary of the US Department of Health and Human Services.[1](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2787205#ild210064r1) Few medical products were authorized for 15 years after the first EUA for an anthrax vaccine was issued in February 2005.[1](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2787205#ild210064r1) During the COVID-19 crisis, EUA was used extensively for rapid authorizations of medical products.[2](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2787205#ild210064r2) In this study, we examined the COVID-19–related products authorized by the FDA and the quality of their supporting evidence.

Full article: [Emergency Use Authorizations of COVID-19–Related Medical Products | Regulatory Agencies | JAMA Internal Medicine | JAMA Network](https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2787205)

recovery

**Title:** All-cause mortality during the COVID-19 pandemic in Chennai, India: an observational study

### The Lancet Infectious Diseases – 22nd December, 2021

### Background India has been severely affected by the ongoing COVID-19 pandemic. However, due to shortcomings in disease surveillance, the burden of mortality associated with COVID-19 remains poorly understood. We aimed to assess changes in mortality during the pandemic in Chennai, Tamil Nadu, using data on all-cause mortality within the district.

**Methods** For this observational study, we analysed comprehensive death registrations in Chennai, from Jan 1, 2016, to June 30, 2021. We estimated expected mortality without the effects of the COVID-19 pandemic by fitting models to observed mortality time series during the pre-pandemic period, with stratification by age and sex. Additionally, we considered three periods of interest: the first 4 weeks of India's first lockdown (March 24 to April 20, 2020), the 4-month period including the first wave of the pandemic in Chennai (May 1 to Aug 31, 2020), and the 4-month period including the second wave of the pandemic in Chennai (March 1 to June 30, 2021). We computed the difference between observed and expected mortality from March 1, 2020, to June 30, 2021, and compared pandemic-associated mortality across socioeconomically distinct communities (measured with use of 2011 census of India data) with regression analyses.

**Findings** Between March 1, 2020, and June 30, 2021, 87 870 deaths were registered in areas of Chennai district represented by the 2011 census, exceeding expected deaths by 25 990 (95% uncertainty interval 25 640–26 360) or 5·18 (5·11–5·25) excess deaths per 1000 people. Stratified by age, excess deaths numbered 21·02 (20·54–21·49) excess deaths per 1000 people for individuals aged 60–69 years, 39·74 (38·73–40·69) for those aged 70–79 years, and 96·90 (93·35–100·16) for those aged 80 years or older. Neighbourhoods with lower socioeconomic status had 0·7% to 2·8% increases in pandemic-associated mortality per 1 SD increase in each measure of community disadvantage, due largely to a disproportionate increase in mortality within these neighbourhoods during the second wave. Conversely, differences in excess mortality across communities were not clearly associated with socioeconomic status measures during the first wave. For each increase by 1 SD in measures of community disadvantage, neighbourhoods had 3·6% to 8·6% lower pandemic-associated mortality during the first 4 weeks of India's country-wide lockdown, before widespread SARS-CoV-2 circulation was underway in Chennai. The greatest reductions in mortality during this early lockdown period were observed among men aged 20–29 years, with 58% (54–62) fewer deaths than expected from pre-pandemic trends.

**Interpretation** Mortality in Chennai increased substantially but heterogeneously during the COVID-19 pandemic, with the greatest burden concentrated in disadvantaged communities. Reported COVID-19 deaths greatly underestimated pandemic-associated mortality.

**Funding** National Institute of General Medical Sciences, Bill & Melinda Gates Foundation, National Science Foundation.

**Translation** For the Hindi translation of the abstract see Supplementary Materials section.

Full paper [All-cause mortality during the COVID-19 pandemic in Chennai, India: an observational study - The Lancet Infectious Diseases](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099%2821%2900746-5/fulltext)

**Title:** Immediate and Longer-Term Changes in the Mental Health and Well-being of Older Adults in England During the COVID-19 Pandemic

JAMA Psychiatry – 22nd December, 2021

**Question**  How have the mental health and well-being of older adults in England changed during the COVID-19 pandemic compared with prepandemic levels?

**Findings**  This cohort study including 5146 older adults participating in the English Longitudinal Study of Ageing found that levels of depression, loneliness, and poor quality of life increased significantly during June and July 2020 compared with prepandemic levels and continued to deteriorate during the second national lockdown in November and December 2020, with further increases in anxiety symptoms from June and July 2020 to November and December 2020. Inequalities in experiences of mental ill health during the COVID-19 pandemic were evident, with women, individuals living alone, and those with less wealth being particularly vulnerable.

**Meaning**  Older individuals did not adapt well to the new psychosocial stressors introduced by the pandemic; policies should be in place for the immediate provision of targeted psychological interventions to support older people, and access to digital mental health services should be improved.

