COVID-19

Scientific literature review

A digest of peer-reviewed articles from top-ranked journals on selected research topics related to SARS-CoV-2 and COVID-19

UPDATE OF

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L'ANRS|Emerging Infectious Diseases shares a selection of the most relevant articles published on COVID-19 on a weekly basis. This literature review not only presents a selection of references, but also highlights the key points and messages from each article. It does not include pre-print articles.

Our objective is to help the scientific community, health-workers and public health decision makers, being up to date with the latest scientific research.

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Additional links:

Haute Autorité de Santé: https://www.scoop.it/topic/coronavirus-covid-19-has-veille?nosug=1
MODCOV19: https://modcov19.math.cnrs.fr/veille_public/

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 18MAY2022	**Omicron BA.1/1.1 SARS-CoV-2 Infection among Vaccinated Canadian Adults**	Brown P.E., *et al.* Canada gotopaper	Variants	**Aim**: to quantify the incidence of SARS-CoV-2 infection during the initial omicron BA.1/1.1 variant wave among Canadian adults and the contribution of previous infection and concurrent vaccination to age-specific active immunity. - 5031 adults who were surveyed in phase 4 of the Ab-C study and whose dried-blood-spot samples were received between January 24 and March 15, 2022, broadly representative of Canadian adults. **Results** - Among 3468 adults who tested negative for the N protein in phase 3 of the study (August through October 2021), 1040 had positive results for the N protein in phase 4 (education-weighted between-phase incidence, 30%; 95% CI, 26 to 33). - Among 91 unvaccinated, uninfected participants in phase 3 of the study, 36 had a positive result in phase 4 (education-weighted between-phase incidence, 40%; 95% CI, 25 to 54). - After the exclusion of participants who had been vaccinated less than 1 month before samples were obtained, spike protein titers were negligible among participants who were uninfected or unvaccinated. - Spike protein titers were lower among participants who had received only one vaccine dose than among those who had received multiple vaccine doses. The spike protein titers were highest among participants who had received three vaccine doses and had been infected. - Analysis of phases 3 and 4 separately: cumulative incidence of N protein positivity before the omicron BA.1/1.1 variant wave was 11% (95% CI, 10 to 12; of 5155 participants tested, 571 had a positive result) but increased during the omicron BA.1/1.1 wave to an education-weighted cumulative incidence of 37% (95% CI, 35 to 39; of 5031 participants tested, 1869 had a positive result). - Estimated 9.0 million adults (95% CI, 7.9 to 10.2 million) had been newly infected during the omicron BA.1/1.1 wave, including 0.9 million infections (95% CI, 0.6 to 1.2 million) among 2.3 million unvaccinated adults. The incidence of infection with the omicron BA.1/1.1 variant increased to a lesser extent among older adults than among younger adults. **Despite the finding of widespread infection, the age-specific patterns caution against the notion that the omicron BA.1/1.1 variant will immunize everyone.**
Clin Infect Dis. 17MAY2022	**A Single Dose of BNT162b2 mRNA Vaccine Induces Airway Immunity in SARS-CoV-2 Naive and recovered COVID-19 subjects**	Martinuzzi E., *et al.* France gotopaper	Vaccines	**Aim**: to investigate whether a booster injection of BNT162b2 promotes stronger mucosal immune responses following prior mucosal infection compared to a mucosally naive subject. **Methods** > 20 recovered COVID-19 subjects (RCS) and 23 SARS-CoV-2 naive subjects vaccinated with respectively one and two doses of the BNT162b2 COVID-19 vaccine - Nasal Epithelial Lining Fluid (NELF) and plasma were collected before and after vaccination and assessed forIgG and IgA levels to Spike, and their binding-neutralisation ability. - Blood was analyzed one week after vaccination for the number of Spike-specific Antibody Secreting Cells (ASCs) with a mucosal tropism. **Results** > All RCS had both nasal and blood SARS-CoV-2 specific antibodies at least 90 days after initial diagnosis. > In RCS, a single dose of vaccine amplified pre-existing Spike-specific IgG and IgA antibody responses in both NELF and blood against both vaccine homologous and variant strains, including delta. These responses were associated with Spike-specific IgG and IgA ASCs with a mucosal tropism in blood. > Nasal IgA and IgG antibody responses were lower in magnitude in SARS-CoV-2 naive subjects after two vaccine doses compared to RCS after one dose. **Mucosal immune response to the SARS-CoV-2 Spike protein is higher in RCS after a single vaccine dose compared to SARS-CoV-2 naive subjects after two doses.**

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NEJM 18MAY2022	**Neutralization of the SARS-CoV-2 Deltacron and BA.3 Variants**	Evans J.P., *et al.* USA gotopaper	Variants	**Aim**: to elucidate the ability of such "deltacron" variants (omicron + delta recombinant) to evade immunity induced by either vaccination or previous infection. - Pseudotyped virus neutralization assay to examine neutralizing-antibody titers in serum samples obtained from vaccinated health care workers as well as from patients with confirmed Covid-19 during the delta and omicron waves (USA). **Results** Serum samples from 10 health care workers 3-4 weeks after the second dose of the mRNA-1273 vaccine: > As compared with the response against the D614G variant, neutralizing-antibody titers were 3.3 times as low against the BA.3 variant and 44.7 times as low against the deltacron variant (P<0.001 for both comparisons) > After an homologous booster dose, neutralizing-antibody titers were 2.9 times as low against the BA.3 variant and 13.3 times as low against the deltacron variant as against the D614G variant (P<0.001 for both comparisons). > Deltacron variant showed similar neutralizing-antibody resistance to the BA.1 and BA.2 variants, whereas the BA.3 variant was more sensitive to both two-dose and boosted samples. Serum samples from 18 patients 3 days after admission to an ICU during the delta wave of the pandemic (12 unvaccinated, 5 fully vaccinated, 1 vaccinated and boosted): > Patients had similar neutralizing-antibody titers against the D614G and BA.3 variants. > Titers against the deltacron variant were 137.8 times as low as the titers against the D614G variant, with only 44.4% of the patients having neutralizing-antibody titers against the deltacron variant. > Neutralization escape of the deltacron variant paralleled that of the BA.1 and BA.2 variants, whereas the BA.3 variant remained largely sensitive to neutralization (> Patients who had been vaccinated had substantially higher titers against the D614G and BA.3 variants than the patients who were unvaccinated, whereas the deltacron variant largely escaped neutralization. Serum samples from 31 patients who were hospitalized during the omicron wave but were not admitted to the ICU: > Neutralization of the deltacron and BA.3 variants was similar to that of the D614G variant. Neutralization of both the deltacron and BA.3 variants was similar to that of the BA.1 and BA.2 variants, regardless of vaccination status. > Patients who were hospitalized during the omicron wave had broader neutralization of all the tested omicron variants than did those hospitalized during the delta wave. > On average, the HCW who had received three doses of vaccine had stronger and broader immunity than the patients who had been evaluated during the omicron wave regardless of vaccination status, with neutralizing-antibody titers against the D614G variant that were 59.9 times as high as those in patients during the omicron wave. > Boosted HCW had neutralizing-antibody titers against the D614G variant that were 4.2 times as high as those among health care workers who had received two doses of vaccine and 2.8 times as high as those among patients who had been assessed during the delta wave. **BA.3 is not a substantial immune-escape variant, however, the deltacron variant retains the strong resistance of other omicron sublineages and has no enhanced sensitivity to serum obtained during the delta wave.**

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Nature 18MAY2022	**Limited cross-variant immunity from SARS-CoV-2 Omicron without vaccination**	Suryawanshi R.K., *et al.* USA gotopaper	Immunology	**Aim**: to show that without vaccination, infection with Omicron induces a limited humoral immune response in mice and humans **Methods** > We studied WA1, Delta, and Omicron infections in mice. Because WA1 and Delta variants cannot infect regular laboratory mice, we used transgenic mice overexpressing, human ACE2 (K18-hACE2). We intranasally infected (104 PFU) these mice with the three viral isolates and over 7 days monitored their body temperature and weight, which serves as indicators of disease progression **Results** > Omicron infection enhances preexisting immunity elicited by vaccines but, on its own, may not confer broad protection against non-Omicron variants in unvaccinated individuals. > Sera from mice overexpressing the human ACE2 receptor and infected with Omicron neutralize only Omicron, but no other VOCs, whereas broader cross-variant neutralization was observed after WA1 and Delta infections. > Unlike WA1 and Delta, Omicron replicates to low levels in the lungs and brains of infected animals, leading to mild disease with reduced pro-inflammatory cytokine expression and diminished activation of lung-resident T cells. > Sera from unvaccinated, Omicron-infected individuals show the same limited neutralization of only Omicron itself. In contrast, Omicron breakthrough infections induce overall higher neutralization titers against all VOCs **While the Omicron variant is immunogenic, infection in unvaccinated individuals may not elicit effective cross-neutralizing antibodies against non Omicron variants. In vaccinated individuals, however, Omicron infection effectively induces immunity against itself and enhances neutralization of other variants. This, together with our finding that Delta infection also elicits broad cross-variant neutralization in vaccinated individuals, supports the inclusion of Omicron- and Delta-based immunogens in future heterologous or multivalent vaccination strategies for broad protection against variants.**
Science Immunol. 17MAY2022	**Recall of pre-existing cross-reactive B cell memory following Omicron BA.1 breakthrough infection**	Kaku C., *et al.* Sweden / USA gotopaper	Immunology	**Aim**: to profile spike (S)-specific B cell responses following Omicron/BA.1 infection in mRNA-vaccinated donors. **Methods:** The authors investigated S-specific serological and peripheral B cell responses in a cohort of mRNA-vaccinated individuals who had recently experienced BA.1 breakthrough infections. **Findings :** > The acute antibody response was characterized by high levels of somatic hypermutation (SHM) and a bias toward recognition of ancestral SARS-CoV-2 strains, suggesting the early activation of vaccine-induced memory B cells (MBCs). > BA.1 breakthrough infection induced a shift in B cell immunodominance hierarchy from the S2 subunit, which is highly conserved across SARS-CoV-2 variants of concern (VOCs), and toward the antigenically variable receptor binding domain (RBD). > A large proportion of RBD-directed neutralizing antibodies isolated from BA.1 breakthrough infection donors displayed convergent sequence features and broadly recognized SARS-CoV-2 VOCs. **These findings provide insights into the role of pre-existing immunity in shaping the B cell response to heterologous SARS-CoV-2 variant exposure.**

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Clin Microbiol Infect 17MAY2022	**Resistance mutations in SARS-CoV-2 omicron variant in patients treated with Sotrovimab**	Vellas C., *et al.* France gotopaper	Variants	**Aim**: to determine the evolution of the virus load, the development of spike mutations and the evolution of the virus complexity in nasopharyngeal (NP) swabs from Sotrovimab-treated ambulatory omicron-infected patients. **Methods** - NP samples from omicron-infected patients, before a single intravenous infusion (Day 0) of Sotrovimab (500mg), 7 days after (Day 7) and weekly until the viral load reached 31 Ct - 51 patients: 42 immunocompromised, 8 had chronic kidney disease with hemodialysis, and one had severe asthma. - 13 patients were infected with BA.1, 30 with BA.1.1, and 5 with BA.2. The SARS-CoV-2 variant infecting 3 patients could not be identified (low viral load). **Results** > The median SARS-CoV-2 NP viral load decreased from 7.1 [IQR, 6.1-7.8] log10copies/ml before Sotrovimab-infusion to 5.1 [IQR, 3.1-6.5] log10copies/ml 7 days post-infusion (p<0.001). > No significant differences in the NP viral load declines between BA.1 (2.1 [IQR, 1.0-4.1] log10copies/ml), BA.1.1 (2.0 [IQR, 0.6-3.6] log10copies/ml), and BA.2 (1.3 [IQR, 0.5-4.1] log10copies/ml) infections (p>0.05) were found. > Of 34 (67%) patients who had viral loads sufficiently high to be sequenced before and post-infusion, 53% had acquired Sotrovimab-resistant mutations 7 to 21 days post-treatment. > The NP viral loads of 5 patients rebounded after the mutation was first detected, those of 8 patients decreased very slowly and those of only 5 patients declined without rebound. > The spike-protein quasispecies complexity increased significantly 7 days after Sotrovimab-infusion compared to day 0 (p<0.001, p=0.002 and p=0.001 respectively). > No significant differences in the viral load decreases of patients infected with BA.1, BA.1.1, and BA.2 variants was observed (but few BA.2 samples in the study). **These results show emergence of Sotrovimab-resistant spike mutations in half of the patients who remained SARS-CoV-2 RNA positive 7 to 21 days post-infusion. This is the first in vivo study showing that Sotrovimab exposure induces the emergence of omicron-variants harboring mutations at positions 340, 337 and 356 and a significant increase in the virus complexity 7 days post-infusion.**
Science Transl Med. 17MAY2022	**The adenosine analog prodrug ATV006 is orally bioavailable and has preclinical efficacy against parental SARS-CoV-2 and variants**	Cao L., *et al.* China gotopaper	Therapeutics	**Aim**: to report a series of ester prodrugs of GS-441524 with improved antiviral potency. **Methods** The authors designed and synthesized a series of derivatives of GS-441524, the parent nucleoside analog of remdesivir, by employing short-chain fatty acid (SCFAs) or amino acid modifications to mask the polar hydroxyl- or amino-groups. **Findings :** > Esterification of the 5′-hydroxyl moieties of GS-441524 markedly improved antiviral potency. > This 5′-hydroxyl-isobutyryl prodrug, ATV006, demonstrated excellent oral bioavailability in rats and cynomolgus monkeys and exhibited potent antiviral efficacy against different SARS-CoV-2 VOCs in vitro and in three mouse models. > Oral administration of ATV006 reduced viral loads and alleviated lung damage when administered prophylactically and therapeutically to K18-hACE2 mice challenged with the Delta variant of SARS-CoV-2. **ATV006 represents a promising oral antiviral drug candidate for SARS-CoV-2.**

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Lancet Digital Health 16MAY2022	**Identifying who has long COVID in the USA: a machine learning approach using N3C data**	Pfaff E.R., *et al.* USA gotopaper	Long Covid	**Aim**: to identify potential patients with Long Covid, based on electronic health records. **Methods** - Machine learning models based on National COVID Cohort Collaborative's (N3C) electronic health record repository - Base population (n=1 793 604): any non-deceased adult patient with either a COVID-19 diagnosis from an inpatient or emergency visit, or a positive SARS-CoV-2 PCR or antigen test, and for whom at least 90 days have passed since COVID-19 index date. - Long Covid population (n=597) **Results** > The models identified, with high accuracy, patients who potentially have long COVID, achieving areas under the receiver operator characteristic curve of 0·92 (all patients), 0·90 (hospitalised), and 0·85 (non-hospitalised). > Important features, as defined by Shapley values, include rate of health-care utilisation, patient age, dyspnoea, and other diagnosis and medication information available within the electronic health record. **Patients identified by these models as potentially having long COVID can be interpreted as patients warranting care at a specialty clinic for long COVID, which is an essential proxy for long COVID diagnosis.**
PNAS 16MAY2022	**The risk of COVID-19 death is much greater and age dependent with type I IFN autoantibodies**	Manry J., *et al.* France gotopaper	Immunology	**Background**: SARS-CoV-2 infection fatality rate (IFR) doubles with every 5 y of age from childhood onward. Circulating autoantibodies neutralizing IFN-α, IFN-ω, and/or IFN-β are found in ∼20% of deceased patients across age groups, and in ∼1% of individuals aged <70 y and in >4% of those >70 y old in the general population. **Aim**: to estimate both IFR and relative risk of death (RRD) across age groups for individuals carrying autoantibodies neutralizing type I IFNs, relative to noncarriers. - Sample: 1,261 unvaccinated deceased patients and 34,159 individuals of the general population sampled before the pandemic. **Results** > The RRD associated with any combination of autoantibodies was higher in subjects under 70 y old. > For autoantibodies neutralizing IFN-α2 or IFN-ω, the RRDs were 17.0 (95% CI: 11.7 to 24.7) and 5.8 (4.5 to 7.4) for individuals <70 y and ≥70 y old, respectively, whereas, for autoantibodies neutralizing both molecules, the RRDs were 188.3 (44.8 to 774.4) and 7.2 (5.0 to 10.3), respectively. > In contrast, IFRs increased with age, ranging from 0.17% (0.12 to 0.31) for individuals <40 y old to 26.7% (20.3 to 35.2) for those ≥80 y old for autoantibodies neutralizing IFN-α2 or IFN-ω, and from 0.84% (0.31 to 8.28) to 40.5% (27.82 to 61.20) for autoantibodies neutralizing both. **Autoantibodies against type I IFNs increase IFRs, and are associated with high RRDs, especially when neutralizing both IFN-α2 and IFN-ω. IFRs increase with age, whereas RRDs decrease with age. Autoimmunity to type I IFNs is a strong and common predictor of COVID-19 death.**

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Nature 16MAY2022	**Characterization and antiviral susceptibility of SARS-CoV-2 Omicron/BA.2**	Uraki R., *et al.* Japan gotopaper	Virology	Aim: to evaluate the replicative ability and pathogenicity of authentic infectious BA.2 isolates in immunocompetent and human ACE2 (hACE2)-expressing mice and hamsters **Results** > In contrast to recent data with chimeric, recombinant SARS-CoV-2 strains expressing the spike proteins of BA.1 and BA.2 on an ancestral WK-521 backbone4, we observed similar infectivity and pathogenicity in mice and hamsters between BA.2 and BA.1, and less pathogenicity compared to early SARS-CoV-2 strains. > We also observed a marked and significant reduction in the neutralizing activity of plasma from COVID-19 convalescent individuals and vaccine recipients against BA.2 compared to ancestral and Delta variant strains. > In addition, we found that some therapeutic monoclonal antibodies (REGN10987/REGN10933, COV2-2196/COV2-2130, and S309) and antiviral drugs (molnupiravir, nirmatrelvir, and S-217622) can restrict viral infection in the respiratory organs of BA.2-infected hamsters **These findings suggest that the replication and pathogenicity of BA.2 is comparable to that of BA.1 in rodents and that several therapeutic monoclonal antibodies and antiviral compounds are effective against Omicron/BA.2 variants.**
PNAS 13MAY2022	**Vaccine-induced systemic and mucosal T cell immunity to SARS-CoV-2 viral variants**	Kingstad-Bakke B., *et al.* USA gotopaper	Immunology	The lack of clarity on the extent to which vaccine-elicited mucosal or systemic memory T cells protect against such antibody-evasive SARS-CoV-2 variants remains a critical knowledge gap in our quest for broadly protective vaccines. Aim: to assess whether systemic or lung-resident CD4 and CD8 T cells protected against SARS-CoV-2 variants in the presence or absence of virus-neutralizing antibodies, using an adjuvanted spike protein–based vaccines. **Results** > Mucosal or parenteral immunization led to effective viral control and protected against lung pathology with or without neutralizing antibodies, > Protection afforded by mucosal memory CD8 T cells was largely redundant in the presence of antibodies that effectively neutralized the challenge virus > "Unhelped" mucosal memory CD8 T cells provided no protection against the homologous SARS-CoV-2 without CD4 T cells and neutralizing antibodies > In the absence of detectable virus-neutralizing antibodies, systemic or lung-resident memory CD4 and "helped" CD8 T cells provided effective protection against the relatively antibody-resistant B1.351 (β) variant, without lung immunopathology. **Induction of systemic and mucosal memory T cells directed against conserved epitopes might be an effective strategy to protect against SARS-CoV-2 variants that evade neutralizing antibodies. Mechanistic insights from this work have significant implications in the development of T cell–targeted immunomodulation or broadly protective SARS-CoV-2 vaccines.**

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JAMA 13MAY2022	**Association of Prior BNT162b2 COVID-19 Vaccination With Symptomatic SARS-CoV-2 Infection in Children and Adolescents During Omicron Predominance**	Fleming-Dutra K.E., *et al.* USA gotopaper	Clinics	**Aim**: to estimate BNT162b2 VE among children 5 to 11 years old and adolescents 12 to 15 years old with COVID-19–like illness tested for SARS-CoV-2 using NAAT at drive-through US pharmacy sites from December 26, 2021, to February 21, 2022. **Methods** > Data from the Increasing Community Access to Testing (ICATT) platform were used. ICATT is an HHS program that contracts with 4 commercial pharmacy chains to facilitate drive-through SARS-CoV-2 testing nationally > When registering for SARS-CoV-2 testing, individuals or parents/guardians of minors answered a questionnaire (available in English or Spanish) to self-report demographic information. > Nasal swabs were self-collected at drive-through sites and tested for SARS-CoV-2 either onsite with the ID Now (Abbott Diagnostics Scarborough Inc) rapid nucleic acid amplification test (NAAT) or at contracted laboratories using laboratory-based NAAT (TaqPath COVID-19 Combo Kit [Thermo Fischer Scientific Inc] or COVID-19 RT-PCR Test [Laboratory Corporation of America]). > A test-negative, case-control analysis was conducted to estimate BNT162b2 VE against symptomatic infection. **Results** > In a test-negative, case-control study conducted from December 2021 to February 2022 during Omicron variant predominance that included 121 952 tests from sites across the US, estimated vaccine effectiveness against symptomatic infection for children 5 to 11 years of age was 60.1% 2 to 4 weeks after dose 2 and 28.9% during month 2 after dose 2. > Among adolescents 12 to 15 years of age, estimated vaccine effectiveness was 59.5% 2 to 4 weeks after dose 2 and 16.6% during month 2; estimated booster dose effectiveness in adolescents 2 to 6.5 weeks after the booster was 71.1%. **Among children and adolescents, estimated vaccine effectiveness for 2 doses of BNT162b2 against symptomatic infection decreased rapidly, and among adolescents increased after a booster dose.**
Lancet Infect Dis. 13MAY2022	**Venous or arterial thrombosis and deaths among COVID-19 cases: a European network cohort study**	Burn E., *et al.* International gotopaper	Clinics	**Aim**: to estimate the incidence of venous thromboembolism, arterial thromboembolism, and death among COVID-19 cases and to assess the impact of these events on the risks of hospitalisation and death. **Methods:** distributed network cohort study using primary care records from the Netherlands, Italy, Spain, and the UK, and outpatient specialist records from Germany. The Spanish database was linked to hospital admissions. Participants were followed up from the date of a diagnosis of COVID-19 or positive RT-PCR test for SARS-CoV-2 (index date) for 90 days. **Findings :** > Overall, 909 473 COVID-19 cases and 32 329 patients hospitalised with COVID-19 on or after Sept 1, 2020, were studied. The latest index dates across the databases ranged from Jan 30, 2021, to July 31, 2021. > Cumulative 90-day incidence of venous thromboembolism ranged from 0·2% to 0·8% among COVID-19 cases, and up to 4·5% for those hospitalised. > For arterial thromboembolism, estimates ranged from 0·1% to 0·8% among COVID-19 cases, increasing to 3·1% among those hospitalised. Case fatality ranged from 1·1% to 2·0% among patients with COVID-19, rising to 14·6% for hospitalised patients. > The occurrence of venous thromboembolism in patients with COVID-19 was associated with an increased risk of death (adjusted HRs 4·42 [3·07–6·36] for those not hospitalised and 1·63 [1·39–1·90] for those hospitalised), as was the occurrence of arterial thromboembolism (3·16 [2·65–3·75] and 1·93 [1·57–2·37]). **Risks of venous thromboembolism and arterial thromboembolism were up to 1% among COVID-19 cases, and increased with age, among males, and in those who were hospitalised.**

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Science Immunology 12MAY2022	**Immune recall improves antibody durability and breadth to SARS-CoV-2 variants**	Chen Y., *et al.* USA gotopaper	Immunology	**Aim**: to assess SARS-CoV-2 variant recognition, dynamics of memory B cells and secreted antibody over time after infection, vaccination, and boosting. - Virus-specific antibody durability and cross-variant breadth, analysis of neutralization breadth per unit function (i.e., evenness of cross-variant neutralization. Evolution of these features over time. **Findings** > A two-dose SARS-CoV-2 vaccination regimen given after natural infection generated greater longitudinal antibody stability and induced maximal antibody magnitudes with enhanced breadth across Beta, Gamma, Delta and Omicron variants. > A homologous 3rd mRNA vaccine dose in COVID-naïve individuals conferred greater cross-variant evenness of neutralization potency with stability that was equal to the hybrid immunity. > In unvaccinated individuals who recovered from COVID, enhanced antibody stability over time was observed in a those who recovered more quickly from COVID and harbored significantly more memory B cells cross-reactive to endemic coronaviruses early after infection. > These cross-reactive clones map to the conserved S2 region of SARS-CoV-2 spike with higher somatic hypermutation levels and greater target affinity. **SARS-CoV-2 antigen challenge histories in humans influence not only the speed and magnitude of antibody responses, but also functional cross-variant antibody repertoire composition and longevity.**
Lancet Respir Med. 11MAY2022	**Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study**	Huang L., *et al.* China gotopaper	Long Covid	**Aim**: to characterise the longitudinal evolution of health outcomes in hospital survivors with different initial disease severity throughout 2 years after acute COVID-19 infection, determine their recovery status. **Methods** > Longitudinal cohort study of 2469 individuals who survived hospitalisation with COVID-19 (Discharge: Jan 7 and May 29, 2020). > Measure of outcomes at month 6 (June 16–Sept 3, 2020), 12 (Dec 16, 2020–Feb 7, 2021), and 2 years (Nov 16, 2021–Jan 10, 2022) after symptom onset: 6-min walking distance (6MWD) test, laboratory tests, questionnaires on symptoms, mental health, health-related quality of life (HRQoL), return to work, health-care use after discharge. > A subset of COVID-19 survivors received pulmonary function tests and chest imaging at each visit. Primary outcomes: symptoms, modified MRC dyspnoea scale, HRQoL, 6MWD, and return to work, assessed in all COVID-19 survivors who attended all three follow-up visits and in controls. **Results** > 1192 COVID-19 survivors were included in the final analysis. > The proportion of COVID-19 survivors with at least one sequelae symptom decreased significantly from 777 (68%) of 1149 at 6 months to 650 (55%) of 1190 at 2 years (p<0·0001), with fatigue or muscle weakness always being the most frequent. > The proportion of COVID-19 survivors with an mMRC score of at least 1 was 168 (14%) of 1191 at 2 years, significantly lower than the 288 (26%) of 1104 at 6 months (p<0·0001). > HRQoL continued to improve in almost all domains, especially in terms of anxiety or depression: the proportion of individuals with symptoms of anxiety or depression decreased from 256 (23%) of 1105 at 6 months to 143 (12%) 1191 at 2 years (p<0·0001). > Survivors with long COVID symptoms at 2 years had lower HRQoL, worse exercise capacity, more mental health abnormality, and increased health-care use after discharge than survivors without long COVID symptoms. > A significantly higher proportion of survivors who had received higher-level respiratory support during hospitalisation had lung diffusion impairment (43 [65%] of 66 vs 24 [36%] of 66, p=0·0009), reduced residual volume (41 [62%] vs 13 [20%], p<0·0001), and total lung capacity (26 [39%] vs four [6%], p<0·0001) than did controls. **Regardless of initial disease severity, COVID-19 survivors had longitudinal improvements in physical and mental health, with most returning to their original work within 2 years; however, the burden of symptomatic sequelae remained high. COVID-19 survivors had a remarkably lower health status than the general population at 2 yrs**

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NEJM 11MAY2022	**Evaluation of mRNA-1273 Covid-19 Vaccine in Children 6 to 11 Years of Age**	Creech C.B., *et al.* USA gotopaper	Vaccines	**Aim**: to evaluate safety, immunogenicity, and efficacy of the mRNA-1273 vaccine in children 6 to 11 years of age are unknown. **Methods** - Part 1 of ongoing phase 2–3 trial: open label for dose selection; part 2: evaluation of the selected dose. - Part 2: children 6 to 11 years of age, 3:1 ratio to receive two injections of mRNA-1273 (50 µg each) or placebo, administered 28 days apart. Primary objectives: evaluation of the safety of the vaccine in children and the noninferiority of the immune response in these children to that in young adults (18 to 25 years of age) in a related phase 3 trial. Secondary objectives: incidences of confirmed Covid-19 and SARS-CoV-2 infection, regardless of symptoms. Interim analysis results are reported. **Results** > In part 1 of the trial, 751 children received 50-µg or 100-µg injections of the mRNA-1273 vaccine, and on the basis of safety and immunogenicity results, the 50-µg dose level was selected for part 2. > In part 2 of the trial, 4016 children were randomly assigned to receive two injections of mRNA-1273 (50 µg each) or placebo and were followed for a median of 82 days (interquartile range, 14 to 94) after the first injection. > This dose level was associated with mainly low-grade, transient adverse events, most commonly injection-site pain, headache, and fatigue. No vaccine-related serious adverse events, multisystem inflammatory syndrome in children, myocarditis, or pericarditis were reported as of the data-cutoff date. > One month after the second injection (day 57), neutralizing antibody titer in children who received mRNA-1273 at a 50-µg level was 1610 (95% CI, 1457 to 1780), as compared with 1300 (95% CI, 1171 to 1443) at the 100-µg level in young adults, with serologic responses in at least 99.0% of the participants in both age groups, findings that met the prespecified noninferiority success criterion. > Estimated vaccine efficacy was 88.0% (95% CI, 70.0 to 95.8) against Covid-19 occurring 14 days or more after the first injection, at a time when B.1.617.2 (delta) was the dominant circulating variant. **Two 50-µg doses of the mRNA-1273 vaccine were found to be safe and effective in inducing immune responses and preventing Covid-19 in children 6 to 11 years of age; these responses were noninferior to those in young adults.**
Nature Commun. 11MAY2022	**Off-the-shelf CAR natural killer cells secreting IL-15 target spike in treating COVID-19**	Lu T., *et al.* USA gotopaper	Therapeutics	**Aim**: to show engineering of NK cells to express (1) soluble interleukin-15 (sIL15) for enhancing their survival and (2) a chimeric antigen receptor (CAR) consisting of an extracellular domain of ACE2, targeting the spike protein of SARS-CoV-2. **Methods:** NK cells were isolated from UCB and generate CAR NK cells using a mutant (m) extracellular domain of ACE2 along with human soluble IL-15 (sIL15). We refer to these cells as mACE2-CAR_sIL15 NK cells. **Findings:** > The CAR NK cells (mACE2-CAR_sIL15 NK cells) bind to VSV-SARS-CoV-2 chimeric viral particles as well as the recombinant SARS-CoV-2 spike protein subunit S1 leading to enhanced NK cell production of TNF-α and IFN-γ and increased *in vitro* and *in vivo* cytotoxicity against cells expressing the spike protein. > Administration of mACE2-CAR_sIL15 NK cells maintains body weight, reduces viral load, and prolongs survival of transgenic mice expressing human ACE2 upon infection with live SARS-CoV-2. > These experiments, and the capacity of mACE2-CAR_sIL15 NK cells to retain their activity following cryopreservation, demonstrate their potential as an allogeneic off-the-shelf therapy for COVID-19 patients who are faced with limited treatment options. **This product provides a novel immunotherapeutic approach for treating COVID-19 infection and other SARS infections expressing the spike protein.**

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Clin Infect Dis. 10MAY2022	**Evidence of transmission and circulation of Deltacron XD recombinant SARS-CoV-2 in Northwest France**	Moisan A., *et al.* France gotopaper	Variants	**Aim**: To study 17 confirmed cases of Deltacron XD recombinant SARS-CoV-2, showing evidence of an extended transmission event and circulation of this form, with low clinical severity. **Methods** - On February 3rd , 2022, samples collected at Rouen University Hospital from a man (DOREC345) and his daughter-in-law (DOREC248), sharing the same household, showed discordant molecular results, between an in-house variant screening test and full genome next generation sequencing. These results led to a more in-depth investigation of the sequencing data. **Results** > Recombination detection algorithms suggested a Delta-Omicron recombinant form, now known as Deltacron XD, with two breakpoints: the first one, with a Delta-Omicron pattern at the beginning of the Spike Region (22034-22194) and the second, with an Omicron-Delta pattern, at the beginning of ORF3a (25469-25584). Three additional coding mutations described as signature mutations of this Deltacron XD recombinant form were observed: ORF1a:I2820V, S:A27S and S:N764K > Epidemiological investigations were conducted by phone between February 2nd and March 3rd, 2022, using a standardized questionnaire to obtain information on demographics, travel history, clinical symptoms and outcomes, risk factors, previous SARS-CoV-2 infection and vaccination status. > A total of five confirmed, one probable and 11 suspected cases of Deltacron XD recombinant SARS-CoV-2 were identified between January 19th and February 17th, 2022. > In-depth virological and epidemiological investigations have proven the transmissibility of the Deltacron XD recombinant form of SARS-CoV-2, in an intrafamilial context and related to at least one transmission cluster in school. **In conclusion, this work has shown evidence of an extended transmission event and the circulation of the Deltacron XD recombinant virus in one area of Normandy, France, which requires close surveillance and monitoring. Multiple questions remain concerning its origin, virulence, resistance and evolution that now need to be addressed**.
Science Immunol. 10MAY2022	**Antibodies induced by ancestral SARS-CoV-2 strain that cross-neutralize variants from Alpha to Omicron BA.1**	Windsor I.W., *et al.* USA gotopaper	Immunology	**Aim**: to determine the Delta- and Omicron BA.1-variant specificity of B cell repertoires established by an initial Wuhan strain infection. - Measure of neutralization potencies of 73 antibodies from an unbiased survey of the early memory B cell response. **Results** > Antibodies recognizing each of three, previously defined, epitopic regions on the spike receptor-binding domain (RBD) varied in neutralization potency and variant-escape resistance. > The ACE2 binding surface (“RBD-2”) harbored the binding sites of the neutralizing antibodies with highest potency but with the greatest sensitivity to viral escape; two other epitopic regions on the RBD (“RBD-1 and “RBD-3”) bound antibodies of more modest potency but greater breadth. > The structures of several Fab:spike complexes that neutralized all five variants of concern tested, including one Fab each from the RBD-1, -2 and -3 clusters, illustrated the determinants of broad neutralization and showed that B cell repertoires can have specificities that avoid immune escape driven by widely distributed (“public”) antibodies. > The structure of the RBD-2-binding, broad neutralizer shows why it retains neutralizing activity for Omicron BA.1, unlike most others in the same public class. **Our results correlate with real-world data on vaccine efficacy, which indicate mitigation of disease caused by Omicron BA.1.**

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Lancet HIV 10MAY2022	**Clinical features of, and risk factors for, severe or fatal COVID-19 among people living with HIV admitted to hospital: analysis of data from the WHO Global Clinical Platform of COVID-19**	Bertagnolio S., *et al.* International gotopaper	Public Health / Epidemiology	**Aim**: to assess whether people living with HIV hospitalised with COVID-19 had increased odds of severe presentation and of in-hospital mortality compared with individuals who were HIV-negative and associated risk factors. **Methods:** Platform pooled dataset from anonymised individual-level data from 338 566 patients in 38 countries reported to WHO. The authors performed descriptive statistics and regression analyses to compare outcomes in the two populations and identify risk factors between Jan 1, 2020, and July 1, 2021, **Findings:** > Of 197 479 patients reporting HIV status, 16 955 (8·6%) were people living with HIV. 16 283 (96.0%) of the 16 955 people living with HIV were from Africa; 10 603 (62·9%) were female and 6271 (37·1%) were male; the mean age was 45·5 years (SD 13·7); 6339 (38·3%) were admitted to hospital with severe illness; and 3913 (24·3%) died in hospital. > Of the 10 166 people living with HIV with known antiretroviral therapy (ART) status, 9302 (91·5%) were on ART. > Compared with individuals without HIV, people living with HIV had 15% increased odds of severe presentation with COVID-19 (aOR 1·15, 95% CI 1·10–1·20) and were 38% more likely to die in hospital (aHR 1·38, 1·34–1·41). > Among people living with HIV, male sex, age 45–75 years, and having chronic cardiac disease or hypertension increased the odds of severe COVID-19; male sex, age older than 18 years, having diabetes, hypertension, malignancy, tuberculosis, or chronic kidney disease increased the risk of in-hospital mortality. **The use of ART or viral load suppression were associated with a reduced risk of poor outcomes; however, HIV infection remained a risk factor for severity and mortality regardless of ART and viral load suppression status.**
Nature 06MAY2022	**Omicron infection enhances Delta antibody immunity in vaccinated persons**	Khan K., *et al.* South Africa gotopaper	Immunology	**Aim**: to measured SARS-CoV-2 variant neutralization capacity in 39 Omicron sub-lineage BA.1 infected individuals in South Africa **Methods** The authors measured SARS-CoV-2 variant neutralization capacity in infected individuals starting at a median of 6 (IQR 3-9) days post-symptoms onset and continuing until a last follow-up sample a median of 23 (IQR 19-27) days post-symptoms to allow BA.1 elicited neutralizing immunity time to develop. **Findings:** > BA.1 neutralization increased from a geometric mean titer (GMT) FRNT50 of 42 at enrollment to 575 at the last follow-up time-point (13.6-fold) in vaccinated and from 46 to 272 (6.0-fold) in unvaccinated participants. > Delta virus neutralization also increased, from 192 to 1091 (5.7-fold) in vaccinated and 28 to 91 (3.0-fold) in unvaccinated participants. > At the last time-point, unvaccinated BA.1 infected individuals had 2.2-fold lower BA.1 neutralization, 12.0-fold lower Delta neutralization, 9.6-fold lower Beta variant neutralization, 17.9-fold lower ancestral virus neutralization, and 4.8-fold lower Omicron sub-lineage BA.2 neutralization relative to vaccinated, with low absolute levels of neutralization for the non-BA.1 viruses. **These results indicate that vaccination combined with Omicron/BA.1 infection hybrid immunity should be protective against Delta and other variants. In contrast, infection with Omicron/BA.1 alone offers limited cross-protection despite moderate enhancement.**

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Lancet Infect Dis. 09MAY2022	**Safety, immunogenicity, and reactogenicity of BNT162b2 and mRNA-1273 COVID-19 vaccines given as fourth-dose boosters following two doses of ChAdOx1 nCoV-19 or BNT162b2 and a third dose of BNT162b2 (COV-BOOST): a multicentre, blinded, phase 2, randomised trial**	Munro A.P.S., *et al.* UK gotopaper	Vaccines	**Aim**: to investigate the safety, reactogenicity, and immunogenicity of fourth-dose booster dose of vaccine against COVID-19. **Methods** - Participants had received BNT162b2 (Pfizer-BioNTech) as their third dose in COV-BOOST and were randomly assigned (1:1) to receive a fourth dose of either BNT162b2 (30 µg in 0.30 mL; full dose) or mRNA-1273 (Moderna; 50 µg in 0.25 mL; half dose) via intramuscular injection into the upper arm. Coprimary outcomes: safety and reactogenicity, and immunogenicity. - Immunogenicity was compared at 28 days after the third dose versus 14 days after the fourth dose and at day 0 versus day 14 relative to the fourth dose. - Safety and reactogenicity were assessed in the per-protocol population, which comprised all participants who received a fourth-dose booster regardless of their SARS-CoV-2 serostatus. - Immunogenicity was primarily analysed in a modified intention-to-treat population comprising seronegative participants who had received a fourth-dose booster and had available endpoint data. **Findings** > Between Jan 11 and Jan 25, 2022, 166 participants received either full-dose BNT162b2 (n=83) or half-dose mRNA-1273 (n=83) as a fourth dose. Median age was 70.1 years (IQR 51.6–77.5) and 52% of 166 participants were female. Median interval between the third and fourth doses was 208.5 days (IQR 203.3–214.8). > Pain was the most common local solicited adverse event and fatigue was the most common systemic solicited adverse event after BNT162b2 or mRNA-1273 booster doses. None of three serious adverse events reported after a fourth dose with BNT162b2 were related to the study vaccine. > In the BNT162b2 group, geometric mean anti-spike protein IgG concentration at day 28 after the third dose was 23 325 ELISA laboratory units (ELU)/mL (95% CI 20 030–27 162), which increased to 37 460 ELU/mL (31 996–43 857) at day 14 after the fourth dose, representing a significant fold change (geometric mean 1.59, 95% CI 1.41–1.78). > There was a significant increase in geometric mean anti-spike protein IgG concentration from 28 days after the third dose (25 317 ELU/mL, 95% CI 20 996–30 528) to 14 days after a fourth dose of mRNA-1273 (54 936 ELU/mL, 46 826–64 452), with a geometric mean fold change of 2.19 (1.90–2.52). > The fold changes in anti-spike protein IgG titres from before (day 0) to after (day 14) the fourth dose were 12.19 (95% CI 10.37–14.32) and 15.90 (12.92–19.58) in the BNT162b2 and mRNA-1273 groups, respectively. > T-cell responses were also boosted after the fourth dose (eg, the fold changes for the wild-type variant from before to after the fourth dose were 7.32 [95% CI 3.24–16.54] in the BNT162b2 group and 6.22 [3.90–9.92] in the mRNA-1273 group). **Fourth-dose COVID-19 mRNA booster vaccines are well tolerated and boost cellular and humoral immunity. Peak responses after the fourth dose were similar to, and possibly better than, peak responses after the third dose.**

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Nature Immunol. 09MAY2022	**Superior immunogenicity and effectiveness of the third compared to the second BNT162b2 vaccine dose**	Lustig Y., *et al.* Israel / USA gotopaper	Vaccines	**Aim**: to assess immunogenicity, vaccine effectiveness and safety of the third BNT162b2 vaccine dose in a prospective cohort study of 12,413 healthcare workers (HCWs). **Methods:** Analysis of vaccine effectiveness, safety and immunogenicity within a large-scale cohort of HCWs in a large tertiary center in Israel, the Sheba HCW COVID cohort **Findings:** > Anti-RBD immunoglobulin G (IgG) levels were increased 1.7-fold after a third dose compared with following the second dose. > Increased avidity from 61.1% (95% confidence interval (CI), 56.1–66.7) to 96.3% (95% CI, 94.2–98.5) resulted in a 6.1-fold increase in neutralization titer. > Peri-infection humoral markers of 13 third-dose Delta variant of concern (VOC) breakthrough cases were lower compared with 52 matched controls. > Vaccine effectiveness of the third dose relative to two doses was 85.6% (95% CI, 79.2–90.1). > No serious adverse effects were reported. **These results suggest that the third dose is superior to the second dose in both quantity and quality of IgG antibodies and safely boosts protection from infection.**
Clin Infect Dis. 06MAY2022	**Clinical Validation of a Novel T-cell Receptor Sequencing Assay for Identification of Recent or Prior SARS-CoV-2 Infection**	Dalai S. C., *et al.* France gotopaper	Clinics	**Aim**: To describe the implementation and clinical validation of T-Detect™ COVID, a novel high-throughput assay that has received Emergency Use Authorization (EUA) for determining recent or prior SARS-CoV-2 infection based on T-cell receptor gene sequencing and subsequent repertoire profiling from whole blood samples. **Methods** - A statistical classifier for identifying prior SARS-CoV-2 infection was trained using >4000 SARS-CoV-2–associated TCRβ sequences identified by comparing 784 cases and 2447 controls from 5 independent cohorts. - The T-Detect™ COVID assay applies this classifier to TCR repertoires sequenced from blood samples to yield a binary assessment of past infection. - Assay performance was assessed in 2 retrospective (n = 346; n = 69) and 1 prospective cohort (n = 87) to determine positive percent agreement (PPA) and negative percent agreement (NPA). PPA was compared to 2 commercial serology assays, and pathogen cross-reactivity was evaluated. **Results** > T-Detect COVID demonstrated high PPA in individuals with prior RT-PCR–confirmed SARS-CoV-2 infection (97.1% 15 + days from diagnosis; 94.5% 15 + days from symptom onset), high NPA (~100%) in presumed or confirmed SARS-CoV-2 negative cases, equivalent or higher PPA than 2 commercial serology tests, and no evidence of pathogen cross-reactivity. **T-Detect COVID is a novel T-cell immunosequencing assay demonstrating high clinical performance for identification of recent or prior SARS-CoV-2 infection from blood samples, with implications for clinical management, risk stratification, surveillance, and understanding protective immunity and long-term sequelae.**