Full paper: [Immediate and Longer-Term Changes in the Mental Health and Well-being of Older Adults in England During the COVID-19 Pandemic | Depressive Disorders | JAMA Psychiatry | JAMA Network](https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2787196)

Infection control

**Title:** Impact of the SARS-CoV-2 pandemic on routine immunisation services: evidence of disruption and recovery from 170 countries and territories

The Lancet Global Health – published 21st December 2021

**Background** The SARS-CoV-2 pandemic has revealed the vulnerability of immunisation systems worldwide, although the scale of these disruptions has not been described at a global level. This study aims to assess the impact of COVID-19 on routine immunisation using triangulated data from global, country-based, and individual-reported sources obtained during the pandemic period.

**Methods** This report synthesised data from 170 countries and territories. Data sources included administered vaccine-dose data from January to December, 2019, and January to December, 2020, WHO regional office reports, and a WHO-led pulse survey administered in April, 2020, and June, 2020. Results were expressed as frequencies and proportions of respondents or reporting countries. Data on vaccine doses administered were weighted by the population of surviving infants per country.

**Findings** A decline in the number of administered doses of diphtheria–pertussis–tetanus-containing vaccine (DTP3) and first dose of measles-containing vaccine (MCV1) in the first half of 2020 was noted. The lowest number of vaccine doses administered was observed in April, 2020, when 33% fewer DTP3 doses were administered globally, ranging from 9% in the WHO African region to 57% in the South-East Asia region. Recovery of vaccinations began by June, 2020, and continued into late 2020. WHO regional offices reported substantial disruption to routine vaccination sessions in April, 2020, related to interrupted vaccination demand and supply, including reduced availability of the health workforce. Pulse survey analysis revealed that 45 (69%) of 65 countries showed disruption in outreach services compared with 27 (44%) of 62 countries with disrupted fixed-post immunisation services.

**Interpretation** The marked magnitude and global scale of immunisation disruption evokes the dangers of vaccine-preventable disease outbreaks in the future. Trends indicating partial resumption of services highlight the urgent need for ongoing assessment of recovery, catch-up vaccination strategy implementation for vulnerable populations, and ensuring vaccine coverage equity and health system resilience.

**Funding** US Agency for International Development.

Full paper: [Impact of the SARS-CoV-2 pandemic on routine immunisation services: evidence of disruption and recovery from 170 countries and territories - The Lancet Global Health](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X%2821%2900512-X/fulltext)

**Title:** Nasal prevention of SARS-CoV-2 infection by intranasal influenza-based boost vaccination in mouse models

EBio Medicine (published by The Lancet) 20th December 2021

**Background** Vaccines in emergency use are efficacious against COVID-19, yet vaccine-induced prevention against nasal SARS-CoV-2 infection remains suboptimal.

**Methods** Since mucosal immunity is critical for nasal prevention, we investigated the efficacy of an intramuscular PD1-based receptor-binding domain (RBD) DNA vaccine (PD1-RBD-DNA) and intranasal live attenuated influenza-based vaccines (LAIV-CA4-RBD and LAIV-HK68-RBD) against SARS-CoV-2.

**Findings** Substantially higher systemic and mucosal immune responses, including bronchoalveolar lavage IgA/IgG and lung polyfunctional memory CD8 T cells, were induced by the heterologous PD1-RBD-DNA/LAIV-HK68-RBD as compared with other regimens. When vaccinated animals were challenged at the memory phase, prevention of robust SARS-CoV-2 infection in nasal turbinate was achieved primarily by the heterologous regimen besides consistent protection in lungs. The regimen-induced antibodies cross-neutralized variants of concerns. Furthermore, LAIV-CA4-RBD could boost the BioNTech vaccine for improved mucosal immunity.

**Interpretation** Our results demonstrated that intranasal influenza-based boost vaccination induces mucosal and systemic immunity for effective SARS-CoV-2 prevention in both upper and lower respiratory systems.

**Funding** This study was supported by the Research Grants Council Collaborative Research Fund, General Research Fund and Health and Medical Research Fund in Hong Kong; Outbreak Response to Novel Coronavirus (COVID-19) by the Coalition for Epidemic Preparedness Innovations; Shenzhen Science and Technology Program and matching fund from Shenzhen Immuno Cure BioTech Limited; the Health@InnoHK, Innovation and Technology Commission of Hong Kong; National Program on Key Research Project of China; donations from the Friends of Hope Education Fund; the Theme-Based Research Scheme.

Full paper: [Nasal prevention of SARS-CoV-2 infection by intranasal influenza-based boost vaccination in mouse models - EBioMedicine (thelancet.com)](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2821%2900556-9/fulltext)

**Title:** Two-dose ChAdOx1 nCoV-19 vaccine protection against COVID-19 hospital admissions and deaths over time: a retrospective, population-based cohort study in Scotland and Brazil

The Lancet – 20th December, 2021

**Background** Reports suggest that COVID-19 vaccine effectiveness is decreasing, but whether this reflects waning or new SARS-CoV-2 variants—especially delta (B.1.617.2)—is unclear. We investigated the association between time since two doses of ChAdOx1 nCoV-19 vaccine and risk of severe COVID-19 outcomes in Scotland (where delta was dominant), with comparative analyses in Brazil (where delta was uncommon).

**Methods** In this retrospective, population-based cohort study in Brazil and Scotland, we linked national databases from the EAVE II study in Scotland; and the COVID-19 Vaccination Campaign, Acute Respiratory Infection Suspected Cases, and Severe Acute Respiratory Infection/Illness datasets in Brazil) for vaccination, laboratory testing, clinical, and mortality data. We defined cohorts of adults (aged ≥18 years) who received two doses of ChAdOx1 nCoV-19 and compared rates of severe COVID-19 outcomes (ie, COVID-19 hospital admission or death) across fortnightly periods, relative to 2–3 weeks after the second dose. Entry to the Scotland cohort started from May 19, 2021, and entry to the Brazil cohort started from Jan 18, 2021. Follow-up in both cohorts was until Oct 25, 2021. Poisson regression was used to estimate rate ratios (RRs) and vaccine effectiveness, with 95% CIs.

**Findings** 1 972 454 adults received two doses of ChAdOx1 nCoV-19 in Scotland and 42 558 839 in Brazil, with longer follow-up in Scotland because two-dose vaccination began earlier in Scotland than in Brazil. In Scotland, RRs for severe COVID-19 increased to 2·01 (95% CI 1·54–2·62) at 10–11 weeks, 3·01 (2·26–3·99) at 14–15 weeks, and 5·43 (4·00–7·38) at 18–19 weeks after the second dose. The pattern of results was similar in Brazil, with RRs of 2·29 (2·01–2·61) at 10–11 weeks, 3·10 (2·63–3·64) at 14–15 weeks, and 4·71 (3·83–5·78) at 18–19 weeks after the second dose. In Scotland, vaccine effectiveness decreased from 83·7% (95% CI 79·7–87·0) at 2–3 weeks, to 75·9% (72·9–78·6) at 14–15 weeks, and 63·7% (59·6–67·4) at 18–19 weeks after the second dose. In Brazil, vaccine effectiveness decreased from 86·4% (85·4–87·3) at 2–3 weeks, to 59·7% (54·6–64·2) at 14–15 weeks, and 42·2% (32·4–50·6) at 18–19 weeks.

**Interpretation** We found waning vaccine protection of ChAdOx1 nCoV-19 against COVID-19 hospital admissions and deaths in both Scotland and Brazil, this becoming evident within three months of the second vaccine dose. Consideration needs to be given to providing booster vaccine doses for people who have received ChAdOx1 nCoV-19.

**Funding** UK Research and Innovation (Medical Research Council), Scottish Government, Research and Innovation Industrial Strategy Challenge Fund, Health Data Research UK, Fiocruz, Fazer o Bem Faz Bem Programme; Conselho Nacional de Desenvolvimento Científico e Tecnológico, Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro.

**Translation** For the Portuguese translation of the abstract see Supplementary Materials section.

Full paper: [Two-dose ChAdOx1 nCoV-19 vaccine protection against COVID-19 hospital admissions and deaths over time: a retrospective, population-based cohort study in Scotland and Brazil - The Lancet](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2821%2902754-9/fulltext)

**Title:** Heterologous ChAdOx1 nCoV-19 and BNT162b2 prime-boost vaccination elicits potent neutralizing antibody responses and T cell reactivity against prevalent SARS-CoV-2 variants

EBioMedicine (Published by The Lancet) – 17th December, 2021)

**Background** Heterologous COVID-19 vaccination regimens combining vector- and mRNA-based vaccines are already administered, but data on solicited adverse reactions, immunological responses and elicited protection are limited.

**Methods** To evaluate the reactogenicity and humoral as well as cellular immune responses towards most prevalent SARS-CoV-2 variants after a heterologous ChAdOx1 nCoV-19 BNT162b2 prime-boost vaccination, we analysed a cohort of 26 clinic employees aged 25-46 (median 30.5) years who received a ChAdOx1 nCoV-19 prime followed by a BNT162b2 boost after an 8-week interval. Serological data were compared to a cohort which received homologous BNT162b2 vaccination with a 3-week interval (14 individuals aged 25-65, median 42).