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Clin Microbiol Infect. 06MAY2022	**An open-label randomized, controlled trial of the effect of lopinavir/ritonavir, lopinavir/ritonavir plus IFN-β-1a and hydroxychloroquine in hospitalized patients with COVID-19 – Final results**	Ader F., *et al.* International gotopaper	Therapeutics	**Aim**: To report final analysis, after completion of data monitoring, of the DisCoVeRy trial evaluating efficacy of lopinavir/ritonavir, lopinavir/ritonavir plus IFN-β-1a and hydroxychloroquine in hospitalized patients with COVID-19. **Methods** - Phase 3 trial evaluating the efficacy and safety of repurposed drugs in adults hospitalized for COVID-19. - Eligible participants were adults (≥ 18-year-old) hospitalized with a PCR-positive (< 72 hours) SARS-CoV-2 infection and pulmonary rales or crackles with a peripheral oxygen saturation ≤ 94% or requiring supplemental oxygen. Primary endpoint: clinical status at day 15 as measured on the WHO 7-point ordinal scale. **Results** > In the final dataset, 603 participants were randomized and 593 were evaluable for analysis: control arm, n=149; lopinavir/ritonavir arm, n=147; lopinavir/ritonavir plus IFN-ß-1a arm, n=147; hydroxychloroquine arm, n=150. > Final adjusted odd ratios (aOR) for clinical improvement at day 15 were not in favour of experimental treatments: lopinavir/ritonavir vs. control, aOR 0.82 (95% CI 0.54; 1.25); lopinavir/ritonavir plus IFN-ß-1a vs. control, aOR 0.69 (95%CI 0.45; 1.05); hydroxychloroquine vs. control, aOR 0.94 (95%CI 0.62; 1.41). > In-hospital mortality was not affected by any treatment arm. > Three-month mortality was significantly higher for participants assigned to the lopinavir/ritonavir plus IFN-ß-1a arm than participants assigned to the control arm, and had a significantly longer time to hospital discharge. > The previously reported higher rate of participants experiencing any adverse event in the lopinavir/ritonavir plus IFN-ß-1a arm was no longer significant in the final dataset. > The proportion of severe adverse events remained significantly higher in both lopinavir/ritonavir-containing arms than in the control arm: control arm, n=58/149 (38.9%); lopinavir/ritonavir arm, n=76/147 (51.7%, P=0.02 vs. control); lopinavir/ritonavir plus IFN-ß-1a arm, n=80/145 (55.2%, P=0.01 vs. control). No significant difference was observed regarding safety data in the hydroxychloroquine arm. **Overall, the final results of the DisCoVeRy trial confirm what was observed in the preliminary report. They support recommendations against the use of hydroxychloroquine and lopinavir/ritonavir in hospitalized patients with COVID-19, while suggesting a detrimental effect of IFN-ß-1a treatment.**
Science Transl Med. 05MAY2022	**Adenovirus type 5 SARS-CoV-2 vaccines delivered orally or intranasally reduced disease severity and transmission in a hamster model**	Langel S.N., *et al.* USA gotopaper	Vaccines	**Background**: we have developed an orally-delivered Adenovirus type (Ad) 5-vectored SARS-CoV-2 vaccine candidate that expresses the spike protein. **Aim**: to demonstrate that hamsters vaccinated by the oral or intranasal route had robust and cross-reactive antibody responses, and to evaluate protection after post-vaccination infection with SARS-CoV-2. **Results** > Oral- or intranasal-vaccinated hamsters had decreased viral RNA and infectious virus in the nose and lungs and experienced less lung pathology compared to mock-vaccinated hamsters after SARS-CoV-2 challenge. > Naïve hamsters exposed in a unidirectional air flow chamber to mucosally-vaccinated, SARS-CoV-2-infected hamsters also had lower nasal swab viral RNA and exhibited fewer clinical symptoms than control animals, suggesting that the mucosal-route reduced viral transmission. > The same platform encoding the SARS-CoV-2 spike and nucleocapsid proteins elicited mucosal cross-reactive SARS-CoV-2-specific IgA responses in a phase 1 clinical trial. **These data demonstrate that mucosal immunization is a viable strategy to decrease SARS-CoV-2 disease and airborne transmission.**

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NEJM 04MAY2022	**Efficacy and Safety of a Recombinant Plant-Based Adjuvanted Covid-19 Vaccine**	Hager K.J., *et al.* International gotopaper	Vaccines	**Aim**: to evaluate a candidate vaccine based on Coronavirus-like particles (CoVLP) that are produced in plants and display the prefusion spike glycoprotein of the original strain of SARS-CoV-2 that are combined with an adjuvant (Adjuvant System 03 [AS03]). **Methods** - Phase 3 trial conducted on adults (≥18 years of age), 1:1 ratio randomization, receiving either two intramuscular injections of the CoVLP+AS03 vaccine or placebo 21 days apart. Primary objective: efficacy of the CoVLP+AS03 vaccine in preventing symptomatic Covid-19 beginning ≥7 days after the second injection. **Results** > A total of 24,141 volunteers participated in the trial; the median age of the participants was 29 years. Covid-19 was confirmed by PCR in 165 participants in the intention-to-treat population; all viral samples that could be sequenced contained variants of the original strain. > Vaccine efficacy was 69.5% (95% CI, 56.7 to 78.8) against any symptomatic Covid-19 caused by 5 variants identified by sequencing. > In a post hoc analysis, vaccine efficacy was 78.8% (95% CI, 55.8 to 90.8) against moderate-to-severe disease and 74.0% (95% CI, 62.1 to 82.5) among the participants who were seronegative at baseline. > No severe cases of Covid-19 occurred in the vaccine group, in which the median viral load for breakthrough cases was lower than that in the placebo group by a factor of more than 100. > Solicited adverse events were mostly mild or moderate and transient and were more frequent in the vaccine group than in the placebo group; local adverse events occurred in 92.3% and 45.5% of participants, respectively, and systemic adverse events in 87.3% and 65.0%. The incidence of unsolicited adverse events was similar in the two groups up to 21 days after each dose (22.7% and 20.4%) and from day 43 through day 201 (4.2% and 4.0%). **The CoVLP+AS03 vaccine was effective in preventing Covid-19 caused by a spectrum of variants, with efficacy ranging from 69.5% against symptomatic infection to 78.8% against moderate-to-severe disease.**
NEJM 04MAY2022	**Efficacy and Safety of the RBD-Dimer–Based Covid-19 Vaccine ZF2001 in Adults**	Dai L., *et al.* China gotopaper	Vaccines	**Aim**: to evaluate efficacy and confirm safety of the ZF2001 vaccine, which contains a dimeric form of the receptor-binding domain of SARS-CoV- 2 and aluminum hydroxide as an adjuvant. **Methods** - Phase 3 trial on adult participants (≥18 years of age), randomly assigned in a 1:1 ratio to receive a total of three 25-µg doses (30 days apart) of ZF2001 or placebo. Primary end point: occurrence of symptomatic Covid-19, as confirmed by PCR, at least 7 days after receipt of the third dose. Key secondary efficacy end point: severe-to-critical Covid-19 (including Covid-19–related death) ≥7 days after receipt of third dose. **Results** > Between December 12, 2020, and December 15, 2021, a total of 28,873 participants received at least one dose of ZF2001 or placebo and were included in the safety analysis; 25,193 participants who had completed the three-dose regimen, for whom there were approximately 6 months of follow-up data, were included in the updated primary efficacy analysis that was conducted at the second data cutoff date of December 15, 2021. > In the updated analysis, primary end-point cases were reported in 158 of 12,625 participants in the ZF2001 group and in 580 of 12,568 participants in the placebo group, for a vaccine efficacy of 75.7% (95% CI, 71.0 to 79.8). > Severe-to-critical Covid-19 occurred in 6 participants in the ZF2001 group and in 43 in the placebo group, for a vaccine efficacy of 87.6% (95% CI, 70.6 to 95.7); Covid-19–related death occurred in 2 and 12 participants, respectively, for a vaccine efficacy of 86.5% (95% CI, 38.9 to 98.5). > The incidence of adverse events and serious adverse events was balanced in the two groups, and there were no vaccine-related deaths. Most adverse reactions (98.5%) were of grade 1 or 2. **The ZF2001 vaccine was safe and effective against symptomatic and severe-to-critical Covid-19 for at least 6 months after full vaccination.**

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NEJM 04MAY2022	**Effectiveness of Ad26.COV2.S and BNT162b2 Vaccines against Omicron Variant in South Africa**	Gray G., *et al.* South Africa gotopaper	Vaccines - Immunisation	**Aim**: to estimate the vaccine effectiveness of the original two-dose series of the BNT162b2 vaccine and a second (booster) dose of the Ad26.COV2.S vaccine against severe Covid-19 (hospitalization or admission to an ICU or to high care) caused by the omicron variant. **Methods** - Comparison of vaccine effectiveness against severe Covid-19 during the period from November 15, 2021, to January 14, 2022 (omicron-driven fourth wave) - Vaccine effectiveness was compared between the two vaccine groups according to the number of days since the second vaccine dose had been administered (0 to 13 days, 14 to 27 days, 28 to 87 days [1 to 2 months], 88 to 147 days [3 to 4 months], and 148 days [5 months] or longer) **Results** > Analysis of the results of 162,637 PCR tests, of which 93,854 (57.7%) had been obtained from participants who had received two doses of the BNT162b2 vaccine given at least 42 days apart or two doses of the Ad26.COV2.S vaccine given 4 to 6 months apart. > Among these participants, the test positivity rate was 34%; of those with a positive PCR test, 1.6% had been admitted to a hospital and 0.5% to an ICU or to high care. > Among the participants in the Ad26.COV2.S vaccine group, the vaccine effectiveness against hospitalization for Covid-19 was 55% (95% CI, 22 to 74) within 13 days after the second dose, 74% (95% CI, 57 to 84) at 14 to 27 days, and 72% (95% CI, 59 to 81) at 1 to 2 months. > Among the participants in the BNT162b2 vaccine group, the vaccine effectiveness was 81% (95% CI, 41 to 94) within 13 days after the second dose, 88% (95% CI, 62 to 96) at 14 to 27 days, 70% (95% CI, 64 to 76) at 1 to 2 months, 71% (95% CI, 68 to 74) at 3 to 4 months, and 67% (95% CI, 63 to 71) at 5 months or longer. > Among the Ad26.COV2.S vaccine recipients, the vaccine effectiveness against ICU admission or high care was 69% (95% CI, 26 to 87) at 14 to 27 days and 82% (95% CI, 57 to 93) at 1 to 2 months after the second dose > Among the BNT162b2 vaccine recipients, the vaccine effectiveness against ICU admission or high care was 70% (95% CI, 56 to 79) at 1 to 2 months, 73% (95% CI, 67 to 77) at 3 to 4 months, and 71% (95% CI, 65 to 76) at 5 months or longer. **After two doses, both vaccines were equally effective against severe disease caused by the omicron variant.** These estimates were calculated in a South African population with a high background prevalence of SARS-CoV-2 exposure during the Covid-19 pandemic.
Science Transl Med. 03MAY2022	**The rapid replacement of the Delta variant by Omicron (B.1.1.529) in England**	Paton R. S., *et al.* UK gotopaper	Public Health / Epidemiology	**Aim**: to develope a set of hierarchical logistic growth models to describe changes in the frequency of S gene target failure (SGTF) PCR tests, which was a proxy for Omicron **Results** > The doubling time of SGTF cases peaked at 1.56 days (95% CI: 1.49, 1.63) on the 5th of December, while triple positive cases were halving every 5.82 days (95% CI: 5.11, 6.67) going into Christmas 2021. > We were unable to characterize the replacement of Delta by Omicron with a single rate. The replacement rate decreased by 53.56% (95% CrI: 45.38, 61.01) between the 14th and 15th of December, meaning the competitive advantage of Omicron approximately halved. > Preceding the changepoint, Omicron was replacing Delta 16.24% (95% CrI: 9.72, 23.41) faster in those with two or more vaccine doses, indicative of vaccine escape being a substantial component of the competitive advantage. Despite the slowdown, Delta had almost entirely been replaced in England within a month of the first sequenced domestic case. **The synchrony of changepoints across regions at various stages of Omicron epidemics suggests that the growth rate advantage was not attenuated due to biological mechanisms related to strain competition. The step-change in replacement could have resulted from behavioral changes, potentially elicited by public health messaging or policies, that differentially affected Omicron.**

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Lancet 02MAY2022	**Remdesivir and three other drugs for hospitalised patients with COVID-19: final results of the WHO Solidarity randomised trial and updated meta-analyses**	WHO Solidarity Trial Consortium International gotopaper	Therapeutics	**Aim**: to report the final results of Solidarity and meta-analyses of mortality in all relevant trials to date. **Methods** - Solidarity enrolled consenting adults (aged ≥18 years) recently hospitalised with definite COVID-19, regardless of any other patient characteristics. - Four study drugs (lopinavir, hydroxychloroquine, IFN-β1a, or remdesivir) were locally available at that time or no study drug (controls). All patients also received the local standard of care. - Protocol-specified primary endpoint: in-hospital mortality, subdivided by disease severity. - Secondary endpoints: progression to ventilation if not already ventilated, and time-to-discharge from hospital. **Findings** > Between March 22, 2020, and Jan 29, 2021, 14 221 patients were recruited from 454 hospitals in 35 countries in all six WHO regions, which included 8275 randomly allocated (1:1) either to remdesivir (ten daily infusions, unless discharged earlier) or to its control (allocated no study drug although remdesivir was locally available). Compliance was high in both groups. > Overall, 602 (14.5%) of 4146 patients assigned to remdesivir died versus 643 (15.6%) of 4129 assigned to control (mortality rate ratio [RR] 0.91 [95% CI 0.82–1.02], p=0.12). > Of those already ventilated, 151 (42.1%) of 359 assigned to remdesivir died versus 134 (38.6%) of 347 assigned to control (RR 1.13 [0.89–1.42], p=0.32). > Of those not ventilated but on oxygen, 14.6% assigned to remdesivir died versus 16.3% assigned to control (RR 0.87 [0.76–0.99], p=0.03). > Of 1730 not on oxygen initially, 2.9% assigned to remdesivir died versus 3.8% assigned to control (RR 0.76 [0.46–1.28], p=0.30). > Combining all those not ventilated initially, 11.9% assigned to remdesivir died versus 13.5% assigned to control (RR 0.86 [0.76–0.98], p=0.02) and 14.1% versus 15.7% progressed to ventilation (RR 0.88 [0.77–1.00], p=0.04). > The non-prespecified composite outcome of death or progression to ventilation occurred in 19.6% assigned to remdesivir versus 22.5% assigned to control (RR 0.84 [0.75–0.93], p=0.001). > Allocation to daily remdesivir infusions (vs open-label control) delayed discharge by about 1 day during the 10-day treatment period. A meta-analysis of mortality in all randomised trials of remdesivir versus no remdesivir yielded similar findings. **Remdesivir has no significant effect on patients with COVID-19 who are already being ventilated. Among other hospitalised patients, it has a small effect against death or progression to ventilation (or both).**
Cell 02MAY2022	**Virological characteristics of the SARS-CoV-2 Omicron BA.2 spike**	Yamasoba D., *et al.* Japan gotopaper	Virology	**Aim**: to study the virological characteristic of Omicron BA.2 as compared with BA.1. **Results** > Statistical analysis showed that the effective reproduction number of BA.2 is 1.4-fold higher than that of BA.1. > Neutralization experiments revealed that immunity induced by COVID vaccines widely administered to human populations is not effective against BA.2, similar to BA.1, and that the antigenicity of BA.2 is notably different from that of BA.1. > Cell culture experiments showed that the BA.2 spike confers higher replication efficacy in human nasal epithelial cells and is more efficient in mediating syncytia formation than the BA.1 spike. > Infection experiments using hamsters indicated that the BA.2 spike-bearing virus is more pathogenic than the BA.1 spike-bearing virus. **The results of this multiscale investigations suggest that the risk of BA.2 to global health is potentially higher than that of BA.1.**

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Lancet HIV 01MAY2022	**Immunogenicity and safety of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine in people living with and without HIV-1 infection: a randomised, controlled, phase 2A/2B trial**	Mahdi S. A., *et al.* South Africa gotopaper	Vaccines	**Aim**: to evaluate the safety and immunogenicity of a Matrix-M adjuvanted recombinant spike protein nanoparticle COVID-19 vaccine (NVX-CoV2373; Novavax) in HIV-negative people and people living with HIV-1. Methods > In this randomised, observer-blinded, multicentre, placebo-controlled phase 2A/B trial in South Africa, participants aged 18–84 years, with and without underlying HIV-1, were enrolled from 16 sites and randomly assigned (1:1) to receive two intramuscular injections of NVX-CoV2373 or placebo, 21 days apart. > People living with HIV-1 were on stable antiretroviral therapy and had an HIV-1 viral load of less than 1000 copies per mL. > Vaccine dosage was 5 µg SARS-CoV-2 recombinant spike protein with 50 µg Matrix-M adjuvant, whereas 0·9% saline was used as placebo injection (volume 0·5 mL each). > All study staff and participants remained masked to study group assignment. **Results** > Participants were enrolled between Aug 17 and Nov 25, 2020. > The safety analysis set included 4164 HIV-negative participants (2089 in the intervention group and 2075 in the placebo group) and 244 people living with HIV-1 (122 in the intervention group and 122 in the placebo group). 1422 (34·1%) of 4164 HIV-negative people and 83 (34·0%) of 244 people living with HIV-1 were categorised as baseline SARS-CoV-2-positive. > In the NVX-CoV2373 group, solicited local and systemic adverse events were more common in HIV-negative participants (427 [30·6%] local and 401 [28·7%] systemic) than in people living with HIV-1 (20 [25·3%] local and 20 [25·3%] systemic) among those who were baseline SARS-CoV-2-seronegative (naive). > Of the serious adverse events that occurred among HIV-negative people (of whom, two [0·1%] were baseline SARS-CoV-2-negative and four [0·6%] were baseline SARS-CoV-2-positive) and people living with HIV-1 (for whom there were no serious adverse events) in the NVX-CoV2373 group, none were assessed as related to the vaccine. > Among participants who were baseline SARS-CoV-2-negative in the NVX-CoV2373 group, the anti-spike IgG geometric mean titres (GMTs) and seroconversion rates (SCRs) were lower in people living with HIV-1 (n=62) than in HIV-negative people (n=1234) following the first vaccination (GMT: 508·6 vs 1195·3 ELISA units [EU]/mL; SCR: 51·6% vs 81·3%); and similarly so 14 days after the second vaccination for GMTs (14 420·5 vs 31 631·8 EU/mL), whereas the SCR was similar at this point (100·0% vs 99·3%). > In the NVX-CoV2373 group, anti-spike IgG GMTs 14 days after the second vaccination were substantially higher in those who were baseline SARS-CoV-2-positive than in those who were baseline SARS-CoV-2-seronegative for HIV-negative participants (100 666·1 vs 31 631·8 EU/mL) and for people living with HIV-1 (98 399·5 vs 14 420·5 EU/mL). This was also the case for angiotensin-converting enzyme 2 receptor-binding antibody and neutralising antibody titres. **The safety of the NVX-CoV2373 vaccine in people living with HIV-1 was similar to that in HIV-negative participants. However, people living with HIV-1 not previously exposed to SARS-CoV-2 had attenuated humoral immune responses to NVX-CoV2373 compared with their HIV-negative vaccine counterparts, but not so if they were baseline SARS-CoV-2-positive.**

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eClinical Medicine 01MAY2022	**Multivariate profile and acute-phase correlates of cognitive deficits in a COVID-19 hospitalised cohort**	Hampshire A., *et al.* UK gotopaper	Clinics	**Aim**: to determine whether cognitive deficits relate to clinical features from the acute phase or to mental health status at the point of assessment, and quantify rate of recovery. **Methods:** Detailed computerised cognitive assessment to assess patients at timepoints ranging from between 1 and 10 months post admission to hospital for severe COVID-19. Global accuracy and response time composites were calculated (G_SScore & G_RT). Linear modelling predicted composite score deficits from acute severity, mental-health status at assessment, and time from hospital admission. The pattern of deficits across tasks was qualitatively compared with normal age-related decline, and early-stage dementia. **Findings:** >COVID-19 survivors were less accurate (G_SScore=-0.53SDs) and slower (G_RT=+0.89SDs) in their responses than expected compared to their matched controls. > Acute illness, but not chronic mental health, significantly predicted cognitive deviation from expected scores (G_SScore (p=0.0037) and G_RT (p = 0.0366)). > The most prominent task associations with COVID-19 were for higher cognition and processing speed, which was qualitatively distinct from the profiles of normal ageing and dementia and similar in magnitude to the effects of ageing between 50 and 70 years of age. **Cognitive deficits after severe COVID-19 relate most strongly to acute illness severity, persist long into the chronic phase, and recover slowly if at all, with a characteristic profile highlighting higher cognitive functions and processing speed.**
Lancet Reg Health Eur. 29APR2022	**Hyper inflammatory syndrome following COVID-19 mRNA vaccine in children: A national post-authorization pharmacovigilance study**	Ouldali N., *et al.* France gotopaper	Vaccines	**Aim**: to assess the risk of hyper-inflammatory syndrome following COVID-19 mRNA vaccine in children. **Methods** > Post-authorization national population-based surveillance using the French enhanced pharmacovigilance surveillance system for COVID-19 vaccines > All cases of suspected hyper-inflammatory syndrome following COVID-19 mRNA vaccine in 12–17-year-old children between June 15th, 2021 and January 1st, 2022, were reported **Results** > Up to January 2022, 8,113,058 COVID-19 mRNA vaccine doses were administered to 4,079,234 12–17-year-old children. Among them, 12 presented a hyper-inflammatory syndrome with multisystemic involvement. > Main clinical features included male predominance (10/12, 83%), cardiac involvement (10/12, 83%), digestive symptoms (10/12, 83%), coagulopathy (7/12, 58%), cytolytic hepatitis (6/12, 50%), and shock (5/12, 42%). > 4/12 (33%) required intensive care unit transfer, and 3/12 (25%) hemodynamic support. All cases recovered. > In eight cases, no evidence of previous SARS-CoV-2 infection was found. The reporting rate was 1.5 (95%CI [0.8; 2.6]) per 1,000,000 doses injected, i.e. 2.9 (95%CI [1.5; 5.1]) per 1,000,000 12–17-year-old vaccinated children. As a comparison, 113 MIS-C (95%CI [95; 135]) occurred per 1,000,000 12–17-year-old children infected by SARS-CoV-2. **Very few cases of hyper-inflammatory syndrome with multi-organ involvement occurred following COVID-19 mRNA vaccine in 12–17-year-old children. The low reporting rate of this syndrome, compared to the rate of post-SARS-CoV-2 MIS-C in the same age-group, largely supports the vaccination in a context of an important circulation of SARS-CoV-2.**

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JAMA Netw Open 29APR2022	**Comparison of Home Antigen Testing With RT-PCR and Viral Culture During the Course of SARS-CoV-2 Infection**	Chu T. V., *et al.* USA gotopaper	Diagnostics	**Aim**: to evaluate the diagnostic performance of home antigen tests compared with RT-PCR and viral culture by days from illness onset, as well as user acceptability. **Methods** > This prospective cohort study was conducted from January to May 2021 in San Diego County, California, and metropolitan Denver, Colorado > The primary outcome was the daily sensitivity of home antigen tests to detect RT-PCR–confirmed cases. **Results** > This study enrolled 225 persons with RT-PCR–confirmed infection (median [range] age, 29 [1-83] years; 117 female participants [52%]; 10 [4%] Asian, 6 [3%] Black or African American, 50 [22%] Hispanic or Latino, 3 [1%] Native Hawaiian or Other Pacific Islander, 145 [64%] White, and 11 [5%] multiracial individuals) who completed 3044 antigen tests and 642 nasopharyngeal swabs. > Antigen test sensitivity was 50% (95% CI, 45%-55%) during the infectious period, 64% (95% CI, 56%-70%) compared with same-day RT-PCR, and 84% (95% CI, 75%-90%) compared with same-day cultures. > Antigen test sensitivity peaked 4 days after illness onset at 77% (95% CI, 69%-83%). Antigen test sensitivity improved with a second antigen test 1 to 2 days later, particularly early in the infection. Six days after illness onset, antigen test result positivity was 61% (95% CI, 53%-68%). > Almost all (216 [96%]) surveyed individuals reported that they would be more likely to get tested for SARS-CoV-2 infection if home antigen tests were available over the counter. **These resultssuggest thatantigen test sensitivity for SARS-CoV-2 was moderate compared with RT-PCR and high compared with viral culture. The results also suggest that symptomatic individuals with an initial negative home antigen test result for SARS-CoV-2 infection should test again 1 to 2 days later because test sensitivity peaked several days after illness onset and improved with repeated testing.**
Nature 28APR2022	**Inflammasome activation in infected macrophages drives COVID-19 pathology**	Sefik E., *et al.* USA gotopaper	Immunology	**Aim**: to assess the role of viral infection on the inflammatory macrophage response, the activation of inflammasomes and pyroptosis. **Methods:** Mechanistic study of the MISTRG6 COVID-19 mice model. **Findings:** > SARS-CoV-2 infection and replication in lung-resident human macrophages is a critical driver of disease. In response to infection mediated by CD16 and ACE2 receptors, human macrophages activate inflammasomes, release IL-1 and IL-18 and undergo pyroptosis thereby contributing to the hyperinflammatory state of the lungs. > Inflammasome activation and its accompanying inflammatory response is necessary for lung inflammation, as inhibition of the NLRP3 inflammasome pathway reverses chronic lung pathology. > Remarkably, this same blockade of inflammasome activation leads to the release of infectious virus by the infected macrophages. **Inflammasomes oppose host infection by SARS-CoV-2 by production of inflammatory cytokines and suicide by pyroptosis to prevent a productive viral cycle.**

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BMJ 27APR2022	**Development and validation of the symptom burden questionnaire for long covid (SBQ-LC): Rasch analysis**	Hughes S. E., *et al.* UK gotopaper	Long Covid	**Aim**: to describe the development and validation of a novel patient reported outcome measure for symptom burden from long covid, the symptom burden questionnaire for long covid (SBQ-LC). **Methods:** Multiphase, prospective mixed methods study. Remote data collection and social media channels in the UK, 14 April-1 Aug 2021. **Findings:** > SBQ-LC (version 1.0) is a modular instrument measuring patient reported outcomes and is composed of 17 independent scales with promising psychometric properties. Respondents rate their symptom burden during the past seven days using a dichotomous response or 4 point rating scale. > Each scale provides coverage of a different symptom domain and returns a summed raw score that can be transformed to a linear (0-100) score. Higher scores represent higher symptom burden. > After rating scale refinement and item reduction, all scales satisfied the Rasch model requirements for unidimensionality (principal component analysis of residuals: first residual contrast values <2.00 eigenvalue units) and item fit (outfit mean square values within 0.5 - 1.5 logits). > Across the 17 scales, person reliability ranged from 0.34 to 0.87, person separation ranged from 0.71 to 2.56, item separation ranged from 1.34 to 13.86, and internal consistency reliability (Cronbach's alpha) ranged from 0.56 to 0.91. **SBQ-LC (version 1.0) is a comprehensive patient reported outcome instrument developed using modern psychometric methods. It measures symptoms of long covid important to people with lived experience of the condition and may be used to evaluate the impact of interventions and inform best practice in clinical management.**
PNAS 27APR2022	**An ensemble model based on early predictors to forecast COVID-19 health care demand in France**	Paireau J., *et al.* France gotopaper	Public Health / Epidemiology	**Aim**: to design an ensemble that combines several models to anticipate French COVID-19 health care needs. - Performance of 12 individual models and 19 predictors to anticipate French COVID-19-related health care needs from September 7, 2020, to March 6, 2021. - Ensemble model by combining the individual forecasts and retrospectively test this model from March 7, 2021, to July 6, 2021. **Findings:** > The inclusion of early predictors (epidemiological, mobility, and meteorological predictors) can halve the rms error for 14-d–ahead forecasts, with epidemiological and mobility predictors contributing the most to the improvement. > On average, the ensemble model is the best or second-best model, depending on the evaluation metric. **This approach facilitates the comparison and benchmarking of competing models through their integration in a coherent analytical framework**
Nature Commun. 27APR2022	**Safety and serum distribution of anti-SARS-CoV-2 monoclonal antibody MAD0004J08 after intramuscular injection**	Lanini S., *et al.* Italy gotopaper	Therapeutics	**Background**: MAD0004J08 is a potent Fc-engineered monoclonal antibody (mAb) able to neutralize in vitro all current SARS-CoV-2 VoCs including omicron variant even if with significantly reduced potency. **Aim**: to evaluate data obtained from the first 30 days of a phase 1 clinical study. Primary endpoint: percentage of severe adverse events. Secondary endpoints: pharmacokinetic and serum neutralization titers. **Results** > A single dose administration of MAD0004J08 via intramuscular (i.m.) route is safe and well tolerated, resulting in rapid serum distribution and sera neutralizing titers higher than COVID-19 convalescent and vaccinated subjects. > A single dose administration of MAD0004J08 is also sufficient to effectively neutralize major SARS-CoV-2 VOCs (alpha, beta, gamma and delta). **MAD0004J08 can be a major advancement in the prophylaxis and clinical management of COVID-19.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
BMJ 27APR2022	**Public health impact of covid-19 vaccines in the US: observational study**	Suthar A.B., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim**: To evaluate the impact of vaccine scale-up on population level covid-19 mortality and incidence in the United States. Methods > Observational study : US county level case surveillance and vaccine administration data reported from 14 December 2020 to 18 December 2021, including residents of 2558 counties from 48 US states. **Results** > In total, 30 643 878 cases of covid-19 and 439 682 deaths associated with covid-19 occurred over 132 791 county weeks. > A 10% improvement in vaccination coverage was associated with an 8% (95% confidence interval 8% to 9%) reduction in mortality rates and a 7% (6% to 8%) reduction in incidence. > Higher vaccination coverage levels were associated with reduced mortality and incidence rates during the eras of alpha and delta variant predominance. **Higher vaccination coverage was associated with lower rates of population level covid-19 mortality and incidence in the US.**
BMC 07APR2022	**Personal and professional quality of life among French health care workers during the first COVID-19 wave: a cross-sectional study**	Grelier A., *et al.* France gotopaper	Public Health / Epidemiology	**Methods** > All health care workers from our hospital were invited to fill-in an anonymous e-questionnaire of 71 questions regarding perceived personal, professional and overall quality of life before and during the first COVID-19 wave, general profile, occupation and job characteristics, change of assignment, COVID-care features if relevant, general perception during the first wave, and personal experience of being encouraged or stigmatised. **Results** > There were 794 participants, with a majority of nursing professionals (n = 416, 56%), including 57 nurse managers, 243 nurses, and 116 nurse assistants. Other participants were physicians (n = 188) and other health care staff (n = 140). > Before the crisis, professional quality of life was low (6.5 on a 10-point scale) overall. The personal quality of life was higher (8.1) particularly for physicians and nurse managers. > The COVID crisis saw a marked decrease in the personal quality of life (− 1.7), more pronounced in younger health care workers. Professional quality of life was less affected (− 0.4) and stayed almost constant for physicians. Staff in COVID units had a more positive perception of the crisis but experienced more fatigue, which resulted in similar quality of life levels in COVID and non-COVID units. > Encouragements originated more often from relatives or colleagues than hospital managers and were exceptionally common: 63.4% of all participants, from 50.5% for other staff to 71.3% for physicians (p = 0.0005). Stigmatisation was reported by 19.3% of participants, with a higher proportion (p = 0.0001) among nurses (26.3%) and assistant nurses (23.3%) than among physicians (8.5%). > From multivariate analysis, higher age, working as a physician and receiving encouragements were independently associated with lower loss of overall quality of life. **The resilience of health care workers was high overall during the first COVID wave although the quality of life decreased more among nursing staff. Social support in the form of encouragements is a key part of management, particularly in times of crisis.**

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Cell 27APR2022	**Protective prototype-Beta and Delta-Omicron chimeric RBD-dimer vaccines against SARS-CoV-2**	Xu K., *et al.* China gotopaper	Vaccines	**Aim**: to develop a chimeric RBD-dimer vaccine approach to adapt SARS-CoV-2 variants. **Results** > A prototype-Beta chimeric RBD-dimer was first designed to adapt the resistant Beta variant. > Compared with its homotypic forms, the chimeric vaccine elicited broader sera neutralization of variants and conferred better protection in mice. The protection of the chimeric vaccine was further verified in macaques. > This approach was generalized to develop Delta-Omicron chimeric RBD-dimer to adapt the currently prevalent variants. > This chimeric vaccine elicited broader sera neutralization of SARS-CoV-2 variants, and conferred better protection against challenge by either Delta or Omicron SARS-CoV-2 in mice. **The chimeric approach is applicable for rapid updating of immunogens, and our data supported the use of variant-adapted multivalent vaccine against circulating and emerging variants.**
Clin Infect Dis. 27APR2022	**Cumulative Incidence and Risk Factors for Severe COVID-19 in French People with Cystic Fibrosis**	Corvol H., *et al.* France gotopaper	Epidemiology	**Aim**: to evaluate data from COVID-19 cases diagnosed in French people with cystic fibrosis (pwCF) followed in one of the 47 French CF center over the first year of the pandemic. **Methods** > Criteria were applied for defining severity (e.g., respiratory failure and/or death). Data were compared to those from all French pwCF using the French CF Registry. **Results** > As of April 30, 2021, 223 pwCF were diagnosed with COVID-19, with higher risks in adults (≥18 years, odds ratio [OR] = 2.52, 95% confidence interval [CI] = 1.82-3.48) and post-transplant individuals (OR = 2.68, 95% CI = 1.98-3.63). > 60 (26.9%) patients were hospitalized, with an increased risk in post-transplant individuals (OR = 4.74, 95% CI = 2.49-9.02). In 34 (15%) cases, COVID-19 was severe; 28/60 (46.7%) hospitalizations occurred in patients without objective criteria of severity. > Severe cases occurred mostly in adults (85.3%) and post-transplant pwCF (61.8%, OR = 6.02, 95% CI = 2.77-13.06). In non-transplanted pwCF, risk factors for severity included low lung function (median ppFEV1 54.6% vs. 75.1%, OR = 1.04, 95% CI = 1.01-1.08) and CF-associated diabetes (OR = 3.26, 95% CI = 1.02-10.4). > While most cases recovered without sequelae (n = 204, 91.5%), 16 (13%) were followed for possible sequelae, and three post-transplant females died. **Severe COVID-19 cases occurred infrequently during the first year of the pandemic in French pwCF. Non-transplanted adults with severe respiratory disease or diabetes and post-transplant individuals were at risk for severe COVID-19.**
Science Immunol. 26APR2022	**An ACE2-blocking antibody confers broad neutralization and protection against Omicron and other SARS-CoV-2 variants of concern**	Du W., *et al.* International gotopaper	Therapeutics	**Aim**: to identify a SARS-CoV-2 human monoclonal antibody with potent and broad neutralizing activity against SARS-CoV-2 and VOC. **Methods:** **- C**haracteriation the antibody binding kinetics and affinity, epitope location and mechanism of neutralization**.** - Analysis *in vivo* of prophylactic and therapeutic activity against ancestral and variant SARS-CoV-2 using two animal disease models **Findings:** > A receptor-blocking human monoclonal antibody was identified, 87G7, that retained potent *in vitro* neutralizing activity against SARS-CoV-2 variants including the Alpha, Beta, Gamma, Delta and Omicron (BA.1/BA.2) VOCs. > 87G7 targets a patch of hydrophobic residues in the ACE2-binding site that are highly conserved in SARS-CoV-2 variants, explaining its broad neutralization capacity. > 87G7 protected mice and/or hamsters prophylactically against challenge with all current SARS-CoV-2 VOCs, and showed therapeutic activity against SARS-CoV-2 challenge in both animal models. **87G7 holds promise as a prophylactic or therapeutic agent for COVID-19 that is more resilient to SARS-CoV-2 antigenic diversity.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Med. 25APR2022	**Effectiveness of a second BNT162b2 booster vaccine against hospitalization and death from COVID-19 in adults aged over 60 years**	Arbel R., *et al.* Israel gotopaper	Vaccines	Retrospective cohort study included all members of Clalit Health Services, aged 60 to 100 years, who were eligible for the second-booster on January 3, 2022. **Methods** > Hospitalizations and mortality due to COVID-19 among participants who received the second-booster were compared with participants who received one booster dose. > Cox proportional-hazards regression models with time-dependent covariates were used to estimate the association between the second-booster and hospitalizations and death due to COVID-19 while adjusting for demographic factors and coexisting illnesses. **Results** > A total of 563,465 participants met the eligibility criteria. Of those, 328,597 (58%) received a second-booster dose during the 40-day study period. > Hospitalizations due to COVID-19 occurred in 270 of the second-booster recipients and in 550 participants who received one booster dose (adjusted hazard ratio 0.36; 95% confidence interval (CI): 0.31 to 0.43). > Death due to COVID-19 occurred in 92 second-booster recipients and in 232 participants who received one booster dose (adjusted hazard ratio 0.22; 95% CI 0.17 to 0.28). **This study demonstrates a substantial reduction in hospitalizations and deaths due to Covid-19 conferred by a second-booster in Israeli adults aged 60 years and over.**
JAMA Netw Open 22APR2022	**Assessment of T-cell Reactivity to the SARS-CoV-2 Omicron Variant by Immunized Individuals**	De Marco L., *et al.* Italy gotopaper	Immunology	**Aim**: to determine T-cell reactivity to the Omicron variant in individuals with established (natural and/or vaccine-induced) immunity to SARS-CoV-2. **Methods** > This was a cohort study conducted between December 20 and 21, 2021, in Italy, among health care worker and scientist volunteers. Lymphocytes from freshly drawn blood samples were isolated and immediately tested for reactivity to the spike protein of SARS-CoV-2. > The main outcomes were the measurement of T-cell reactivity to the mutated regions of the spike protein of the Omicron BA.1 SARS-CoV-2 variant and the assessment of remaining T-cell immunity to the spike protein by stimulation with peptide libraries. **Results** > A total of 61 volunteers (mean (range) age, 41.62 (21-62) years; 38 women [62%]) with different vaccination and SARS-CoV-2 infection backgrounds were enrolled. > The median (range) frequency of CD4+ T cells reactive to peptides covering the mutated regions in the Omicron variant was 0.039% (0%-2.356%), a decrease of 64% compared with the frequency of CD4+ cells specific for the same regions of the ancestral strain (0.109% [0%-2.376%]). > Within CD8+ T cells, a median (range) of 0.02% (0%-0.689%) of cells recognized the mutated spike regions, while 0.039% (0%-3.57%) of cells were reactive to the equivalent unmutated regions, a reduction of 49%. > However, overall reactivity to the peptide library of the full-length protein was largely maintained (estimated 87%). No significant differences in loss of immune recognition were identified between groups of participants with different vaccination or infection histories. **This cohort study of immunized adults in Italy found that despite the mutations in the spike protein, the SARS-CoV-2 Omicron variant was recognized by the cellular component of the immune system. It is reasonable to assume that protection from hospitalization and severe disease will be maintained.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nat. Commun. 22APR2022	**Comparing COVID-19-related hospitalization rates among individuals with infection-induced and vaccine-induced immunity in Israel**	Waxman J.G., *et al.* Israel / USA gotopaper	Public Health / Epidemiology	**Aim**: to compare COVID-19-related hospitalization incidence rates in 2,412,755 individuals across four exposure levels: non-recent vaccine immunity (two BNT162b2 COVID-19 vaccine doses five or more months prior), boosted vaccine immunity (three BNT162b2 doses), infection-induced immunity (previous COVID-19 without a subsequent BNT162b2 dose), and enhanced infection-induced immunity (previous COVID-19 with a subsequent BNT162b2 dose) **Methods** > Rates, adjusted for potential demographic, clinical and health-seeking-behavior confounders, were assessed from July-November 2021 when the Delta variant was predominant. **Results** > Of a total of 3,199,145 individuals considered for the analysis, 2,412,755 (75.4%) were found eligible (Fig. 1). The median age of the study population was 47 (IQR 33–65) and 51% were female. The total time under follow-up was 235,552,274 person-days. > Compared with non-recent vaccine immunity, COVID-19-related hospitalization incidence rates were reduced by 89% (87–91%) for boosted vaccine immunity, 66% (50–77%) for infection-induced immunity and 75% (61–83%) for enhanced infection-induced immunity. **In conclusion, we demonstrate that, while infection-induced immunity (with or without an enhancer dose of BNT162b2) provides more protection against COVID-19-related hospitalization than non-recent vaccine immunity, booster vaccination provides an even greater level of relative protection.**
JAMA Netw Open 22APR2022	**Estimated Health Outcomes and Costs of COVID-19 Prophylaxis With Monoclonal Antibodies Among Unvaccinated Household Contacts in the US**	Flaxman A.D., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim**: To estimate the health outcomes and net cost of implementing postexposure prophylaxis (PEP) with monoclonal antibodies (mAbs) against household exposure to COVID-19. **Methods:** Decision analytical model of results from a randomized clinical trial of casirivimab with imdevimab administered as subcutaneous injections to unvaccinated, SARS-CoV-2–negative household contacts of people with confirmed COVID-19 with complementary data on household demographic structure, vaccine coverage, and confirmed COVID-19 case counts. **Findings:** > In a month of transmission intensity similar to that of May 2021, a mAb PEP program reaching 50% of exposed, unvaccinated household members aged 50 years and older was estimated to avert 1820 symptomatic infections (95% uncertainty interval [UI], 1220-2454 symptomatic infections), 528 hospitalizations (95% UI, 354-724 hospitalizations), and 84 deaths (95% UI, 55-116 deaths) In a low-transmission scenario > In a high-transmission scenario : 4834 symptomatic infections (95% UI, 3375-6257 symptomatic infections), 1404 hospitalizations (95% UI, 974-1827 hospitalizations), and 223 deaths (95% UI, 152-299 deaths). > Without mAb PEP, the estimated cost of hospitalizations due to COVID-19 infections from household exposure in the lower transmission scenario was $149 million, whereas the estimated hospitalization cost in the higher transmission scenario was $400 million. > In the lower transmission scenario, mAb PEP administered to 50% of eligible contacts aged 80 years and older was estimated to have 82% probability of saving costs, but was not associated with cost savings at age thresholds of 50 years and older or 20 years and older. > In contrast, in the high-transmission scenario, mAb PEP administered to 50% of eligible household contacts had estimated cost savings in 100% of simulations at the 80-year age threshold, 96% of simulations at the 50-year threshold, and 2% of simulations at the 20-year thresholds.

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Nature 21APR2022	**Increased Memory B Cell Potency and Breadth After a SARS-CoV-2 mRNA Boost**	Muecksch F., *et al.* USA gotopaper	Immunology	**Aim**: to examine the memory B cell repertoire in a longitudinal cohort of individuals receiving 3 mRNA vaccine doses **Methods:** - Immune responses to SARS-CoV-2 mRNA vaccination was studied in a longitudinal cohort of 42 volunteers with no prior history of SARS-CoV-2 infection (January 21, 2021, and December 14, 2021). Volunteers received either the Moderna (mRNA-1273; n=8) or Pfizer-BioNTech (BNT162b2; n=34) mRNA vaccines. **Findings:** > the 3rd dose is accompanied by an increase in, and evolution of, anti-receptor binding domain-specific memory B cells. > The increase is due to expansion of memory B cell clones that were present after the 2nd dose as well as the emergence of new clones. The antibodies encoded by these cells showed significantly increased potency and breadth when compared to antibodies obtained after the 2nd dose. > The increase in potency was especially evident among newly developing clones of memory cells that differed from the persisting clones in targeting more conserved regions of the RBD. > More than 50% of analyzed neutralizing antibodies in the memory compartment after a 3rd mRNA vaccine dose neutralized Omicron. **Individuals receiving 3 doses of an mRNA vaccine, have a diverse memory B cell repertoire that can respond rapidly and produce antibodies capable of clearing even diversified variants such as Omicron.**
Science Immunol. 21APR2022	**SARS-CoV-2 epitope-specific CD4+ memory T cell responses across COVID-19 disease severity and antibody durability**	Nelson R.W., *et al.* USA gotopaper	Immunology	**Aim**: to better understand the role of Th1 and T follicular helper cells in COVID-19 immunity. Longitudinal study of SARS-CoV-2-specific CD4+ T cell and antibody responses in convalescent subjects who seroconverted during the first wave of the pandemic (US). **Methods** > We generated peptide:MHCII tetramers to analyze SARS-CoV-2-specific CD4+ T cell responses to spike and nucleocapsid epitopes, along with paired antibody responses, from peripheral blood samples. > For each individual, basic demographic information including age and sex, as well as medical history and COVID-19 history were obtained. **Results** > We utilized a peptide:MHCII tetramer-based enrichment strategy to analyze CD4+ T cell responses to two DR7:S epitopes and two DR7:N epitopes. Our analysis found different CD4+ T cell epitope-specific responses had relatively stable half-lives between ~4-6 months. SARS-CoV-2-specific CD4+ T cell response frequencies were not significantly different between cases of mild (non-hospitalized) and moderate to severe (previously hospitalized) COVID-19 when normalized to total CD4+ T cells in circulation, though the trend appeared to be toward increased frequencies of SARS-CoV-2-specific cells in the more severe cases. > We also found a relationship between antibody durability and percent of SARS-CoV-2-specific cells with a cTfh phenotype that persisted into the late memory phase, which was not previously appreciated without methods for directly identifying SARS-CoV-2-specific responses. > Our pMHCII tetramer-based analysis did not find evidence for strong pre-existing immunity to the 2 spike and 2 nucleocapsid CD4+ T cell epitopes assessed. It should be noted, however, that these epitopes do not have significant sequence homology with common cold coronaviruses, which may account for the lack of significant pre-existing T cell immunity detected in unexposed subjects, as has been documented with larger-scale screens of SARS-CoV-2 CD4+ T cell epitopes using different methods **In conclusion, our study demonstrates the usefulness of directly tracking SARS-CoV-2-specific responses with pMHCII tetramers, an approach that has been underutilized for characterizing correlates of SARS-CoV-2 immunity.**

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Clin Infect Dis. 21APR2022	**Favipiravir for treatment of outpatients with asymptomatic or uncomplicated COVID-19: a double-blind randomized, placebo-controlled, phase 2 trial**	Holubar M., *et al.* USA gotopaper	Therapeutics	**Methods** > Phase 2 double-blind randomized controlled outpatient trial of favipiravir in asymptomatic or mildly symptomatic adults with a positive SARS-CoV2 RT-PCR within 72 hours of enrollment. > Participants were randomized 1: 1 to receive placebo or favipiravir (1800mg BID Day 1, 800 mg BID Days 2-10). > The primary outcome was SARS-CoV-2 shedding cessation in a modified intention-to-treat (mITT) cohort of participants with positive enrollment RT-PCRs. > Using SARS-CoV-2 amplicon-based sequencing, we assessed favipiravir's impact on mutagenesis. **Results** > From July 8, 2020 - March 23, 2021, we randomized 149 participants with 116 included in the mITT cohort. > The participants' mean age was 43 years (SD 12.5) and 57 (49%) were women. > We found no difference in time to shedding cessation by treatment arm overall (HR 0.76 favoring placebo, 95% confidence interval [CI] 0.48–1.20) or in sub-group analyses (age, sex, high-risk comorbidities, seropositivity or symptom duration at enrollment). > We observed no difference in time to symptom resolution (initial: HR 0.84, 95% CI 0.54–1.29; sustained: HR 0.87, 95% CI 0.52–1.45). > We detected no difference in accumulation of transition mutations in the viral genome during treatment. **Our data do not support favipiravir use at commonly used doses in outpatients with uncomplicated COVID-19. Further research is needed to ascertain if higher doses of favipiravir are effective and safe for patients with COVID-19.**
JAMA Cardiol. 20APR2022	**SARS-CoV-2 Vaccination and Myocarditis in a Nordic Cohort Study of 23 Million Residents**	Karlstad Ø., *et al.* International gotopaper	Public Health / Epidemiology	**Aim**: to evaluate the risks of myocarditis and pericarditis following SARS-CoV-2 vaccination by vaccine product, vaccination dose number, sex, and age. **Methods** - 23 122 522 residents aged 12 years or older from 4 cohort studies (Denmark, Finland, Norway, and Sweden), followed up from December 27, 2020, until incident myocarditis or pericarditis, censoring, or study end (October 5, 2021). - Exposures: 28-day risk periods after administration date of the first and second doses of a SARS-CoV-2 vaccine (BNT162b2, mRNA-1273, and AZD1222 or combinations thereof). - Incident outcome events were defined as the date of first inpatient hospital admission based on primary or secondary discharge diagnosis for myocarditis or pericarditis from December 27, 2020, onward. - Secondary outcome was myocarditis or pericarditis combined from either inpatient or outpatient hospital care. **Results** > Among 23 122 522 Nordic residents (81% vaccinated by study end; 50.2% female), 1077 incident myocarditis events and 1149 incident pericarditis events were identified. > Within the 28-day period, for males and females 12 years or older combined who received a homologous schedule, the second dose was associated with higher risk of myocarditis, with adjusted IRRs of 1.75 (95% CI, 1.43-2.14) for BNT162b2 and 6.57 (95% CI, 4.64-9.28) for mRNA-1273. > Among males 16 to 24 years of age, adjusted IRRs were 5.31 (95% CI, 3.68-7.68) for a second dose of BNT162b2 and 13.83 (95% CI, 8.08-23.68) for a second dose of mRNA-1273, and numbers of excess events were 5.55 (95% CI, 3.70-7.39) events per 100 000 vaccinees after the second dose of BNT162b2 and 18.39 (9.05-27.72) events per 100 000 vaccinees after the second dose of mRNA-1273. > Estimates for pericarditis were similar. **Both first and second doses of mRNA vaccines were associated with increased risk of myocarditis and pericarditis. For individuals receiving 2 doses of the same vaccine, risk of myocarditis was highest among young males (aged 16-24 years) after the second dose.**

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NEJM 20APR2022	**Intramuscular AZD7442 (Tixagevimab–Cilgavimab) for Prevention of Covid-19**	Levin M.J., *et al.* International gotopaper	Therapeutics	**Aim**: to evaluate efficacy of a single dose of AZD7442 for the prevention of Covid-19 **Methods** - Phase 3 trial in adults who had an increased risk of an inadequate response to vaccination against Covid-19, an increased risk of exposure to SARS-CoV-2, or both. - Randomisation in a 2:1 ratio to receive a single dose of either 300 mg of AZD7442 or saline placebo. Follow for up to 183 days in the primary analysis. Primary safety end point: incidence of adverse events after a single dose of AZD7442. Primary efficacy end point: symptomatic Covid-19 occurring after administration of AZD7442 or placebo and on or before day 183. **Results** > 5197 participants underwent randomization and received one dose of AZD7442 or placebo (3460 in the AZD7442 group and 1737 in the placebo group). The primary analysis was conducted after 30% of the participants had become aware of their randomized assignment. > In total, 1221 of 3461 participants (35.3%) in the AZD7442 group and 593 of 1736 participants (34.2%) in the placebo group reported having at least one adverse event, most of which were mild or moderate in severity. > Symptomatic Covid-19 occurred in 8 of 3441 participants (0.2%) in the AZD7442 group and in 17 of 1731 participants (1.0%) in the placebo group (relative risk reduction, 76.7%; 95% CI, 46.0 to 90.0; P<0.001); extended follow-up at a median of 6 months showed a relative risk reduction of 82.8% (95% CI, 65.8 to 91.4). > Five cases of severe or critical Covid-19 and two Covid-19–related deaths occurred, all in the placebo group. **A single dose of AZD7442 had efficacy for the prevention of Covid-19, without evident safety concerns.**
Science Transl Med. 19APR2022	**An antibody class with a common CDRH3 motif broadly neutralizes sarbecoviruses**	Liu L., *et al.* USA gotopaper	Immunology	**Aim**: to assess three mAbs that broadly neutralize or bound all sarbecoviruses. **Methods** Comprehensive comparative analysis of three mAbs that broadly neutralize sarbecoviruses together with nine other mAbs that have previously been reported to have broad activity. **Findings:** > One of the mAbs identified in this study, 10-40, was the only mAb to neutralize or bind all sarbecoviruses tested. > 10-40 and many other broadly neutralizing mAbs utilize a common motif in their heavy chain complementarity determining region 3 (CDRH3) gene, suggesting that it may be possible to elicit such antibodies in a general manner. > Comparative studies with other receptor-binding domain (RBD)-directed antibodies showed 10-40 to have the greatest breadth against sarbecoviruses, suggesting that 10-40 is a promising agent for pandemic preparedness. > Structural analyses on 10-40 and similar antibodies not only defined an epitope cluster in the inner face of the RBD that is well-conserved among sarbecoviruses, but also uncovered a distinct antibody class with a common CDRH3 motif. **Elicitation of this class of antibodies may not be overly difficult, an observation that bodes well for the development of a pan-sarbecovirus vaccine.**

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Science Adv. 15APR2022	**One-year surveillance of SARS-CoV-2 transmission of the ELISA cohort: A model for population-based monitoring of infection risk**	Klein C., *et al.* Germany gotopaper	Public Health / Epidemiology	**Aim**: to survey a catchment area of 300,000 inhabitants from March 2020 to February 2021 by polymerase chain reaction and antibody testing of 1% of the local population and >90,000 app-based datasets. **Results** > Cohort (56% female; mean age, 45.6 years) retention was 75 to 98%. > Increased risk for seropositivity was detected in several high-exposure groups, especially nurses. > Unreported infections dropped from 92 to 29% during the study. "Contact to COVID-19–affected" was the strongest risk factor, whereas public transportation, having children in school, or tourism did not affect infection rates. > The development of symptoms, behavior, and quality of life during the pandemic is based on self-reports from 3051 study participants reported in 90,923 electronic questionnaires until February 2021. Frequencies of symptoms of infection rose between lockdown periods and dropped during the second lockdown. Behaviors were either stable (e.g., use of face masks) or increased in frequency between lockdowns in relation to the alleviation of the lockdown measures (e.g., eating out) and dropped again sharply during the second lockdown. **The ELISA study is the first to provide longitudinal data throughout the SARS-CoV-2 pandemic on a prospectively followed, population-based cohort. In conclusion, we (i) demonstrate that infection rates were vastly underestimated at the beginning of the pandemic, highlighting the necessity of intense testing; (ii) provide an easy-to-be-adapted model for effective, population-based surveillance of the current (and future) pandemic(s); and (iii) demonstrate that easing of lockdown measures appears safe even over several months at times of low prevalence rates, suggesting that a well-working surveillance system may serve as a feasible alternative to strict lockdown measures and as key for future protection against SARS-CoV-2, as well as for preparedness for future pandemics due to potential novel infectious agents.**
JAMA Pedratrics 15APR2022	**Acute Upper Airway Disease in Children With the Omicron (B.1.1.529) Variant of SARS-CoV-2—A Report From the US National COVID Cohort Collaborative**	Martin B., *et al.* USA gotopaper	Clinic	**Aim**: to conduct a retrospective cohort study to determine if cases of upper airway infection (UAI) among children increased when Omicron became the dominant SARS-CoV-2 variant in the US. **Methods** - Children in N3C (US National COVID Cohort Collaborative) younger than 19 years with a positive SARS-CoV-2 test result and a UAI diagnosis. - Comparison of demographic, comorbidity, and clinical outcome variables between patients from the pre-Omicron (March 1, 2020, to December 25, 2021) and Omicron (December 26, 2021, to February 17, 2022) periods. **Results** > 18 849 children hospitalized with SARS-CoV-2, 384 of whom (2.0%) had UAIs. Severe disease (defined as requiring invasive ventilation, vasopressors, or extracorporeal membrane oxygenation or death) occurred in 81 children (21%). > SARS-CoV-2–positive UAI rates have increased with progression from the pre-Omicron to Omicron periods (206 of 14 473 [1.5%] vs 178 of 4376 [4.1%], respectively; P < .001), with 178 of 384 cases (46%) occurring during the Omicron period. > Children with UAIs during the Omicron period were more likely to be younger and Hispanic or Latino and less likely to receive dexamethasone or develop severe disease compared with those in the pre-Omicron period. > The proportion of children with a pediatric complex chronic condition was not significantly different in the pre-Omicron period compared with the Omicron period (74 of 206 [36%] vs 39 of 178 [22%], respectively; P = 0.54). **SARS-CoV-2–positive pediatric UAI rates increased during the Omicron surge. More than one-fifth of children hospitalized with SARS-CoV-2 and UAI developed severe disease.**

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JAMA Netw Open 14APR2022	**Surveillance of Safety of 3 Doses of COVID-19 mRNA Vaccination Using Electronic Health Records**	Niesen M.J.M., *et al.* USA gotopaper	Vaccines	**Aim**: To evaluate the safety of third-dose vaccination with US Food and Drug Administration (FDA)–approved COVID-19 mRNA vaccines. **Methods** > This cohort study was conducted using electronic health record (EHR) data from December 2020 to October 2021 from the multistate Mayo Clinic Enterprise. > Participants included all 47 999 individuals receiving 3-dose COVID-19 mRNA vaccines within the study setting who met study inclusion criteria. **Results** > Among 47 999 individuals who received 3-dose COVID-19 mRNA vaccines, 38 094 individuals (21 835 [57.3%] women; median [IQR] age, 67.4 [52.5-76.5] years) received BNT162b2 (79.4%) and 9905 individuals (5099 [51.5%] women; median [IQR] age, 67.7 [59.5-73.9] years) received mRNA-1273 (20.6%). > Reporting of severe adverse events remained low after the third vaccine dose, with rates of pericarditis (0.01%; 95% CI, 0%-0.02%), anaphylaxis (0%; 95% CI, 0%-0.01%), myocarditis (0%; 95% CI, 0%-0.01%), and cerebral venous sinus thrombosis (no individuals) consistent with results from earlier studies. > Significantly more individuals reported low-severity adverse events after the third dose compared with after the second dose, including fatigue (2360 individuals [4.92%] vs 1665 individuals [3.47%]; P < .001), lymphadenopathy (1387 individuals [2.89%] vs 995 individuals [2.07%]; P < .001), nausea (1259 individuals [2.62%] vs 979 individuals [2.04%]; P < .001), headache (1185 individuals [2.47%] vs 992 individuals [2.07%]; P < .001), arthralgia (1019 individuals [2.12%] vs 816 individuals [1.70%]; P < .001), myalgia (956 individuals [1.99%] vs 784 individuals [1.63%]; P < .001), diarrhea (817 individuals [1.70%] vs 595 individuals [1.24%]; P < .001), fever (533 individuals [1.11%] vs 391 individuals [0.81%]; P < .001), vomiting (528 individuals [1.10%] vs 385 individuals [0.80%]; P < .001), and chills (224 individuals [0.47%] vs 175 individuals [0.36%]; P = .01). **This study found that although third-dose vaccination against SARS-CoV-2 infection was associated with increased reporting of low-severity adverse events, risk of severe adverse events remained comparable with risk associated with the standard 2-dose regime. These findings suggest the safety of third vaccination doses in individuals who were eligible for booster vaccination at the time of this study**.
Nature Commun. 13APR2022	**Protection following BNT162b2 booster in adolescents substantially exceeds that of a fresh 2-dose vaccine**	Amir O., *et al.* Israel gotopaper	Vaccines - Immunisation	**Aim**: to compare the real-world effectiveness against Delta of a fresh (up to 60 days) booster dose of BNT162b2 with that of a fresh 2-dose BNT162b2 vaccine in Israel. - Comparison of the confirmed infection rates in adolescents aged 12–14 (215,653 individuals) who received the 2-dose vaccine and in adolescents aged 16–18 (103,454 individuals) who received the booster dose. **Results** > The confirmed infection rate was lower by a factor of 3.7 (95% CI: 2.7 to 5.2) in the booster group as compared to the 2-doses group > The infection rate in the booster cohort was 3.3 (95% CI: 2.4–4.6) per 100,000 at-risk days, compared to 12.4 (95% CI: 11.4–14) in the doubly-vaccinated cohort. > Compared to unvaccinated individuals 16–18 years old, the confirmed infection rate in the booster cohort was lower by a factor of 26.3 (95% CI: 19.2, 36), while in the two-dose group the rate was lower by a factor of 9.8-fold (95% CI: 5, 16) (which is 2.7-fold lower than that of the booster group). > In the doubly-vaccinated 12–14 cohort, the confirmed infection rate was 12.5-fold (95% CI: 11.2, 13.8) lower compared to the unvaccinated group of that age, which is 2.1-fold lower than the 26.3-fold reduction in confirmed infection rate observed in the booster cohort. **This analysis shows that a fresh booster dose of the BNT162b2 mRNA vaccine provides improved protection against confirmed infection from the Delta variant compared to fresh two doses of the same vaccine.**

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Nature Commun. 13APR2022	**Modeling the disruption of respiratory disease clinical trials by non-pharmaceutical COVID-19 interventions**	Arsène S., *et al.* International gotopaper	Public Health / Epidemiology	**Aim**: to determine, rationalize and interpret the possible changes induced by lockdown and other non-pharmaceutical interventions (NPIs) for pandemic containment on respiratory disease trials with emphasis on RTI prophylaxis. **Methods** - A mechanistic in silico clinical trial approach in RTI prophylaxis which can incorporate available disease burden data to output efficacy metrics relevant for assessing clinical benefits and estimating sample sizes in perturbed scenarios (or evaluating impact on the post-hoc power of a trial for a given sample size) as well as recruitment times. **Results** > With the adjusted transmission rate and otherwise unchanged parameters, the root mean square deviation (RMSD) for the weekly incidence per 100,000 of the simulation vs. data are 82 and 96 (unperturbed simulation vs. 5-year average data and perturbed simulation vs. 2019–2020, data, respectively), which is smaller than the variability within the observed data before lockdown (RMSD of 102 for the 5-year average vs. 2019–2020 data for the time points considered). > Furthermore, reproduction of RTI incidence broken down into URTIs and LRTIs shows convincing capability to describe the effect of transmission perturbation on RTIs. Supported by this agreement, we applied this epidemiological model to modulate the instantaneous hazard of exposure to RTI-causing viruses in our in silico trials with four different NPI scenarios. **Our simulation setup for this analysis (year 1: patient selection, year 2: treatment and follow-up period) reflects RTI prophylaxis trials whose conduction takes place during the current pandemic. Therefore, we concluded that the benefit-risk assessment of these trials should account for the currently reduced disease burden, and that supporting data (such as observational studies and models) should be used to demonstrate that a low number of prevented episodes under pandemic conditions does not necessarily mean that under normal conditions equally few episodes will be prevented.**

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NEJM 13APR2022	**Fourth Dose of BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Setting**	Magen O., *et al.* USA gotopaper	Vaccines	**Aim**: to evaluate the early effectiveness of a fourth dose of the BNT162b2 vaccine for the prevention of Covid-19–related outcomes. **Methods** - Data recorded by the largest health care organization in Israel from January 3 to February 18, 2022. - Evaluation of relative effectiveness of a fourth vaccine dose as compared with that of a third dose given at least 4 months earlier among persons 60 years of age or older. **Results** > Primary analysis included 182,122 matched pairs. > Relative vaccine effectiveness in days 7 to 30 after the fourth dose was estimated to be 45% (95% CI, 44 to 47) against PCR–confirmed SARS-CoV-2 infection, 55% (95% CI, 53 to 58) against symptomatic Covid-19, 68% (95% CI, 59 to 74) against Covid-19–related hospitalization, 62% (95% CI, 50 to 74) against severe Covid-19, and 74% (95% CI, 50 to 90) against Covid-19–related death. > The corresponding estimates in days 14 to 30 after the fourth dose were 52% (95% CI, 49 to 54), 61% (95% CI, 58 to 64), 72% (95% CI, 63 to 79), 64% (95% CI, 48 to 77), and 76% (95% CI, 48 to 91). > In days 7 to 30 after a fourth vaccine dose, the difference in the absolute risk (three doses vs. four doses) was 180.1 cases per 100,000 persons (95% CI, 142.8 to 211.9) for Covid-19–related hospitalization and 68.8 cases per 100,000 persons (95% CI, 48.5 to 91.9) for severe Covid-19. > In sensitivity analyses, estimates of relative effectiveness against documented infection were similar to those in the primary analysis. **A fourth dose of the BNT162b2 vaccine was effective in reducing the short-term risk of Covid-19–related outcomes among persons who had received a third dose at least 4 months earlier.**
Nature Commun. 12APR2022	**Persistent COVID-19 symptoms in a community study of 606,434 people in England**	Whitaker M., *et al.* UK gotopaper	Long Covid	**Aim**: to report persistent COVID-19 symptoms in a community study of 606,434 people in England. **Methods** We use data from rounds 3–5 of the REACT-2 study (n = 508,707; September 2020 – February 2021), a representative community survey of adults in England, and replication data from round 6 (n = 97,717; May 2021) to estimate the prevalence and identify predictors of persistent symptoms lasting 12 weeks or more; and unsupervised learning to cluster individuals by reported symptoms. **Findings** > At 12 weeks in rounds 3–5, 37.7% experienced at least one symptom, falling to 21.6% in round 6. > Female sex, increasing age, obesity, smoking, vaping, hospitalisation with COVID-19, deprivation, and being a healthcare worker are associated with higher probability of persistent symptoms in rounds 3–5, and Asian ethnicity with lower probability. > Clustering analysis identifies a subset of participants with predominantly respiratory symptoms. **In conclusion, the scale of morbidity identified in this study post COVID-19 presents significant challenges for the affected individuals and their families, and indicates a high potential population health burden. Managing the long-term sequelae of COVID-19 will remain a major challenge for affected individuals and their families and for health services.**

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Clin Infect Dis. 11APR2022	**COVID-19 Disease Severity in Children Infected with the Omicron Variant**	Butt A. A., *et al.* Qatar gotopaper	Clinic	**Aim**: to assess COVID-19 disease severity in children/adolescents infected with the Omicron variant. **Methods** We identified children and adolescents <18 years with SARS-CoV-2 infection with Delta and propensity-score matched controls with Omicron variant infection from the National COVID-19 Database in Qatar. Primary outcome was disease severity, determined by hospital admission, admission to ICU, or mechanical ventilation within 14 days of diagnosis, or death within 28 days. **Findings** > Among 1,735 cases with Delta variant infection between June 1 and November 6, 2021 and 32 635 cases with Omicron variant infection between January 1 and January 15, 2022 who did not have prior infection and were not vaccinated, we identified 985 propensity-score matched pairs. > Among Delta infected, 84.2% had mild, 15.7% had moderate, and 0.1% had severe/critical disease. > Among Omicron infected, 97.8% had mild, 2.2% had moderate, and none had severe/critical disease (P < .001). > Omicron variant infection (vs. Delta) was associated with significantly lower odds of moderate or severe/critical disease (adjusted odds ratio, 0.12; 95% CI 0.07-0.18). > Those aged 6–11, and 12-<18 years had lower odds of developing moderate or severe/critical disease compared with those younger than six years (aOR, 95% CI 0.47; 0.33-0.66 for 6-11 year old; aOR 0.45, 95% CI 0.21-0.94 for 12-<18 years old). **Omicron variant infection in children/adolescents is associated with less severe disease than Delta variant infection as measured by hospitalization rates and need for ICU care or mechanical ventilation. Those 6 to <18 years also have less severe disease than those <6 years old.**
Clin Infect Dis. 11APR2022	**Risk factors and multidimensional assessment of long COVID fatigue: a nested case-control study**	Margalit I., *et al.* Israel gotopaper	Long Covid	**Aim**: to assess risk factors for long COVID fatigue and explored its possible pathophysiology. **Findings** > Total of 141 individuals were included. Mean age was 47 (SD 13) years; 115 (82%) were recovering from mild COVID-19. Mean time for evaluation was 8 months following COVID-19. Sixty-six (47%) individuals were classified with significant long COVID fatigue. They had significantly higher number of children, lower proportion of hypothyroidism, higher proportion of sore throat during acute illness and long COVID symptoms, and of physical limitation in daily activities. > Individuals with fatigue had poorer sleep quality and higher degree of depression. They had significantly lower heart rate [153.52 (22.64) vs 163.52 (18.53), p=0.038] and oxygen consumption per Kg [27.69 (7.52) vs 30.71 (7.52), p=0.036] at peak exercise. > The two independent risk factors for fatigue identified in multivariable analysis were peak exercise heart rate (odds ratio [OR] 0.79 per 10 beats/minute, 95% confidence interval [CI] 0.65-0.96, p=0.019); and long COVID memory impairment (OR 3.76, 95% CI 1.57-9.01, p=0.003). **Long COVID fatigue may be related to autonomic dysfunction, impaired cognition and decreased mood. This may suggest a limbic-vagal pathophysiology.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 08APR2022	**Estimating global, regional, and national daily and cumulative infections with SARS-CoV-2 through Nov 14, 2021: a statistical analysis**	COVID-19 Cumulative Infection Collaborators International gotopaper	Public health / Epidemiology	**Aim**: to provide a novel approach to estimating past SARS-CoV-2 daily infections, cumulative infections, and the proportion of the population infected, for 190 countries and territories from the start of the pandemic to Nov 14, 2021. **Methods** - Set of global and location-specific estimates of daily and cumulative SARS-CoV-2 infections through Nov 14, 2021, using data from Johns Hopkins University and national databases for reported cases, hospital admissions, and reported deaths, seroprevalence surveys, SeroTracker, and governmental organisations. - Data were corrected for known biases such as lags in reporting, waning antibody sensitivity, vaccinations, and reinfection from SARS-CoV-2 escape variants. - Modelled estimations based on an empirical database of infection–detection ratios (IDRs), infection–hospitalisation ratios (IHRs), and infection–fatality ratios (IFRs). - Daily infections were converted into a historical time series of effective reproductive number (Reffective) by location and day. **Results** > Global daily SARS-CoV-2 infections fluctuated between 3 million and 17 million new infections per day between April, 2020, and October, 2021, peaking in mid-April, 2021, primarily as a result of surges in India. > Between the start of the pandemic and Nov 14, 2021, there were an estimated 3,80 billion (95% uncertainty interval 3,44–4,08) total SARS-CoV-2 infections and reinfections combined, and an estimated 3·39 billion (3,08–3,63) individuals, or 43,9% (39,9–46,9) of the global population, had been infected one or more times. > 1·34 billion (1,20–1,49) of these infections occurred in south Asia, the highest among the seven super-regions, although the sub-Saharan Africa super-region had the highest infection rate (79,3 per 100 population [69,0–86,4]). > The high-income super-region had the fewest infections (239 million [226–252]), and southeast Asia, east Asia, and Oceania had the lowest infection rate (13,0 per 100 population [8,4–17,7]). > The cumulative proportion of the population ever infected varied greatly between countries and territories, with rates higher than 70% in 40 countries and lower than 20% in 39 countries. > There was no discernible relationship between Reffective and total immunity, and even at total immunity levels of 80%, we observed no indication of an abrupt drop in Reffective, indicating that there is not a clear herd immunity threshold observed in the data. **COVID-19 has already had a staggering impact on the world up to the beginning of the omicron (B.1.1.529) wave, with over 40% of the global population infected at least once by Nov 14, 2021.**
Nature Med. 08APR2022	**Infectious viral load in unvaccinated and vaccinated individuals infected with ancestral, Delta or Omicron SARS-CoV-2**	Puhach O., *et al.* Switzerland gotopaper	Public Health / Epidemiology	**Methods** > Quantification of infectious viral load (VL) in SARS-CoV-2 infected individuals during the first 5 symptomatic days by in vitro culturability assay in unvaccinated or vaccinated individuals infected with pre-variant of concern (pre-VOC) SARS-CoV-2, Delta, or Omicron. **Findings** > Unvaccinated individuals infected with pre-VOC SARS-CoV-2 had lower infectious VL compared to Delta-infected unvaccinated individuals > Full vaccination (defined as >2weeks after reception of 2nd dose during primary vaccination series) significantly reduced infectious VL for Delta breakthrough cases compared to unvaccinated individuals > For Omicron breakthrough cases, reduced infectious VL was only observed in boosted but not in fully vaccinated individuals compared to unvaccinated subjects. > In addition, infectious VL was lower in fully vaccinated Omicron-compared to fully vaccinated Delta-infected individuals, suggesting that other mechanisms than increased infectious VL contribute to the high infectiousness of SARS-CoV-2 Omicron. **Our findings indicate that vaccines may lower transmission risk and therefore have a public health benefit beyond the individual protection from severe disease.**

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Cell 08APR2022	**Efficient recall of Omicron-reactive B cell memory after a third dose of SARS-CoV-2 mRNA vaccine**	Goel R. R., *et al.* Australia / USA gotopaper	Immunology	**Aim**: to examine antibody and memory B cell responses longitudinally for ~9-10 months after primary 2-dose SARS-CoV-2 mRNA vaccination and 3 months after a 3rd dose. **Findings** > Antibody decay stabilized between 6 to 9 months and antibody quality continued to improve for at least 9 months after 2-dose vaccination. > Spike- and RBD-specific memory B cells remained durable over time, and 40-50% of RBD-specific memory B cells simultaneously bound the Alpha, Beta, Delta, and Omicron variants. > Omicron-binding memory B cells were efficiently re-activated by a 3rd dose of wild-type vaccine and correlated with the corresponding increase in neutralizing antibody titers. > In contrast, pre-3rd dose antibody titers inversely correlated with the fold-change of antibody boosting, suggesting that high levels of circulating antibodies may limit the added protection afforded by repeat short interval boosting. **This study supports the utility of a 3rd vaccine dose to recall immunological memory and boost circulating antibody levels. A 3rd dose of mRNA vaccine encoding the original Wuhan Spike reengaged Omicron-reactive memory B cells generated by the first two doses.**
Lancet Infect Dis. 08APR2022	**COVID-19 vaccine waning and effectiveness and side-effects of boosters: a prospective community study from the ZOE COVID Study**	Menni C., *et al.* UK gotopaper	Vaccines	**Aim**: to investigate COVID-19 primary vaccine series effectiveness and its waning, and the safety and effectiveness of booster doses, in a UK community setting. **Methods** - SARS-CoV-2 positivity rates in individuals from a longitudinal, prospective, community-based study (ZOE COVID Study). Data were self-reported through an app, to assess the effectiveness of three COVID-19 vaccines (ChAdOx1 nCov19, BNT162b2, and mRNA1273) against infection in the 8 months after completion of primary vaccination series. - In individuals receiving boosters, vaccine effectiveness and reactogenicity were investigated, by assessing 16 self-reported systemic and localised side-effects. **Findings** > We included 620 793 participants who received two vaccine doses (204 731 [33·0%] received BNT162b2, 405 239 [65·3%] received ChAdOx1 nCoV-19, and 10 823 [1·7%] received mRNA-1273) and subsequently had a SARS-CoV-2 test result between May 23 (chosen to exclude the period of alpha [B.1.1.7] variant dominance) and Nov 23, 2021. 62 172 (10·0%) vaccinated individuals tested positive for SARS-CoV-2 and were compared with 40 345 unvaccinated controls (6726 [16·7%] of whom tested positive). > Vaccine effectiveness waned after the second dose: at 5 months, BNT162b2 effectiveness was 82·1% (95% CI 81·3–82·9), ChAdOx1 nCoV-19 effectiveness was 75·7% (74·9–76·4), and mRNA-1273 effectiveness was 84·3% (81·2–86·9). > Vaccine effectiveness decreased more among individuals aged 55 years or older and among those with comorbidities. > 135 932 individuals aged 55 years or older received a booster (2123 [1·6%] of whom tested positive). > Vaccine effectiveness for booster doses in 0–3 months after BNT162b2 primary vaccination was higher than 92·5%, and effectiveness for heterologous boosters after ChAdOx1 nCoV-19 was at least 88·8%. > For the booster reactogenicity analysis, in 317 011 participants, the most common systemic symptom was fatigue (in 31 881 [10·1%] participants) and the most common local symptom was tenderness (in 187 767 [59·2%]). > Systemic side-effects were more common for heterologous schedules (32 632 [17·9%] of 182 374) than for homologous schedules (17 707 [13·2%] of 134 637; odds ratio 1·5, 95% CI 1·5–1·6, p<0·0001). **After 5 months, vaccine effectiveness remained high among individuals younger than 55 years. Booster doses restore vaccine effectiveness. Adverse reactions after booster doses were similar to those after the second dose. Homologous booster schedules had fewer reported systemic side-effects than heterologous boosters.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 07APR2022	**Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study**	Menni C., *et al.* UK gotopaper	Public Health / Epidemiology	**Aim**: to quantify the differences in symptom prevalence, risk of hospital admission, and symptom duration among the vaccinated population. **Methods** > Prospective longitudinal observational study, we collected data from participants who were self-reporting test results and symptoms in the ZOE COVID app. > The primary outcome was the likelihood of developing a given symptom (of the 32 monitored in the app) or hospital admission within 7 days before or after the positive test in participants infected during omicron prevalence compared with those infected during delta prevalence. **Findings** > Between June 1, 2021, and Jan 17, 2022, we identified 63 002 participants who tested positive for SARS-CoV-2 and reported symptoms in the ZOE app. These patients were matched 1:1 for age, sex, and vaccination dose, across two periods (June 1 to Nov 27, 2021, delta prevalent at >70%; n=4990, and Dec 20, 2021, to Jan 17, 2022, omicron prevalent at >70%; n=4990). > Loss of smell was less common in participants infected during omicron prevalence than during delta prevalence (16·7% vs 52·7%, odds ratio [OR] 0·17; 95% CI 0·16–0·19, p<0·001). Sore throat was more common during omicron prevalence than during delta prevalence (70·5% vs 60·8%, 1·55; 1·43–1·69, p<0·001). > There was a lower rate of hospital admission during omicron prevalence than during delta prevalence (1·9% vs 2·6%, OR 0·75; 95% CI 0·57–0·98, p=0·03). **The prevalence of symptoms that characterise an omicron infection differs from those of the delta SARS-CoV-2 variant, apparently with less involvement of the lower respiratory tract and reduced probability of hospital admission. These data indicate a shorter period of illness and potentially of infectiousness which should impact work–health policies and public health advice.**
Nature 06APR2022	**FcγR-mediated SARS-CoV-2 infection of monocytes activates inflammation**	Junqueira C., *et al.* UK / USA gotopaper	Immunology	**Aim**: to understand how SARS-CoV-2 triggers inflammation and to determine if pyroptosis biomarkers correlate with COVID-19 disease severity, **Findings:** >6% of blood monocytes in COVID-19 patients are infected with SARS-CoV-2. > Monocyte infection depends on uptake of antibody-opsonized virus by Fcγ receptors. > Vaccine recipient plasma does not promote antibody-dependent monocyte infection. SARS-CoV-2 begins to replicate in monocytes, but infection is aborted, and infectious virus is not detected in infected monocyte culture supernatants. > Instead, infected cells undergo inflammatory cell death (pyroptosis) mediated by activation of NLRP3 and AIM2 inflammasomes, caspase-1 and GSDMD. > Moreover, tissue-resident macrophages, but not infected epithelial and endothelial cells, from COVID-19 lung autopsies have activated inflammasomes. **Antibody-mediated SARS-CoV-2 uptake by monocytes/macrophages triggers inflammatory cell death that aborts production of infectious virus but causes systemic inflammation that contributes to COVID-19 pathogenesis.**

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Lancet Resp Med 06APR2022	**Early Th2 inflammation in the upper respiratory mucosa as a predictor of severe COVID-19 and modulation by early treatment with inhaled corticosteroids: a mechanistic analysis**	Baker J.R., *et al.* UK gotopaper	Immunology	**Aim**: to understand the inflammatory mechanism of budesonide in the treatment of early COVID-19. **Methods**: The STOIC trial was a randomised, open label, parallel group, phase 2 clinical intervention trial where patients were randomly assigned (1:1) to receive usual care (as needed antipyretics were only available treatment) or inhaled budesonide at a dose of 800 µg twice a day plus usual care. F**indings:** > In early COVID-19 disease, there was an enhanced inflammatory airway response with the induction of an anti-viral and T-helper 1 and 2 (Th1/2) inflammatory response compared with healthy individuals. > Individuals with COVID-19 who clinically deteriorated (ie, who met the primary outcome) showed an early blunted respiratory interferon response and pronounced and persistent Th2 inflammation, mediated by CC chemokine ligand (CCL)-24, compared with those with COVID-19 who did not clinically deteriorate. > Over time, the natural course of COVID-19 showed persistently high respiratory interferon concentrations and elevated concentrations of the eosinophil chemokine, CCL-11, despite clinical symptom improvement. > There was persistent systemic inflammation after 28 days following COVID-19, including elevated concentrations of interleukin (IL)-6, tumour necrosis factor-α, and CCL-11. Budesonide treatment modulated inflammation in the nose and blood and was shown to decrease IL-33 and increase CCL17. **The clinical benefit of inhaled budesonide in early COVID-19 is likely to be as a consequence of its inflammatory modulatory effect, suggesting efficacy by reducing epithelial damage and an improved T-cell response.**
Immunity 06APR2022	**Analysis of mRNA vaccination-elicited RBD-specific memory B cells reveals strong but incomplete immune escape of the SARS-CoV-2 Omicron variant**	Sokal A., *et al.* France gotopaper	Immunology	**Aim**: to understand whether MBCs elicited by mRNA vaccines can recognize Omicron variant remains unclear. - Assessment of affinity and neutralization potency against the Omicron variant of several hundred naturally expressed MBC-derived monoclonal IgG antibodies from vaccinated COVID-19-recovered and -naïve individuals. **Results** > Compared to other variants of concern, Omicron evaded recognition of a larger proportion of MBC-derived antibodies. > Only 30% MBCs retaining high affinity against the Omicron-RBD, and the reduction in neutralization potency was even more pronounced. > Neutralizing MBC clones could be found in all individuals analysed. **Despite the strong immune escape potential of the Omicron variant, these results suggest that the MBC repertoire generated by mRNA vaccines still provide some protection against the Omicron variant in vaccinated individuals.**

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BMJ 06APR2022	**Risks of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19: nationwide self-controlled cases series and matched cohort study**	Katsoularis I., *et al.* Sweden gotopaper	Clinic	**Aim**: to quantify the risk of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19. **Methods** - Participants: 1 057 174 people who tested positive for SARS-CoV-2 (1 Feb 2020-25 May 2021) in Sweden, matched on age, sex, and county of residence to 4 076 342 control participants. - Incidence rate ratio and risk ratio for a first deep vein thrombosis, pulmonary embolism, or bleeding event. **Results** > Compared with the control period, incidence rate ratios were significantly increased 70 days after covid-19 for deep vein thrombosis, 110 days for pulmonary embolism, and 60 days for bleeding. > Incidence rate ratios for a first pulmonary embolism were 36.17 (95% CI, 31.55 to 41.47) during the first week after covid-19 and 46.40 (40.61 to 53.02) during the second week. > Incidence rate ratios during days 1-30 after covid-19 were 5.90 (5.12 to 6.80) for deep vein thrombosis, 31.59 (27.99 to 35.63) for pulmonary embolism, and 2.48 (2.30 to 2.68) for bleeding. > Similarly, the risk ratios during days 1-30 after covid-19 were 4.98 (4.96 to 5.01) for deep vein thrombosis, 33.05 (32.8 to 33.3) for pulmonary embolism, and 1.88 (1.71 to 2.07) for bleeding, after adjusting for the effect of potential confounders. > The rate ratios were highest in patients with critical covid-19 and highest during the first pandemic wave in Sweden compared with the second and third waves. > In the same period, the absolute risk among patients with covid-19 was 0.039% (401 events) for deep vein thrombosis, 0.17% (1761 events) for pulmonary embolism, and 0.101% (1002 events) for bleeding. **These findings suggest that covid-19 is a risk factor for deep vein thrombosis, pulmonary embolism, and bleeding.**
Immunity 06APR2022	**Analysis Of Memory B Cells Identifies Conserved Neutralizing Epitopes On The N-Terminal Domain Of Variant SARS-Cov-2 Spike Proteins**	Wang Z., *et al.* USA gotopaper	Immunology	**Aim**: to understand the inflammatory mechanism of budesonide in the treatment of early COVID-19. **Methods:** The authors used NTD-specific probes to capture anti-NTD memory B cells in a longitudinal cohort of infected individuals, some of whom were vaccinated. **Findings:** > Six complementation groups of neutralizing antibodies were founded. 58% targeted epitopes outside the NTD supersite, 58% neutralized either Gamma or Omicron, and 14% were broad neutralizers that also neutralized Omicron. > Structural characterization revealed that broadly active antibodies targeted three epitopes outside the NTD supersite including a class that recognized both the NTD and SD2 domain. > Rapid recruitment of memory B cells producing these antibodies into the plasma cell compartment upon re-infection likely contributes to the relatively benign course of subsequent infections with SARS-CoV-2 variants, including Omicron. **This diverse collection of memory cells and their cognate memory T cells are likely to make a major contribution to the generally milder course of infection in individuals that have been infected and/or vaccinated with SARS-CoV-2.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 06APR2022	**Protection with a Third Dose of mRNA Vaccine against SARS-CoV-2 Variants in Frontline Workers**	Yoon S.K., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: to report effectiveness of two or three doses of a mRNA vaccine against infection caused by SARS-CoV-2 omicron and delta variants. - Cohort: health care personnel first responders, and other essential and frontline workers who received three doses of BNT162b2 (administered in 74%), mRNA-1273 (in 24%), or a combination of the two vaccines (in 2%). - Study period: August 2021 – January 2022 **Results** > 202 infections with the delta variant and 419 with the omicron variant were detected in samples obtained from 3241 participants. > Among unvaccinated adults, % of asymptomatic infection was higher in infections with omicron than in infections with delta (21% and 8%, respectively; odds ratio 3.10 (95% confidence interval [CI], 0.96 to 9.70)). > Participants who had symptomatic Covid-19 sought medical care for infection with omicron less frequently than they did for infection with delta (22% and 41%, respectively; odds ratio of 0.40 (95% CI, 0.17 to 0.94)). > Adjusted vaccine effectiveness against delta infection was 65% (95% CI, 49 to 76) after two doses and 91% (95% CI, 84 to 95) after three doses. The relative vaccine effectiveness of three doses as compared with two doses against the delta variant was 86% (95% CI, 69 to 94). > After adjustment, the vaccine effectiveness against omicron infection was 46% (95% CI, 25 to 61) after two doses and 60% (95% CI, 42 to 72) after three doses, for a relative effectiveness of 60% (95% CI, 40 to 73) for three doses as compared with two doses. > Estimate of vaccine effectiveness of three doses against omicron infection was lower than the corresponding effectiveness against medically attended Covid-19 (82 to 90%) in the same study. **Despite indicating a decline in vaccine effectiveness, these results show continued effectiveness against clinically severe outcomes related to both delta and omicron variants.**
NEJM 05APR2022	**Protection by a Fourth Dose of BNT162b2 against Omicron in Israel**	Bar-On Y.M., *et al.* Israel gotopaper	Vaccines - Immunisation	**Aim**: to evaluate the effect of the fourth dose on rates of confirmed SARS-CoV-2 infection and of severe Covid-19 in persons 60 years of age or older. - Data on 1,252,331 persons ≥60 years of age and eligible for the fourth dose during a period in which the B.1.1.529 (omicron) variant of SARS-CoV-2 was predominant (January 10 - March 2, 2022). - Estimation of rate of confirmed infection and severe Covid-19 as a function of time starting at 8 days after receipt of a fourth dose (four-dose groups) as compared with that among persons who received three doses (three-dose group) and persons who received a fourth dose 3 to 7 days earlier (internal control group). **Results** > The number of cases of severe Covid-19 per 100,000 person-days (unadjusted rate) was 1.5 in the aggregated four-dose groups, 3.9 in the three-dose group, and 4.2 in the internal control group. > The adjusted rate of severe Covid-19 in the fourth week after receipt of the fourth dose was lower than that in the three-dose group by a factor of 3.5 (95% CI, 2.7 to 4.6) and was lower than that in the internal control group by a factor of 2.3 (95% CI, 1.7 to 3.3). > Protection against severe illness did not wane during the 6 weeks after receipt of the fourth dose. > The number of cases of confirmed infection per 100,000 person-days (unadjusted rate) was 177 in the aggregated four-dose groups, 361 in the three-dose group, and 388 in the internal control group. > The adjusted rate of confirmed infection in the fourth week after receipt of the fourth dose was lower than that in the three-dose group by a factor of 2.0 (95% CI, 1.9 to 2.1) and was lower than that in the internal control group by a factor of 1.8 (95% CI, 1.7 to 1.9). However, this protection waned in later weeks. **Rates of confirmed SARS-CoV-2 infection and severe Covid-19 were lower after a fourth dose of BNT162b2 vaccine than after three doses. Protection against confirmed infection appeared short-lived, whereas protection against severe illness did not wane during the study period.**

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Nature Immunol. 05APR2022	**SARS-CoV-2 antigen exposure history shapes phenotypes and specificity of memory CD8+ T cells**	Minervina A.A., *et al.* USA gotopaper	Immunology	**Aim**: to investigate the effects of repeated antigen exposures (SARS-CoV-2 infections and vaccinations with Pfizer-BioNTech BNT162b2) on the key features of the CD8+ T cell response, including response magnitude, functional gene expression profiles (assessed directly ex vivo), and the constituent TCR repertoire. **Methods :** The authors utilize major histocompatibility complex multimers with single-cell RNA sequencing to profile SARS-CoV-2-responsive T cells ex vivo from humans with one, two or three antigen exposures, including vaccination, primary infection and breakthrough infection. **Findingss:** > Exposure order determined the distribution between spike-specific and non-spike-specific responses, with vaccination after infection leading to expansion of spike-specific T cells and differentiation to CCR7−CD45RA+ effectors. In contrast, individuals after breakthrough infection mount vigorous non-spike-specific responses. > Analysis of over 4,000 epitope-specific T cell antigen receptor (TCR) sequences demonstrates that all exposures elicit diverse repertoires characterized by shared TCR motifs, confirmed by monoclonal TCR characterization, with no evidence for repertoire narrowing from repeated exposure. **These findings suggest that breakthrough infections diversify the T cell memory repertoire and current vaccination protocols continue to expand and differentiate spike-specific memory.**
Science Trans Med. 05APR2022	**SARS-CoV-2 BA.1 variant is neutralized by vaccine booster-elicited serum, but evades most convalescent serum and therapeutic antibodies**	Lusvarghi S., *et al.* USA gotopaper	Immunology	**Aim**: measuring neutralization of the Omicron BA.1 variant pseudovirus by post-vaccination serum samples after two and three immunizations with Pfizer/BNT162b2 vaccine, convalescent serum samples from unvaccinated individuals infected by different variants, and clinical-stage therapeutic antibodies **Findings** > Titers against the Omicron variant were low or undetectable after two immunizations and in many convalescent serum samples, regardless of the infecting variant. > A booster vaccination increased titers more than 30-fold against Omicron to values comparable to those seen against the D614G variant after two immunizations. > Neither age nor sex were associated with differences in post-vaccination antibody responses. > Among eighteen clinical-stage therapeutic antibody products and an antibody mimetic protein product: five monoclonal antibodies, the antibody mimetic protein, three antibody cocktails, and two polyclonal antibody preparations retained measurable neutralization activity against Omicron with a varying degree of potency. > Of these, only three retained potencies comparable to the D614G variant. Two therapeutic antibody cocktails in the tested panel that are authorized for emergency use in the United States did not neutralize Omicron. **These findings underscore the potential benefit of mRNA vaccine boosters for protection against Omicron and the need for rapid development of antibody therapeutics that maintain potency against emerging variants.**