**Findings** Self-reported solicited symptoms after ChAdOx1 nCoV-19 prime were in line with previous reports and more severe than after the BNT162b2 boost. Antibody titres increased significantly over time resulting in strong neutralization titres two weeks after the BNT162b2 boost and subsequently slightly decreased over the course of 17 weeks. At the latest time point measured, all analysed sera retained neutralizing activity against the currently dominant Delta (B.1.617.2) variant. Two weeks post boost, neutralizing activity against the Alpha (B.1.1.7) and immune-evading Beta (B.1.351) variant was ∼4-fold higher than in individuals receiving homologous BNT162b2 vaccination. No difference was observed in neutralization of Kappa (B.1.617.1). In addition, heterologous vaccination induced CD4+ and CD8+ T cells reactive to SARS-CoV-2 spike peptides of all analysed variants; Wuhan-Hu-1, Alpha, Beta, Gamma (P.1), and Delta.

**Interpretation** In conclusion, heterologous ChAdOx1 nCoV-19 / BNT162b2 prime-boost vaccination is not associated with serious adverse events and induces potent humoral and cellular immune responses. The Alpha, Beta, Delta, and Kappa variants of spike are potently neutralized by sera from all participants and reactive T cells recognize spike peptides of all tested variants. These results suggest that this heterologous vaccination regimen is at least as immunogenic and protective as homologous vaccinations and also offers protection against current variants of concern.

**Funding** This project has received funding from the European Union's Horizon 2020 research and innovation programme, the German Research Foundation, the BMBF, the Robert Koch Institute (RKI), the Baden-Württemberg Stiftung, the county of Lower Saxony, the Ministry for Science, Research and the Arts of Baden-Württemberg, Germany, and the National Institutes of Health.

Full paper: [Heterologous ChAdOx1 nCoV-19 and BNT162b2 prime-boost vaccination elicits potent neutralizing antibody responses and T cell reactivity against prevalent SARS-CoV-2 variants - EBioMedicine (thelancet.com)](https://www.thelancet.com/journals/ebiom/article/PIIS2352-3964%2821%2900555-7/fulltext)

**Title:** Incidence and Estimated Vaccine Effectiveness Against Symptomatic SARS-CoV-2 Infection Among Persons Tested in US Retail Locations, May 1 to August 7, 2021

JAMA Netw Open – 22nd December 2021

As of August 17, 2021, the US Centers for Disease Control and Prevention (CDC) reported that 168.7 million people in the US, more than half of the US population, had received full doses of SARS-CoV-2 vaccines.[1](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2787363#zld210296r1) This study evaluates whether estimated vaccine effectiveness against infection changes over time to help inform public health policy and clinical practices.

Full paper: [Incidence and Estimated Vaccine Effectiveness Against Symptomatic SARS-CoV-2 Infection Among Persons Tested in US Retail Locations, May 1 to August 7, 2021 | Infectious Diseases | JAMA Network Open | JAMA Network](https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2787363)

**Title:** Vaccination Doesn’t Eliminate Delta Variant Household Transmission

JAMA – 21st December 2021

Being fully vaccinated against SARS-CoV-2 makes it less likely but far from impossible to become infected when another member of the household has a highly transmissible Delta variant infection, according to a [study](https://www.thelancet.com/lancet/article/s1473309921006484) in the United Kingdom.

Altogether, the study enrolled 621 participants: 440 household contacts and 162 nonhousehold contacts of people with SARS-CoV-2 infection as well as 19 index cases. Among the contacts, 369 were recruited for the study between mid-September 2020 and mid-March 2021 when the Alpha variant predominated in London. Another group of 233 contacts and the 19 index cases were recruited between late May and mid-September 2021 after the Delta variant emerged. Contacts collected daily nasal swab samples for up to 20 days and submitted them for diagnostic reverse transcriptase–polymerase chain reaction testing.

Epidemiologic analysis showed that 25% of fully vaccinated individuals who were exposed to the Delta variant through household contact became infected compared with 38% of unvaccinated individuals. The vaccine was 34% effective against the Delta variant—substantially lower than the 40% to 50% effectiveness against household transmission [reported](https://www.nejm.org/doi/10.1056/NEJMc2107717) before the variant became widespread. Vaccination status among index cases didn’t change the likelihood of household transmission. Although the peak viral load was similar among participants regardless of their vaccination status or variant, viral load decreased faster among those who were vaccinated. Susceptibility to infection increased as early as 2 to 3 months after vaccination.

Co-lead researcher Ajit Lalvani, DM, chair of infectious diseases at Imperial College London, said in a [statement](https://www.eurekalert.org/news-releases/933075) that ongoing transmission between vaccinated people makes it essential for those who remain unvaccinated to get the vaccine, especially as more people spend time indoors during the winter months.

Full paper: [Vaccination Doesn’t Eliminate Delta Variant Household Transmission | Vaccination | JAMA | JAMA Network](https://jamanetwork.com/journals/jama/fullarticle/2787307)

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