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Nature Commun. 05APR2022	**Course of post COVID-19 disease symptoms over time in the ComPaRe long COVID prospective e-cohort**	Tran V.J., *et al.* France gotopaper	Long Covid	**Aim**: to analyse data from 968 adult patients (5350 person-months) with a confirmed infection enroled in the ComPaRe long COVID cohort, a disease prevalent prospective e-cohort of such patients in France. **Methods** Day-by-day prevalence of post COVID-19 symptoms was determined from patients' responses to the Long COVID Symptom Tool, a validated self-reported questionnaire assessing 53 symptoms **Findings** > Among patients symptomatic after 2 months, 85% still reported symptoms one year after their symptom onset. > Evolution of symptoms showed a decreasing prevalence over time for 27/53 symptoms (e.g., loss of taste/smell); a stable prevalence over time for 18/53 symptoms (e.g., dyspnoea), and an increasing prevalence over time for 8/53 symptoms (e.g., paraesthesia). > The disease impact on patients' lives began increasing 6 months after onset. **Our results are of importance to understand the natural history of post COVID-19 disease.**
Lancet 02APR2022	**Efficacy, safety, and immunogenicity of the DNA SARS-CoV-2 vaccine (ZyCoV-D): the interim efficacy results of a phase 3, randomised, double-blind, placebo-controlled study in India**	Khobragade A., *et al.* India gotopaper	Vaccines	**Aim**: to report the interim efficacy results of phase 3 clinical trial with ZyCoV-D DNA-based vaccine in India. **Methods** > Interim analysis of a multicentre, double-blind, randomised, placebo-controlled phase 3 trial at 49 centres in India. > Healthy participants aged at least 12 years randomly assigned (1:1) to receive either ZyCov-D vaccine (Cadila Healthcare; 2 mg per dose) or placebo. > The primary outcome was the number of participants with first occurrence of symptomatic RT-PCR-positive COVID-19 28 days after the third dose, until the targeted number of cases (interim analysis n=79, full analysis n=158) have been achieved. **Findings** > Between Jan 16, and June 23, 2021 (data cutoff), 33 194 individuals were screened, of whom 5241 did not meet screening criteria and 27 703 were enrolled and randomly assigned to receive ZyCoV-D (n=13 851) or placebo (n=13 852). > Per-protocol, 81 cases were eligible and included in efficacy analysis (20 of 12 350 in the ZyCoV-D group and 61 of 12 320 in placebo group). > The ZyCoV-D vaccine efficacy was found to be 66·6% (95% CI 47·6–80·7). > The occurrence of solicited adverse events was similar between the treatment groups (623 [4·49%] in the ZyCoV-D group vs 620 [4·47%] in the placebo group). There were two deaths (one in each group) reported at the data cutoff, neither of which was considered related to the study treatments. **In this interim analysis, ZyCoV-D vaccine was found to be efficacious, safe, and immunogenic in a phase 3 trial.**
Cell 01APR2022	**Circular RNA Vaccines against SARS-CoV-2 and Emerging Variants**	Qu L., *et al.* China gotopaper	Vaccines	**Aim**: to report a highly stable circular RNA (circRNA) vaccine against SARS-CoV-2 variants of concern. **Results** > The circRNA vaccine elicited potent neutralizing antibodies and T cell responses by expressing the trimeric RBD of the spike protein, providing robust protection against SARS-CoV-2 in both mice and rhesus macaques. > The circRNA vaccine enabled higher and more durable antigen production than the 1mΨ-modified mRNA vaccine, and elicited a higher proportion of neutralizing antibodies and distinct Th1-skewed immune responses. > The circRNARBD-Omicron vaccine induced effective neutralizing antibodies against the Omicron but not the Delta variant. In contrast, the circRNARBD-Delta vaccine protected against both Delta and Omicron or functioned as a booster after two doses of either native- or Delta-specific vaccination, making it a favorable choice against the current variants of concern (VOCs) of SARS-CoV-2.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Infect Dis. 01APR2022	**Screening and vaccination against COVID-19 to minimise school closure: a modelling study**	Colosi E., *et al.* France gotopaper	Public Health / Epidemiology	**Aim**: to evaluate costs and benefits of different protocols for SARS-CoV-2 control at school, by estimating school-specific transmissibility. **Methods** - Empirical contact data in a primary and a secondary school and data from pilot screenings in 683 schools during the alpha variant (B.1.1.7) wave in March–June, 2021, in France. - Estimate of school-specific effective reproductive number for the alpha (Ralpha) and delta (B.1.617.2; Rdelta) variants, cost–benefit analysis examining different intervention protocols. **Results** > Ralpha was estimated to be 1·40 (95% CI 1·35–1·45) in the primary school and 1·46 (1·41–1·51) in the secondary school during the spring wave, higher than the time-varying reproductive number estimated from community surveillance. > Considering the delta variant and vaccination coverage in Europe as of mid-September 2021, Rdelta was estimated to be 1·66 (1·60–1·71) in primary schools and 1·10 (1·06–1·14) in secondary schools. > Under these conditions, weekly testing of 75% of unvaccinated students (PCR tests on saliva samples in primary schools and lateral flow tests in secondary schools), in addition to symptom-based testing, would reduce cases by 34% (95% CI 32–36) in primary schools and 36% (35–39) in secondary schools compared with symptom-based testing alone. Insufficient adherence was recorded in pilot screening (median ≤53%). > Regular testing would also reduce student-days lost up to 80% compared with reactive class closures. > Moderate vaccination coverage in students would still benefit from regular testing for additional control – weekly testing 75% of unvaccinated students would reduce cases compared with symptom-based testing only, by 23% in primary schools when 50% of children are vaccinated. **Extending vaccination coverage in students, complemented by regular testing with good adherence, are essential steps to keep schools open when highly transmissible variants are circulating.**
JAMA Pediatr. 01APR2022	**Incidence Rates and Clinical Outcomes of SARS-CoV-2 Infection With the Omicron and Delta Variants in Children Younger Than 5 Years in the US**	Wang L., *et al.* USA gotopaper	Clinic	**Aim**: to examine incidence rates and clinical outcomes of Omicron infection before and after Omicron became the predominant variant in the US. Study population: 3 cohorts of children younger than 5 years with no prior SARS-CoV-2 infection: (1) Omicron cohort, infected between December 26, 2021 - January 25, 2022; (2) Delta (B.1.617.2) cohort, infected between September 1 - November 15, 2021; (3) Delta2 cohort, infected between 16 - November 30, 2021 (control for later time periods and shorter infection window). **Results** > 651 640 children younger than 5 years: (1) Omicron cohort, 22 772 children; (2) Delta cohort, 66 692 children; and (3) Delta2 cohort, 10 496 children. > Monthly incidence rate of SARS-CoV-2 infections was mostly stable (1.0-1.5 cases per 1000 persons per day) between September and November 2021 (Delta-predominant period) but rapidly increased to 2.4 to 5.6 cases per 1000 persons per day in December 2021 (Omicron emergence). > Monthly incidence rate of SARS-CoV-2 infections peaked at 8.6 cases per 1000 persons per day in the first half of January 2022 (Omicron-predominant period) and 8.2 in the second half of January 2022. > Incidence rate of Omicron infection was higher in children aged 0 to 2 years than in those aged 3 to 4 years. > Risks for severe clinical outcomes in children infected with Omicron variant were significantly lower than those in the matched Delta cohort, whereas the risks for severe clinical outcomes in Delta2 cohort did not differ from those in Delta cohort. > There were fewer than 10 deaths in all cohorts. **Incidence rate of SARS-CoV-2 infection with Omicron variant was 6 to 8 times that of Delta variant in children younger than 5 years, but severe clinical outcomes were less frequent than with Delta variant.**

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Nature Commun. 01APR2022	**Neuropathology and virus in brain of SARS-CoV-2 infected non-human primates**	Rutkai I., *et al.* USA gotopaper	Clinic	Aim: to develop animal models that recapitulate the neuropathological findings of autopsied brain tissue from patients who died from SARS-CoV-2 infection to elucide the neuropathogenesis of infection and disease. **Findings** > Neuroinflammation, microhemorrhages, brain hypoxia, and neuropathology is consistent with hypoxic-ischemic injury in SARS-CoV-2 infected non-human primates (NHPs), including evidence of neuron degeneration and apoptosis. > This is seen among infected animals that do not develop severe respiratory disease, which may provide insight into neurological symptoms associated with "long COVID". > Sparse virus is detected in brain endothelial cells but does not associate with the severity of central nervous system (CNS) injury. **These findings will advance the current understanding of the neuropathogenesis of SARS-CoV-2 infection and demonstrate SARS-CoV-2 infected NHPs are a highly relevant animal model for investigating COVID-19 neuropathogenesis among human subjects.**
Nature Med. 31MAR2022	**Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge in young adults**	Killingley B., *et al.* UK gotopaper	Clinic	**Aim**: to establish a novel SARS-CoV-2 human challenge model that enables controlled investigation of pathogenesis, correlates of protection and efficacy testing of forthcoming interventions. **Methods** - 36 volunteers aged 18–29 years without evidence of previous infection or vaccination, inoculated with 10 TCID50 of a wild-type virus (SARS-CoV-2/human/GBR/484861/2020) intranasally in an open-label, non-randomized study. Two participants were excluded from the per-protocol analysis owing to seroconversion between screening and inoculation. - Study's primary objective: to identify an inoculum dose that induced well-tolerated infection in more than 50% of participants. - Secondary objectives: to assess virus and symptom kinetics during infection. **Results** > Eighteen (~53%) participants became infected, with viral load (VL) rising steeply and peaking at ~5 days after inoculation. > Virus was first detected in the throat but rose to significantly higher levels in the nose, peaking at ~8.87 log10 copies per milliliter (median, 95% CI (8.41, 9.53)). Viable virus was recoverable from the nose up to ~10 days after inoculation, on average. > There were no serious adverse events. > Mild-to-moderate symptoms were reported by 16 (89%) infected participants, beginning 2–4 days after inoculation, whereas two (11%) participants remained asymptomatic (no reportable symptoms). > Anosmia or dysosmia developed more slowly in 15 (83%) participants. > No quantitative correlation was noted between VL and symptoms, with high VLs present even in asymptomatic infection. > All infected individuals developed serum spike-specific IgG and neutralizing antibodies. > Results from lateral flow tests were strongly associated with viable virus, and modeling showed that twice-weekly rapid antigen tests could diagnose infection before 70–80% of viable virus had been generated. **With detailed characterization and safety analysis of this first SARS-CoV-2 human challenge study in young adults, viral kinetics over the course of primary infection with SARS-CoV-2 were established, with implications for public health recommendations and strategies to affect SARS-CoV-2 transmission.**

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Nature Commun. 31MAR2022	**Protein-based SARS-CoV-2 spike vaccine booster increases cross-neutralization against SARS-CoV-2 variants of concern in non-human primates**	Pavot V., *et al.* International gotopaper	Immunology	**Aim**: to assess a protein-based subunit vaccine booster in macaques vaccinated 7 months before with either mRNA–LNP or subunit CoV2 preS dTM-AS03 Sanofi vaccine candidates. **Methods :** Various formulations, namely AS03-adjuvanted parental (D614), variant (B.1.351), and bivalent (D614 + B.1.351) CoV2 preS dTM or non-adjuvanted CoV2 preS dTM (B.1.351), were evaluated for their ability to boost neutralizing antibodies (NAbs) against the parental strain and to induce cross-neutralization against the five VOC described so far (Alpha, Beta, Gamma, Delta, and Omicron) and SARS-CoV-1 (from the 2003 outbreak) to further explore the breadth of neutralization. **Findings:** > In macaques primed with mRNA or protein-based subunit vaccine candidates, one booster dose of CoV2 preS dTM-AS03 (monovalent D614 or B.1.351, or bivalent D614 + B.1.351 formulations), significantly boosts the pre-existing neutralizing antibodies against the parental strain from 177- to 370-fold. > The booster dose elicits high and persistent cross-neutralizing antibodies covering five former or current SARS-CoV-2 variants of concern (Alpha, Beta, Gamma, Delta and Omicron) and, unexpectedly, SARS-CoV-1. > The booster specifically increases the functional antibody responses as compared to the receptor binding domain (RBD)-specific responses. **These vaccine candidates, when used as a booster, have the potential to offer cross-protection against a broad spectrum of variants.**
Science Immunol. 31MAR2022	**A modified vaccinia Ankara vaccine expressing spike and nucleocapsid protects rhesus macaques against SARS-CoV-2 delta infection**	Kishore Routhu N., *et al.* USA gotopaper	Immunology	**Aim**: to evaluate the immunogenicity and efficacy of a modified vaccinia Ankara (MVA) virus vector-based SARS-CoV-2 vaccine co-expressing the furin-cleavage site inactivated spike and nucleocapsid (MVA/SdFCS-N) against heterologous SARS-CoV-2 challenge. **Methods :** Improved MVA-based SARS-CoV-2 vaccine expressing S with furin-cleavage site inactivation (SdFCS) and N proteins, evaluating its immunogenicity and efficacy when administered via either intramuscular (IM) or oral needle-free route against heterologous SARS-CoV-2 challenge in rhesus macaques. **Findings:** > Following vaccination of mice, the MVA/SdFCS vaccine induced 8-fold higher neutralizing antibodies compared to MVA/S, which expressed spike without FCS inactivation, and protected against the beta variant. > In rhesus macaques, IM vaccination induced spike-specific IgG in serum and mucosae (nose, throat, lung, rectum) which neutralized the homologous (WA-1/2020) and heterologous VOCs, including delta, with minimal loss (<2-fold) of activity. > IM vaccination also induced both S and N specific CD4 and CD8 T cell responses in the blood. In contrast, the SL and BU vaccinations induced less spike-specific IgG in secretions and lower levels of polyfunctional IgG in serum compared to IM vaccination. > Following challenge with SARS-CoV-2 delta variant, the IM route induced robust protection, BU moderate protection and the SL no protection. > Vaccine-induced neutralizing and non-neutralizing antibody effector functions positively correlated with protection, but only the effector functions correlated with early protection. **IM vaccination with MVA/SdFCS-N vaccine elicited cross-reactive antibody and T cell responses, protecting against heterologous SARS-CoV-2 VOC more effectively than other routes of vaccination.**

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Lancet Infect Dis. 31MAR2022	**Effectiveness of CoronaVac, ChAdOx1 nCoV-19, BNT162b2, and Ad26.COV2.S among individuals with previous SARS-CoV-2 infection in Brazil: a test-negative, case-control study**	Cerqueira-Silva T., *et al.* International gotopaper	Vaccines - Immunisation	**Aim**: to estimate the effectiveness of four COVID-19 vaccines against symptomatic infection, hospitalisation, and death for individuals with laboratory-confirmed previous SARS-CoV-2 infection. **Methods :** test-negative, case-control study to assess the effectiveness of four vaccines (CoronaVac [Sinovac], ChAdOx1 nCoV-19 [AstraZeneca], Ad26.COV2.S [Janssen], and BNT162b2 [Pfizer-BioNtech]) for individuals with laboratory-confirmed previous SARS-CoV-2 infection. **Findings:** > 213 457 individuals who had a subsequent, symptomatic illness with RT-PCR testing done at least 90 days after their initial SARS-CoV-2 infection and after the vaccination programme started were identified. > Among these, 30 910 (14·5%) had a positive RT-PCR test consistent with reinfection, and we matched 22 566 of these cases with 145 055 negative RT-PCR tests from 68 426 individuals as controls. > Among individuals with previous SARS-CoV-2 infection, vaccine effectiveness against symptomatic infection 14 or more days from vaccine series completion was 39·4% (95% CI 36·1–42·6) for CoronaVac, 56·0% (51·4–60·2) for ChAdOx1 nCoV-19, 44·0% (31·5–54·2) for Ad26.COV2.S, and 64·8% (54·9–72·4) for BNT162b2. > For the two-dose vaccine series (CoronaVac, ChAdOx1 nCoV-19, and BNT162b2), effectiveness against symptomatic infection was significantly greater after the second dose than after the first dose. > Effectiveness against hospitalisation or death 14 or more days from vaccine series completion was 81·3% (75·3–85·8) for CoronaVac, 89·9% (83·5–93·8) for ChAdOx1 nCoV-19, 57·7% (−2·6 to 82·5) for Ad26.COV2.S, and 89·7% (54·3–97·7) for BNT162b2.
Lancet Infect Dis. 31MAR2022	**Risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals with natural and hybrid immunity: a retrospective, total population cohort study in Sweden**	Nordström P., *et al.* Sweden gotopaper	Vaccines - Immunisation	**Aim**: to investigate the long-term protection from a previous infection (natural immunity) and whether natural immunity plus vaccination (hybrid immunity) was associated with additional protection. **Methods :** **R**etrospective cohort study from three cohorts using Swedish nationwide registers managed by the Public Health Agency of Sweden, the National Board of Health and Welfare, and Statistics Sweden. Cohort 1 included unvaccinated individuals with natural immunity matched pairwise on birth year and sex to unvaccinated individuals without natural immunity at baseline. Cohort 2 and cohort 3 included individuals vaccinated with one dose (one-dose hybrid immunity) or two doses (two-dose hybrid immunity) of a COVID-19 vaccine respectively. **Findings:** > After the first 3 months, natural immunity was associated with a 95% lower risk of SARS-CoV-2 infection (adjusted hazard ratio [aHR] 0·05 [95% CI 0·05–0·05] p<0·001) and an 87% (0·13 [0·11–0·16]; p<0·001) lower risk of COVID-19 hospitalisation for up to 20 months of follow-up. > During a mean follow-up of 52 days (SD 38) in cohort 2, 639 individuals with one-dose hybrid immunity were registered with a SARS-CoV-2 reinfection, compared with 1662 individuals with natural immunity (numbers of hospitalisations were eight and 113, respectively). > One-dose hybrid immunity was associated with a 58% lower risk of SARS-CoV-2 reinfection (aHR 0·42 [95% CI 0·38–0·47]; p<0·001) than natural immunity up to the first 2 months, with evidence of attenuation thereafter up to 9 months (p<0·001) of follow-up. > Two-dose hybrid immunity was associated with a 66% lower risk of SARS-CoV-2 reinfection (aHR 0·34 [95% CI 0·31–0·39]; p<0·001) than natural immunity, with no significant attenuation up to 9 months (p=0·07). **The risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals who have survived and recovered from a previous infection remained low for up to 20 months.**

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NEJM 30MAR2022	**Early Outpatient Treatment for Covid-19 with Convalescent Plasma**	Sullivan D.J., *et al.* USA gotopaper	Therapeutics	**Aim**: to evaluate the efficacy and safety of polyclonal convalescent plasma in preventing serious complications in outpatients with recent-onset Covid-19. - Symptomatic adults (≥18 years of age) who had tested positive for SARS-CoV-2, regardless of their risk factors for disease progression or vaccination status. - Participants were enrolled within 8 days after symptom onset and received a transfusion within 1 day after randomization (June 3, 2020, through October 1, 2021). Primary outcome: Covid-19–related hospitalization within 28 days after transfusion. **Results** > 1225 participants underwent randomization, and 1181 received a transfusion. > In the prespecified modified intention-to-treat analysis that included only participants who received a transfusion, the primary outcome occurred in 17 of 592 participants (2.9%) who received convalescent plasma and 37 of 589 participants (6.3%) who received control plasma (absolute risk reduction, 3.4 percentage points; 95% CI, 1.0 to 5.8; P=0.005), which corresponded to a relative risk reduction of 54%. > Evidence of efficacy in vaccinated participants cannot be inferred from these data because 53 of the 54 participants with Covid-19 who were hospitalized were unvaccinated and 1 participant was partially vaccinated. > A total of 16 grade 3 or 4 adverse events (7 in the convalescent-plasma group and 9 in the control-plasma group) occurred in participants who were not hospitalized. **In participants with Covid-19, most of whom were unvaccinated, the administration of convalescent plasma within 9 days after the onset of symptoms reduced the risk of disease progression leading to hospitalization.**
NEJM 30MAR2022	**BNT162b2 Protection against the Omicron Variant in Children and Adolescents**	Price A.M., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: to study immune evasion and the duration of protection from vaccines against Covid-19 due to SARS-CoV-2 B.1.1.529 (omicron) variant in children and adolescents. **Methods** - Vaccine effectiveness against laboratory-confirmed Covid-19 leading to hospitalization and against critical Covid-19 (i.e., leading to receipt of life support or to death) was assessed. - Vaccine effectiveness was estimated by comparing the odds of antecedent full vaccination (two doses of BNT162b2 mRNA vaccine) ≥14 days before illness among case patients and controls, according to time since vaccination for patients 12 to 18 years of age and in periods coinciding with circulation of B.1.617.2 (delta) (July 1, 2021, to Dec 18, 2021) and omicron (Dec 19, 2021, to Feb 17, 2022) among patients 5 to 11 and 12 to 18 years of age. **Results** > 1185 case patients (1043 [88%] unvaccinated, 291 [25%] received life support, 14 died) and 1627 controls. > During the delta-predominant period, vaccine effectiveness against hospitalization for Covid-19 among adolescents 12 to 18 years of age was 93% (95% CI, 89 to 95) 2 to 22 weeks after vaccination and was 92% (95% CI, 80 to 97) at 23 to 44 weeks. > During the omicron-predominant period, among adolescents 12 to 18 years of age (median interval since vaccination, 162 days), vaccine effectiveness was 40% (95% CI, 9 to 60) against hospitalization for Covid-19, 79% (95% CI, 51 to 91) against critical Covid-19, and 20% (95% CI, −25 to 49) against noncritical Covid-19. > During the omicron period, vaccine effectiveness against hospitalization among children 5 to 11 years of age was 68% (95% CI, 42 to 82; median interval since vaccination, 34 days). **BNT162b2 vaccination reduced the risk of omicron-associated hospitalization by two thirds among children 5 to 11 years of age. Although two doses provided lower protection against omicron-associated hospitalization than against delta-associated hospitalization among adolescents 12 to 18 years of age, vaccination prevented critical illness caused by either variant.**

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NEJM 30MAR2022	**Effect of Early Treatment with Ivermectin among Patients with Covid-19**	Reis G., *et al.* International gotopaper	Therapeutics	**Aim**: to evaluate efficacy of ivermectin in preventing hospitalization or extended observation in an emergency setting among outpatients with acutely symptomatic Covid-19. - Patients who had had symptoms of Covid-19 for up to 7 days and had at least one risk factor for disease progression - Treatment: ivermectin (400 µg per kilogram of body weight) once daily for 3 days or placebo. Primary composite outcome: hospitalization due to Covid-19 within 28 days after randomization or an emergency department visit due to clinical worsening of Covid-19 within 28 days after randomization. **Results** > 3515 patients, receiving ivermectin (679 patients), placebo (679), or another intervention (2157). > Overall, 100 patients (14.7%) in the ivermectin group had a primary-outcome event, as compared with 111 (16.3%) in the placebo group (relative risk, 0.90; 95% Bayesian credible interval, 0.70 to 1.16). > Of the 211 primary-outcome events, 171 (81.0%) were hospital admissions. > Findings were similar to the primary analysis in a modified intention-to-treat analysis that included only patients who received at least one dose of ivermectin or placebo (relative risk, 0.89; 95% Bayesian credible interval, 0.69 to 1.15) and in a per-protocol analysis that included only patients who reported 100% adherence to the assigned regimen (relative risk, 0.94; 95% Bayesian credible interval, 0.67 to 1.35). > There were no significant effects of ivermectin use on secondary outcomes or adverse events. **Treatment with ivermectin did not result in a lower incidence of medical admission to a hospital due to progression of Covid-19 or of prolonged emergency department observation among outpatients with an early diagnosis of Covid-19.**
Science Transl Med. 29MAR2022	**mRNA-1273 and BNT162b2 COVID-19 vaccines elicit antibodies with differences in Fc-mediated effector functions**	Kaplocek P., *et al.* USA gotopaper	Immunology	**Aim**: to understand the subtle variation in immune responses induced by the BNT162b2 and mRNA-1273 vaccines that may confer differential protection. - Profiling the post-boost binding and functional capacity of humoral immune responses induced by the BNT162b2 and mRNA-1273 vaccines in a cohort of 73 hospital staff. **Results** > Both BNT162b2 and mRNA-1273 vaccines induced robust humoral immune responses to wild-type SARS-CoV-2 and to variants of concern. > Both vaccinations induced FcR-binding responses to multiple VOCs and induced more robust Fc-functional antibodies compared to infection. > Differences emerged across epitope-specific responses, with higher concentrations of RBD- and N-terminal domain-specific IgA observed in recipients of mRNA-1273. > Antibodies eliciting neutrophil phagocytosis and natural killer cell activation were also increased in mRNA-1273 vaccine recipients as compared to BNT162b2 recipients. > RBD-specific antibody depletion highlighted the different roles of non-RBD-specific antibody effector functions induced across the mRNA vaccines. **These data provide insights into potential differences in protective immunity conferred by these vaccines.**

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Lancet Rheumatol. 29MAR2022	**Ruxolitinib in addition to standard of care for the treatment of patients admitted to hospital with COVID-19 (RUXCOVID): a randomised, double-blind, placebo-controlled, phase 3 trial**	Han K.M., *et al.* International gotopaper	Therapeutics	**Aim**: assess whether treatment with the JAK1/JAK2 inhibitor ruxolitinib would be beneficial in patients with COVID-19 admitted to hospital. **Methods** > RUXCOVID was an international, randomised, double-blind, phase 3 trial of ruxolitinib plus standard of care versus placebo plus standard of care in patients with COVID-19. > The primary endpoint was a composite of death, respiratory failure (invasive ventilation), or ICU care by day 29 **Findings** > Between May 4 and Sept 19, 2020, 432 patients were randomly assigned to ruxolitinib (n=287) or placebo (n=145) plus standard of care; the mean age was 56·5 years (SD 13·3), 197 (46%) were female, and 235 (54%) were male. > The primary objective was not met: the composite endpoint occurred in 34 (12%) of 284 ruxolitinib-treated patients versus 17 (12%) of 144 placebo-treated patients (odds ratio 0·91, 95% CI 0·48–1·73; p=0·77). > By day 29, nine (3%) of 286 ruxolitinib-treated patients had died compared with three (2%) of 145 placebo-treated patients; 22 (8%) of 286 ruxolitinib-treated patients had received invasive ventilation compared with ten (7%) of 145 placebo-treated patients; and 30 (11%) of 284 ruxolitinib-treated patients had received ICU care compared with 17 (12%) of 144 placebo-treated patients. > In an exploratory analysis, median time to recovery was 1 day faster with ruxolitinib versus placebo (8 days vs 9 days; hazard ratio 1·10, 95% CI 0·89–1·36). > Adverse events included headache (23 [8%] of 281 on ruxolitinib vs 11 [8%] of 143 on placebo) and diarrhoea (21 [7%] vs 12 [8%]). **Ruxolitinib 5 mg twice per day showed no benefit in the overall study population. A larger sample is required to determine the clinical importance of trends for increased efficacy in patient subgroups.**
Lancet Child Adolesc Health 28MAR2022	**Risk of SARS-CoV-2 reinfections in children: a prospective national surveillance study between January, 2020, and July, 2021, in England**	Mensah A.A., *et al.* UK gotopaper	Public health / Epidemiology	**Aim**: to assess the risk of SARS-CoV-2 reinfection in children and compare this with the risk in adults, by analysis of national testing data for England. **Findings** > Reinfection rates closely followed community infection rates, with a small peak during the alpha wave and a larger peak during the delta wave. In children aged 16 years and younger, 688 418 primary infections and 2343 reinfections were identified. > The overall reinfection rate was 66·88 per 100 000 population, which was higher in adults (72·53 per 100 000) than children (21·53 per 100 000). > The reinfection rate after primary infection was 0·68% overall, 0·73% in adults compared with 0·18% in children age younger than 5 years, 0·24% in those aged 5–11 years, and 0·49% in those aged 12–16 years. > Of the 109 children admitted to hospital with reinfection, 78 (72%) had comorbidities. Hospital admission rates were similar for the first (64 [2·7%] of 2343) and second episode (57 [2·4%] of 2343) and intensive care admissions were rare (seven children for the first episode and four for reinfections). There were 44 deaths within 28 days after primary infection (0·01%) and none after reinfection. **The risk of SARS-CoV-2 reinfection is strongly related to exposure due to community infection rates, especially during the delta variant wave. Children had a lower risk of reinfection than did adults, but reinfections were not associated with more severe disease or fatal outcomes.**

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Nature 28MAR2022	**A TMPRSS2 inhibitor acts as a pan-SARS-CoV-2 prophylactic and therapeutic**	Shapira T., *et al.* Canada / USA gotopaper	Therapeutics	**Aim**: to identify and characterize a small-molecule compound, N-0385, which exhibits low nanomolar potency and a selectivity index of >106 at inhibiting SARS-CoV-2 infection in human lung cells and in donor-derived colonoids. **Methods:** The peptidomimetics' antiviral activities against SARS-CoV-2 and four variants B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta) in human lung cells were analysed. The lead highly potent antiviral, N-0385 was tested, against SARS-CoV-2 (lineage A strain) and SARS-CoV-2 Delta VOC-induced morbidity and mortality in K18-hACE2 mice. **Findings:** > The authors developed and characterized N-0385, a novel highly potent inhibitor of TMPRSS2-like proteases that blocks SARS-CoV-2 VOCs (B.1.1.7, P.1, B.1.351 and B.1.617.2) and is broadly protective against infection and mortality in mice. > The nanomolar potency of N-0385 against SARS-CoV-2 infection in human Calu-3 cells and patient-derived colonoids without detectable toxicity yields a striking selectivity index of >10x6. > In the K18-hACE2 mouse model, treating with N-0385 resulted in complete protection against SARS-CoV-2 induced mortality and significantly protected against weight loss, lung pathology, and viral infection when treatment occurred at the time of, or 12 hours after, infection with the SARS-CoV-2 B.1.617.2, suggesting that N-0385 may provide a novel effective early treatment option against emerging SARS-CoV-2 Variants of Concern (VOCs). > N-0385 provides a novel effective early treatment option against SARS-CoV-2 and the B.1.617.2 Delta VOC. **N-0385 analogs may have broader applications in combating other widespread respiratory viruses that usurp TMPRSS2-related proteases for viral entry, including other established coronaviruses, influenza viruses, and additional viruses that depend on TTSPs for entering host cells.**
Cell 28MAR2022	**Boosting with variant-matched or historical mRNA vaccines protects against Omicron infection in mice**	Ying B. *et al.* USA gotopaper	Vaccines	**Aim**: to evaluate in mice the protective efficacy of the Moderna mRNA-1273 vaccine against BA.1 before or after boosting. **Results** > In rhesus macaques, whereas two doses of mRNA-1273 vaccine induced high levels of neutralizing antibodies against historical WA1/2020 strains, lower levels against BA.1 were associated with breakthrough infection and inflammation in the lung. > A primary vaccination series with mRNA-1273.529, an Omicron-matched vaccine, potently neutralized BA.1 but inhibited historical or other SARS-CoV-2 variants less effectively. > Boosting with either mRNA-1273 or mRNA-1273.529 vaccines increased neutralizing titers and protection against BA.1 and BA.2 infection. Similar expansion of cross-reactive S-2P-specific memory B cells following boosting. > Nonetheless, the neutralizing antibody titers were higher, and lung viral burden and cytokines were slightly lower in mice boosted with mRNA-1273.529 and challenged with BA.1. **Boosting with mRNA-1273 or mRNA-1273.529 enhances protection against Omicron infection with limited differences in efficacy measured.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Cell 25MAR2022	**mRNA-1273 or mRNA-Omicron boost in vaccinated macaques elicits similar B cell expansion, neutralizing antibodies and protection against Omicron**	Gagne M., *et al.* USA gotopaper	Vaccines	**Aim**: to understand whether boosting with Omicron-matched vaccines after immunization with ancestral spike-matched vaccines enhances protection. - Nonhuman primates that received mRNA-1273 at weeks 0 and 4 were boosted at week 41 with mRNA-1273 or mRNA-Omicron. **Results** > mRNA-1273 prime induces cross-reactive B cells to Omicron and ancestral strains. Boosting with mRNA-1273 or mRNA-Omicron enhances neutralization of Omicron > Neutralizing titers against D614G were 4760 and 270 reciprocal ID50 at week 6 (peak) and week 41 (pre-boost), respectively, and 320 and 110 for Omicron. > Two weeks after boost, titers against D614G and Omicron increased to 5360 and 2980 for mRNA-1273 boost and 2670 and 1930 for mRNA-Omicron. > Similar increases against BA.2 were observed. > Following either boost, 70-80% of spike-specific B cells were cross-reactive against WA1 and Omicron. > Equivalent control of virus replication in lower airways was observed following Omicron challenge one month after either boost. **These data show that mRNA-1273 and mRNA-Omicron elicit comparable immunity and protection shortly after the boost.**
JAMA Netw Open 24MAR2022	**Association of Early Aspirin Use With In-Hospital Mortality in Patients With Moderate COVID-19**	Chow J. H., *et al.* USA gotopaper	Therapeutics	**Aim**: to assess whether early aspirin use is associated with lower odds of in-hospital mortality in patients with moderate COVID-19. **Methods** > Observational cohort study of 112 269 hospitalized patients with moderate COVID-19, enrolled from January 1, 2020, through September 10, 2021, at 64 health systems in the United States participating in the National Institute of Health's National COVID Cohort Collaborative (N3C). **Findings** > Among the 2 446 650 COVID-19–positive patients who were screened, 189 287 were hospitalized and 112 269 met study inclusion. > For the full cohort, Median age was 63 years (IQR, 47-74 years); 16.1% of patients were African American, 3.8% were Asian, 52.7% were White, 5.0% were of other races and ethnicities, 22.4% were of unknown race and ethnicity. In-hospital mortality occurred in 10.9% of patients. > After inverse probability treatment weighting, 28-day in-hospital mortality was significantly lower in those who received aspirin (10.2% vs 11.8%; odds ratio [OR], 0.85; 95% CI, 0.79-0.92; P < .001). > The rate of pulmonary embolism, but not deep vein thrombosis, was also significantly lower in patients who received aspirin (1.0% vs 1.4%; OR, 0.71; 95% CI, 0.56-0.90; P = .004). > Patients who received early aspirin did not have higher rates of gastrointestinal hemorrhage (0.8% aspirin vs 0.7% no aspirin; OR, 1.04; 95% CI, 0.82-1.33; P = .72), cerebral hemorrhage (0.6% aspirin vs 0.4% no aspirin; OR, 1.32; 95% CI, 0.92-1.88; P = .13), or blood transfusion (2.7% aspirin vs 2.3% no aspirin; OR, 1.14; 95% CI, 0.99-1.32; P = .06). > The composite of hemorrhagic complications did not occur more often in those receiving aspirin (3.7% aspirin vs 3.2% no aspirin; OR, 1.13; 95% CI, 1.00-1.28; P = .054). Subgroups who appeared to benefit the most included patients older than 60 years (61-80 years: OR, 0.79; 95% CI, 0.72-0.87; P < .001; >80 years: OR, 0.79; 95% CI, 0.69-0.91; P < .001) and patients with comorbidities (1 comorbidity: 6.4% vs 9.2%; OR, 0.68; 95% CI, 0.55-0.83; P < .001; 2 comorbidities: 10.5% vs 12.8%; OR, 0.80; 95% CI, 0.69-0.93; P = .003; 3 comorbidities: 13.8% vs 17.0%, OR, 0.78; 95% CI, 0.68-0.89; P < .001; >3 comorbidities: 17.0% vs 21.6%; OR, 0.74; 95% CI, 0.66-0.84; P < .001). **In this cohort study of US adults hospitalized with moderate COVID-19, early aspirin use was associated with lower odds of 28-day in-hospital mortality. A randomized clinical trial that includes diverse patients with moderate COVID-19 is warranted to adequately evaluate aspirin's efficacy in patients with high-risk conditions.**

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JAMA 24MAR2022	**Association of COVID-19 Vaccination in Pregnancy With Adverse Peripartum Outcomes**	Fell D. B., *et al.* International gotopaper	Vaccines	**Aim**: To evaluate peripartum outcomes following COVID-19 vaccination during pregnancy. **Methods:** Population-based retrospective cohort study in Ontario, Canada, using a birth registry linked with the provincial COVID-19 immunization database. All births between December 14, 2020, and September 30, 2021, were included. **Results** > Among 97 590 individuals (mean [SD] age, 31.9 [4.9] years), 22 660 (23%) received at least 1 dose of COVID-19 vaccine during pregnancy (63.6% received dose 1 in the third trimester; 99.8% received an mRNA vaccine). > Comparing those vaccinated during vs after pregnancy (n = 44 815), there were no significantly increased risks of postpartum hemorrhage (incidence: 3.0% vs 3.0%; aRD, −0.28 per 100 individuals [95% CI, −0.59 to 0.03]; aRR, 0.91 [95% CI, 0.82-1.02]), chorioamnionitis (0.5% vs 0.5%; aRD, −0.04 per 100 individuals [95% CI, −0.17 to 0.09]; aRR, 0.92 [95% CI, 0.70-1.21]), cesarean delivery (30.8% vs 32.2%; aRD, −2.73 per 100 individuals [95% CI, −3.59 to −1.88]; aRR, 0.92 [95% CI, 0.89-0.95]), NICU admission (11.0% vs 13.3%; aRD, −1.89 per 100 newborns [95% CI, −2.49 to −1.30]; aRR, 0.85 [95% CI, 0.80-0.90]), or low Apgar score (1.8% vs 2.0%; aRD, −0.31 per 100 newborns [95% CI, −0.56 to −0.06]; aRR, 0.84 [95% CI, 0.73-0.97]). > Findings were qualitatively similar when compared with individuals who did not receive COVID-19 vaccination at any point (n = 30 115). **In this population-based cohort study in Ontario, Canada, COVID-19 vaccination during pregnancy, compared with vaccination after pregnancy and with no vaccination, was not significantly associated with increased risk of adverse peripartum outcomes. Study interpretation should consider that the vaccinations received during pregnancy were primarily mRNA vaccines administered in the second and third trimester.**
JAMA 24MAR2022	**Association of SARS-CoV-2 Vaccination During Pregnancy With Pregnancy Outcomes**	Magnus M.C., *et al.* International gotopaper	Vaccines	**Aim**: To examine the risk of adverse pregnancy outcomes after vaccination against SARS-CoV-2 during pregnancy. **Methods:** This registry-based retrospective cohort study included 157 521 singleton pregnancies ending after 22 gestational weeks from January 1, 2021, until January 12, 2022 (Sweden), or January 15, 2022 (Norway). The Pregnancy Register in Sweden and the Medical Birth Registry of Norway were linked to vaccination and other registries for identification of exposure and background characteristics. **Results** > Among the 157 521 singleton births included in the study (103 409 in Sweden and 54 112 in Norway), the mean maternal age at the time of delivery was 31 years, and 28 506 (18%) were vaccinated against SARS-CoV-2 (12.9% with BNT162b2, 4.8% with mRNA-1273, and 0.3% with AZD1222) while pregnant. > A total of 0.7%, 8.3%, and 9.1% of individuals delivering were vaccinated during the first, second, and third trimester, respectively. > Vaccination against SARS-CoV-2 was not significantly associated with increased risk of preterm birth (6.2 vs 4.9 per 10 000 pregnancy days; adjusted hazard ratio [aHR], 0.98 [95% CI, 0.91 to 1.05]; I2 = 0%; P for heterogeneity = .60), stillbirth (2.1 vs 2.4 per 100 000 pregnancy days; aHR, 0.86 [95% CI, 0.63 to 1.17]), small for gestational age (7.8% vs 8.5%; difference, –0.6% [95% CI, –1.3% to 0.2%]; adjusted OR [aOR], 0.97 [95% CI, 0.90 to 1.04]), low Apgar score (1.5% vs 1.6%; difference, –0.05% [95% CI, –0.3% to 0.1%]; aOR, 0.97 [95% CI, 0.87 to 1.08]), or neonatal care admission (8.5% vs 8.5%; difference, 0.003% [95% CI, –0.9% to 0.9%]; aOR, 0.97 [95% CI, 0.86 to 1.10]). **In this population-based study conducted in Sweden and Norway, vaccination against SARS-CoV-2 during pregnancy, compared with no SARS-CoV-2 vaccination during pregnancy, was not significantly associated with an increased risk of adverse pregnancy outcomes. The majority of the vaccinations were with mRNA vaccines during the second and third trimesters of pregnancy, which should be considered in interpreting the findings.**

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Science 24MAR2022	**Structural basis for potent antibody neutralization of SARS-CoV-2 variants including B.1.1.529**	Zhou T., *et al.* USA gotopaper	Therapeutics	**Aim**: to provide insight into effective neutralization of receptor-binding domain (RBD) antibodies for their ability to bind and neutralize B.1.1.529. **Methods:** Cryo-EM structures were determined and receptor-binding domain (RBD) antibodies were evaluated for their ability to bind and neutralize B.1.1.529. **Findings:** > In the context of trimeric spike proteins, variant amino acid changes did not provide a biologically meaningful alteration in affinity to ACE2. > Mutations altered 16% of the B.1.1.529 RBD surface, clustered on a RBD ridge overlapping the ACE2-binding surface and reduced binding of most antibodies. > Significant inhibitory activity was retained by select monoclonal antibodies including A19-58.1, B1-182.1, COV2-2196, S2E12, A19-46.1, S309 and LY-CoV1404, which accommodated these changes and neutralized B.1.1.529. **The authors identified combinations of antibodies with synergistic neutralization. The analysis revealed structural mechanisms for maintenance of potent neutralization against emerging variants.**
Nature Med. 23MAR2022	**Serum neutralization of SARS-CoV-2 Omicron sublineages BA.1 and BA.2 in patients receiving monoclonal antibodies**	Bruel T., *et al.* Belgium / France gotopaper	Variants	**Aim**: to compare the sensitivity of BA.1 and BA.2 to neutralization by 9 therapeutic monoclonal antibodies (mAbs). **Methods:** No statistical methods were used to predetermine sample size. The experiments were not randomized and the investigators were not blinded to allocation during experiments and outcome assessment. **Results** > We isolated a BA.2 variant from a nasopharyngeal swab which was initially sequenced at the National Reference Center of UZ/KU Leuven (Belgium). The virus was amplified by two passages on Vero E6 cells and re-sequenced (Pango lineage BA.2, 21L (Omicron) according to Nextstrain, GISAID accession ID: (EPI_ISL_10654979). > When compared to the Delta variant (B.1.617), the BA.2 spike protein contained 28 changes, with 18 modifications that are shared with BA.1. The modifications are dispersed throughout the spike but display a preferential accumulation in the N-terminal domain (NTD) and the RBD. > Seven antibodies (Bamlanivimab, Etesevimab, Casirivimab, Sotrovimab, Adintrevimab, Regdanvimab and Tixagevimab) were inactive against BA.2. The two other antibodies (Imdevimab and Cilgavimab) displayed an IC50 of 693 and 9 ng/ml, against BA.2, respectively. > The addition of Tixagevimab to Cilgavimab in the Evusheld cocktail was not more efficient than Cilgavimab alone. > In agreement with the decreased sero-neutralization activity of Evusheld-treated individuals against BA.1, we observed 4 breakthrough infections among the 29 participants. > Our results also show that measuring antibody levels with standard serology assays that currently use an ancestral spike antigen does not inform on protection. Future work will help determining whether adapted, lineage-specific, serological or neutralization assays can be used as a marker of clinical efficacy. **Collectively, BA.1 and BA.2 exhibit noticeable differences in their sensitivity to therapeutic mAbs. Anti-Omicron neutralizing activity of Ronapreve, and to a lesser extent that of Evusheld, is reduced in patients' sera.**

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eClinical Medicine 24MAR2022	**Tocilizumab plus dexamethasone versus dexamethasone in patients with moderate-to-severe COVID-19 pneumonia: A randomised clinical trial from the CORIMUNO-19 study group**	Hermine O., *et al.* France gotopaper	Therapeutics	**Aim**: to investigate the efficacy and safety of dexamethasone (DEX) + tocilizumab (TCZ) in an open randomized clinical trial. **Methods:** - Patients with moderate-to-severe COVID-19 pneumonia requiring oxygen (>3 L/min), July 24, 2020-May 18, 2021. - Treatment: DEX (10 mg/d 5 days tapering up to 10 days) alone or combined with TCZ (8 mg/kg IV) at day 1, possibly repeated with a fixed dose of 400 mg i.v. at day 3. Primary outcome: time from randomization to mechanical ventilation support or death up to day 14, analysed on an intent-to-treat basis. **Findings:** > 450 patients analysed, of whom 226 and 224 patients were assigned to receive DEX or TCZ+DEX, respectively. > At day 14, mechanical ventilation or death occurred in 32/226 (14%) and 27/224 (12%) in the DEX and TCZ+DEX arms, respectively (hazard ratio [HR] 0·85, 90% credible interval [CrI] 0·55 to 1·31). > At day 14, the World health Organization (WHO) clinical progression scale (CPS) was significantly improved in the TCZ+DEX arm (OR 0·69, 95% CrI, 0·49 to 0.97). > At day 28, the cumulative incidence of oxygen supply independency was 82% in the TCZ+DEX arms and 72% in the DEX arm (HR 1·36, 95% CI 1·11 to 1·67). > On day 90, 24 deaths (11%) were observed in the DEX arm and 18 (8%) in the TCZ+DEX arm (HR 0·77, 95% CI 0·42–1·41). > Serious adverse events were observed in 25% and 21% in DEX and TCZ+DEX arms, respectively. **Mechanical ventilation need and mortality were not improved with TCZ+DEX compared with DEX alone. Given the wide confidence intervals for the estimate of effect, definitive interpretation cannot be drawn.**
Lancet Microbe 23MAR2022	**SARS-CoV-2-specific antibody and T-cell responses 1 year after infection in people recovered from COVID-19: a longitudinal cohort study**	Guo L., *et al.* China gotopaper	Immunology	**Aim**: to investigate the durability and functionality of the humoral and T-cell response to the original SARS-CoV-2 strain and variants in recovered patients 12 months after infection. **Methods:** - Longitudinal cohort study, participants recovered from COVID-19 (Jan 7 and May 29, 2020). Follow-up visit: Dec 16, 2020-Jan 27, 2021. - Study of IgM, IgA, and IgG against the SARS-CoV-2 nucleoprotein, Spike protein, and the RBD 12 months after initial infection. **Findings:** > 1096 patients were enrolled, including 289 (26·4%) patients with moderate initial disease, 734 (67·0%) with severe initial disease, and 73 (6·7%) with critical initial disease. > N-IgG (899 [82·0%]), S-IgG (1043 [95·2%]), RBD-IgG (1032 [94·2%]), and neutralising (115 [81·6%] of 141) antibodies were detectable 12 months after initial infection in most individuals. > Neutralising antibodies remained stable 6 and 12 months after initial infection in most individuals younger than 60 years. > Multifunctional T-cell responses were detected for all SARS-CoV-2 viral proteins tested. > There was no difference in the magnitude of T-cell responses or cytokine profiles in individuals with different symptom severity. > The degree of reduced in-vitro neutralising antibody responses to the D614G and delta variants, but not to the beta variant, was associated with the neutralising antibody titres after SARS-CoV-2 infection. > Poor neutralising antibody responses to the beta variant were found; 83 (72·2%) of 115 patients showed no response at all. > The neutralising antibody titre reduction of the recovered patient plasma against the delta variant was similar to that of the D614G variant and lower than that of the beta variant. > T-cell responses were cross-reactive to the beta variant in most individuals. Importantly, T-cell responses could be detected in all individuals who had lost the neutralising antibody response to SARS-CoV-2 12 months after the initial infection. **Cross-reactive SARS-CoV-2-specific T-cell responses could be particularly important in the protection against severe disease whereas neutralising antibody responses seem to reduce over time.**

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NEJM 23MAR2022	**Neutralization Profile after Recovery from SARS-CoV-2 Omicron Infection**	Rössler A., *et al.* Austria gotopaper	Immunology	**Aim**: to report the results on neutralization profiles against six SARS-CoV-2 variants in serum samples obtained from persons who had recovered from infection with the omicron BA.1 variant, with or without preexisting SARS-CoV-2 immunity. - Serum samples 5 to 42 days after first positive PCR during infection with the omicron BA.1 variant. - Immunity profiles i) vaccinated without previous SARS-CoV-2 infection (n = 15); ii) unvaccinated without previous SARS-CoV-2 infection (n = 18); iii) vaccinated, with previous infection with the D614G (wild-type), alpha, or delta variant (n = 11); iv) unvaccinated, with previous infection with the wild-type, alpha, or delta variant (n = 15). - Neutralizing antibodies against wild-type, alpha, beta, P.1 (gamma), delta, and omicron BA.1. **Results** > Neutralizing antibody titers against all the variants were high among vaccinated persons after omicron BA.1 breakthrough infection and among vaccinated or unvaccinated persons who had had previous infection with the wild-type, alpha, or delta variant before infection with the omicron BA.1. > Mean neutralizing antibody titers against the omicron BA.1 variant were lower than those against the other variants among previously vaccinated persons but were similar to those against the other variants among unvaccinated persons who had had infection with the wild-type, alpha, or delta variant before infection with the omicron BA.1 variant. > Samples obtained from unvaccinated persons who had not had previous SARS-CoV-2 infection before infection with the omicron BA.1 variant contained mainly neutralizing antibodies against omicron BA.1 but only occasionally contained neutralizing antibodies against the other variants. **These data support the hypothesis that the omicron BA.1 variant is an extremely potent immune-escape variant that shows little cross-reactivity with the earlier variants.** Unvaccinated persons who are infected with the omicron BA.1 variant only (without previous infection) might not be sufficiently protected against infection with a variant other than omicron BA.1.
NEJM 23MAR2022	**Safety and Efficacy of a Third Dose of BNT162b2 Covid-19 Vaccine**	Moreira E.D., *et al.* Brazil / USA gotopaper	Vaccines	**Aim**: to evaluate safety and efficacy of offering a third (booster) dose in persons 16 years of age or older. - Participants who had received two 30-µg doses of the BNT162b2 vaccine at least 6 months earlier were injected with a third dose of the BNT162b2 vaccine or with placebo. - Safety and efficacy against Covid-19 were assessed starting 7 days after the third dose. **Results** > 5081 participants received a third BNT162b2 dose and 5044 received placebo. Median interval between dose 2 and dose 3 was 10.8 months in the vaccine group and 10.7 months in the placebo group; the median follow-up was 2.5 months. > Local and systemic reactogenicity events from the third dose were generally of low grade. > No new safety signals were identified, and no cases of myocarditis or pericarditis were reported. > Among the participants without evidence of previous SARS-CoV-2 infection, Covid-19 with onset at least 7 days after dose 3 was observed in 6 participants in the vaccine group and in 123 participants in the placebo group, corresponding to a relative vaccine efficacy of 95.3% (95% CI, 89.5 to 98.3). **A third dose of the BNT162b2 vaccine administered a median of 10.8 months after the second dose provided 95.3% efficacy against Covid-19 as compared with two doses of the BNT162b2 vaccine during a median follow-up of 2.5 months.**

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Nature Commun. 23MAR2022	**Comparative effectiveness and safety of homologous two-dose ChAdOx1 versus heterologous vaccination with ChAdOx1 and BNT162b2**	Hermosilla E., *et al.* International gotopaper	Vaccines	**Aim:** To study if heterologous vaccination with first-dose ChAdOx1 and second-dose BNT162b2 may generate a better immune response than homologous vaccination with two doses of ChAdOx1. **Methods** > In this cohort analysis, we use linked data from Catalonia (Spain), where those aged <60 who received a first dose of ChAdOx1 could choose between ChAdOx1 and BNT162b2 for their second dose. > Comparable cohorts were obtained after exact-matching 14,325/17,849 (80.3%) people receiving heterologous vaccination to 14,325/149,386 (9.6%) receiving homologous vaccination by age, sex, region, and date of second dose. Of these, 464 (3.2%) in the heterologous and 694 (4.8%) in the homologous groups developed COVID-19 between 1st June 2021 and 5th December 2021. **Results** > The resulting hazard ratio (95% confidence interval) is 0.66 [0.59–0.74], favouring heterologous vaccination. > The two groups had similar testing rates and safety outcomes. > Sensitivity and negative control outcome analyses confirm these findings. **In conclusion, we demonstrate that a heterologous vaccination schedule with ChAdOx1 followed by BNT162b2 was more efficacious than and similarly safe to homologous vaccination with two doses of ChAdOx1. Most of the infections in our study occurred when Delta was the predominant SARS-CoV-2 variant in Spain. These data agree with previous phase 2 randomised trials.**
Science Transl Med. 22MAR2022	**Therapeutic treatment with an oral prodrug of the remdesivir parental nucleoside is protective against SARS-CoV-2 pathogenesis in mice**	Schäfer A., *et al.* USA gotopaper	Therapeutics	**Aim**: to demonstrate the in vitro antiviral activity and in vivo therapeutic efficacy of GS-621763, an orally bioavailable prodrug of GS-441524, the parent nucleoside of remdesivir, which targets the highly conserved virus RNA-dependent RNA polymerase **Findings** > GS-621763 exhibited antiviral activity against SARS-CoV-2 in lung cell lines and two different human primary lung cell culture systems. > GS-621763 was also potently antiviral against a genetically unrelated emerging coronavirus, Middle East Respiratory Syndrome CoV (MERS-CoV). > The dose-proportional pharmacokinetic profile observed after oral administration of GS-621763 translated to dose-dependent antiviral activity in mice infected with SARS-CoV-2. > Therapeutic GS-621763 administration reduced viral load and lung pathology; treatment also improved pulmonary function in COVID-19 mouse model. > A direct comparison of GS-621763 with molnupiravir, an oral nucleoside analog antiviral which has recently received EUA approval, proved both drugs to be similarly efficacious in mice. **These data support the exploration of GS-441524 oral prodrugs for the treatment of COVID-19.**

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Clin Microbiol Infect. 22MAR2022	**Post-COVID-19 syndrome and humoral response association after one year in vaccinated and unvaccinated patients**	Peghin M., *et al.* Italy gotopaper	Long Covid	**Aim**: to describe the impact of vaccination and the role of humoral responses on post-coronavirus disease 2019 (COVID-19) syndrome one year after the onset of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). **Methods** > A prospective study. Interviews investigated post-COVID-19 syndrome 6 and 12 months after the disease onset of all adult in- and outpatients with COVID-19 attending Udine Hospital (March–May 2020). Vaccination status and two different serological assays to distinguish between response to vaccination (receptor-binding domain –RBD SARS-CoV-2 IgG) and/or natural infection (non-RBD-SARS-CoV-2 IgG) were also assessed. **Findings** > 479 individuals (52.6% female, mean age 53 years) were interviewed 13.5 months (0.6 SD) after acute infection. Post-COVID-19 syndrome was observed in 47.2% (226/479) of patients after one year. > There were no significant differences in the worsening of post-COVID 19 symptoms (22.7% vs 15.8%, p = 0.209) among vaccinated (n=132) and unvaccinated (n=347) patients. > The presence of non-RBD SARS-CoV-2 IgG induced by natural infection showed a significant association with post-COVID-19 syndrome (OR 1.35, 95% CI 1.11–1.64, p = 0.003), and median non-RBD SARS-CoV-2 IgG titres were significantly higher in long-haulers than in patients without symptoms 22 (IQR 9.7–37.2) vs 14.1 (IQR 5.4–31.3) kAU/L, p = 0.009) after one year. > In contrast, the presence of RBD SARS-CoV-2 IgG was not associated with the occurrence of post-COVID-19 syndrome (>2500 U/mL vs 0.9–2500 U/mL, OR 1.36, 95% CI 0.62–3.00, p = 0.441) and RBD SARS-CoV-2 IgG titres were similar in long-haulers than in patients without symptoms (50% values > 2500 U/mL vs 55.6% values > 2500 U/mL, p = 0.451) **The SARS-CoV-2 vaccination is not associated with the emergence of post-COVID-19 symptoms over one year after acute infection. The persistence of high serological titres response induced by natural infection but not by vaccination, may play a role in long-COVID-19.**
Clin Infect Dis. 21MAR2022	**Efficacy and Safety of Sarilumab in Hospitalized Patients With COVID-19: A Randomized Clinical Trial**	Sivapalasingam S., *et al.* USA gotopaper	Therapeutics	Open-label platform trials and a prospective meta-analysis suggest efficacy of anti–IL-6R therapies in hospitalized patients with COVID-19 receiving corticosteroids. **Methods** > In this adaptive, phase 2/3, randomized, double-blind, placebo-controlled trial, adults hospitalized with COVID-19 (ClinicalTrials.gov: NCT04315298) received intravenous sarilumab or placebo. The phase 3 primary analysis population included patients with critical COVID-19 receiving mechanical ventilation randomized to sarilumab 400 mg or placebo. > The primary outcome was proportion of patients with ≥1-point improvement in clinical status from baseline to day 22. **Findings** > There were 457 and 1365 patients randomized and treated in phases 2 and 3, respectively. In phase 3, patients with critical COVID-19 receiving mechanical ventilation (n = 298; 28.2% on corticosteroids), the proportion with ≥1-point improvement in clinical status (alive, not receiving mechanical ventilation) at day 22 was 43.2% in sarilumab and 35.5% in placebo (risk difference +7.5%; 95% CI, –7.4 to 21.3; P = .3261), a relative risk improvement of 21.7%. > In post-hoc analyses pooling phase 2 and 3 critical patients receiving mechanical ventilation, the hazard ratio for death in sarilumab versus placebo was 0.76 (95% CI, .51–1.13) overall and 0.49 (95% CI, .25–.94) in patients receiving corticosteroids at baseline. **This study did not establish the efficacy of sarilumab in hospitalized patients with severe/critical COVID-19. Post-hoc analyses were consistent with other studies that found a benefit of sarilumab in patients receiving corticosteroids.**

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Lancet Diabetes Endocrinol. 21MAR2022	**Risks and burdens of incident diabetes in long COVID: a cohort study**	Xie Y., et al. USA gotopaper	Long Covid	**Aim**: to examine the post-acute risk and burden of incident diabetes in people who survived the first 30 days of SARS-CoV-2 infection. **Methods** - Cohort: 181 280 participants who had a positive COVID-19 test between March 1, 2020, and Sept 30, 2021, and survived the first 30 days of COVID-19. - Contemporary control: 4 118 441 individuals enrolled between March 1, 2020, and Sept 30, 2021 - Historical control: 4 286 911 individuals enrolled between March 1, 2018, and Sept 30, 2019. - Both control groups had no evidence of SARS-CoV-2 infection. Participants in all three comparison groups were free of diabetes before cohort entry and were followed up for a median of 352 days (IQR 245–406). - Measures of risk: hazard ratio (HR) and burden per 1000 people at 12 months. **Results** > In the post-acute phase of the disease, compared with the contemporary control group, people with COVID-19 exhibited an increased risk (HR 1·40, 95% CI 1·36–1·44) and excess burden (13·46, 95% CI 12·11–14·84, per 1000 people at 12 months) of incident diabetes; and an increased risk (1·85, 1·78–1·92) and excess burden (12·35, 11·36–13·38) of incident antihyperglycaemic use. > Analyses to estimate the risk of a composite endpoint of incident diabetes or antihyperglycaemic use yielded a HR of 1·46 (95% CI 1·43–1·50) and an excess burden of 18·03 (95% CI 16·59–19·51) per 1000 people at 12 months. > Risks and burdens of post-acute outcomes increased in a graded fashion according to the severity of the acute phase of COVID-19 (whether patients were non-hospitalised, hospitalised, or admitted to intensive care). > All the results were consistent in analyses using the historical control as the reference category. **In the post-acute phase, an increased risks and 12-month burdens of incident diabetes and antihyperglycaemic use is reported in people with COVID-19 compared to a non-infected pandemic cohort and a pre-pandemic cohort.**
Nature Commun. 21MAR2022	**Comparative effectiveness of the BNT162b2 and ChAdOx1 vaccines against Covid-19 in people over 50**	Xie J., *et al.* UK gotopaper	Vaccines	**Aim:** To conduct a head-to-head comparison of BNT162b2 versus ChAdOx1 against Covid-19 in people over 50 **Methods** > To analyse 235,181 UK Biobank participants aged 50 years or older and vaccinated with one or two doses of BNT162b2 or ChAdOx1. > People are followed from the vaccination date until 18/10/2021. > Inverse probability weighting is used to minimise confounding and the Cox models to derive hazard ratio. **Results** > Compared with one dose of ChAdOx1, vaccination with BNT162b2 is associated with a 28% (95% CI, 12-42) decreased risk of SARS-CoV-2 infection. > Also, two doses of BNT162b2 vs ChAdOx1 confers 30% (95% CI, 25-35) and 29% (95% CI, 10-45) lower risks of both infection and hospitalisation during the study period when the Delta variant is dominant. > Furthermore, the comparative protection against the infection persists for at least six months among the fully vaccinated, suggesting no differential waning between the two vaccines. **These findings support evidence from pivotal trials suggesting that BNT162b2 provides additional protection against Covid-19 and hospitalisation than ChAdOx1 vaccination. For the first time, it was demonstrated that this comparative effectiveness endured over six months when the Delta variant was predominant, and community transmission kept increasing in the UK. These findings highlight the importance of continuous monitoring of the effectiveness of different vaccines against emerging SARS-CoV-2 variants to inform future booster campaigns and vaccine combinations strategies.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Immunol. 21MAR2022	**Establishment and recall of SARS-CoV-2 spike epitope-specific CD4+ T cell memory**	Wragg K.M., *et al.* Australia gotopaper	Immunology	**Aim**: to quantitatively and qualitatively characterize memory CD4+ T cells and cTFH cells following infection and vaccination. **Methods :** Use a novel HLA-DRB1*15:01 tetramer presenting a SARS-CoV-2 spike epitope (S751–767) to quantitatively and qualitatively characterize memory CD4+ T cells and cTFH cells. **Findings :** > Pprimary infection or vaccination induces robust S751-specific CXCR5− and cTFH cell memory responses. > Secondary exposure induced recall of CD4+ T cells with a transitory CXCR3+ phenotype, and drove expansion of cTFH cells transiently expressing ICOS, CD38 and PD-1. > In both contexts, cells exhibited a restricted T cell antigen receptor repertoire, including a highly public clonotype and considerable clonotypic overlap between CXCR5− and cTFH populations. > Following a third vaccine dose, the rapid re-expansion of spike-specific CD4+ T cells contrasted with the comparatively delayed increase in antibody titers. **Stable pools of cTFH and memory CD4+ T cells established by infection and/or vaccination are efficiently recalled upon antigen reexposure and may contribute to long-term protection against SARS-CoV-2.**
Lancet 19MAR2022	**Effectiveness of the Ad26.COV2.S vaccine in health-care workers in South Africa (the Sisonke study): results from a single-arm, open-label, phase 3B, implementation study**	Bekker L.G., *et al.* International gotopaper	Vaccines	**Aim** Assessement of the effectiveness of a single dose of the Ad26.COV2.S vaccine (Johnson & Johnson) in health-care workers in South Africa during two waves of the South African COVID-19 epidemic. **Methods** > HCW popuation (over 18 years of age) within the Sisonke study (Single-arm, open-label, phase 3B) > Administration of a single dose of 5 × 10exp10 viral particles of the Ad26.COV2.S vaccine. Primary outcome: vaccine effectiveness against severe COVID-19, defined as COVID-19-related admission to hospital, hospitalisation requiring critical or intensive care, or death, in health-care workers compared with the general population, ascertained 28 days or more after vaccination **Findings** > 477 102 health-care workers were enrolled and vaccinated > 74·9% were female and 25·1% were male > Median age of 42·0 years (33·0–51·0) 215 813 vaccinated individuals were matched with 215 813 unvaccinated individuals. > Vaccine effectiveness derived from the total matched cohort was: - 83% (95% CI 75–89) to prevent COVID-19-related deaths, - 75% (69–82) to prevent COVID-19-related hospital admissions requiring critical or intensive care, - 67% (62–71) to prevent COVID-19-related hospitalisations. > The vaccine effectiveness was maintained in older health-care workers and those with comorbidities including HIV infection. > During the course of the study, the beta (B.1.351) and then the delta (B.1.617.2) SARS-CoV-2 variants of concerns were dominant, and vaccine effectiveness remained consistent: - effectiveness against COVID-19-related hospital admission during beta wave was 62% [95% CI 42–76] and during delta wave was 67% [62–71], - effectiveness against COVID-19-related death during beta wave was 86% [57–100] and during delta wave was 82% [74–89]. **Conclusions** The single-dose Ad26.COV2.S vaccine shows effectiveness against severe COVID-19 disease and COVID-19-related death after vaccination, and against both beta and delta variants, providing real-world evidence for its use globally.

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA Netw Open 18MAR2022	**Age-Varying Susceptibility to the Delta Variant (B.1.617.2) of SARS-CoV-2**	Chun J.Y., *et al.* South Korea gotopaper	Public health / Epidemiology	**Aim**: to gain a better understanding of the association of age with susceptibility to the Delta variant of SARS-CoV-2. **Methods :** Decision analytic model using symptom onset (S), exposure (E), infectious (I), and quarantine (Q) (SEIQ) to estimate the age-specific force of infection. **Findings :** > Among 106 866 confirmed COVID-19 infections (including 26 597 infections and 80 269 infections during the third and fourth waves of COVID-19 in Korea, respectively), a significant difference in age-specific susceptibility to the Delta vs pre-Delta variant was found in the younger age group. > After adjustment for contact pattern and vaccination status, the increase in susceptibility to the Delta vs pre-Delta variant was estimated to be highest in the group aged 10 to 15 years, approximately doubling (1.92-fold increase [95% CI, 1.86-fold to 1.98-fold]), whereas in the group aged 50 years or more, susceptibility to the Delta vs pre-Delta variant remained stable at an approximately 1-fold change (eg, among individuals aged 50-55 years: 0.997-fold [95% CI, 0.989-fold to 1.001-fold). **The Delta variant of SARS-CoV-2 was estimated to propagate more easily among children and adolescents than pre-Delta strains, even after adjusting for contact pattern and vaccination status.**
Lancet Infect Dis. 17MAR2022	**Neutralisation sensitivity of the SARS-CoV-2 omicron (B.1.1.529) variant: a cross-sectional study**	Sheward D.J., *et al.* Sweden gotopaper	Variants	**Aim**: to characterise the sensitivity of the omicron variant to neutralisation. - omicron pseudotyped virus neutralisation assay to quantify the neutralising antibody ID50 (the reciprocal dilution that produces 50% inhibition) against the omicron spike protein, and the fold-change in ID50 relative to the spike of wild-type SARS-CoV-2 - one convalescent reference plasma pool, three reference serum pools from vaccinated individuals, and two cohorts: one comprising previously infected hospital workers (17 sampled in November, 2021, after vaccine rollout and 9 in June or July, 2020, before vaccination) and one comprising serum from 40 randomly sampled blood donors donated during week 48 (Nov 29–Dec 5) of 2021. - assessment of neutralisation of omicron by five clinically relevant monoclonal antibodies (mAbs). **Results** > Neutralising antibody responses in reference sample pools sampled shortly after infection or vaccination were substantially less potent against the omicron variant than against wild-type SARS-CoV-2 (7- to 42-fold reduction in ID50 titres). > For sera obtained before vaccination in 2020 from a cohort of convalescent hospital workers, neutralisation of the omicron variant was low to undetectable (all ID50 titres <20). > In serum samples obtained in 2021 from two cohorts, substantial cross-neutralisation of the omicron variant was observed. Sera from 17 hospital workers after infection and subsequent vaccination had a reduction in average potency of only 5-fold relative to wild-type SARS-CoV-2 (geometric mean ID50 titre 495 vs 105), and two donors had no reduction in potency. > A similar pattern was observed in randomly sampled blood donors (n=40), who had an 8-fold reduction in average potency against the omicron variant compared with wild-type SARS-CoV-2 (geometric mean ID50 titre 369 vs 45). > Omicron variant was resistant to neutralisation (50% inhibitory concentration [IC50] >10 µg/mL) by mAbs casirivimab (REGN-10933), imdevimab (REGN-10987), etesevimab (Ly-CoV016), and bamlanivimab (Ly-CoV555). However, S309, the parent of sotrovimab, retained most of its activity, with only an approximately 2-fold reduction in potency against the omicron variant compared with D614G strain (IC50 0·1–0·2 µg/mL). **These data highlight the extensive, but incomplete, evasion of neutralising antibody responses by the omicron variant, and suggest that a vaccine booster might be sufficient to raise neutralising antibody titres to protective levels.**

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Cell 18MAR2022	**Neutralizing immunity in vaccine breakthrough infections from the SARS-CoV-2 Omicron and Delta variants**	Servellita V., *et al.* USA gotopaper	Immunology	**Aim**: to investigate neutralizing immunity against Delta and Omicron SARS-CoV-2 variants. - Virus-like particle (VLP) and live virus assays on 259 samples from 128 vaccinated individuals. **Results** > Following Delta breakthrough infection, titers against WT rose 57-fold and 3.1-fold compared to uninfected boosted and unboosted individuals, respectively, versus only a 5.8-fold increase and 3.1-fold decrease for Omicron breakthrough infection. > Among immunocompetent, unboosted patients, Delta breakthrough infections induced 10.8-fold higher titers against WT compared to Omicron (p=0.037). > Decreased antibody responses in Omicron breakthrough infections relative to Delta were potentially related to a higher proportion of asymptomatic or mild breakthrough infections (55.0% versus 28.6%, respectively), which exhibited 12.3-fold lower titers against WT compared to moderate-severe infections (p=0.020). > Following either Delta or Omicron breakthrough infection, limited variant-specific cross-neutralizing immunity was observed. **These results suggest that Omicron breakthrough infections are less immunogenic than Delta, thus providing reduced protection against reinfection or infection from future variants.**
JAMA 17MAR2022	**Myocarditis Following a Third BNT162b2 Vaccination Dose in Military Recruits in Israel**	Friedensohn L., *et al.* Israel gotopaper	Vaccines	**Aim**: to assess whether a third vaccine dose was associated with the risk of myocarditis. - All military personnel (IDF, Israel Defense Forces) vaccinated with a third dose of BNT162b2 until September 30, 2021, and diagnosed with myocarditis up to October 14, 2021 were included. All suspected myocarditis cases in the IDF are referred to the hospital. - Incidence of myocarditis in the week and 2 weeks following vaccination was calculated. **Results** > 126 029 IDF members were vaccinated. 79% of the men and 90% of the women were 18 to 24 years old. > During follow-up, 9 members, all young men, were diagnosed with myocarditis. One case occurred after COVID-19 and was excluded. The 8 remaining cases had a negative result on a SARS-CoV-2 PCR test at the time of diagnosis. > Four developed symptoms within a week of vaccination, 3 had symptoms beginning 8 to 10 days after vaccination, and 1 developed symptoms >2 weeks after vaccination. > All cases were mild, without arrhythmia or signs of congestive heart failure. All remained without residual cardiac injury on hospital discharge. > The overall incidence rates of myocarditis in the week and 2 weeks following a third vaccine dose were 3.17 (95% CI, 0.64-6.28) and 5.55 (95% CI, 1.44-9.67) per 100 000 vaccines given, respectively. > The incidence in young men was estimated to be 6.43 (95% CI, 0.13-12.73) and 11.25 (95% CI, 2.92-19.59) per 100 000 vaccines given in the week and 2 weeks after a third vaccine dose, respectively. **This study found a low risk of myocarditis after a third dose of BNT162b2 in Israeli military recruits. The incidence was lower than observed a week after a second dose of the vaccine in a similar population. However, the myocarditis incidence for 18- to 24-year-old men was higher than observed for a US male population.**

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Nature Commun. 17MAR2022	**Agent-based modelling of reactive vaccination of workplaces and schools against COVID-19**	Faucher B., *et al.* France gotopaper	Public health / Epidemiology	- Reactive" (ring) vaccination: targeting contacts of confirmed cases or contacts of such contacts, and vaccinating these contacts in workplaces or schools. - Non-reactive vaccination: mass vaccination, workplace/school strategies. **Objective**: to study the impact of reactive vaccination targeting schools and workplaces vs. mass vaccination. **Results** > Reactive vaccination + contact tracing, home-working and social restrictions: - In most scenarios, reactive vaccination results in greater case reduction compared to non-reactive strategies using the same number of vaccine doses. - The reactive strategy may be less effective than a moderate/high mass vaccination programme (~ 45-60% of the total population) if vaccination coverage is high or if disease incidence is low. > Combining reactive and mass vaccination to manage the sustained spread of COVID-19: - For the same number of doses, the combined strategy is more effective than mass vaccination in reducing the attack rate. A cap on the number of doses (50-250 per 100,000 population, compared to unlimited vaccine availability) limits the impact of the reactive strategy. > Combining reactive and mass vaccination to manage a COVID-19 outbreak: - Reactive vaccination could better mitigate the spread if implemented early, supported by a strengthened test-trace-isolate strategy, and triggering increased vaccine uptake. **Reactive vaccination in universities and workplaces could have a stronger impact in several circumstances than simply increasing vaccination in these settings. The effectiveness of the reactive strategy depends on the epidemic context, the use of contact tracing, vaccination coverage and vaccine administration.**
Clin Microbiol Infect. 17MAR2022	**Long-term evolution of humoral immune response after SARS-CoV-2 infection**	Teyssou E., *et al.* France gotopaper	Immunology	**Aim**: to characterize the evolution of humoral immune response up to one year after SARS-CoV-2 infection in health care workers (HCWs) during the first wave of COVID-19 in Paris **Methods** >Serum samples from 92 HCWs were tested at month 0 (M0), M6 and M12 after SARS-CoV-2 infection for IgG targeting the nucleocapsid (N), IgG targeting the receptor-binding domain (RBD) of spike (S) protein, IgA targeting S, and anti-RBD neutralizing antibodies. After M6, 46 HCWs received a single-dose of COVID-19 vaccine. **Findings** > We observed a significant decrease of all SARS-CoV-2 immunologic markers at M6 post-infection: median decreases were 0.26 log binding antibody units (BAU)/mL (M0: 1.9 [interquartile range (IQR) 1.47 – 2.27]; M6: 1.64 [IQR: 1.22 – 1.92]) for anti-RBD IgG, 4.10 (index) (M0: 4.94 [IQR: 2.72 – 6.82]; M6: 0.84 [IQR: 0.25 – 1.55]) for anti-N IgG, 0.64 (index) (M0: 2.50 [IQR: 1.18 – 4.62]; M6: 1.86 [IQR: 0.85 – 3.54]) for anti-S IgA, and 24.4% (M0: 66.4 [IQR: 39.7 – 82.5]; M6: 42.0 [IQR: 16.8 – 68.8]) inhibition activity for the RBD neutralizing antibodies. > Between M6 and M12, anti-RBD IgG level, anti-S IgA index, and anti-RBD neutralizing activity, significantly increased among COVID-19 vaccinated HCWs, whereas they remained stable among unvaccinated HCWs. Anti-N IgG index significantly decreased between M6 and M12 among both vaccinated (median: 0.73 [IQR: 0.23 – 1.11] at M6 and 0.52 [IQR: 0.20 – 0.73] at M12) and unvaccinated HCWs (median: 0.79 [IQR: 0.21 – 4.67] at M6 and 0.34 [IQR: 0.24 – 2.78] at M12). **A steady decline in the anti-N IgG response was observed during the first year following SARS-CoV-2 infection among HCWs, whereas the anti-RBD IgG and the anti-S IgA responses remained stable and could be enhanced by COVID-19 vaccination.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA Netw Open 17MAR2022	**Incidence of Cerebral Venous Thrombosis Following SARS-CoV-2 Infection vs mRNA SARS-CoV-2 Vaccination in Singapore**	Ming Tu T., *et al.* Singapore gotopaper	Clinic	**Aim**: To compare the incidence rates and clinical characteristics of CVT following either SARS-CoV-2 infection or mRNA-based SARS-CoV-2 vaccines. **Methods** > Between January 23, 2020, and August 3, 2021, this observational cohort study was conducted at all public acute hospitals in Singapore, where patients hospitalized with CVT within 6 weeks of SARS-CoV-2 infection or after mRNA-based SARS-CoV-2 vaccination (BNT162b2 [Pfizer-BioNTech] or mRNA-1273 [Moderna]) were identified. > Diagnosis of SARS-CoV-2 infection was based on quantitative reverse transcription-polymerase chain reaction or positive serology. > National SARS-CoV-2 infection data were obtained from the National Centre for Infectious Disease, Singapore, and vaccination data were obtained from the National Immunisation Registry, Singapore. **Results** > Among 62 447 individuals diagnosed with SARS-CoV-2 infections included in this study, 58 989 (94.5%) were male; the median (range) age was 34 (0-102) years; 6 CVT cases were identified (all were male; median [range] age was 33.5 [27-40] years). > Among 3 006 662 individuals who received at least 1 dose of mRNA-based SARS-CoV-2 vaccine, 1 626 623 (54.1%) were male; the median (range) age was 50 (12-121) years; 9 CVT cases were identified (7 male individuals [77.8%]; median [range] age: 60 [46-76] years). > The crude IR of CVT after SARS-CoV-2 infections was 83.3 per 100 000 person-years (95% CI, 30.6-181.2 per 100 000 person-years) and 2.59 per 100 000 person-years (95% CI, 1.19-4.92 per 100 000 person-years) after mRNA-based SARS-CoV-2 vaccination. > Six (66.7%) received BNT162b2 (Pfizer-BioNTech) vaccine and 3 (33.3%) received mRNA-1273 (Moderna) vaccine. > The crude IRR of CVT hospitalizations with SARS-CoV-2 infection compared with those who received mRNA SARS-CoV-2 vaccination was 32.1 (95% CI, 9.40-101; P < .001). **The incidence rate of CVT after SARS-CoV-2 infection was significantly higher compared with after mRNA-based SARS-CoV-2 vaccination. CVT remained rare after mRNA-based SARS-CoV-2 vaccines, reinforcing its safety.**
Cell 17MAR2022	**Vaccine Protection Against the SARS-CoV-2 Omicron Variant in Macaques**	Chandrashekar A., *et al.* USA gotopaper	Vaccines	**Aim:** To evaluate the immunogenicity and protective efficacy of BNT162b2 and Ad26.COV2.S, including homologous and heterologous boost regimens, against SARS-CoV-2 Omicron challenge in nonhuman primates. **Results** > In this study, we demonstrate that the BNT162b2 and Ad26.COV2.S vaccines led to rapid virologic control in the upper and lower respiratory tracts following high dose, heterologous challenge with the SARS-CoV-2 Omicron variant in the majority of macaques. However, 4 vaccinated animals with moderate Omicron-specific NAb titers but negligible Omicron-specific CD8+ T cell responses failed to control viral replication in NS by day 7. > In the present study, Omicron-specific NAbs were markedly lower than WA1/2020 NAbs, whereas Omicron-specific T cell responses were comparable WA1/2020 T cell responses, indicating substantial cross-reactivity of cellular immune responses against SARS-CoV-2 variants. > We observed that virus persisted longer in NS compared with BAL in sham controls following Omicron challenge, which differs from prior SARS-CoV-2 variants in macaques. **Data suggest that protection against a highly mutated SARS-CoV-2 variant involves the combination of humoral and cellular immunity, and not NAbs alone unless antibody titers are exceptionally high. Specifically, moderate NAb titers without CD8+ T cell responses may be insufficient for virologic control. Future studies could also compare the relative importance of neutralizing vs. functional non-neutralizing antibodies for protection. Taken together, these data have important implications for understanding immune correlates of protection against highly mutated SARS-CoV-2 variants.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Cell 17MAR2022	**Imprinted SARS-CoV-2-specific memory lymphocytes define hybrid immunity**	Rodda L.B., *et al.* USA gotopaper	Immunology	**Aim**: to assess how vaccine-induced memory is shaped by previous infection. **Methods :** Track of circulating SARS-CoV-2-specific antibodies and memory lymphocytes in a cohort of Naive (N) or SARS-CoV-2-Previously Infected (PI) subjects over the course of three vaccinations. Focusing on RBD-specific antibodies and B cells, and spike (S)-specific CD4+ T cells. **Findings :** > Following vaccination, previously infected individuals generated more SARS-CoV-2 RBD-specific memory B cells and variant-neutralizing antibodies and a distinct population of IFN-γ and IL-10-expressing memory SARS-CoV-2 spike-specific CD4+ T cells than previously naive individuals. > Hybrid immunity is associated with more virus-specific memory B cells and Omicron nAb. > While additional vaccination could increase humoral memory in previously naive individuals, it did not recapitulate the distinct CD4+ T cell cytokine profile observed in previously infected subjects. > Infection-induced Th1/IFNγ signature is not reproduced by three vaccinations **T cell priming by infection or vaccination promotes distinct effector states in which phenotypic outcomes can be normalized by additional antigen exposure, while functional differences persist through multiple vaccine doses.**
Science Advances 16MAR2022	**SARS-CoV-2 receptor binding domain displayed on HBsAg virus–like particles elicits protective immunity in macaques**	Dalvie N.C., *et al.* USA gotopaper	Vaccines	**Aim:** Evalution of the immunogenicity of a modular protein subunit vaccine, comprising a SARS-CoV-2 spike protein subunit RBD displayed on a hepatitis B VLP, constructed using a covalent peptide–mediated linkage (SpyTag/SpyCatcher) **Results** > Immunization of three groups of six cynomolgus macaques with two doses of either vaccine formulation (alum or alum combined with CpG 1018) or a placebo, spaced 3 weeks apart > Assessement of spike protein–specific antibody titers after each dose -full seroconversion and high antibody titers for both RBD-VLP vaccine formulations -formulation with only alum elicited significantly higher-binding antibody titers > Assesement of neutralizing activity of the sera against a SARS-CoV-2 pseudovirus - high titers of neutralizing antibodies for both formulation with alum only and formulation with alum and CpG 1018 - formulation with only alum appeared to yield higher neutralization but was not significantly higher than the vaccine formulated with both alum and CpG 1018 > Assesement of the neutralizing activity of sera from week 5 against SARS-CoV-2 pseudoviruses with spike proteins from several VOC - sera from animals immunized with RBD-VLP in both vaccine formulations exhibited similar neutralizing activities against D614G and B.1.1.7 variants - neutralizing activities of sera from animals immunized with RBD-VLP with only alum were significantly reduced against B.1.351 > Neutralization of SARS-CoV-2 pseudovirus correlated well with spike protein–specific antibody titer > Challenge studies showed that - both formulations of the RBD-VLP vaccine significantly reduced the levels of detected sgRNA in the upper respiratory tract and exhibited nearly complete protection from viral infection in the lower respiratory tract **Conclusion** Preclinical data of RBD-VLP support the potential benefit of its design for a low-cost modular vaccine platform for SARS-CoV-2 and other variants of concern or betacoronaviruses.

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JAMA Netw Open 17MAR2022	**Durability of the Single-Dose Ad26.COV2.S Vaccine in the Prevention of COVID-19 Infections and Hospitalizations in the US Before and During the Delta Variant Surge**	Polinski J.M., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: To assess the association between receiving the Ad26.COV2.S vaccine and COVID-19–related infections and hospitalizations before and during the Delta variant surge. **Methods :** Adults aged 18 years and older who were newly Ad26.COV2.S-vaccinated matched to as many as 10 unvaccinated individuals by date, location, age, sex, and comorbidity index. This was followed by 1:4 propensity score matching on COVID-19 risk factors. **Findings :** > Among 422 034 vaccinated individuals (mean [SD] age, 54.7 [17.4] years; 236 437 [56.0%] women) and 1 645 397 matched unvaccinated individuals (mean [SD] age, 54.5 [17.5] years; 922 937 [56.1%] women), Vaccine effectiveness (VE) was 76% for COVID-19 infections and 81% for COVID-19–related hospitalizations. > VE was stable for at least 180 days after vaccination and over calendar time. > Among states with high Delta variant incidence, VE during June to August 2021 was 74% for infections and 81% for hospitalizations. > VE for COVID-19 was higher in individuals younger than 65 years (78%) and lower in immunocompromised patients (64%). **This cohort study in US clinical practice showed stable VE of Ad26.COV2.S for at least 6 months before as well as during the time the Delta variant emerged and became dominant.**
BMJ 16MAR2022	**SARS-CoV-2 positivity in offspring and timing of mother-to-child transmission: living systematic review and meta-analysis**	Allotey J., *et al.* International gotopaper	Public health / Epidemiology	**Aim:** To assess the rates of SARS-CoV-2 positivity in babies born to mothers with SARS-CoV-2 infection, the timing of mother-to-child transmission and perinatal outcomes, and factors associated with SARS-CoV-2 status in offspring. **Methods** > Living systematic review and meta-analysis. > Data sources: Major databases between 1 December 2019 and 3 August 2021. > Study selection: Cohort studies of pregnant and recently pregnant women (including after abortion or miscarriage) who sought hospital care for any reason and had a diagnosis of SARS-CoV-2 infection, and also provided data on offspring SARS-CoV-2 status and risk factors for positivity. Case series and case reports were also included to assess the timing and likelihood of mother-to-child transmission in SARS-CoV-2 positive babies. **Results** > 472 studies (206 cohort studies, 266 case series and case reports; 28 952 mothers, 18 237 babies) were included. > Overall, 1.8% (95% confidence interval 1.2% to 2.5%; 140 studies) of the 14 271 babies born to mothers with SARS-CoV-2 infection tested positive for the virus with reverse transcriptase polymerase chain reaction (RT-PCR). > Of the 592 SARS-CoV-2 positive babies with data on the timing of exposure and type and timing of tests, 14 had confirmed mother-to-child transmission: seven in utero (448 assessed), two intrapartum (18 assessed), and five during the early postnatal period (70 assessed). > Of the 800 SARS-CoV-2 positive babies with outcome data, 20 were stillbirths, 23 were neonatal deaths, and eight were early pregnancy losses; 749 babies were alive at the end of follow-up. > Severe maternal covid-19 (odds ratio 2.4, 95% confidence interval 1.3 to 4.4), maternal death (14.1, 4.1 to 48.0), maternal admission to an intensive care unit (3.5, 1.7 to 6.9), and maternal postnatal infection (5.0, 1.2 to 20.1) were associated with SARS-CoV-2 positivity in offspring. > Positivity rates using RT-PCR varied between regions, ranging from 0.1% (95% confidence interval 0.0% to 0.3%) in studies from North America to 5.7% (3.2% to 8.7%) in studies from Latin America and the Caribbean. **SARS-CoV-2 positivity rates were found to be low in babies born to mothers with SARS-CoV-2 infection. Evidence suggests confirmed vertical transmission of SARS-CoV-2, although this is likely to be rare. Severity of maternal covid-19 appears to be associated with SARS-CoV-2 positivity in offspring.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
BMJ 16MAR2022	**Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events: population based cohort and self-controlled case series analysis**	Li X., *et al.* International gotopaper	Public Health / Epidemiology	**Aim**: to study the association between covid-19 vaccines, SARS-CoV-2 infection, and risk of immune mediated neurological events. **Methods** > 8 330 497 people who received at least one dose of covid-19 vaccines ChAdOx1 nCoV-19, BNT162b2, mRNA-1273, or Ad.26.COV2.S between the rollout of the vaccination campaigns and end of data availability (UK: 9 May 2021; Spain: 30 June 2021). The study sample also comprised a cohort of 735 870 unvaccinated individuals with a first positive reverse transcription polymerase chain reaction test result for SARS-CoV-2 from 1 September 2020, and 14 330 080 participants from the general population. **Findings** > The study included 4 376 535 people who received ChAdOx1 nCoV-19, 3 588 318 who received BNT162b2, 244 913 who received mRNA-1273, and 120 731 who received Ad26.CoV.2; 735 870 people with SARS-CoV-2 infection; and 14 330 080 people from the general population. > Overall, post-vaccine rates were consistent with expected (background) rates for Bell's palsy, encephalomyelitis, and Guillain-Barré syndrome. Self-controlled case series was conducted only for Bell's palsy, given limited statistical power, but with no safety signal seen for those vaccinated. > Rates were, however, higher than expected after SARS-CoV-2 infection. For example, in the data from the UK, the standardised incidence ratio for Bell's palsy was 1.33 (1.02 to 1.74), for encephalomyelitis was 6.89 (3.82 to 12.44), and for Guillain-Barré syndrome was 3.53 (1.83 to 6.77). Transverse myelitis was rare (<5 events in all vaccinated cohorts) and could not be analysed. **No safety signal was observed between covid-19 vaccines and the immune mediated neurological events of Bell's palsy, encephalomyelitis, Guillain-Barré syndrome, and transverse myelitis. An increased risk of Bell's palsy, encephalomyelitis, and Guillain-Barré syndrome was, however, observed for people with SARS-CoV-2 infection.**
Science Transl Med. 15MAR2022	**Omicron variant Spike-specific antibody binding and Fc activity is preserved in recipients of mRNA or inactivated COVID-19 vaccines**	Bartsch Y.C., *et al.* Chile / USA gotopaper	Immunology	**Aim**: to probe the ability of vaccine-induced antibodies to drive Fc-effector activity against the Omicron variant using samples from individuals receiving one of three SARS-CoV-2 vaccines. **Methods :** Samples were obtained from individuals who were vaccinated with full dose regimens. **Findings :** > Despite a substantial loss of IgM, IgA, and IgG binding to the Omicron variant Receptor Binding Domain (RBD) in samples from individuals receiving BNT162b2, mRNA-1273, and CoronaVac vaccines, stable binding was maintained against the full-length Omicron Spike protein. > Compromised RBD binding IgG was accompanied by a loss of cross RBD-specific antibody Fcγ receptor (FcγR) binding in samples from individuals who received the CoronaVac vaccine, but RBD-specific FcγR2a and FcγR3a binding was preserved in recipients of mRNA vaccines. > Conversely, Spike protein-specific antibodies exhibited persistent but reduced binding to FcγRs across all three vaccines, though higher binding was observed in samples from recipients of mRNA vaccines. This was associated with preservation of FcγR2a and FcγR3a binding antibodies and maintenance of Spike protein-specific antibody-dependent natural killer cell activating antibodies. **Despite the loss of Omicron neutralization, vaccine-induced Spike protein-specific antibodies continue to drive Fc-effector functions, suggesting a capacity for extra-neutralizing antibodies to contribute to disease control.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 16MAR2022	**Efficacy of a Fourth Dose of Covid-19 mRNA Vaccine against Omicron**	Regev-Yochay G., *et al.* Israel gotopaper	Vaccines - Immunisation	**Aim**: to assess immunogenicity and safety of a fourth dose of either BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) administered 4 months after the third dose in a series of three BNT162b2 doses. - 1050 eligible health care workers: 154 received the fourth dose of BNT162b2 and, 1 week later, 120 received mRNA-1273. **Results** > After the fourth dose, both mRNA vaccines induced IgG antibodies against SARS-CoV-2 RBD and increased neutralizing antibody titers by a factor of 9 to 10, to titers that were slightly higher than those achieved after the third dose, with no significant difference between the two vaccines. > Antibody levels in the control group continued to wane. > Both vaccines induced an increase in live neutralization of the B.1.1.529 (omicron) variant and other viral strains by a factor of approximately 10, similar to the response after the third dose. > The fourth dose did not lead to substantial adverse events despite triggering mild systemic and local symptoms in the majority of recipients. > Overall, 25.0% of the participants in the control group were infected with the omicron variant, as compared with 18.3% of the participants in the BNT162b2 group and 20.7% of those in the mRNA-1273 group. > Vaccine efficacy against any SARS-CoV-2 infection was 30% (95% CI, −9 to 55) for BNT162b2 and 11% (95% CI, −43 to 44) for mRNA-1273. Most infected health care workers reported negligible symptoms, both in the control group and the intervention groups. > Most of the infected participants were potentially infectious, with relatively high viral loads (nucleocapsid gene cycle threshold, ≤25). Vaccine efficacy was estimated to be higher for the prevention of symptomatic disease (43% for BNT162b2 and 31% for mRNA-1273). > The cohort was too small to allow for accurate determination of vaccine efficacy. However, within the wide confidence intervals of our estimates, vaccine efficacy against symptomatic disease was 65% at most. **A fourth dose of mRNA vaccine is immunogenic, safe, and somewhat efficacious (primarily against symptomatic disease). Maximal immunogenicity of mRNA vaccines appears to be achieved after three doses and antibody levels can be restored by a fourth dose. Low vaccine efficacy against infections and relatively high viral loads suggest that fourth vaccination of healthy young health care workers may have only marginal benefits.**
Clin Microbiol Infect. 16MAR2022	**Inhaled ciclesonide for outpatient treatment of COVID-19 in adults at risk of adverse outcomes: a randomised controlled trial**	Duvignaud A., *et al.* France gotopaper	Therapeutics	**Aim**: to assess the efficacy of inhaled ciclesonide in reducing the risk of adverse outcomes in COVID-19 outpatients at risk of developing severe illness. **Methods** - COVERAGE clinical trial on outpatients with documented COVID-19, risk factors for aggravation, symptoms <7 days and absence of criteria for hospitalisation. - Primary efficacy endpoint: COVID-19 worsening (hospitalisation, oxygen therapy at home, or death) by Day 14. **Results** > 217 participants (control 107, ciclesonide 110); 111 women and 106 men; median age 63 years [Interquartile range (IQR) 59-68]; 157/217 (72.4%) had at least one comorbidity. > The median time since first symptom was 4 days [IQR 3-5]. > During the 28-day follow-up, 2 participants died (control 2/107 [1.9%], ciclesonide 0), 4 received oxygen therapy at home and were not hospitalized (control 2/107 [1.9%], ciclesonide 2/110 [1.8%]) and 24 were hospitalised (control 10/107 [9.3%], ciclesonide 14/110 [12.7%]). > In intent-to-treat analysis of observed data, 26 participants reached the composite primary endpoint by Day14, including 12/106 (11. 3%, 95% CI 6.0 to 18.9%) in the control arm and 14/106 (13.2%; 95% CI 7.4 to 21.2%) in the ciclesonide arm. > Secondary outcomes were similar for both arms. **These findings are consistent with the EMA's COVID-19 taskforce statement that there is currently insufficient evidence that inhaled corticosteroids are beneficial for people with COVID-19.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 16MAR2022	**Comparative analysis of the risks of hospitalisation and death associated with SARS-CoV-2 omicron (B.1.1.529) and delta (B.1.617.2) variants in England: a cohort study**	Nyberg T., *et al.* UK gotopaper	Clinic	**Aim**: to better characterise omicron severity relative to delta by assessing the relative risk of hospital attendance, hospital admission, or death in a large national cohort. **Methods** - Laboratory-confirmed COVID-19 cases in England, Nov 29, 2021-Jan 9, 2022. - The relative risk of hospital attendance or admission within 14 days, or death within 28 days after confirmed infection, was estimated. - Secondary analysis: estimation of variant-specific and vaccine-specific vaccine effectiveness and the intrinsic relative severity of omicron infection compared with delta (ie, relative risk in unvaccinated cases). **Results** > The adjusted hazard ratio (HR) of hospital attendance (not necessarily resulting in admission) with omicron compared with delta was 0.56 (95% CI 0.54–0.58); for hospital admission and death, HR estimates were 0.41 (0.39–0.43) and 0.31 (0.26–0.37), respectively. > Omicron versus delta HR estimates varied with age for all endpoints examined. The adjusted HR for hospital admission was 1.10 (0.85–1.42) in <10-year-old, decreasing to 0.25 (0.21–0.30) in 60–69-year-olds, and then increasing to 0.47 (0.40–0.56) in ≥80-year-old. > For both variants, past infection gave some protection against death both in vaccinated (HR 0.47 [0.32–0.68]) and unvaccinated (0.18 [0.06–0.57]) cases. > In vaccinated cases, past infection offered no additional protection against hospital admission beyond that provided by vaccination (HR 0.96 [0.88–1.04]); however, for unvaccinated cases, past infection gave moderate protection (HR 0.55 [0.48–0.63]). > Omicron versus delta HR estimates were lower for hospital admission (0.30 [0.28–0.32]) in unvaccinated cases than the corresponding HR estimated for all cases in the primary analysis. > Booster vaccination with an mRNA vaccine was highly protective against hospitalisation and death in omicron cases (HR for hospital admission 8–11 weeks post-booster vs unvaccinated: 0.22 [0.20–0.24]), with the protection afforded after a booster not being affected by the vaccine used for doses 1 and 2. **Conclusions** - Risk of severe outcomes following SARS-CoV-2 infection is substantially lower for omicron than for delta, with higher reductions for more severe endpoints and significant variation with age. - Underlying the observed risks is a larger reduction in intrinsic severity (in unvaccinated individuals) counterbalanced by a reduction in vaccine effectiveness. - Documented previous SARS-CoV-2 infection offered some protection against hospitalisation and high protection against death in unvaccinated individuals, but only offered additional protection in vaccinated individuals for the death endpoint. - Booster vaccination with mRNA vaccines maintains over 70% protection against hospitalisation and death in breakthrough confirmed omicron infections.

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 16MAR2022	**Neutralization of the SARS-CoV-2 Omicron BA.1 and BA.2 Variants**	Yu J., *et al.* USA gotopaper	Variants	**Aim**: to assess the ability of omicron sublineage BA.2 to evade neutralizing antibodies induced by vaccination or infection. - 24 persons who had been vaccinated and boosted with the BNT162b2 mRNA vaccine and had not had infection with SARS-CoV-2 and in 8 persons with a history of SARS-CoV-2 infection, irrespective of vaccination status. **Results** > After the initial two doses of the BNT162b2 vaccine, the median pseudovirus neutralizing antibody titers against WA1/2020, BA.1, and BA.2 were 658, 29, and 24, respectively (titer against WA1/2020 was 23 and 27 times those for BA.1 and BA.2, respectively). > Six months after the initial vaccination, the median neutralizing antibody titers declined to 129 for WA1/2020 and to less than 20 for both BA.1 and BA.2. > Two weeks after the third dose (booster) of the BNT162b2 vaccine, the median neutralizing antibody titers increased substantially to 6539 for WA1/2020, 1066 for BA.1, and 776 for BA.2, (titer against WA1/2020 was 6.1 and 8.4 times those for BA.1 and BA.2, respectively). The median BA.2 neutralizing antibody titer was lower than the median BA.1 neutralizing antibody titer by a factor of 1.4. > In persons with a history of SARS-CoV-2 infection at a median of 14 days post-infection, median neutralizing antibody titers were 4046 for WA1/2020, 3249 for BA.1, and 2448 for BA.2. The median BA.1 neutralizing antibody titer was 1.3 times the median BA.2 neutralizing antibody titer. **Neutralizing antibody titers against BA.2 were similar to those against BA.1. In vaccinated persons who had presumably been infected with BA.1, robust neutralizing antibody titers against BA.2 developed, suggesting a substantial degree of cross-reactive natural immunity. Increasing frequency of BA.2 in the context of the BA.1 surge is probably related to increased transmissibility rather than to enhanced immunologic escape.**
Science 15MAR2022	**Increased risk of SARS-CoV-2 reinfection associated with emergence of Omicron in South Africa**	Pulliam J.C., *et al.* South Africa gotopaper	Variants	**Aim**: to provide two methods for monitoring reinfection trends in routine surveillance data to identify signatures of changes in reinfection risk and apply these approaches to data from South Africa's SARS-CoV-2 epidemic to date. **Results** > 105,323 individuals with at least two suspected infections, 1,778 individuals with at least three suspected infections, and 18 individuals with four suspected infections. > 1,492 out of 1,778 individuals with multiple reinfections (83.9%) experienced their third infection after 31 October 2021, during the period of Omicron circulation. > No evidence of increased reinfection risk associated with circulation of Beta (B.1.351) or Delta (B.1.617.2) variants was found. > Population-level evidence to suggest immune evasion by the Omicron (B.1.1.529) variant in previously infected individuals in South Africa was identified. > Reinfections occurring between 01 November 2021 and 31 January 2022 were detected in individuals infected in all three previous waves, and there has been an increase in the risk of having a third infection since mid-November 2021. **A substantial increase in the risk of reinfection that was temporally consistent with the timing of the emergence of the Omicron variant in South Africa, suggesting that Omicron's selection advantage is at least partially driven by an increased ability to infect previously infected individuals.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Ann Intern Med. 15MAR2022	**Comparison of Patients Infected With Delta Versus Omicron COVID-19 Variants Presenting to Paris Emergency Departments**	Bouzid D., *et al.* France gotopaper	Clinic	**Aim:** To compare baseline characteristics and in-hospital outcomes of patients with SARS-CoV-2 infection with the Delta variant versus the Omicron variant in the emergency department (ED). **Methods:** Retrospective chart reviews that includes patients with a positive reverse transcriptase polymerase chain reaction (RT-PCR) test result for SARS-CoV-2 and variant identification. **Results** > A total of 3728 patients had a positive RT-PCR test result for SARS-CoV-2 during the study period; 1716 patients who had a variant determination (818 Delta and 898 Omicron) were included. > Median age was 58 years, and 49% were women. > Patients infected with the Omicron variant were younger (54 vs. 62 years; difference, 8.0 years [95% CI, 4.6 to 11.4 years]), had a lower rate of obesity (8.0% vs. 12.5%; difference, 4.5 percentage points [CI, 1.5 to 7.5 percentage points]), were more vaccinated (65% vs. 39% for 1 dose and 22% vs. 11% for 3 doses), had a lower rate of dyspnea (26% vs. 50%; difference, 23.6 percentage points [CI, 19.0 to 28.2 percentage points]), and had a higher rate of discharge home from the ED (59% vs. 37%; difference, 21.9 percentage points [−26.5 to −17.1 percentage points]). > Compared with Delta, Omicron infection was independently associated with a lower risk for ICU admission (adjusted difference, 11.4 percentage points [CI, 8.4 to 14.4 percentage points]), mechanical ventilation (adjusted difference, 3.6 percentage points [CI, 1.7 to 5.6 percentage points]), and in-hospital mortality (adjusted difference, 4.2 percentage points [CI, 2.0 to 6.5 percentage points]). **Compared with the Delta variant, infection with the Omicron variant in patients in the ED had different clinical and biological patterns and was associated with better in-hospital outcomes, including higher survival.**
Lancet 15MAR2022	**Effectiveness of rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV vaccines for risk of infection with SARS-CoV-2 and death due to COVID-19 in people older than 60 years in Argentina: a test-negative, case-control, and retrospective longitudinal study**	Rearte A., et al. Argentina gotopaper	Vaccine - Immunisation	**Aim**: to estimate vaccine effectiveness at reducing risk of SARS-CoV-2 infection and COVID-19 deaths in people older than 60 years. **Methods:** Test-negative, case-control, and retrospective longitudinal study done in Argentina. The effectiveness of three vaccines (rAd26-rAd5, ChAdOx1 nCoV-19, and BBIBP-CorV) on SARS-CoV-2 infection and risk of death in people with RT-PCR confirmed COVID-19, using data from the National Surveillance System (SNVS 2.0) was evaluated. All individuals aged 60 years or older reported to SNVS 2.0 as being suspected to have COVID-19 who had disease status confirmed with RT-PCR were included in the study. **Findings:** **>** From Jan 31, to Sept 14, 2021, 1 282 928 individuals were included, of whom 687 167 (53·6%) were in the rAd26-rAd5 analysis, 358 431 (27·6%) in the ChAdOx1 nCoV-19 analysis, and 237 330 (18·5%) in the BBIBP-CorV analysis. > Vaccine effectiveness after two doses was high for all three vaccines, adjusted odds ratio 0·36 (95% CI 0·35–0·37) for rAd26-rAd5, 0·32 (0·31–0·33) for ChAdOx1 nCoV-19, and 0·56 (0·55–0·58) for BBIBP-CorV. > After two doses, the effect on deaths was higher than that on risk of infection: adjusted hazard ratio 0·19 (95% CI 0·18–0·21) for rAd26-rAd5, 0·20 (0·18–0·22) for ChAdOx1 nCoV-19, and 0·27 (0·25–0·29) for BBIBP-CorV. > The indirectly estimated effectiveness on deaths was 93·1% (95% CI 92·6–93·5) for rAd26-rAd5, 93·7% (93·2–94·3) for ChAdOx1 nCoV-19, and 85·0% (84·0–86·0) for BBIBP-CorV following two doses. > First dose effect of viral vector vaccines remained stable over time.

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA Netw Open 14MAR2022	**Effect of Sotrovimab on Hospitalization or Death Among High-risk Patients With Mild to Moderate COVID-19**	Gupta,A., *et al.* International gotopaper	Therapeutics	**Aim**: to evaluate the efficacy and adverse events of sotrovimab in preventing progression of mild to moderate COVID-19 to severe disease. **Methods** > Randomized clinical trial including 1057 nonhospitalized patients with symptomatic, mild to moderate COVID-19 and at least 1 risk factor for progression conducted at 57 sites in Brazil, Canada, Peru, Spain, and the US from August 27, 2020, through March 11, 2021; follow-up data were collected through April 8, 2021. > The primary outcome was the proportion of patients with COVID-19 progression through day 29 (all-cause hospitalization lasting >24 hours for acute illness management or death) **Findings** > Enrollment was stopped early for efficacy at the prespecified interim analysis.Among 1057 patients randomized (median age, 53 years [IQR, 42-62], 20% were ≥65 years of age, and 65% Latinx), the median duration of follow-up was 103 days for sotrovimab and 102 days for placebo. > All-cause hospitalization lasting longer than 24 hours or death was significantly reduced with sotrovimab (6/528 [1%]) vs placebo (30/529 [6%]) (adjusted relative risk [RR], 0.21 [95% CI, 0.09 to 0.50]; absolute difference, –4.53% [95% CI, –6.70% to –2.37%]; P < .001). > Four of the 5 secondary outcomes were statistically significant in favor of sotrovimab, including reduced ED visit, hospitalization, or death (13/528 [2%] for sotrovimab vs 39/529 [7%] for placebo; adjusted RR, 0.34 [95% CI, 0.19 to 0.63]; absolute difference, –4.91% [95% CI, –7.50% to –2.32%]; P < .001) and progression to severe or critical respiratory COVID-19 (7/528 [1%] for sotrovimab vs 28/529 [5%] for placebo; adjusted RR, 0.26 [95% CI, 0.12 to 0.59]; absolute difference, –3.97% [95% CI, –6.11% to –1.82%]; P = .002). > Adverse events were infrequent and similar between treatment groups (22% for sotrovimab vs 23% for placebo); the most common events were diarrhea with sotrovimab (n = 8; 2%) and COVID-19 pneumonia with placebo (n = 22; 4%). **Among nonhospitalized patients with mild to moderate COVID-19 and at risk of disease progression, a single intravenous dose of sotrovimab, compared with placebo, significantly reduced the risk of a composite end point of all-cause hospitalization or death through day 29. However, efficacy against SARS-CoV-2 variants that have emerged since the study was completed is unknown.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Public Health 14MAR2022	**Acute COVID-19 severity and mental health morbidity trajectories in patient populations of six nations: an observational study**	Magnúsdóttir O., *et al.* International gotopaper	Public Health / Epidemiology	**Aim**: to assess the prevalence of adverse mental health symptoms among individuals diagnosed with COVID-19 in the general population by acute infection severity up to 16 months after diagnosis. **Methods:** Observational follow-up study included seven prospectively planned cohorts across six countries (Denmark, Estonia, Iceland, Norway, Sweden, and the UK). Participants were recruited from March 27, 2020, to Aug 13, 2021. Individuals aged 18 years or older were eligible to participate. In a cross-sectional analysis, we contrasted symptom prevalence of depression, anxiety, COVID-19-related distress, and poor sleep quality (screened with validated mental health instruments) among individuals with and without a diagnosis of COVID-19 at entry, 0–16 months from diagnosis. **Findings:** > The analytical cohort consisted of 247 249 individuals, 9979 (4·0%) of whom were diagnosed with COVID-19 during the study period. Mean follow-up was 5·65 months (SD 4·26). > Participants diagnosed with COVID-19 presented overall with a higher prevalence of symptoms of depression (prevalence ratio [PR] 1·18 [95% CI 1·03–1·36]) and poorer sleep quality (1·13 [1·03–1·24]) but not symptoms of anxiety (0·97 [0·91–1·03]) or COVID-19-related distress (1·05 [0·93–1·20]) compared with individuals without a COVID-19 diagnosis. > Although the prevalence of depression and COVID-19-related distress attenuated with time, individuals diagnosed with COVID-19 but never bedridden due to their illness were consistently at lower risk of depression (PR 0·83 [95% CI 0·75–0·91]) and anxiety (0·77 [0·63–0·94]) than those not diagnosed with COVID-19, whereas patients who were bedridden for more than 7 days were persistently at higher risk of symptoms of depression (PR 1·61 [95% CI 1·27–2·05]) and anxiety (1·43 [1·26–1·63]) than those not diagnosed throughout the study period. **Severe acute COVID-19 illness—indicated by extended time bedridden—is associated with long-term mental morbidity among recovering individuals in the general population.**
Clin Infect Dis. 10MAR2022	**Rapid spread of SARS-CoV-2 Omicron subvariant BA.2 in a single-source community outbreak**	Chin-Chung Cheng V, *et al.* China gotopaper	Variants	**Aim**: to report the epidemiological and genomic analysis of a large single source BA.2 outbreak in a housing estate. **Findings** > The community outbreak of BA.2 (STY outbreak) involved a total of 768 individuals as of 5 th February 2022, including 432 residents, visitors or staff (56.3%) from a single housing estate (KC Estate). The outbreak at the KC Estate has a short doubling time of 1.28 days (95% confidence interval: 0.560-1.935). The outbreak was promptly controlled with the lockdown of 3 buildings within the housing estate. > Whole genome sequencing was performed for 133 patients in the STY outbreak, including 106 residents of the KC Estate. > All 133 sequences from the STY outbreak belonged to the BA.2 sublineage, and phylogenetic analysis showed that these sequences cluster together. All individuals in the STY cluster had the unique mutation C12525T. **Our study highlights the exceptionally high transmissibility of the Omicron variant BA.2 sublineage in Hong Kong where stringent measures are implemented as part of the elimination strategy. Continual genomic surveillance is crucial in monitoring the emergence of epidemiologically important Omicron sub-variants.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Infect Dis. 14MAR2022	**SARS-CoV-2 incidence, transmission, and reinfection in a rural and an urban setting: results of the PHIRST-C cohort study, South Africa, 2020–21**	Cohen C, *et al.* South Africa gotopaper	Public Health / Epidemiology	**Aim:** to evaluate SARS-CoV-2 burden and transmission in one rural and one urban community in South Africa. **Methods** > We conducted a prospective cohort study of households in Agincourt, Mpumalanga province (rural site) and Klerksdorp, North West province (urban site) from July, 2020 to August, 2021. > Main outcomes: cumulative incidence of SARS-CoV-2 infection, frequency of reinfection, symptomatic fraction (% of infected individuals with ≥1 symptom), the duration of viral RNA shedding (number of days of SARS-CoV-2 RT-rtPCR positivity), and the household cumulative infection risk (HCIR; number of infected household contacts divided by the number of susceptible household members). **Findings** > 222 households (114 at the rural site and 108 at the urban site), and 1200 household members (643 at the rural site and 557 at the urban site) were included in the analysis. > For 115 759 nasal specimens from 1200 household members (follow-up 92·5%), 1976 (1·7%) were SARS-CoV-2-positive on RT-rtPCR. By RT-rtPCR and serology combined, 749 of 1200 individuals (62·4% [95% CI 58·1–66·4]) had at least one SARS-CoV-2 infection episode, and 87 of 749 (11·6% [9·4–14·2]) were reinfected. > Of 662 RT-rtPCR-confirmed episodes (>14 days after the start of follow-up) with available data, 97 (14·7% [11·9–17·9]) were symptomatic with at least one symptom (in individuals aged <19 years, 28 [7·5%] of 373 episodes symptomatic; in individuals aged ≥19 years, 69 [23·9%] of 289 episodes symptomatic). Among 222 households, 200 (90·1% [85·3–93·7]) had at least one SARS-CoV-2-positive individual on RT-rtPCR or serology. > HCIR overall was 23·9% (195 of 817 susceptible household members infected [95% CI 19·8–28·4]). HCIR was 23·3% (20 of 86) for symptomatic index cases and 23·9% (175 of 731) for asymptomatic index cases (univariate odds ratio [OR] 1·0 [95% CI 0·5–2·0]). > On multivariable analysis, accounting for age and sex, low minimum cycle threshold value (≤30 vs >30) of the index case (OR 5·3 [2·3–12·4]) and beta and delta variant infection (vs Wuhan-Hu-1, OR 3·3 [1·4–8·2] and 10·4 [4·1–26·7], respectively) were associated with increased HCIR. People living with HIV who were not virally supressed (≥400 viral load copies per mL) were more likely to develop symptomatic illness when infected with SAR-CoV-2 (OR 3·3 [1·3–8·4]), and shed SARS-CoV-2 for longer (hazard ratio 0·4 [95% CI 0·3–0·6]) compared with HIV-uninfected individuals. **In this study, 565 (85·3%) SARS-CoV-2 infections were asymptomatic and index case symptom status did not affect HCIR, suggesting a limited role for control measures targeting symptomatic individuals. Increased household transmission of beta and delta variants was likely to have contributed to successive waves of SARS-CoV-2 infection, with more than 60% of individuals infected by the end of follow-up.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Infect Dis. 11MAR2022	**Efficacy and safety of CD24Fc in hospitalised patients with COVID-19: a randomised, double-blind, placebo-controlled, phase 3 study**	Welker J., *et al.* USA gotopaper	Therapeutics	**Aim:** To evaluate the safety and efficacy of CD24Fc in hospitalised adults with COVID-19 receiving oxygen support. **Methods:** A randomised, double-blind, placebo-controlled, phase 3 study was conducted at nine medical centres in the USA. Hospitalised patients (age ≥18 years) with confirmed SARS-CoV-2 infection who were receiving oxygen support and standard of care were randomly assigned (1:1) by site-stratified block randomisation to receive a single intravenous infusion of CD24Fc 480 mg or placebo. The study funder, investigators, and patients were masked to treatment group assignment. **Results** > Between April 24 and Sept 22, 2020, 243 hospitalised patients were assessed for eligibility and 234 were enrolled and randomly assigned to receive CD24Fc (n=116) or placebo (n=118). > The prespecified interim analysis was done when 146 participants reached the time to clinical improvement endpoint among 197 randomised participants. In the interim analysis, the 28-day clinical improvement rate was 82% (81 of 99) for CD24Fc versus 66% (65 of 98) for placebo; median time to clinical improvement was 6·0 days (95% CI 5·0–8·0) in the CD24Fc group versus 10·0 days (7·0–15·0) in the placebo group (hazard ratio [HR] 1·61, 95% CI 1·16–2·23; log-rank p=0·0028, which crossed the prespecified efficacy boundary [α=0·0147]). > 37 participants were randomly assigned after the interim analysis data cutoff date; among the 234 randomised participants, median time to clinical improvement was 6·0 days (95% CI 5·0–9·0) in the CD24Fc group versus 10·5 days (7·0–15·0) in the placebo group (HR 1·40, 95% CI 1·02–1·92; log-rank p=0·037). > The proportion of participants with disease progression within 28 days was 19% (22 of 116) in the CD24Fc group versus 31% (36 of 118) in the placebo group (HR 0·56, 95% CI 0·33–0·95; unadjusted p=0·031). The incidences of adverse events and serious adverse events were similar in both groups. No treatment-related adverse events were observed. **CD24Fc is generally well tolerated and accelerates clinical improvement of hospitalised patients with COVID-19 who are receiving oxygen support. These data suggest that targeting inflammation in response to tissue injuries might provide a therapeutic option for patients hospitalised with COVID-19.**
Cell 10MAR2022	**Broad neutralization of SARS-CoV-2 variants by an inhalable bispecific single-domain antibody**	Li C. *et al.* China gotopaper	Therapeutics	**Findings** > Two highly-conserved regions on Omicron variant RBD recognized by broadly neutralizing antibodies were identified. > A bispecific single-domain antibody (bn03) was generated that was able to simultaneously and synergistically bind these two regions on a single Omicron variant RBD as revealed by cryo-EM structures. > This bispecific antibody can be effectively delivered to lung via inhalation administration, and exhibites exquisite neutralization breadth and therapeutic efficacy in mouse models of SARS-CoV-2 infections. **An uncommon and highly-conserved cryptic epitope was identified within the spike trimeric interface that may have implications for the design of broadly protective SARS-CoV-2 vaccines and therapeutics.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA Netw Open 09MAR2022	**Comparison of Seroconversion in Children and Adults With Mild COVID-19**	Quan Toh., *et al.* Australia / UK gotopaper	Immunology	**Aim:** To compare seroconversion in nonhospitalized children and adults with mild SARS-CoV-2 infection and identify factors that are associated with seroconversion. **Methods** - Weekly nasopharyngeal and throat swabs and blood samples during the acute (median, 7 days for children and 12 days for adults [IQR, 4-13] days) and convalescent (median, 41 [IQR, 31-49] days) periods after PCR diagnosis for analysis (May 10 to Oct 28, 2020). **Results** > Among 108 participants with SARS-CoV-2–positive PCR findings, 57 were children (35 boys [61.4%]; median age, 4 [IQR, 2-10] years), 51 were adults (28 women [54.9%]; median age, 37 [IQR, 34-45] years). > Using the 3 established serological assays, a lower proportion of children had seroconversion to IgG compared with adults (20 of 54 [37.0%] vs 32 of 42 [76.2%]; P < .001). This result was not associated with viral load, which was similar in children and adults (mean [SD] cycle threshold [Ct] value, 28.58 [6.83] vs 24.14 [8.47]; P = .09). > In addition, age and sex were not associated with seroconversion within children (median age, 4 [IQR, 2-14] years for both seropositive and seronegative groups; seroconversion by sex, 10 of 21 girls [47.6%] vs 10 of 33 boys [30.3%]) or adults (median ages, 37 years for seropositive and 40 years for seronegative adults [IQR, 34-39 years]; seroconversion by sex, 18 of 24 women [75.0%] vs 14 of 18 men [77.8%]) (P > .05 for all comparisons between seronegative and seropositive groups). > Symptomatic adults had 3-fold higher SARS-CoV-2 IgG levels than asymptomatic adults (median, 227.5 [IQR, 133.7-521.6] vs 75.3 [IQR, 36.9-113.6] IU/mL), whereas no differences were observed in children regardless of symptoms. Moreover, differences in cellular immune responses were observed in adults compared with children with seroconversion. **Among patients with mild COVID-19, children may be less likely to have seroconversion than adults despite similar viral loads.**
Lancet 10MAR2022	**Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21**	COVID-19 Excess Mortality Collaborators International gotopaper	Public Health / Epidemiology	**Aim**: to estimate excess mortality from the COVID-19 pandemic in 191 countries and territories, and 252 subnational units for selected countries, from Jan 1, 2020, to Dec 31, 2021. **Methods** All-cause mortality reports were collected for 74 countries and territories and 266 subnational locations (including 31 locations in low-income and middle-income countries) that had reported either weekly or monthly deaths from all causes during the pandemic in 2020 and 2021, and for up to 11 year previously. **Findings** > Although reported COVID-19 deaths between Jan 1, 2020, and Dec 31, 2021, totalled 5·94 million worldwide, we estimate that 18·2 million (95% uncertainty interval 17·1–19·6) people died worldwide because of the COVID-19 pandemic (as measured by excess mortality) over that period. > The global all-age rate of excess mortality due to the COVID-19 pandemic was 120·3 deaths (113·1–129·3) per 100 000 of the population, and excess mortality rate exceeded 300 deaths per 100 000 of the population in 21 countries. > The number of excess deaths due to COVID-19 was largest in the regions of south Asia, north Africa and the Middle East, and eastern Europe. > At the country level, the highest numbers of cumulative excess deaths due to COVID-19 were estimated in India (4·07 million [3·71–4·36]), the USA (1·13 million [1·08–1·18]), Russia (1·07 million [1·06–1·08]), Mexico (798 000 [741 000–867 000]), Brazil (792 000 [730 000–847 000]), Indonesia (736 000 [594 000–955 000]), and Pakistan (664 000 [498 000–847 000]). > Among these countries, the excess mortality rate was highest in Russia (374·6 deaths [369·7–378·4] per 100 000) and Mexico (325·1 [301·6–353·3] per 100 000), and was similar in Brazil (186·9 [172·2–199·8] per 100 000) and the USA (179·3 [170·7–187·5] per 100 000). **The full impact of the pandemic has been much greater than what is indicated by reported deaths due to COVID-19 alone.**

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Nature 09MAR2022	**Autoantibodies targeting GPCRs and RAS-related molecules associate with COVID-19 severity**	Cabral-Marques O., *et al.* International gotopaper	Clinic	**Aim**: to identify new autoantibodies that are dysregulated by SARS-CoV-2. **Methods:** Cross-sectional study of 246 individuals. Anlysis of autoantibodies targeting G protein-coupled receptors (GPCR) and RAS-related molecules associate with the clinical severity of COVID-19. **Findings:** > Patients with moderate and severe disease are characterized by higher autoantibody levels than healthy controls and those with mild COVID-19 disease. > Among the anti-GPCR autoantibodies, machine learning classification identifies the chemokine receptor CXCR3 and the RAS-related molecule AGTR1 as targets for antibodies with the strongest association to disease severity. > Besides antibody levels, autoantibody network signatures are also changing in patients with intermediate or high disease severity. The production of autoantibodies is deregulated in COVID-19 and their level and pattern alterations might predict COVID-19 disease severity.
BMJ 09MAR2022	**Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: prospective observational study**	Lauring A. S., *et al.* USA gotopaper	Variants	**Aim**: to characterize the clinical severity of covid-19 associated with the alpha, delta, and omicron SARS-CoV-2 variants among adults admitted to hospital and to compare the effectiveness of mRNA vaccines to prevent hospital admissions related to each variant. **Methods** > Case-control study in 21 hospitals across the United States > 11 690 adults (≥18 years) admitted to hospital: 5728 covid-19 cases and 5962 controls. Patients were classified into SARS-CoV-2 variant groups based on viral sequencing, or on predominant circulating variant at the time of hospital admission: alpha (11 March-3 July 2021), delta (4 July-25 December 2021), and omicron (26 December 2021-14 January 2022). > Main outcomes: Vaccine effectiveness calculated using a test negative design for mRNA vaccines to prevent covid-19 related hospital admissions by each variant (alpha, delta, omicron). **Findings** > Effectiveness of the mRNA vaccines to prevent covid-19 associated hospital admissions was 85% (95% CI 82% to 88%) for two vaccine doses against the alpha variant, 85% (83% to 87%) for two doses against the delta variant, 94% (92% to 95%) for three doses against the delta variant, 65% (51% to 75%) for two doses against the omicron variant; and 86% (77% to 91%) for three doses against the omicron variant. > In-hospital mortality was 7.6% (81/1060) for alpha, 12.2% (461/3788) for delta, and 7.1% (40/565) for omicron. > Among unvaccinated patients with covid-19 admitted to hospital, severity was higher for the delta versus alpha variant (adjusted proportional odds ratio 1.28, 95% CI 1.11 to 1.46), and lower for the omicron versus delta variant (0.61, 0.49 to 0.77). Compared with unvaccinated patients, severity was lower for vaccinated patients for each variant, including alpha (adjusted proportional odds ratio 0.33, 0.23 to 0.49), delta (0.44, 0.37 to 0.51), and omicron (0.61, 0.44 to 0.85). **mRNA vaccines were highly effective in preventing covid-19 associated hospital admissions related to the alpha, delta, and omicron variants, but three vaccine doses were required to achieve protection against omicron similar to the protection that two doses provided against delta and alpha variants. Among adults admitted to hospital with covid-19, the omicron variant was associated with less severe disease than the delta variant but still resulted in substantial morbidity and mortality. Vaccinated patients admitted to hospital with covid-19 had significantly lower disease severity than unvaccinated patients for all the variants.**

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Lancet Microbe 09MAR2022	**Safety and immunogenicity of a synthetic multiantigen modified vaccinia virus Ankara-based COVID-19 vaccine (COH04S1): an open-label and randomised, phase 1 trial**	Chiuppesi F., *et al.* USA gotopaper	Vaccines	**Aim:** To test a synthetic attenuated modified vaccinia virus Ankara vector co-expressing SARS-CoV-2 spike and nucleocapsid antigens for safety and immunogenicity in healthy adults. **Methods:** - Open-label and randomised, phase 1 trial, USA, in participants aged 18–54 years with a negative SARS-CoV-2 antibody and PCR test, normal haematology and chemistry panels, normal electrocardiogram and troponin concentration, negative pregnancy test if female, body-mass index of 30 kg/m2 or less, and no modified vaccinia virus Ankara or poxvirus vaccine in the past 12 months. **Results** > Between Dec 13, 2020, and May 24, 2021, 56 participants initiated vaccination. On day 0 and 28, 17 participants received low-dose COH04S1, eight received medium-dose COH04S1, nine received high-dose COH04S1, five received placebo, 13 received low-dose COH04S1 followed by placebo, and four discontinued early. > Grade 3 fever was observed in one participant who received low-dose COH04S1 and placebo, and grade 2 anxiety or fatigue was seen in one participant who received medium-dose COH04S1. No severe adverse events were reported. > Seroconversion was observed in all 34 participants for spike protein and 32 (94%) for nucleocapsid protein (p<0·0001 vs placebo for each comparison). > Four times or more increase in SARS-CoV-2 neutralising antibodies within 56 days was measured in nine of 17 participants in the low-dose COH04S1 group, all eight participants in the medium-dose COH04S1 group, and eight of nine participants in the high-dose COH04S1 group (p=0·0035 combined dose levels vs placebo). > Post-prime and post-boost four times increase in spike-specific or nucleocapsid-specific T cells secreting interferon-γ was measured in 48 (98%; 95% CI 89–100) of 49 participants who received at least one dose of COH04S1 and provided a sample for immunological analysis. **COH04S1 was well tolerated and induced spike-specific and nucleocapsid-specific antibody and T-cell responses. Future evaluation of this COVID-19 vaccine candidate as a primary or boost vaccination is warranted.**
Lancet Public Health 08MAR2022	**Maintaining face mask use before and after achieving different COVID-19 vaccination coverage levels: a modelling study**	Bartsch S.M., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim**: to assess the value of maintaining face masks use indoors according to different COVID-19 vaccination coverage levels in the USA. - Computational simulation-model study comparing face masks use versus no-use until given final vaccination coverages were achieved. - Different scenarios varied the target vaccination coverage (70–90%), date of coverage achievement (Jan 1, 2022, to July 1, 2022), and date of face mask use discontinuation. **Results** > Maintaining face mask use (at the coverage seen in the USA from March to July, 2020) until target vaccination coverages were achieved was cost-effective and in many cases cost saving from the societal and third-party payer perspectives across nearly all scenarios explored. > Face mask use was estimated to be cost-effective and usually cost saving when the cost of face masks per person per day was ≤US$1.25. > In all scenarios, it was estimated to be cost-effective to maintain face mask use for about 2–10 weeks beyond the date that target vaccination coverage (70–90%) was achieved, with this added duration being longer when the target coverage was achieved during winter versus summer. > Factors that might increase the transmissibility of the virus (eg, emergence of the delta and omicron variants), or decrease vaccine effectiveness (eg, waning immunity or escape variants), or increase social interactions among certain segments of the population, only increased the cost savings or cost-effectiveness provided by maintaining face mask use. **This study provides strong support for maintaining face mask use until and a short time after achieving various final vaccination coverage levels, given that maintaining face mask use can be not just cost-effective, but even cost saving.**

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NEJM 09MAR2022	**Efficacy of Antiviral Agents against the SARS-CoV-2 Omicron Subvariant BA.2**	Takashita E., *et al.* Japan gotopaper	Variants	**Aim**: to examine by live-virus focus reduction neutralization test (FRNT) the neutralizing ability of FDA approved therapeutic monoclonal antibodies against the omicron BA.2 subvariant. **Results** > Both LY-CoV016 (etesevimab) and LY-CoV555 (bamlanivimab), individually and in combination, lost neutralizing activity against BA.2. > REGN10987 (imdevimab), which was previously shown to lose neutralizing activity against BA.1, had neutralizing activity against BA.2. > The combination of REGN10987 and REGN10933 (casirivimab) also inhibited BA.2 but did not inhibit BA.1 or BA.1.1. However, the FRNT50 value of this combination therapy was higher by a factor of 43.0 to 143.6 for BA.2 than for an ancestral strain and other VOC. > REGN10933, COV2-2196 (tixagevimab), and COV2-2130 (cilgavimab) neutralized BA.2. The COV2-2196–COV2-2130 combination inhibited BA.2, however, the FRNT50 values were higher by a factor of 1.4 to 8.1 for BA.2 than for the ancestral strain and other VOC. > S309 (the precursor of sotrovimab), had even less neutralizing activity against BA.2 in our study than BA.1 (and therefore ancestral strain and other VOC). The FRNT50 value was higher by a factor of 12.2 to 49.7 for omicron/BA.2 than for the ancestral strain and other VOC. > The susceptibilities of BA.2 to remdesivir, molnupiravir, and nirmatrelvir were similar to those of the ancestral strain and other variants of concern **Clinical studies are warranted to determine whether these antiviral therapies are indeed effective against omicron/BA.2 infections.**
NEJM 09MAR2022	**Resistance Mutations in SARS-CoV-2 Delta Variant after Sotrovimab Use**	Rockett R., *et al.* Australia gotopaper	Therapeutics	**Aim**: to study the mutation profile of SARS-CoV-2 in patients treated with Sotrovimab. - 8 patients who received sotrovimab during the B.1.617.2 (delta) variant outbreak (August - November 2021), with RT-PCR assays that were persistently positive for SARS-CoV-2 and for whom respiratory tract specimens obtained before and after treatment were available. **Results** > 4 of these 8 patients acquired previously defined RBD mutations within 6 to 13 days after they received sotrovimab. Mutations in S:E340 developed in all 4 patients. > Cultures obtained from these patients remained positive for 23, 24, 12, and 15 days, respectively, after they received sotrovimab. The proportion of the viral population carrying S:E340K/A/V mutations exceeded 75% by day 7 in Patient R002, by day 13 in Patient R003, and by day 37 in Patient R004. > Retrospective review of 11,841 SARS-CoV-2 genomes reported in New South Wales, Australia, identified 4 additional patients with S:E340 mutations. In 1 patient, the SARS-CoV-2 genome was detected 5 days after sotrovimab treatment, and in another it was detected 11 days after treatment. **These data show the persistence of viable SARS-CoV-2 in patients after sotrovimab infusions and the rapid development of spike gene mutations associated with high-level sotrovimab resistance in vitro. These findings underscore the importance of stewardship of monoclonal antibodies and postmarketing genomic surveillance.**

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NEJM 09MAR2022	**Effect of mRNA Vaccine Boosters against SARS-CoV-2 Omicron Infection in Qatar**	Abu-Raddad L.J., *et al.* Qatar gotopaper	Vaccines	**Aim**: to evaluate protection conferred against symptomatic SARS-CoV-2 infection and Covid-19–related hospitalization and death by booster doses of the BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) vaccines in Qatar, as compared with protection conferred by the two-dose primary series, during the Omicron wave (Dec 2021-Jan 2022). **Results** > In a population of 2,239,193 persons who had received at least two doses of BNT162b2 (Pfizer–BioNTech) or mRNA-1273 (Moderna) vaccine, those who had also received a booster were matched with persons who had not received a booster. > Among the BNT162b2-vaccinated persons, the cumulative incidence of symptomatic omicron infection was 2.4% (95% CI, 2.3 to 2.5) in the booster cohort and 4.5% (95% CI, 4.3 to 4.6) in the nonbooster cohort after 35 days of follow-up. > Booster effectiveness against symptomatic omicron infection, as compared with that of the primary series, was 49.4% (95% CI, 47.1 to 51.6). > Booster effectiveness against Covid-19–related hospitalization and death due to omicron infection, as compared with the primary series, was 76.5% (95% CI, 55.9 to 87.5). > BNT162b2 booster effectiveness against symptomatic infection with the delta variant, as compared with the primary series, was 86.1% (95% CI, 67.3 to 94.1). > Among the mRNA-1273–vaccinated persons, the cumulative incidence of symptomatic omicron infection was 1.0% (95% CI, 0.9 to 1.2) in the booster cohort and 1.9% (95% CI, 1.8 to 2.1) in the nonbooster cohort after 35 days; booster effectiveness against symptomatic omicron infection, as compared with the primary series, was 47.3% (95% CI, 40.7 to 53.3). > Few severe Covid-19 cases were noted in the mRNA-1273–vaccinated cohorts. **The mRNA boosters were highly effective against symptomatic delta infection, but they were less effective against symptomatic omicron infection. However, with both variants, mRNA boosters led to strong protection against Covid-19–related hospitalization and death.**
Nature 07MAR2022	**Whole genome sequencing reveals host factors underlying critical Covid-19**	Kousathanas A., *et al.* UK gotopaper	Clinic	**Aim**: to study the comparison of genomes from critically-ill cases with population controls in order to find underlying disease mechanisms. **Methods:** Whole genome sequencing (WGS) from a cohort of 7,491 critically-ill patients from 224 intensive care units, compared with 48,400 controls, describing discovery and validation of 23 gene loci for susceptibility to critical Covid-19. **Findings :** > 16 new independent associations, including variants within genes involved in interferon signalling (IL10RB, PLSCR1), leucocyte differentiation (BCL11A), and blood type antigen secretor status (FUT2) were identified. > Using transcriptome-wide association and colocalisation to infer the effect of gene expression on disease severity, the authors find evidence implicating multiple genes, including reduced expression of a membrane flippase (ATP11A), and increased mucin expression (MUC1), in critical disease. > Myeloid cell adhesion molecules (SELE, ICAM5, CD209) and coagulation factor F8 are potentially druggable targets **Comparison between critically-ill cases and population controls is highly efficient for detection of therapeutically-relevant mechanisms of disease.**

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Clin Infect Dis. 07MAR22	**Reduced immune response to inactivated SARS-CoV-2 vaccine in a cohort of immunocompromised patients in Chile**	Balcells M.E., *et al.* Chile gotopaper	Vaccines	**Aim:** To evaluate immune response to CoronaVac vaccine in immunocompromised patients. **Methods:** This prospective cohort study included 193 participants with five different immunocompromising conditions and 67 controls, receiving two doses of CoronaVac 8-12 weeks before enrollment. The study was conducted between May and August 2021, at Red de Salud UC-CHRISTUS, Chile. Neutralizing antibodies (NAb) positivity, total anti-SARS-CoV-2 IgG antibodies (TAb) concentration, and T cell response were determined. **Results** > NAb positivity and median neutralizing activity were 83.1% and 51.2% for the control group versus 20.6% (p<0.0001) and 5.7% (p<0.0001) in the solid organ transplant (SOT) group, 41.5% (p<0.0001) and 19.2% (p<0.0001) in the autoimmune rheumatic diseases group, 43.3% (p=0.0002) and 21.4% (p=0.0013) in the cancer patients with solid tumors group, 45.5% (p<0.0001) and 28.7% (p=0.0006) in the HIV infected group, 64.3% (p=n.s.) and 56.6% (p=n.s.) in the hematopoietic stem cell transplantation (HSCT) group, respectively. > TAb seropositivity was also lower for the SOT (20.6%, p<0.0001), rheumatic diseases (61%, p=0.0001) and HIV groups (70.9%, p=0.0032), compared to control group (92.3%). > The number of IFN-γ Spot Forming T Cells specific for SARS-CoV-2 tended to be lower but did not differ significantly between groups. **Diverse immunocompromising conditions markedly reduce the humoral response to CoronaVac vaccine. These findings suggest a boosting vaccination strategy should be considered in these vulnerable patients.**
Nature 07MAR2022	**SARS-CoV-2 is associated with changes in brain structure in UK Biobank**	Douaud G., *et al.* UK / USA gotopaper	Clinic	**Aim:** To study the impact of SARS-CoV-2 infection in milder cases of brain-related abnormalities and the possible mechanisms contributing to brain pathology **Methods:** Investigation of brain changes in 785 UK Biobank participants (aged 51–81) imaged twice, including 401 cases who tested positive for infection with SARS-CoV-2 between their two scans, with 141 days on average separating their diagnosis and second scan, and 384 controls. **Results** > Signifcant longitudinal efects were identified when comparing the two groups, including: (i) greater reduction in grey matter thickness and tissue-contrast in the orbitofrontal cortex and parahippocampal gyrus, (ii) greater changes in markers of tissue damage in regions functionally-connected to the primary olfactory cortex, and (iii) greater reduction in global brain size. > The infected participants also showed on average larger cognitive decline between the two timepoints. > These imaging and cognitive longitudinal efects were still seen after excluding the 15 cases who had been hospitalised. > These mainly limbic brain imaging results may be the in vivo hallmarks of a degenerative spread of the disease via olfactory pathways, of neuroinfammatory events, or of the loss of sensory input due to anosmia. **By using automated, objective and quantitative methods, a consistent spatial pattern of longitudinal abnormalities in limbic brain regions was uncovered forming a mainly olfactory network. Whether these abnormal changes are the hallmark of the spread of the pathogenic effects, or of the virus itself in the brain, and whether these may prefigure a future vulnerability of the limbic system in particular, including memory, for these participants, remains to be investigated.**

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Lancet Infect Dis. 07MAR2022	**Safety of mRNA vaccines administered during the initial 6 months of the US COVID-19 vaccination programme: an observational study of reports to the Vaccine Adverse Event Reporting System and v-safe**	Rosenblum H.G., *et al.* USA gotopaper	Vaccines	**Aim**: to describe US surveillance data collected through the Vaccine Adverse Event Reporting System (VAERS), a passive system, and v-safe, a new active system, during the first 6 months of the US COVID-19 vaccination programme (Dec 2020 – June 2021) **Results** > 298 792 852 doses of mRNA vaccines were administered in the USA. > VAERS processed 340 522 reports: 313 499 (92·1%) were non-serious, 22 527 (6·6%) were serious (non-death), and 4496 (1·3%) were deaths. > Over half of 7 914 583 v-safe participants self-reported local and systemic reactogenicity, more frequently after dose two (4 068 447 [71·7%] of 5 674 420 participants for local reactogenicity and 4 018 920 [70·8%] for systemic) than after dose one (4 644 989 [68·6%] of 6 775 515 participants for local reactogenicity and 3 573 429 [52·7%] for systemic). > Injection-site pain (4 488 402 [66·2%] of 6 775 515 participants after dose one and 3 890 848 [68·6%] of 5 674 420 participants after dose two), fatigue (2 295 205 [33·9%] participants after dose one and 3 158 299 participants [55·7%] after dose two), and headache (1 831 471 [27·0%] participants after dose one and 2 623 721 [46·2%] participants after dose two) were commonly reported during days 0–7 following vaccination. > Reactogenicity was reported most frequently the day after vaccination; most reactions were mild. More reports of being unable to work, do normal activities, or of seeking medical care occurred after dose two (1 821 421 [32·1%]) than after dose one (808 963 [11·9%]); less than 1% of participants reported seeking medical care after vaccination (56 647 [0·8%] after dose one and 53 077 [0·9%] after dose two). **Safety data from more than 298 million doses of mRNA COVID-19 vaccine show that most reported adverse events were mild and short in duration.**
Science Transl Med. 07MAR2022	**Characterization of immune responses in fully vaccinated individuals following breakthrough infection with the SARS-CoV-2 delta variant**	Collier A.Y., *et al.* USA gotopaper	Vaccines	**Aim**: to describe humoral and cellular immune responses in a large, well described cluster of breakthrough infections with the SARS-CoV-2 delta variant in fully vaccinated individuals in the United States **Methods:** Vaccinated individuals who were part of the MA DPH outbreak investigation or enhanced surveillance and who tested positive or negative for COVID-19 by nasopharyngeal swabs were recruited. These individuals participated in a detailed immunologic study at Beth Israel Deaconess Medical Center (BIDMC) in Boston, Massachusetts. **Findings :** > Vaccinated individuals who tested positive for SARS-CoV-2 (n=16) demonstrated substantially higher serum antibody responses than vaccinated individuals who tested negative for SARS-CoV-2 (n=23), including 32-fold higher binding antibody titers and 31-fold higher neutralizing antibody titers against the SARS-CoV-2 delta variant. > Vaccinated individuals who tested positive also showed higher mucosal antibody responses in nasal secretions and higher Spike protein-specific CD8+ T cell responses in peripheral blood than did vaccinated individuals who tested negative. **Fully vaccinated individuals developed robust anamnestic antibody and T cell responses following infection with the SARS-CoV-2 delta variant.**

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Clin Microbiol Infect. 04MAR2022	**Anti-SARS-CoV-2 antibody response after 2 and 3 doses of BNT162b2 mRNA vaccine in patients with lymphoid malignancies**	Gressens S.B., *et al.* France gotopaper	Vaccines	The present study aims to evaluate the humoral response after mRNA vaccination as well as the impact of a third vaccine dose in patients with lymphoid malignancies. **Methods** > Single center study, evaluating the serological responses of mRNA vaccination amongst a cohort of 200 patients affected by lymphoid malignancies after two or three doses using an industrial SARS-CoV-2 serology assay for anti-RBD Spike IgG detection and quantification **Findings** > Among patients with plasma cell disorders, 59/96 (61%) had a seroconversion (anti-RBD > 50 AU/mL), and recent anti-CD38 therapies were associated with lower serological anti-RBD IgG concentrations (median IgG concentration 137 (IQR 0-512) AU/mL vs 543 (IQR 35-3496) AU/mL, p<0.001) > Patients with B-cell malignancies had a lower seroconversion rate (20/84, 24%) mainly due to the broad usage of anti-CD20 monoclonal antibodies, only 2/53 (4%) patients treated by anti-CD20 antibodies during the last 12 months experienced a seroconversion. > A total of 78 patients (44 with plasma cell disorders, 27 with B-cell malignancies and 7 with other lymphomas) received a third dose of vaccine. The seroconversion rate and antibody concentrations increased significantly, especially in patients with plasma cell disorders where an increment of anti-RBD IgG concentrations was observed in 31/44 (70%) of the patients, with an anti-RBD concentration median-fold increase of 10.6 (IQR 2.4-25.5), while its benefit in B-cell malignancies is uncertain, only 2/25 (8%) patients having seroconverted after the vaccine booster, without increased median antibody concentration. **A third mRNA vaccine dose improved significantly humoral responses among patients with plasma cell disorders, while the effect was limited among patients with B-cell malignancies.**
JAMA Netw Open 03MAR2022	**Assessment of Clinical Effectiveness of BNT162b2 COVID-19 Vaccine in US Adolescents**	Oliveira C.R., *et al.* USA gotopaper	Vaccines	**Aim:** To study the association between the BNT162b2 COVID-19 vaccine and SARS-CoV-2 positivity among adolescents **Methods:** Participants were Connecticut individuals aged 12-18 years who had a RT-PCR assay of a nasopharyngeal swab for SARS-CoV-2 between June 1 and August 15, 2021, and had an associated medical encounter in the Yale–New Haven Health System (YNHHS), where symptoms (or their absence) at the time of testing were noted. **Results** > A total of 6901 adolescents were tested for SARS-CoV-2 in the YNHHS between June 1, 2021, and August 19, 2021. Among the 197 adolescents who tested positive for SARS-CoV-2, 186 (94%) met inclusion criteria. Two closely matched control participants were identified for 170 case participants (91%); the remaining 16 case participants were each matched with 1 control participant. > In the unadjusted model, the vaccine effectiveness (VE) against any infection with SARS-CoV-2 for fully immunized adolescents was 91% (95% CI, 80%-96%); for partly immunized adolescents, 74% (95% CI, 18%-92%). > After the second dose, estimated VE against any infection peaked between 9 and 12 weeks (94%; 95% CI, 79%-99%) and was its lowest between 13 and 17 weeks (83%; 95% CI, 34%-96%). > The aVE after 2 doses was 90% (95% CI, 69%-94%). Two doses of the vaccine were slightly less effective against asymptomatic infection (VE, 85%; 95% CI, 57%-95%). > Results of sensitivity analyses using models derived from different approaches were similar to those of the primary analysis. > In an analysis restricted to cases infected with the Delta variant, the VE after 2 doses was 94% (95% CI, 75%-98%). > The proportion of case and control participants who had received an influenza vaccine during the preceding respiratory season were the same (45 [24%] and 87 [24%]). **In this retrospective case-control study of US adolescents, 2 doses of BNT162b2 vaccine appeared to provide excellent protection for at least 4 months after immunization against both symptomatic and asymptomatic SARS-CoV-2 infections.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 03MAR2022	**Antibody evasion properties of SARS-CoV-2 Omicron sublineages**	Iketani S., *et al.* USA gotopaper	Variants	**Background**: surveillance of Omicron evolution has revealed the rise in prevalence of two sublineages, BA.1 with an R346K mutation (BA.1+R346K, also known as BA.1.1) and B.1.1.529.2 (BA.2), with the latter containing 8 unique spike mutations while lacking 13 spike mutations found in BA.1. **Aim**: to study efficacy of vaccines and authorized therapeutic monoclonal antibodies against Omicron BA.2 **Findings** > Polyclonal sera from patients infected by wild-type SARS-CoV-2 or recipients of current mRNA vaccines showed a substantial loss in neutralizing activity against both BA.1+R346K and BA.2, with drops comparable to that already reported for BA.1 > These findings indicate that these three sublineages of Omicron are antigenically equidistant from the wild-type SARS-CoV-2 and thus similarly threaten the efficacies of current vaccines > BA.2 also exhibited marked resistance to 17 of 19 neutralizing monoclonal antibodies tested, including S309 (sotrovimab)7, which had retained appreciable activity against BA.1 and BA.1+R346K **This new finding shows that no authorized monoclonal antibody therapy could adequately cover all sublineages of the Omicron variant, except for the recently authorized LY-CoV1404 (bebtelovimab)**
BMJ 02MAR2022	**Efficacy of covid-19 vaccines in immunocompromised patients: systematic review and meta-analysis**	Lee A.R.Y.B., *et al.* Singapore gotopaper	Vaccines	**Aim**: to compare the efficacy of covid-19 vaccines between immunocompromised and immunocompetent people. - Systematic review and meta-analysis (Dec 2020 – Nov 2021) **Results** > 82 studies were included in the meta-analysis. Of these studies, 77 (94%) used mRNA vaccines, 16 (20%) viral vector vaccines, and 4 (5%) inactivated whole virus vaccines. 63 studies were assessed to be at low risk of bias and 19 at moderate risk of bias. > After one vaccine dose, seroconversion was about half as likely in patients with haematological cancers (risk ratio 0.40, 95% CI 0.32 to 0.50, I2=80%; absolute risk 0.29, 95% confidence interval 0.20 to 0.40, I2=89%), immune mediated inflammatory disorders (0.53, 0.39 to 0.71, I2=89%; 0.29, 0.11 to 0.58, I2=97%), and solid cancers (0.55, 0.46 to 0.65, I2=78%; 0.44, 0.36 to 0.53, I2=84%) compared with immunocompetent controls, whereas organ transplant recipients were 16 times less likely to seroconvert (0.06, 0.04 to 0.09, I2=0%; 0.06, 0.04 to 0.08, I2=0%). > After a second dose, seroconversion remained least likely in transplant recipients (0.39, 0.32 to 0.46, I2=92%; 0.35, 0.26 to 0.46), with only a third achieving seroconversion. > Seroconversion was increasingly likely in patients with haematological cancers (0.63, 0.57 to 0.69, I2=88%; 0.62, 0.54 to 0.70, I2=90%), immune mediated inflammatory disorders (0.75, 0.69 to 0.82, I2=92%; 0.77, 0.66 to 0.85, I2=93%), and solid cancers (0.90, 0.88 to 0.93, I2=51%; 0.89, 0.86 to 0.91, I2=49%). > Seroconversion was similar between people with HIV and immunocompetent controls (1.00, 0.98 to 1.01, I2=0%; 0.97, 0.83 to 1.00, I2=89%). > Systematic review of 11 studies showed that a third dose of a covid-19 mRNA vaccine was associated with seroconversion among vaccine non-responders with solid cancers, haematological cancers, and immune mediated inflammatory disorders, although response was variable in transplant recipients and inadequately studied in people with HIV and those receiving non-mRNA vaccines. **Seroconversion rates after covid-19 vaccination were significantly lower in immunocompromised patients, especially organ transplant recipients. A second dose was associated with consistently improved seroconversion across all patient groups, albeit at a lower magnitude for organ transplant recipients.**

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NEJM 02MAR2022	**Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant**	Andrews N., *et al.* UK gotopaper	Vaccines	**Aim**: to estimate vaccine effectiveness against symptomatic disease caused by the omicron and delta (B.1.617.2) variants in England. - Vaccine effectiveness was calculated after primary immunization with two doses of BNT162b2 (Pfizer–BioNTech), ChAdOx1 nCoV-19 (AstraZeneca), or mRNA-1273 (Moderna) vaccine and after a booster dose of BNT162b2, ChAdOx1 nCoV-19, or mRNA-1273. **Results** > Between November 27, 2021, and January 12, 2022, a total of 886,774 eligible persons infected with the omicron variant, 204,154 eligible persons infected with the delta variant, and 1,572,621 eligible test-negative controls were identified. > At all time points investigated and for all combinations of primary course and booster vaccines, vaccine effectiveness against symptomatic disease was higher for the delta variant than for the omicron variant. > No effect against the omicron variant was noted from 20 weeks after two ChAdOx1 nCoV-19 doses, whereas vaccine effectiveness after two BNT162b2 doses was 65.5% (95% CI, 63.9 to 67.0) at 2 to 4 weeks, dropping to 8.8% (95% CI, 7.0 to 10.5) at 25 or more weeks. > Among ChAdOx1 nCoV-19 primary course recipients, vaccine effectiveness increased to 62.4% (95% CI, 61.8 to 63.0) at 2 to 4 weeks after a BNT162b2 booster before decreasing to 39.6% (95% CI, 38.0 to 41.1) at 10 or more weeks. > Among BNT162b2 primary course recipients, vaccine effectiveness increased to 67.2% (95% CI, 66.5 to 67.8) at 2 to 4 weeks after a BNT162b2 booster before declining to 45.7% (95% CI, 44.7 to 46.7) at 10 or more weeks. > Vaccine effectiveness after a ChAdOx1 nCoV-19 primary course increased to 70.1% (95% CI, 69.5 to 70.7) at 2 to 4 weeks after an mRNA-1273 booster and decreased to 60.9% (95% CI, 59.7 to 62.1) at 5 to 9 weeks. > After a BNT162b2 primary course, the mRNA-1273 booster increased vaccine effectiveness to 73.9% (95% CI, 73.1 to 74.6) at 2 to 4 weeks; vaccine effectiveness fell to 64.4% (95% CI, 62.6 to 66.1) at 5 to 9 weeks. **Primary immunization with two doses of ChAdOx1 nCoV-19 or BNT162b2 vaccine provided limited protection against symptomatic disease caused by the omicron variant. A BNT162b2 or mRNA-1273 booster after either the ChAdOx1 nCoV-19 or BNT162b2 primary course substantially increased protection, but that protection waned over time.**
JAMA Netw Open 02MAR2022	**Effectiveness of Ad26.COV2.S Vaccine vs BNT162b2 Vaccine for COVID-19 Hospitalizations**	Botton J., *et al.* France gototpaper	Vaccines - Immunisation	**Aim**: to compare the effectiveness of full vaccination with Ad26.COV2.S vs BNT162b2 against COVID-19–related hospitalization. **Methods:** Anonymized data from the French National Health Data System. The authors constructed a matched cohort of participants aged 55 years or older vaccinated with either Ad26.COV2.S or BNT162b2 between April 24, 2021, and July 31, 2021 (ie, 99 days). **Results:** >The cohort included 689 275 participants vaccinated with Ad26.COV2.S (94% of all individuals of this age category vaccinated with Ad26.COV2.S) and 689 275 participants vaccinated with BNT162b2. > The mean (SD) age was 65.8 (9.0) years, and 341 490 participants in each group (49.5%) were women. The 2 groups were similar in terms of socioeconomic and health characteristics. > During a median (IQR) follow-up of 54 (22-74) days from day 28 after injection, 129 COVID-19–related hospitalizations occurred in participants vaccinated with Ad26.COV2.S, and 23 hospitalizations occurred in those vaccinated with BNT162b2. > The risk of hospitalization for COVID-19 from day 28 after injection was 5.2 times higher in individuals vaccinated with Ad26.COV2.S compared with those vaccinated with BNT162b2 (adjusted hazard ratio, 5.2; 95% CI, 3.4-7.9). On the basis of these results and according to an effectiveness of BNT162b2 of 92% (95% CI, 90%-94%) estimated from the same data set,an absolute effectiveness of Ad26.COV2.S of 59% was obteined (95% CI, 33%-75%).

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Clin Infect Dis. 02MAR2022	**Antibody response in immunocompromised patients after the administration of SARS-CoV-2 vaccine BNT162b2 or mRNA-1273: A randomised controlled trial**	Speich B., *et al.* Switzerland gotopaper	Vaccines - Immunisation	BNT162b2 by Pfizer-BioNTech and mRNA-1273 by Moderna are the most commonly used vaccines to prevent SARS-CoV-2 infections. Head-to-head comparison of the efficacy of these vaccines in immunocompromised patients is lacking. **Methods** > Parallel, two-arm (allocation 1:1), open-label, non-inferiority randomised clinical trial nested into the Swiss HIV Cohort Study and the Swiss Transplant Cohort Study. > Patients living with HIV (PLWH) or solid organ transplant recipients (SOTR; i.e. lung and kidney) from these cohorts were randomised to mRNA-1273 or BNT162b2 **Findings** > 430 patients were randomised and 412 were included in the intention-to-treat analysis (341 PLWH and 71 SOTR). > The percentage of patients showing an immune response was 92.1% (95% confidence interval [CI] 88.4-95.8%; 186/202) for mRNA-1273 and 94.3% (95% CI 91.2-97.4; 198/210) for BNT162b2 (difference: 2.2%; 95% CI -7.1 to 2.7), fulfilling non-inferiority of mRNA-1273. > With the ABCORA 2 test 89.1% had an immune response to mRNA-1273 (95% CI 84.8-93.4%; 180/202) and 89.5% to BNT162b2 (95% CI 85.4-93.7%; 188/210). > Based on the Elecsys test, all PLWH had an antibody response (100.0%; 341/341), while for SOTR only 60.6% (95% CI 49.2-71.9%; 43/71) had titres above the cut-off. **In immunocompromised patients the antibody response of mRNA-1273 was non-inferior to BNT162b2. PLWH had in general an antibody response, while a high proportion of SOTR had no antibody response.**
Clin Infect Dis. 01MAR2022	**Mechanically ventilated patients shed high titre live SARS-CoV2 for extended periods from both the upper and lower respiratory tract**	Saud Z., *et al.* UK gotopaper	Virology	**Aim**: to determine the duration of viable virus shedding from the respiratory tract in patients with SARS-CoV-2 infection and severe acute respiratory distress syndrome. **Methods** - Analysis of upper and lower airway respiratory secretions for both viral RNA and infectious virions in mechanically ventilated patients admitted to the intensive care unit. - Samples: oral cavity (saliva), oropharynx (sub-glottic aspirate), or lower respiratory tract (non-directed bronchoalveolar lavage (NBL) or bronchoalveolar lavage (BAL)). **Results** > 117 samples were obtained from 25 patients. qPCR showed extremely high rates of positivity across all sample types, however live virus was far more common in saliva (68%) than in BAL/NBAL (32%). > Average titres of live virus were higher in subglottic aspirates (4.5x10 7) than in saliva (2.2x10 6) or BAL/NBAL (8.5x10 6) and reached >10 8 PFU/ml in some samples. > The longest duration of shedding was 98 days, while most patients (14/25) shed live virus for 20 days or longer. **Intensive care unit patients infected with SARS-CoV-2 can shed high titres of virus both in the upper and lower respiratory tract and tend to be prolonged shedders.**

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JAMA Netw Open 28FEB2022	**Mortality Rates Among Hospitalized Patients With COVID-19 Infection Treated With Tocilizumab and Corticosteroids**	Albuquerque A. M., *et al.* Brazil gotopaper	Therapeutics	To use bayesian methods to assess the magnitude of mortality benefit associated with tocilizumab and the differences between respiratory support subgroups in hospitalized patients with COVID-19. **Methods** > A bayesian hierarchical reanalysis of the WHO meta-analysis of tocilizumab studies published in 2020 and 2021 was performe. The studies featured in the meta-analysis were randomized clinical tocilizumab trials of hospitalized patients with COVID-19. Only patients receiving corticosteroids were included. **Findings** > Among the 5339 patients included in this analysis, most were men, with mean ages between 56 and 66 years. There were 2117 patients receiving simple oxygen only, 2505 receiving noninvasive ventilation (NIV), and 717 receiving invasive mechanical ventilation (IMV) in 15 studies from multiple countries and continents. > Assuming weakly informative priors, the overall odds ratios (ORs) for survival were 0.70 (95% credible interval [CrI], 0.50-0.91) for patients receiving simple oxygen only, 0.81 (95% CrI, 0.63-1.03) for patients receiving NIV, and 0.89 (95% CrI, 0.61-1.22) for patients receiving IMV, respectively. The posterior probabilities of any benefit (OR <1) were notably different between patients receiving simple oxygen only (98.9%), NIV (95.5%), and IMV (75.4%). > The posterior probabilities of a clinically meaningful association (absolute mortality risk difference >1%) were greater than 95% in patients receiving simple oxygen only and greater than 90% in patients receiving NIV. In contrast, the posterior probability of this clinically meaningful association was only approximately 67% in patients receiving IMV > The probabilities of tocilizumab superiority in the simple oxygen only subgroup compared with the NIV and IMV subgroups were 85% and 90%, respectively. Predictive intervals highlighted that only 72.1% of future tocilizumab IMV studies would show benefit. The conclusions did not change with different prior distributions. **In this bayesian reanalysis of a previous meta-analysis of 15 studies of hospitalized patients with COVID-19 treated with tocilizumab and corticosteroids, use of simple oxygen only and NIV was associated with a probability of a clinically meaningful mortality benefit from tocilizumab. Future research should clarify whether patients receiving IMV also benefit from tocilizumab.**
Clin Infect Dis. 26FEB2022	**Efficacy and Safety of Sarilumab in Hospitalized Patients With COVID-19: A Randomized Clinical Trial**	Sivapalasingam S., *et al.* USA gotopaper	Therapeutics	This study evaluated the efficacy and safety of sarilumab, an anti–IL-6R monoclonal antibody, in the treatment of hospitalized patients with COVID-19. **Methods** > In this adaptive, phase 2/3, randomized, double-blind, placebo-controlled trial, adults hospitalized with COVID-19 (ClinicalTrials.gov: NCT04315298) received intravenous sarilumab or placebo. The phase 3 primary analysis population included patients with critical COVID-19 receiving mechanical ventilation randomized to sarilumab 400 mg or placebo. > The primary outcome was proportion of patients with ≥1-point improvement in clinical status from baseline to day 22. **Findings** > There were 457 and 1365 patients randomized and treated in phases 2 and 3, respectively. In phase 3, patients with critical COVID-19 receiving mechanical ventilation (n = 298; 28.2% on corticosteroids), the proportion with ≥1-point improvement in clinical status (alive, not receiving mechanical ventilation) at day 22 was 43.2% in sarilumab and 35.5% in placebo (risk difference +7.5%; 95% CI, –7.4 to 21.3; P = .3261), a relative risk improvement of 21.7%. > In post-hoc analyses pooling phase 2 and 3 critical patients receiving mechanical ventilation, the hazard ratio for death in sarilumab versus placebo was 0.76 (95% CI, .51–1.13) overall and 0.49 (95% CI, .25–.94) in patients receiving corticosteroids at baseline. **This study did not establish the efficacy of sarilumab in hospitalized patients with severe/critical COVID-19. Post-hoc analyses were consistent with other studies that found a benefit of sarilumab in patients receiving corticosteroids.**

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NEJM 23FEB2022	**Population Immunity and Covid-19 Severity with Omicron Variant in South Africa**	Madhi S.A., *et al.* South Africa gotopaper	Variants	**Aim**: to obtain data regarding the seroprevalence of SARS-CoV-2 IgG in Gauteng before the fourth wave of Covid-19, in which the omicron variant was dominant. **Methods:** Seroepidemiologic survey from October 22 to December 9, 2021, in Gauteng to determine the seroprevalence of SARS-CoV-2 IgG. Households included in a previous seroepidemiologic survey (conducted from November 2020 to January 2021) were contacted; to account for changes in the survey population. Samples were obtained from 7010 participants, of whom 1319 (18.8%) had received a Covid-19 vaccine. **Results:** > The seroprevalence of SARS-CoV-2 IgG ranged from 56.2% (95% confidence interval [CI], 52.6 to 59.7) among children younger than 12 years of age to 79.7% (95% CI, 77.6 to 81.5) among adults older than 50 years of age. > Vaccinated participants were more likely to be seropositive for SARS-CoV-2 than unvaccinated participants (93.1% vs. 68.4%). > Epidemiologic data showed that the incidence of SARS-CoV-2 infection increased and subsequently declined more rapidly during the fourth wave than it had during the three previous waves. > The incidence of infection was decoupled from the incidences of hospitalization, recorded death, and excess death during the fourth wave, as compared with the proportions seen during previous waves. **Widespread underlying SARS-CoV-2 seropositivity was observed in Gauteng before the omicron-dominant wave of Covid-19. Epidemiologic data showed a decoupling of hospitalizations and deaths from infections while omicron was circulating.**
Science Transl Med. 22FEB2022	**A homologous or variant booster vaccine after Ad26.COV2.S immunization enhances SARS-CoV-2-specific immune responses in rhesus macaques**	He X., *et al.* USA gotopaper	Vaccines	**Aim**: to report the correlates of durability of humoral and cellular immune responses in 20 rhesus macaques immunized with single-shot Ad26.COV2.S and the immunogenicity of a booster shot at 8 to 10 months following the initial immunization. **Results** > Ad26.COV2.S elicited durable binding and neutralizing antibodies as well as memory B cells and long-lived bone marrow plasma cells. Innate immune responses and bone marrow plasma cell responses correlated with durable antibody responses. > Following Ad26.COV2.S boost immunization, binding and neutralizing antibody responses against multiple SARS-CoV-2 variants increased 31- to 69-fold and 23- to 43-fold, respectively, compared with pre-boost concentrations. Antigen-specific B cell and T cell responses also increased substantially following the boost immunization. > Boosting with a modified Ad26.COV2.S.351 vaccine expressing the SARS-CoV-2 spike protein from the beta variant led to largely comparable responses with slightly higher beta- and omicron-specific humoral immune responses. **A late boost with Ad26.COV2.S or Ad26.COV2.S.351 resulted in a dramatic increase in humoral and cellular immune responses that were highly cross-reactive across multiple SARS-CoV-2 variants in rhesus macaques.**

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JAMA Neurol. 25FEB2022	**Omicron-Specific Cytotoxic T-Cell Responses After a Third Dose of mRNA COVID-19 Vaccine Among Patients With Multiple Sclerosis Treated With Ocrelizumab**	Madelon N., *et al.* Switzerland gotopaper	Vaccines	**Aim**: to determine T-cell responses to the Omicron spike protein in anti-CD20–treated patients with multiple sclerosis (MS) before and after a third mRNA COVID-19 vaccination. - Prospective cohort study (March 2021 to November 2021) on 20 adults with MS receiving anti-CD20 treatment (ocrelizumab) and who received their third dose of mRNA COVID-19 vaccine **Results** > Of 20 included patients, 11 were male, and the median (IQR) age was 45.8 (37.8-53.3) years. > Spike-specific CD4 and CD8 T-cell memory against all variants were maintained in 9 to 12 patients 6 months after their second dose, albeit at lower median frequencies against the Delta and Omicron variants compared with the vaccine strain (CD8 T cells: Delta, 83.0%; 95% CI, 73.6-114.5; Omicron, 78.9%; 95% CI, 59.4-100.0; CD4 T cells: Delta, 72.2%; 95% CI, 67.4-90.5; Omicron, 62.5%; 95% CI, 51.0-89.0). > A third dose enhanced the number of responders to all variants (11 to 15 patients) and significantly increased CD8 T-cell responses, but the frequencies of Omicron-specific CD8 T cells remained 71.1% (95% CI, 41.6-96.2) of the responses specific to the vaccine strain. **T-cell responses recognizing spike proteins from the Delta and Omicron variants were observed, suggesting that COVID-19 vaccination in patients taking B-cell–depleting drugs may protect them against serious complications from COVID-19 infection. T-cell response rates increased after the third dose.**
Lancet Child Adolesc Health 22FEB2022	**Reported cases of multisystem inflammatory syndrome in children aged 12–20 years in the USA who received a COVID-19 vaccine, December, 2020, through August, 2021: a surveillance investigation**	Yousaf A.R., *et al.* USA gotopaper	Clinic	**Aim**: to investigate reports of individuals aged 12–20 years with Multisystem inflammatory syndrome in children (MIS-C) after COVID-19 vaccination reported to passive surveillance systems or through clinician outreach to the US Centers for Disease Control and Prevention (CDC). **Results:** > Using surveillance results from Dec 14, 2020, to Aug 31, 2021, 21 individuals with MIS-C after COVID-19 vaccination were identified. > Of these 21 individuals, median age was 16 years (range 12–20); 13 (62%) were male and eight (38%) were female. All 21 were hospitalised: 12 (57%) were admitted to an intensive care unit and all were discharged home. 15 (71%) of 21 individuals had laboratory evidence of past or recent SARS-CoV-2 infection, and six (29%) did not. > As of Aug 31, 2021, 21 335 331 individuals aged 12–20 years had received one or more doses of a COVID-19 vaccine, making the overall reporting rate for MIS-C after vaccination 1·0 case per million individuals receiving one or more doses in this age group. > The reporting rate in only those without evidence of SARS-CoV-2 infection was 0·3 cases per million vaccinated individuals. **MIS-C after COVID-19 vaccination is rare. Continued reporting of potential cases and surveillance for MIS-C illnesses after COVID-19 vaccination is warranted.**
Nature Med. 21FEB2022	**Effectiveness of mRNA-1273 against SARS-CoV-2 Omicron and Delta variants**	Fu Tseng H., *et al.* USA gotopaper	Vaccines	**Aim**: to conduct a test-negative case-control study to evaluate mRNA-1273 vaccine effectiveness (VE) against infection and hospitalization with Omicron or Delta. - 26,683 SARS-CoV-2 test-positive cases with variants determined by S-gene target failure status (16% Delta, 84% Omicron). **Results** > The 2-dose VE against Omicron infection at 14–90 days was 44.0% (95% CI, 35.1–51.6%) but declined quickly. > The 3-dose VE was 93.7% (92.2–94.9%) and 86.0% (78.1–91.1%) against Delta infection and 71.6% (69.7–73.4%) and 47.4% (40.5–53.5%) against Omicron infection at 14–60 days and >60 days, respectively. > The 3-dose VE was 29.4% (0.3–50.0%) against Omicron infection in immunocompromised individuals. > The 3-dose VE against hospitalization with Delta or Omicron was >99% across the entire study population. **These findings demonstrate high, durable 3-dose VE against Delta infection but lower effectiveness against Omicron infection, particularly among immunocompromised people. 3-dose VE of mRNA-1273 was high against hospitalization with Delta and Omicron**

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Lancet Health Longev. 21FEB2022	**Real-world serological responses to extended-interval and heterologous COVID-19 mRNA vaccination in frail, older people (UNCoVER): an interim report from a prospective observational cohort study**	Vinh D.C., *et al.* Canada gotopaper	Vaccines	**Aim**: to assess the antigenicity of mRNA-based COVID-19 vaccines in frail, older people in a real-world setting, with a rationed interval dosing of 16 weeks between the prime and boost doses. **Methods** - Prospective observational cohort study on adults aged 65 years and older residing in long-term care facilities with or without previously documented SARS-CoV-2 infection who received homologous or heterologous mRNA vaccines, with an extended 16-week interval between doses. - Participants were enrolled from Dec 31, 2020, to Feb 16, 2021, and data were collected up to June 9, 2021. - Two cohorts: a discovery cohort, for which blood samples were collected before administration of the first vaccine dose and longitudinally thereafter; and a confirmatory cohort, for which blood samples were only collected from 4 weeks after the prime dose. **Results** > 185 participants: 65 participants received two doses of mRNA-1273, 36 received two doses of BNT162b2, and 84 received mRNA-1273 followed by BNT162b2. > In the discovery cohort, after a significant increase in anti-RBD and anti-spike IgG concentrations 4 weeks after the prime dose (from 4·86 log binding antibody units [BAU]/mL to 8·53 log BAU/mL for anti-RBD IgG and from 5·21 log BAU/mL to 8·05 log BAU/mL for anti-spike IgG), there was a significant decline in anti-RBD and anti-spike IgG concentrations until the boost dose (7·10 log BAU/mL for anti-RBD IgG and 7·60 log BAU/mL for anti-spike IgG), followed by an increase 4 weeks later for both vaccines (9·58 log BAU/mL for anti-RBD IgG and 9·23 log BAU/mL for anti-spike IgG). > SARS-CoV-2-naive individuals showed lower antibody responses than previously infected individuals at all timepoints tested up to 16 weeks after the prime dose, but achieved similar antibody responses to previously infected participants by 4 weeks after the second dose. > Individuals primed with the BNT162b2 vaccine showed a larger decrease in mean anti-RBD and anti-spike IgG concentrations with a 16-week interval between doses (from 8·12 log BAU/mL to 4·25 log BAU/mL for anti-RBD IgG responses and from 8·18 log BAU/mL to 6·66 log BAU/mL for anti-spike IgG responses) than did those who received the mRNA-1273 vaccine (two doses of mRNA-1273: from 8·06 log BAU/mL to 7·49 log BAU/mL for anti-RBD IgG responses and from 6·82 log BAU/mL to 7·56 log BAU/mL for anti-spike IgG responses; mRNA-1273 followed by BNT162b2: from 8·83 log BAU/mL to 7·95 log BAU/mL for anti-RBD IgG responses and from 8·50 log BAU/mL to 7·97 log BAU/mL for anti-spike IgG responses). > No differences in antibody responses 4 weeks after the second dose were noted between the two vaccines, in either homologous or heterologous combinations. **Interim results of this ongoing longitudinal study show that among frail, older people, previous SARS-CoV-2 infection and the type of mRNA vaccine influenced antibody responses when used with a 16-week interval between doses. Homologous and heterologous use of mRNA vaccines was not associated with significant differences in antibody responses 4 weeks following the second dose, supporting their interchangeability.**

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Lancet 21FEB2022	**Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression**	Feikin D. R., *et al.* International gotopaper	Vaccines	**Aim**: to systematically review the evidence for the duration of protection of COVID-19 vaccines against various clinical outcomes, and to assess changes in the rates of breakthrough infection caused by the delta variant with increasing time since vaccination. **Methods** > systematic review of preprint and peer-reviewed published article databases from June 17, 2021, to Dec 2, 2021. > Randomised controlled trials of COVID-19 vaccine efficacy and observational studies of COVID-19 vaccine effectiveness were eligible **Findings** > Of 13 744 studies screened, 310 underwent full-text review, and 18 studies were included (all studies were carried out before the omicron variant began to circulate widely). We included 78 vaccine-specific vaccine efficacy or effectiveness evaluations (Pfizer–BioNTech-Comirnaty, n=38; Moderna-mRNA-1273, n=23; Janssen-Ad26.COV2.S, n=9; and AstraZeneca-Vaxzevria, n=8) > On average, vaccine efficacy or effectiveness against SARS-CoV-2 infection decreased from 1 month to 6 months after full vaccination by 21·0 percentage points (95% CI 13·9–29·8) among people of all ages and 20·7 percentage points (10·2–36·6) among older people (as defined by each study, who were at least 50 years old) > For symptomatic COVID-19 disease, vaccine efficacy or effectiveness decreased by 24·9 percentage points (95% CI 13·4–41·6) in people of all ages and 32·0 percentage points (11·0–69·0) in older people > For severe COVID-19 disease, vaccine efficacy or effectiveness decreased by 10·0 percentage points (95% CI 6·1–15·4) in people of all ages and 9·5 percentage points (5·7–14·6) in older people. Most (81%) vaccine efficacy or effectiveness estimates against severe disease remained greater than 70% over time. **COVID-19 vaccine efficacy or effectiveness against severe disease remained high, although it did decrease by 6 months after full vaccination. By contrast, vaccine efficacy or effectiveness against infection and symptomatic disease decreased approximately by 20–30% by 6 months. This is likely caused by, at least in part, waning immunity, although an effect of bias cannot be ruled out. Evaluating vaccine efficacy or effectiveness beyond 6 months will be crucial.**
Clin Infect Dis. 18FEB2022	**Prospective evaluation of COVID-19 vaccine responses across a broad spectrum of immunocompromising conditions: the COVICS study**	Haidar G., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: to study humoral responses after COVID-19 vaccination across varying causes of immunodeficiency. **Methods:** Prospective study of fully-vaccinated immunocompromised adults (solid organ transplant (SOT), hematologic malignancy, solid cancers, autoimmune conditions, HIV infection) versus non-immunocompromised healthcare-workers (HCW). 1271 participants enrolled: 1,099 immunocompromised and 172 HCW. **Results:** > Compared to HCW (92.4% seropositive), seropositivity was lower among participants with SOT (30.7%), hematological malignancies (50.0%), autoimmune conditions (79.1%), solid tumors (78.7%), and HIV (79.8%) ($p<0.01$). > Factors associated with poor seropositivity included age, greater immunosuppression, time since vaccination, anti-CD20 monoclonal antibodies, and vaccination with BNT162b2 (Pfizer) or adenovirus vector vaccines versus mRNA-1273 (Moderna). > mRNA-1273 was associated with higher antibody levels than BNT162b2 or adenovirus vector vaccines, after adjusting for time since vaccination, age, and underlying condition. > Antibody levels were strongly correlated with pseudovirus neutralization titers (Spearman $r=0.89$, $p<0.0001$), but in seropositive participants with intermediate antibody levels, neutralization titers were significantly lower in immunocompromised individuals versus HCW. **Antibody responses to COVID-19 vaccines were lowest among SOT and anti-CD20 monoclonal recipients, and recipients of vaccines other than mRNA-1273. Among those with intermediate antibody levels, pseudovirus neutralization titers were lower in immunocompromised patients than HCW.**

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Nature Med. 17FEB2022	**Immunopathological signatures in multisystem inflammatory syndrome in children and pediatric COVID-19**	Sacco K., *et al.* USA gotopaper	Immunology	**Aim**: to profile children with COVID-19 (n = 110) and MIS-C (n = 76), along with pediatric healthy controls (pHCs; n = 76) through multi-omics (analysis of soluble biomarkers, proteomics, single-cell gene expression and immune repertoire analysis). **Results** > Pediatric COVID-19 (pCOVID-19) was characterized by robust type I interferon (IFN) responses, whereas prominent type II IFN-dependent and NF-κB-dependent signatures, matrisome activation and increased levels of circulating spike protein were detected in multisystem inflammatory syndrome in children (MIS-C), with no correlation with SARS-CoV-2 PCR status around the time of admission. > Transient expansion of TRBV11-2 T cell clonotypes in MIS-C was associated with signatures of inflammation and T cell activation. > The association of MIS-C with the combination of HLA A*02, B*35 and C*04 alleles suggests genetic susceptibility. > MIS-C B cells showed higher mutation load than pCOVID-19 and pHC. **These results identify distinct immunopathological signatures in pCOVID-19 and MIS-C that might help better define the pathophysiology of these disorders and guide therapy.**
NEJM 16FEB2022	**Protection against SARS-CoV-2 after Covid-19 Vaccination and Previous Infection**	Hall V., *et al.* UK gotopaper	Vaccins - Immunisation	**Aim**: to investigate the duration and effectiveness of immunity from infection with and vaccination against SARS-CoV-2. - Prospective cohort of asymptomatic health care workers in the UK who underwent routine PCR testing. - Vaccine effectiveness (≤10 months after the first dose of vaccine) and infection-acquired immunity were assessed by comparing the time to PCR-confirmed infection in vaccinated persons with that in unvaccinated persons, stratified according to previous infection status. **Results** > Of 35,768 participants, 27% (9488) had a previous SARS-CoV-2 infection. Vaccine coverage was high: 97% of the participants had received two doses (78% had received BNT162b2 with a long interval between doses, 9% BNT162b2 with a short interval between doses, and 8% ChAdOx1 nCoV-19). > Between December 7, 2020, and September 21, 2021, a total of 2747 primary infections and 210 reinfections were observed. > Among previously uninfected participants who received long-interval BNT162b2 vaccine, adjusted vaccine effectiveness decreased from 85% (95% CI, 72 to 92) 14 to 73 days after the second dose to 51% (95% CI, 22 to 69) at a median of 201 days (interquartile range, 197 to 205) after the second dose > Effectiveness did not differ significantly between the long-interval and short-interval BNT162b2 vaccine recipients. > At 14 to 73 days after the second dose, adjusted vaccine effectiveness among ChAdOx1 nCoV-19 recipients was 58% (95% CI, 23 to 77) — considerably lower than that among BNT162b2 vaccine recipients. > Infection-acquired immunity waned after 1 year in unvaccinated participants but remained consistently higher than 90% in those who were subsequently vaccinated, even in persons infected more than 18 months previously. **Two doses of BNT162b2 vaccine were associated with high short-term protection against SARS-CoV-2 infection; this protection waned considerably after 6 months. Infection-acquired immunity boosted with vaccination remained high more than 1 year after infection.**

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NEJM 16FEB2022	**Effectiveness of the BNT162b2 Vaccine after Recovery from Covid-19**	Hammerman A., *et al.* Israel gotopaper	Vaccins - Immunisation	**Aim**: to study how long protective immunity against SARS-CoV-2 reinfection lasts after recovering from a previous SARS-CoV-2 infection. **Methods** - Assessment of reinfection rates in patients who had recovered from SARS-CoV-2 infection before any vaccination against Covid-19. - Comparison of reinfection rates among patients who had subsequently received the BNT162b2 vaccine (Pfizer–BioNTech) and those who had not been vaccinated (March 1 - November 26, 2021). **Results** > A total of 149,032 patients who had recovered from SARS-CoV-2 infection met the eligibility criteria. Of these, 83,356 (56%) received subsequent vaccination during the 270-day study period. > Reinfection occurred in 354 of the vaccinated patients (2.46 cases per 100,000 persons per day) and in 2168 of 65,676 unvaccinated patients (10.21 cases per 100,000 persons per day). > Vaccine effectiveness was estimated at 82% (95% CI, 80 to 84) among patients who were 16 to 64 years of age and 60% (95% CI, 36 to 76) among those 65 years of age or older. > No significant difference in vaccine effectiveness was found for one dose as compared with two doses. **Among patients who had recovered from Covid-19, the receipt of at least one dose of the BNT162b2 vaccine was associated with a significantly lower risk of recurrent infection.**
NEJM 16FEB2022	**Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19**	Hammond J., *et al.* USA gotopaper	Therapeutics	**Aim**: to test efficacy of Nirmatrelvir (an orally administered SARS-CoV-2 main protease (Mpro) inhibitor with potent pan–human-coronavirus activity in vitro) in High-Risk, Nonhospitalized Adults with Covid-19. - Phase 2–3 trial on symptomatic, unvaccinated, nonhospitalized adults at high risk for progression to severe Covid-19 - Treatment: 300 mg of nirmatrelvir plus 100 mg of ritonavir (a pharmacokinetic enhancer) or placebo every 12 hours for 5 days. - Covid-19–related hospitalization or death from any cause through day 28, viral load, and safety were evaluated. **Results** > A total of 2246 patients underwent randomization; 1120 patients received nirmatrelvir plus ritonavir (nirmatrelvir group) and 1126 received placebo (placebo group). > In the planned interim analysis of patients treated within 3 days after symptom onset (modified intention-to treat population, comprising 774 of the 1361 patients in the full analysis population), the incidence of Covid-19–related hospitalization or death by day 28 was lower in the nirmatrelvir group than in the placebo group by 6.32 percentage points (95% CI, −9.04 to −3.59; P<0.001; relative risk reduction, 89.1%) > Incidence was 0.77% (3 of 389 patients) in the nirmatrelvir group, with 0 deaths, as compared with 7.01% (27 of 385 patients) in the placebo group, with 7 deaths. > Efficacy was maintained in the final analysis involving the 1379 patients in the modified intention-to-treat population, with a difference of −5.81 percentage points (95% CI, −7.78 to −3.84; P<0.001; relative risk reduction, 88.9%). All 13 deaths occurred in the placebo group. > The viral load was lower with nirmaltrelvir plus ritonavir than with placebo at day 5 of treatment, with an adjusted mean difference of −0.868 log10 copies per milliliter when treatment was initiated within 3 days after the onset of symptoms. > The incidence of adverse events that emerged during the treatment period was similar in the two groups (any adverse event, 22.6% with nirmatrelvir plus ritonavir vs. 23.9% with placebo; serious adverse events, 1.6% vs. 6.6%; and adverse events leading to discontinuation of the drugs or placebo, 2.1% vs. 4.2%). Dysgeusia (5.6% vs. 0.3%) and diarrhea (3.1% vs. 1.6%) occurred more frequently with nirmatrelvir plus ritonavir than with placebo. **Treatment of symptomatic Covid-19 with nirmatrelvir plus ritonavir resulted in a risk of progression to severe Covid-19 that was 89% lower than the risk with placebo, without evident safety concerns.**

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Clin Microbiol Infect. 16FEB2022	**Reactogenicity among healthcare workers following a BNT162b2 or mRNA-1273 second dose after priming with a ChAdOx1 nCOV-19 vaccine**	Baldolli A., *et al.* France gotopaper	Vaccines	We performed a single center prospective observational cohort study among healthcare workers (HCW) in a tertiary care hospital to assess reactogenicity of BNT162b2 and mRNA-1273 vaccines administered as a second dose in participants primed with ChAdOx1 nCoV-19. **Findings** > Among 1184 HCW, 356 (30%) agreed to participate. Of the participants, 32.3% were men, and the mean age was 35 years (SD 10.1). 229 HCW received BNT162b2 and 127 received mRNA-1273. A systemic reaction was observed in 130/229 (56.8%) and 100/127 (78.7%) HCW respectively. Injection site reactions were generally limited (grade 1 or 2 in 163/229 [97.6%] and 90/127 [85.7 %] respectively). > After adjustment for age, sex and HCW role, receiving the mRNA-1273 vaccine was associated with higher reactogenicity with more grade 3 side effects (aOR=3.34, 95% CI 1.91-5.85), more systemic symptoms (aOR=2.82, 95% CI 1.69-4.7), and not being able to work (aOR=8.35, 95% CI 3.78-18.44), in comparison to receiving the BNT162b2 vaccine. **Among patients receiving the mRNA1273 vaccine as a second dose, our study confirms good tolerance of the heterologous schedule with a higher risk of short term side effects in comparison to patients receiving the BNT162b2 vaccine.**
Science Transl Med. 15FEB2022	**Neutralizing antibody responses elicited by SARS-CoV-2 mRNA vaccination wane over time and are boosted by breakthrough infection**	Evans J.P., *et al.* USA gotopaper	Vaccins - Immunisation	**Aim**: to examine the neutralizing antibody response against the spike protein of five major SARS-CoV-2 variants, D614G, Alpha (B.1.1.7), Beta (B.1.351), Delta (B.1.617.2), and Omicron (B.1.1.529), in health care workers (HCWs) vaccinated with SARS-CoV-2 mRNA vaccines. - Serum samples were collected pre-vaccination, three weeks post-first vaccination, one month post-second vaccination, and six months post-second vaccination. **Results** > Minimal neutralizing antibody titers were detected against Omicron pseudovirus at all four time points, including for a majority of patients who had SARS-CoV-2 breakthrough infections. > Neutralizing antibody titers against all other variant spike protein-bearing pseudoviruses declined dramatically from one to six months after the second mRNA vaccine dose, although SARS-CoV-2 infection boosted vaccine responses. > NT50 values of anti-N protein positive HCWs (infected either previous to, during, or after vaccination scheme) were approximately six times higher than that of anti-N protein negative HCWs at six months post-vaccination (30% below the background of detection vs 60%). This suggests that breakthrough infection can improve the durability of the SARS-CoV-2 nAb response > Vaccine type and sex, but not age, impact nAb responses elicited by SARS-CoV-2 vaccination. > mRNA-1273-vaccinated HCWs exhibited about two-fold higher neutralizing antibody titers than BNT162b2-vaccinated HCWs following two vaccine doses. However, the trend for declining nAb titers was consistent for both vaccines. > Male HCWs exhibited significantly higher NT50 titers ($p < 0.001$) compared to females against all five variants over the post-vaccination time points. However, this difference was not significant when examined for individual viruses at individual time points ($p > 0.05$). **These results demonstrate possible waning of antibody-mediated protection against SARS-CoV-2 variants that is dependent on prior infection status and the mRNA vaccine received. They also show that the Omicron variant spike protein can almost completely escape from neutralizing antibodies elicited in recipients of only two mRNA vaccine doses.**

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Nature 15FEB2022	**Germinal centre-driven maturation of B cell response to mRNA vaccination**	Kim W., *et al.* USA gotopaper	Immunology	**Aim**: to assess whether persistent germinal centre (GC) responses lead to the generation of affinity-matured memory B cells (MBCs) and long-lived bone marrow-resident plasma cells (BMPCs) **Methods:** Combined approach of sequencing the B cell receptors of responding blood plasmablasts and MBCs, lymph node GC and plasma cells and BMPCs from eight individuals and expression of the corresponding monoclonal antibodies (mAbs), the evolution of 1540 S-specific B cell clones were tracked. **Results:** > Early blood S-specific plasmablasts — on average — exhibited the lowest SHM frequencies. > In comparison, SHM frequencies of S-specific GC B cells increased by 3.5-fold within six months after vaccination. > S-specific MBCs and BMPCs accumulated high levels of SHM, which corresponded with enhanced anti-S antibody avidity in blood and affinity as well as neutralization capacity of BMPC-derived mAbs. **This study documents how the striking persistence of SARS-CoV-2 vaccination-induced GC reaction in humans culminates in affinity-matured long-term antibody responses that potently neutralize the virus.**
Nature Commun. 14FEB2022	**Humoral and cellular responses after a third dose of SARS-CoV-2 BNT162b2 vaccine in patients with lymphoid malignancies**	Re D., *et al.* France gotopaper	Immunology	**Aim:** to report the monitoring of humoral and cellular responses to a third vaccine dose (dose 3), in patients with poor or no response to two previous vaccine doses. **Methods:** Observational study (registration number HDH F20210324145532), SARS-CoV-2 anti-Spike antibodies, neutralizing antibodies and T-cell responses after immune stimulation with a third dose (D3) of the same vaccine were measured in patients with chronic lymphocytic leukemia (n = 13), B cell non-Hodgkin lymphoma (n = 14), and multiple myeloma (n = 16)). **Results :** > No unexpected novel side effects are reported. > Among 25 patients with positive anti-S titers before D3, 23 (92%) patients increase their anti-S and neutralizing antibody titer after D3. > All 18 (42%) initially seronegative patients remain negative. > D3 increases the median IFN-γ secretion in the whole cohort and induces IFN-γ secretion in a fraction of seronegative patients. T**hese data support the use of a third vaccine dose amongst patients with lymphoid malignancies, even though some of them will still have vaccine failure.**
Nature Med. 14FEB2022	**Antibody responses and correlates of protection in the general population after two doses of the ChAdOx1 or BNT162b2 vaccines**	Wei J., *et al.* UK gotopaper	Vaccines - Immunisation	In this study, we investigated anti-spike IgG antibody responses and correlates of protection after second doses of ChAdOx1 or BNT162b2 vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the United Kingdom general population **Findings** > In 222,493 individuals, we found significant boosting of anti-spike IgG by the second doses of both vaccines in all ages and using different dosing intervals, including the 3-week interval for BNT162b2 > After second vaccination, BNT162b2 generated higher peak levels than ChAdOX1. Older individuals and males had lower peak levels with BNT162b2 but not ChAdOx1, whereas declines were similar across ages and sexes with ChAdOX1 or BNT162b2. Prior infection significantly increased antibody peak level and half-life with both vaccines > Anti-spike IgG levels were associated with protection from infection after vaccination and, to an even greater degree, after prior infection > At least 67% protection against infection was estimated to last for 2–3 months after two ChAdOx1 doses, for 5–8 months after two BNT162b2 doses in those without prior infection and for 1–2 years for those unvaccinated after natural infection. A third booster dose might be needed, prioritized to ChAdOx1 recipients and those more clinically vulnerable.

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Lancet Public Health 14FEB2022	**The effect of social deprivation on the dynamic of SARS-CoV-2 infection in France: a population-based analysis**	Vandentorren S., *et al.* France gotopaper	Public Health / Epidemiology	**Aim**: to analyse the association between an area-based deprivation indicator and SARS-CoV-2 incidence, positivity, and testing rates (May 2020 - April 2021). **Methods** - Analysis of records of results of all SARS-CoV-2 tests in France. - Residential addresses of tested individuals were geocoded to retrieve the associated aggregated units for the statistical information (IRIS) scale (area comprising 2000 inhabitants relatively homogenous in terms of socioeconomic characteristics). - A social deprivation score was assigned to each area using the European Deprivation Index (EDI). **Findings** > Analyses were based on 70 990 478 SARS-CoV-2 tests, of which 5 000 972 were positive. > SARS-CoV-2 incidence was higher in the most deprived areas than the least deprived areas (IRR 1.148 [95% CI 1.138–1.158]) and positivity rates were also higher (IRR 1.283 [1.273–1.294]), whereas testing rates were lower in the most deprived areas than the least deprived areas (IRR 0.905 [0.904–0.907]). > SARS-CoV-2 incidence and positivity rates remained higher in the most deprived areas than the least deprived areas during the second and third national lockdowns, and variation in testing rate was observed according to population density. **These results highlight a positive social gradient between deprivation and the risk of testing positive for SARS-CoV-2, with the highest risk among individuals living in the most deprived areas and a negative social gradient for testing rate. These findings might reflect structural barriers to health-care access in France and lower capacity of deprived populations to benefit from protective measures.**
JAMA 11FEB2022	**Association of Homologous and Heterologous Vaccine Boosters With COVID-19 Incidence and Severity in Singapore**	Hui Xuan Tan S., *et al.* Singapore gotopaper	Vaccines - Immunisation	**Aim**: to estimate SARS-CoV-2 infections and disease severity with the receipt of a booster and by type of booster. **Results** > Among 703 209 eligible individuals during the study period, 576 132 received boosters. The study included 22 643 521 and 9 339 981 person-days among the nonbooster and booster groups, respectively. By person-days, 59% were 60 to 69 years, 29% were 70 to 79 years, and 11% were aged 80 years and older, with 53% being female. > Among individuals who received BNT162b2 for their primary series, the incidences (per million person-days) of confirmed and severe infections were 227.9 and 1.4 for the homologous boosted compared with 600.4 and 20.5 for the nonboosted. > The IRRs were 0.272 (95% CI, 0.258-0.286) for the confirmed cases among the homologous-boosted individuals and 0.047 (95% CI, 0.026-0.084) for severe cases. > For the heterologous-boosted individuals, the incidences of confirmed and severe infections were 147.9 and 2.3 cases per million person-days, respectively, with IRRs of 0.177 (95% CI, 0.138-0.227) and 0.078 (95% CI, 0.011-0.560). > For individuals who received mRNA-1273 for their primary series, the incidence of confirmed infections for the homologous boosted was 133.9 cases per million person-years (IRR, 0.198 [95% CI, 0.144-0.271]). > For heterologous-boosted individuals, the incidence of confirmed infections was 100.6 per million person-days (IRR, 0.140 [95% CI, 0.052-0.376]). > The number of severe infections among individuals receiving mRNA-1273 for their primary series was too small to assess IRRs. **Heterologous boosting was associated with lower SARS-CoV-2 incidence rates than homologous boosting. Severe infections were lower among those receiving a booster after BNT162b2 as the primary series compared with the nonboosted individuals, regardless of the type of booster.**

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JAMA Pediatrics 10FEB2022	**Association of BNT162b2 COVID-19 Vaccination During Pregnancy With Neonatal and Early Infant Outcomes**	Goldshtein I., *et al.* Israel gotopaper	Vaccins	**Aim**: to examine whether BNT162b2 mRNA vaccination during pregnancy is associated with adverse neonatal and early infant outcomes among the newborns. **Methods** - Population-based cohort study comprising all singleton live births (March - September 2021), followed up until October 31, 2021, from mothers who had or had not received the BNT162b2 mRNA vaccination during pregnancy - Main Outcomes: risk ratios (RR) of preterm birth, small birth weight for gestational age (SGA), congenital malformations, all-cause hospitalizations, and infant death. **Results** > The cohort included 24 288 eligible newborns (49% female, 96% born at ≥37 weeks' gestation), of whom 16 697 were exposed (n = 2134 and n = 9364 in the first and second trimesters, respectively) to maternal vaccination in utero. Median (IQR) follow-up after birth was 126 days (76-179) among exposed and 152 days (88-209) among unexposed newborns. > No substantial differences were observed in preterm birth rates between exposed and unexposed newborns (RR = 0.95; 95% CI, 0.83-1.10) or SGA (RR = 0.97; 95% CI, 0.87-1.08). > No significant differences were observed in the incidence of all-cause neonatal hospitalizations (RR = 0.99; 95% CI, 0.88-1.12), postneonatal hospitalizations after birth (RR = 0.95; 95% CI, 0.84-1.07), congenital anomalies (RR = 0.69; 95% CI, 0.44-1.04), or infant mortality over the study period (RR = 0.84; 95% CI, 0.43-1.72). **No evident differences between newborns of women who received BNT162b2 mRNA vaccination during pregnancy, vs those of women who were not vaccinated, were found.**
Science 10FEB2022	**Broad anti-SARS-CoV-2 antibody immunity induced by heterologous ChAdOx1/mRNA-1273 vaccination**	Kaku C.I., *et al.* Sweden / USA gotopaper	Vaccines - Immunisation	**Aim**: to longitudinally profile SARS-CoV-2 spike (S)-specific serological and memory B cell (MBC) responses in individuals receiving either homologous (ChAdOx1:ChAdOx1) or heterologous (ChAdOx1:mRNA-1273) prime-boost vaccination. **Methods** : Recruitment of 55 healthcare workers receiving either homologous ChAdOx1:ChAdOx1 or heterologous ChAdOx1:mRNA-1273 prime-boost vaccination for blood donation (table S1). None of the volunteers had a documented history of prior SARS-CoV-2 infection. Participants received one dose of ChAdOx1 and 9-12 weeks later, a second dose of either ChAdOx1 (n = 28) or mRNA-1273 (n = 27). Collection of the first blood sample on the day of booster immunization to analyze ChAdOx1-primed immune responses and a second sample 7-10 days following the second dose to study the early secondary B cell response induced by homologous or heterologous booster vaccination. **Results** > Heterologous mRNA booster immunization induced higher serum neutralizing antibody and MBC responses against SARS-CoV-2 variants of concern (VOCs) compared to homologous ChAdOx1 boosting. > Specificity mapping of circulating B cells revealed that mRNA-1273 boost immunofocused ChAdOx1-primed responses onto epitopes expressed on prefusion-stabilized S. Monoclonal antibodies isolated from mRNA-1273 boosted participants displayed overall higher binding affinities and increased breadth of reactivity against VOCs relative to those isolated from ChAdOx1-boosted individuals. **Heterologous ChAdOx1:mRNA-1273 prime-boost immunization induces significantly broader and more potent serum neutralizing antibody and MBC responses against WT SARS-CoV-2 and VOCs relative to homologous ChAdOx1 vaccination, and this difference appears to be driven by both the magnitude and quality of the early secondary B cell response.**

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Lancet 12FEB2022	**Casirivimab and imdevimab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial**	RECOVERY Collaborative Group UK gotopaper	Therapeutics	**Aim**: to evaluate the efficacy and safety of casirivimab and imdevimab administered in combination in patients admitted to hospital with COVID-19. - Participants: patients aged at least 12 years admitted to hospital with clinically suspected or laboratory-confirmed SARS-CoV-2 infection. - Treatments: usual standard of care alone or usual care plus casirivimab 4 g and imdevimab 4 g administered in a single IV infusion. Primary outcome: 28-day all-cause mortality assessed by intention to treat, first only in patients without detectable antibodies to SARS-CoV-2 infection at randomisation, and then in the overall population. **Results** > Between Sept 18, 2020, and May 22, 2021, 9785 patients enrolled in RECOVERY were eligible for casirivimab and imdevimab, of which 4839 were randomly assigned to casirivimab and imdevimab plus usual care and 4946 to usual care alone. 3153 (32%) of 9785 patients were seronegative, 5272 (54%) were seropositive, and 1360 (14%) had unknown baseline antibody status. 812 (8%) patients were known to have received at least one dose of a SARS-CoV-2 vaccine. > In the primary efficacy population of seronegative patients, 396 (24%) of 1633 patients allocated to casirivimab and imdevimab versus 452 (30%) of 1520 patients allocated to usual care died within 28 days (rate ratio [RR] 0·79, 95% CI 0·69–0·91; p=0·0009). > Analysis of all randomly assigned patients (regardless of baseline antibody status): 943 (19%) of 4839 patients allocated to casirivimab and imdevimab versus 1029 (21%) of 4946 patients allocated to usual care died within 28 days (RR 0·94, 95% CI 0·86–1·02; p=0·14). > The proportional effect of casirivimab and imdevimab on mortality differed significantly between seropositive and seronegative patients (p value for heterogeneity=0·002). > There were no deaths attributed to the treatment, or meaningful between-group differences in the pre-specified safety outcomes of cause-specific mortality, cardiac arrhythmia, thrombosis, or major bleeding events. > Serious adverse reactions reported in seven (<1%) participants were believed by the local investigator to be related to treatment with casirivimab and imdevimab. **In patients admitted to hospital with COVID-19, the monoclonal antibody combination of casirivimab and imdevimab reduced 28-day mortality in patients who were seronegative at baseline but not in those who were seropositive at baseline.**
Nature Med. 10FEB2022	**Initial analysis of viral dynamics and circulating viral variants during the mRNA-1273 Phase 3 COVE trial**	Pajon R., *et al.* USA gotopaper	Vaccines	**Aim**: exploratory analyses to assess the impact of mRNA-1273 vaccination in the ongoing COVE trial on SARS-CoV-2 copy number and shedding, burden of disease and infection, and viral variants. **Methods** > Viral variants were sequenced in all COVID-19 and adjudicated COVID-19 cases (n = 832), from July 2020 in the blinded part A of the study to May 2021 of the open-label part B of the study, in which participants in the placebo arm started to receive the mRNA-1273 vaccine after US FDA emergency use authorization (Dec 2020). **Findings** > mRNA-1273 vaccination significantly reduced SARS-CoV-2 viral copy number (95% CI) by 100-fold on the day of diagnosis compared with placebo (4.1 (3.4–4.8) versus 6.2 (6.0–6.4) log10 copies per ml) > Median times to undetectable viral copies were 4 days for mRNA-1273 and 7 days for placebo. Vaccination also substantially reduced the burden of disease and infection scores > Vaccine efficacies (95% CI) against SARS-CoV-2 variants circulating in the United States during the trial assessed in this post hoc analysis were 82.4% (40.4–94.8%) for variants Epsilon and Gamma and 81.2% (36.1–94.5%) for Epsilon. > The detection of other, non-SARS-CoV-2, respiratory viruses during the trial was similar between groups. **These data show that in SARS-CoV-2-infected individuals, vaccination reduced both the viral copy number and duration of detectable viral RNA, which may be markers for the risk of virus transmission**.

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BMJ 10FEB2022	**Effectiveness of mRNA vaccines and waning of protection against SARS-CoV-2 infection and severe covid-19 during predominant circulation of the delta variant in Italy: retrospective cohort study**	Fabiani M., *et al.* Italy gotopaper	Vaccines - Immunisation	**Aim**: to estimate the effectiveness of mRNA vaccines against SARS-CoV-2 infection and severe covid-19 at different time after vaccination (27 Dec 2020 to 7 Nov 2021). Participants: 33 250 344 people aged ≥16 years who received a first dose of BNT162b2 (Pfizer-BioNTech) or mRNA-1273 (Moderna) vaccine and did not have a previous diagnosis of SARS-CoV-2 infection. Main outcomes: SARS-CoV-2 infection and severe covid-19 (admission to hospital or death). **Results** > During the epidemic phase when the delta variant was the predominant strain of the SARS-CoV-2 virus, vaccine effectiveness against SARS-CoV-2 infection significantly decreased (P<0.001) from 82% (95% CI 80% to 84%) at 3-4 weeks after the second dose of vaccine to 33% (27% to 39%) at 27-30 weeks after the second dose. > In the same time intervals, vaccine effectiveness against severe covid-19 also decreased (P<0.001), although to a lesser extent, from 96% (95% to 97%) to 80% (76% to 83%). > High risk people (vaccine effectiveness −6%, −28% to 12%), those aged ≥80 years (11%, −15% to 31%), and those aged 60-79 years (2%, −11% to 14%) did not seem to be protected against infection at 27-30 weeks after the second dose of vaccine. **The results support the vaccination campaigns targeting high risk people, those aged ≥60 years, and healthcare workers to receive a booster dose of vaccine six months after the primary vaccination cycle.**
BMJ 09FEB2022	**Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: retrospective cohort study**	Cohen K., *et al.* USA gotopaper	Long Covid	**Aim**: to characterize the risk of persistent and new clinical sequelae in adults aged ≥65 years after the acute phase of SARS-CoV-2 infection. Participants: individuals aged ≥65 years from January 2019 to the date of diagnosis of SARS-CoV-2 infection, matched by propensity score to three comparison groups that did not have covid-19: 2020 comparison group (n=87 337), historical 2019 comparison group (n=88 070), and historical comparison group with viral lower respiratory tract illness (n=73 490). Main outcomes: presence of persistent and new sequelae at ≥21 or more days after a diagnosis of covid-19. Excess risk for sequelae caused by SARS-CoV-2 infection was estimated for the 120 days after the acute phase of the illness. **Results** > Among individuals who were diagnosed with SARS-CoV-2, 32% (27 698 of 87 337) sought medical attention in the post-acute period for one or more new or persistent clinical sequelae, which was 11% higher than the 2020 comparison group. > Respiratory failure (risk difference 7.55, 95% CI 7.18 to 8.01), fatigue (5.66, 5.03 to 6.27), hypertension (4.43, 2.27 to 6.37), memory difficulties (2.63, 2.23 to 3.13), kidney injury (2.59, 2.03 to 3.12), mental health diagnoses (2.50, 2.04 to 3.04), hypercoagulability 1.47 (1.2 to 1.73), and cardiac rhythm disorders (2.19, 1.76 to 2.57) had the greatest risk differences compared with the 2020 comparison group, with similar findings to the 2019 comparison group. > Compared with the group with viral lower respiratory tract illness, however, only respiratory failure, dementia, and post-viral fatigue had increased risk differences of 2.39 (95% CI 1.79 to 2.94), 0.71 (0.3 to 1.08), and 0.18 (0.11 to 0.26) per 100 patients, respectively. > Individuals with severe covid-19 disease requiring admission to hospital had a markedly increased risk for most but not all clinical sequelae. **The results confirm an excess risk for persistent and new sequelae in adults aged ≥65 years after acute infection with SARS-CoV-2. Other than respiratory failure, dementia, and post-viral fatigue, the sequelae resembled those of viral lower respiratory tract illness in older adults.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 09FEB2022	**Effectiveness of Homologous or Heterologous Covid-19 Boosters in Veterans**	Mayr F.B., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: to understand whether the choice of a homologous or heterologous booster affects real-world vaccine effectiveness. - 4,806,026 veteran. Two analysis cohorts based on the primary vaccine that each veteran received (adenoviral-vector or mRNA) to compare the effectiveness of heterologous and homologous boosters. Each participant who had received a heterologous booster was matched with a control who had received a homologous booster. - Primary outcome: incidence of documented SARS-CoV-2 infection after a booster dose. - Additional outcomes: incidence of moderate disease (defined as Covid-19–related hospitalization within 14 days after infection) and severe or critical disease (defined as admission to an ICU or death within 28 days after infection). **Results** > 43,394 individuals who received a booster after vaccination with Ad26.COV2, 965,063 who received a booster after primary vaccination with either BNT162b2 or mRNA-1273. Matched analysis cohorts: 25,972 veterans with Ad26.COV2.S primed boosters (Ad26.COV2.S vaccine cohort: 12,986 homologous and 12,986 heterologous boosters) and 35,850 veterans with mRNA-primed boosters (mRNA vaccine cohort: 17,925 homologous and 17,925 heterologous boosters). > In the Ad26.COV2.S-primed vaccine cohort, we observed 415 documented infections, including 34 participants with moderate disease and 12 with severe or critical disease. > Of these infections, 278 occurred in participants who had received a homologous booster and 137 in those who had received a heterologous booster. The incidence of infection after heterologous boosting was approximately 50% lower than that after homologous boosting (adjusted rate ratio, 0.49; 95 CI, 0.40 to 0.60). Similarly, adjusted rate ratios for moderate and severe or critical disease were lower after heterologous boosting. > In the mRNA-primed cohort, we observed 362 documented infections, including 23 participants with moderate disease and 8 with severe or critical disease. No material difference was noted in the incidence of SARS-CoV-2 infection, including moderate and severe or critical disease, among participants who had received heterologous or homologous boosting after primary mRNA vaccination (adjusted rate ratio, 1.10; 95% CI, 0.90 to 1.35). Outcomes for the individual mRNA vaccines were similar to those in the combined mRNA category. **Overall, documented infections were uncommon among veterans who had received either homologous or heterologous boosters. Heterologous mRNA boosting may better protect against incident infection in persons who were initially vaccinated with an adenoviral-vector vaccine.**
Nature Med. 09FEB2022	**Vaccine effectiveness of heterologous CoronaVac plus BNT162b2 in Brazil**	Cerqueira-Silva T., *et al.* Brazil gotopaper	Vaccines - Immunisation	**Aim**: to estimate VE of CoronaVac over time and VE of BNT162b2 booster vaccination against RT–PCR-confirmed SARS-CoV-2 infection and severe COVID-19 outcomes (hospitalization or death). - test-negative design study involving almost 14 million people (~16 million tests) **Results** > Compared with unvaccinated individuals, CoronaVac VE at 14–30 d after the second dose was 55.0% (95% CI: 54.3–55.7) against confirmed infection and 82.1% (95% CI: 81.4–82.8) against severe outcomes. > VE decreased to 34.7% (95% CI: 33.1–36.2) against infection and 72.5% (95% CI: 70.9–74.0) against severe outcomes over 180 d after the second dose. > A BNT162b2 booster, 6 months after the second dose of CoronaVac, improved VE against infection to 92.7% (95% CI: 91.0–94.0) and VE against severe outcomes to 97.3% (95% CI: 96.1–98.1) 14–30 d after the booster. > Compared with younger age groups, individuals 80 years of age or older had lower protection after the second dose but similar protection after the booster. **Our findings support a BNT162b2 booster vaccine dose after two doses of CoronaVac, particularly for the elderly.**

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NEJM 09FEB2022	**Final Analysis of Efficacy and Safety of Single-Dose Ad26.COV2.S**	Sadoff J., *et al.* International gotopaper	Vaccines	**Aim:** to report the final analysis of the double-blind phase of ENSEMBLE **Methods:** final analysis of Ad26.COV2.S trial, in which adults were assigned in a 1:1 ratio to receive single-dose Ad26.COV2.S (5×1010 viral particles) or placebo. Median follow-up in this analysis was 4 months; 8940 participants had at least 6 months of follow-up. **Findings:** **>** In the per-protocol population (39,185 participants), vaccine efficacy against moderate to severe–critical Covid-19 at least 14 days after administration was 56.3% (95% CI, 51.3 to 60.8; 484 cases in the vaccine group vs. 1067 in the placebo group); at least 28 days after administration, vaccine efficacy was 52.9% (95% CI, 47.1 to 58.1; 433 cases in the vaccine group vs. 883 in the placebo group). > Efficacy in the United States, primarily against the reference strain (B.1.D614G) and the B.1.1.7 (alpha) variant, was 69.7% (95% CI, 60.7 to 76.9); efficacy was reduced elsewhere against the P.1 (gamma), C.37 (lambda), and B.1.621 (mu) variants. **>** Efficacy was 74.6% (95% CI, 64.7 to 82.1) against severe–critical Covid-19 (with only 4 severe–critical cases caused by the B.1.617.2 [delta] variant), 75.6% (95% CI, 54.3 to 88.0) against Covid-19 leading to medical intervention (including hospitalization), and 82.8% (95% CI, 40.5 to 96.8) against Covid-19–related death, with protection lasting 6 months or longer. > Efficacy against any severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was 41.7% (95% CI, 36.3 to 46.7). Ad26.COV2.S was associated with mainly mild-to-moderate adverse events, and no new safety concerns were identified. **A single dose of Ad26.COV2.S provided 52.9% protection against moderate to severe–critical Covid-19. Protection varied according to variant; higher protection was observed against severe Covid-19, medical intervention, and death than against other end points and lasted for 6 months or longer.**
NEJM 09FEB2022	**Protection against the Omicron Variant from Previous SARS-CoV-2 Infection**	Altarawneh H.N., *et al.* Qatar gotopaper	Variants	**Aim**: to estimate the effectiveness of previous infection in preventing symptomatic new cases hospitalisation or death caused by omicron and other SARS-CoV-2 variants in Qatar. - Sensitivity analyses that included adjustment for vaccination status and that excluded vaccinated persons from the analysis were performed. **Results** > The median interval between previous infection and PCR testing among cases and controls was 279 days (interquartile range [IQR], 194 to 313) for analysis of the alpha variant, 285 days (IQR, 213 to 314) for analysis of the beta variant, 254 days (IQR, 159 to 376) for analysis of the delta variant, and 314 days (IQR, 268 to 487) for analysis of the omicron variant. > The effectiveness of previous infection in preventing reinfection was estimated to be 90.2% (95% CI, 60.2 to 97.6) against the alpha variant, 85.7% (95% CI, 75.8 to 91.7) against the beta variant, 92.0% (95% CI, 87.9 to 94.7) against the delta variant, and 56.0% (95% CI, 50.6 to 60.9) against the omicron variant. > Among the patients with reinfection, progression to severe Covid-19 occurred in one patient with the alpha variant, in two patients with the beta variant, in no patients with the delta variant, and in two patients with the omicron variant. None of the reinfections progressed to critical or fatal Covid-19. > The effectiveness with respect to severe, critical, or fatal Covid-19 was estimated to be 69.4% (95% CI, −143.6 to 96.2) against the alpha variant, 88.0% (95% CI, 50.7 to 97.1) against the beta variant, 100% (95% CI, 43.3 to 100) against the delta variant, and 87.8% (95% CI, 47.5 to 97.1) against the omicron variant. **Effectiveness of previous infection in preventing reinfection with the alpha, beta, and delta variants of SARS-CoV-2 was robust (at approximately 90%). Such protection against reinfection with the omicron variant was lower (approximately 60%) but still considerable. Protection of previous infection against hospitalization or death caused by reinfection appeared to be robust, regardless of variant.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Cell 09FEB2022	**Respiratory mucosal delivery of next-generation COVID-19 vaccine provides robust protection against both ancestral and variant strains of SARS-CoV-2**	Afkami S., *et al.* Canada gotopaper	Vaccines	**Findings** > Two trivalent adenoviral-vectored COVID-19 vaccines were developed and evaluated > Intranasal, but not intramuscular, immunization induces tripartite mucosal immunity > Intranasal immunization protects against ancestral and variant strains of SARS-CoV-2 > Optimal protection requires B and T cell immunity and trained innate immunity
Lancet Microbe 08FEB2022	**Safety and immunogenicity of two recombinant DNA COVID-19 vaccines containing the coding regions of the spike or spike and nucleocapsid proteins: an interim analysis of two open-label, non-randomised, phase 1 trials in healthy adults**	Ahn J.Y., *et al.* South Korea gotopaper	Vaccines	**Aim**: to assess the safety and immunogenicity of two recombinant DNA vaccines for COVID-19: GX-19 containing plasmid DNA encoding the SARS-CoV-2 spike protein, and GX-19N containing plasmid DNA encoding the SARS-CoV-2 receptor-binding domain (RBD) foldon, nucleocapsid protein, and plasmid DNA encoding the spike protein. **Methods** Two open-label non-randomised phase 1 trials, one of GX-19 and the other of GX-19N were done at two hospitals in South Korea **Findings** > Between June 17 and July 30, 2020, we screened 97 individuals, of whom 40 (41%) participants were enrolled in the GX-19 trial (20 [50%] in the 1·5 mg group and 20 [50%] in the 3·0 mg group) > Between Dec 28 and 31, 2020, we screened 23 participants, of whom 21 (91%) participants were enrolled on the GX-19N trial. 32 (52%) of 61 participants reported 80 treatment-emergent adverse events after vaccination > All solicited adverse events were mild except one (2%) case of moderate fatigue in the 1·5 mg GX-19 group; no serious vaccine-related adverse events were detected > Binding antibody responses increased after second dose of vaccination in all groups (p=0·0002 in the 1·5 mg GX-19 group; p<0·0001 in the 3·0 mg GX-19; and p=0·0004 for the spike protein and p=0·0001 for the RBD in the 3·0 mg GX-19N group). **GX-19 and GX-19N are safe and well tolerated. GX-19N induces humoral and broad SARS-CoV-2-specific T-cell responses. GX-19N shows lower neutralising antibody responses and needs improvement to enhance immunogenicity.**
Science 08FEB2022	**Rapid increase in Omicron infections in England during December 2021: REACT-1 study**	Elliot P., *et al.* UK gotopaper	Variants	**Aim:** to analyze prevalence of SARS-CoV-2 and its dynamics in England. The REal-time Assessment of Community Transmission-1 (REACT-1) study **Methods:** Analysis from end November to mid-December 2021 among almost 100,000 participants from the REACT-1 study. **Findings:** > Prevalence was high with rapid growth nationally and particularly in London during December 2021, and an increasing proportion of infections due to Omicron. > Large falls were observed in swab positivity among mostly vaccinated older children (12-17 years) compared with unvaccinated younger children (5-11 years), and in adults who received a third (booster) vaccine dose vs. two doses. **These results reinforce the importance of vaccination and booster campaigns, although additional measures have been needed to control the rapid growth of the Omicron variant.**

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Nature Med. 07FEB2022	**Long-term cardiovascular outcomes of COVID-19**	Wie Y., *et al.* USA gotopaper	Long Covid	**Aim**: to estimate risks and 1-year burdens of a set of pre-specified incident cardiovascular outcomes. - National healthcare databases from the US Department of Veterans Affairs - Cohort of 153,760 individuals with COVID-19, as well as two sets of control cohorts with 5,637,647 (contemporary controls) and 5,859,411 (historical controls) individuals. **Results** > Beyond the first 30 d after infection, individuals with COVID-19 are at increased risk of incident cardiovascular disease spanning several categories, including cerebrovascular disorders, dysrhythmias, ischemic and non-ischemic heart disease, pericarditis, myocarditis, heart failure and thromboembolic disease. > These risks and burdens were evident even among individuals who were not hospitalized during the acute phase of the infection and increased in a graded fashion according to the care setting during the acute phase (non-hospitalized, hospitalized and admitted to intensive care). **These results provide evidence that the risk and 1-year burden of cardiovascular disease in survivors of acute COVID-19 are substantial.**
Lancet Child Adolesc Health 07FEB2022	**Long COVID symptoms in SARS-CoV-2-positive adolescents and matched controls (LongCOVIDKidsDK): a national, cross-sectional study**	Kikkenborg Berg S., *et al.* Denmark gotopaper	Long Covid	**Aim**: to investigate health, including symptoms of long COVID, in adolescents (aged 15–18 years) who tested positive for SARS-CoV-2 compared with a control group. - All Danish adolescents aged 15–18 years with a positive SARS-CoV-2 test, Jan 1, 2020, to July 12, 2021, and a control group matched (1:4) by age and sex were sent a survey. **Results** > 6630 individuals in the case group, 21 640 in the control group. Across both groups, median age was 17.6 years (IQR 16.4–18.5), 57.6% responders were female, and 42.4% male. > Participants in the case group had greater odds of having at least one long COVID symptom lasting at least 2 months compared with the control group (3159 [61.9%] vs 12 340 [57.0%], odds ratio 1.22 [95% CI 1.15–1.30]; p<0.0001). > Participants in the case group reported significantly lower symptom scores (ie, less somatic distress) on the Children's Somatic Symptoms Inventory-24 (CSSI-24) than in the control group: mean 10.7 (SD 11.4; median 7.0 [IQR 2.0–15.0]) versus 11,9 (10.6; 9.0 [4.0–17.0]; p<0.0001). > Participants in the case group had better quality of life scores on the Paediatric Quality of Life Inventory (PedsQL) than in the control group: physical functioning mean score 88.7 (SD 13.9; median 93.8 [IQR 84.4–100.0]) versus 86.5 (14.3; 90.6 [81.3–96.9]; p<0.0001); emotional functioning 77.1 (20.3; 80.0 [65.0–95.0]) versus 71.7 (21.4; 75.0 [60.0–90.0]; p<0.0001); social functioning 93.1 (12.5; 100.0 [90.0–100.0]) versus 88.4 (16.2; 95.0 [80.0–100.0]; p<0.0001); and school functioning 66.9 (22.5; 65.0 [60.0–85.0]) versus 62.9 (22.1; 65.0 [50.0–80.0]; p<0.0001). > More participants in the case group than in the control group reported 16 or more sick days (1205 [18.2%] vs 2518 [11.6%]; p<0.0001) and 16 or more days of school absence (695 [10.5%] vs 1777 [8.2%]; p<0.0001). **Participants with SARS-CoV-2-positive tests had more long-lasting symptoms and sick leave, whereas participants in the control group had more short-lasting symptoms and worse quality of life.**

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Lancet Child Adolesc Health 07FEB2022	**Physical and mental health 3 months after SARS-CoV-2 infection (long COVID) among adolescents in England (CLoCk): a national matched cohort study**	Stephenson T., *et al.* UK gotopaper	Long Covid	**Aim**: to describe post-COVID symptomatology in a non-hospitalised, UK national sample of adolescents aged 11–17 years with PCR-confirmed SARS-CoV-2 infection compared with matched adolescents with negative PCR status. - Cohort: adolescents aged 11–17 years from the Public Health England database who tested positive for SARS-CoV-2 (Jan-March, 2021), matched by month of test, age, sex, and geographical region to adolescents who tested negative. - 3 months after testing, a subsample of adolescents were contacted to complete a detailed questionnaire. **Results** > 6804 adolescents (3065 who tested positive and 3739 who tested negative) completed the questionnaire. > At PCR testing, 1084 (35.4%) who tested positive and 309 (8.3%) who tested negative were symptomatic and 936 (30.5%) from the test-positive group and 231 (6.2%) from the test-negative group had three or more symptoms. > 3 months after testing, 2038 (66.5%) who tested positive and 1993 (53.3%) who tested negative had any symptoms, and 928 (30.3%) from the test-positive group and 603 (16.2%) from the test-negative group had three or more symptoms. > At 3 months after testing, the most common symptoms among the test-positive group were tiredness (1196 [39.0%]), headache (710 [23.2%]), and shortness of breath (717 [23.4%]), and among the test-negative group were tiredness (911 [24.4%]), headache (530 [14.2%]), and other (unspecified; 590 [15.8%]). > Latent class analysis identified two classes, characterised by few or multiple symptoms. The estimated probability of being in the multiple symptom class was 29.6% (95% CI 27.4–31.7) for the test-positive group and 19.3% (17.7–21.0) for the test-negative group (risk ratio 1.53; 95% CI 1.35–1.70). > The multiple symptoms class was more frequent among those with positive PCR results than negative results, in girls than boys, in adolescents aged 15–17 years than those aged 11–14 years, and in those with lower pretest physical and mental health. **Adolescents who tested positive for SARS-CoV-2 had similar symptoms to those who tested negative, but had a higher prevalence of single and, particularly, multiple symptoms at the time of PCR testing and 3 months later.**
Nature 07FEB2022	**Pyrimidine inhibitors synergize with nucleoside analogues to block SARS-CoV-2**	Schultz D., *et al.* USA gotopaper	Therapeutics	**Aim:** to screen small molecule libraries that contained approved drugs, drugs in clinical trials and drugs with known targets to uncover both direct-acting and host directed antivirals using the ancestral SARS-CoV-2 virus (WA1) and a cell-based, high-content assay in respiratory cells. **Methods:** ~18,000 drugs for antiviral activity were screened using live virus infection in human respiratory cells. **Findings:** > 122 drugs with antiviral activity and selectivity against SARS-CoV-2 were validated. Amongst these candidates are 16 nucleoside analogues, the largest category of clinically used antivirals. This included the antivirals remdesivir and molnupiravir, which have been approved for use in COVID-19. > RNA viruses rely on a high supply of nucleoside triphosphates from the host to efficiently replicate, and the authors identified a panel of host nucleoside biosynthesis inhibitors as antiviral. **> combining pyrimidine biosynthesis inhibitors with antiviral nucleoside analogues synergistically inhibits SARS-CoV-2 infection in vitro and in vivo against emerging strains of SARS-CoV-2 suggesting a clinical path forward.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 07FEB2022	**Association of SARS-CoV-2 Infection With Serious Maternal Morbidity and Mortality From Obstetric Complications**	Torri D., *et al.* USA South Korea gotopaper	Public Health / Epidemiology	**Aim**: to evaluate the association of SARS-CoV-2 infection with serious maternal morbidity or mortality from common obstetric complications. **Methods** - Retrospective cohort study of 14 104 pregnant and postpartum patients delivered between March 1, 2020, and December 31, 2020 (with final follow-up to February 11, 2021). - All patients with SARS-CoV-2 were included and compared with those without a positive SARS-CoV-2 test result who delivered on randomly selected dates over the same period. **Findings** > Of the 14 104 included patients (mean age, 29.7 years), 2352 patients had SARS-CoV-2 infection and 11 752 did not have a positive SARS-CoV-2 test result. > Compared with those without a positive SARS-CoV-2 test result, SARS-CoV-2 infection was significantly associated with the primary outcome which is composite of maternal death or serious morbidity related to hypertensive disorders of pregnancy, postpartum hemorrhage, or infection other than SARS-CoV-2 (13.4% vs 9.2%; difference, 4.2% [95% CI, 2.8%-5.6%]; adjusted relative risk [aRR], 1.41 [95% CI, 1.23-1.61]). > All 5 maternal deaths were in the SARS-CoV-2 group > SARS-CoV-2 infection was not significantly associated with cesarean birth (34.7% vs 32.4%; aRR, 1.05 [95% CI, 0.99-1.11]) > Compared with those without a positive SARS-CoV-2 test result, moderate or higher COVID-19 severity (n = 586) was significantly associated with the primary outcome (26.1% vs 9.2%; difference, 16.9% [95% CI, 13.3%-20.4%]; aRR, 2.06 [95% CI, 1.73-2.46]) and the major secondary outcome of cesarean birth (45.4% vs 32.4%; difference, 12.8% [95% CI, 8.7%-16.8%]; aRR, 1.17 [95% CI, 1.07-1.28]), but mild or asymptomatic infection (n = 1766) was not significantly associated with the primary outcome (9.2% vs 9.2%; difference, 0% [95% CI, −1.4% to 1.4%]; aRR, 1.11 [95% CI, 0.94-1.32]) or cesarean birth (31.2% vs 32.4%; difference, −1.4% [95% CI, −3.6% to 0.8%]; aRR, 1.00 [95% CI, 0.93-1.07]) **Among pregnant and postpartum individuals at 17 US hospitals, SARS-CoV-2 infection was associated with an increased risk for a composite outcome of maternal mortality or serious morbidity from obstetric complications.**
Molecular Therapy 07FEB2022	**Elicitation of potent SARS-CoV-2 neutralizing antibody responses through immunization with a versatile adenovirus-inspired multimerization platform**	Chevillard C., *et al.* France gotopaper	Immunology	Virus like particles (VLPs) are highly suited platforms for protein-based vaccines. **Aim**: to adapt a previously designed non-infectious adenovirus-inspired 60-merdodecahedric VLP (ADDomer) to display a multimeric array of large antigens through a SpyTag/SpyCatcher system. **Findings** > To validate the platform as a potential COVID-19 vaccine approach, we decorated the newly designed VLP with the glycosylated receptor binding domain (RBD) of SARS-CoV-2. Cryo-Electron Microscopy structure revealed that up to 60 copies of this antigenic domain could be bound on a single ADDomer particle, with the symmetrical arrangements of a dodecahedron. > Mouse immunization with the RBD decorated VLPs already showed a significant specific humoral response following prime vaccination, greatly reinforced by a single boost. > Neutralization assays with SARS-CoV-2 spike pseudo-typed-virus demonstrated the elicitation of strong neutralization titers, superior to those of COVID-19 convalescent patients. > Notably, the presence of pre-existing immunity against the adenoviral-derived particles did not hamper the immune response against the antigen displayed on its surface. **This plug and play vaccine platform represents a promising new highly versatile tool to combat emergent pathogens.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Cell 03FEB2022	**T-cell reactivity to the SARS-CoV-2 Omicron variant is preserved in most but not all individuals**	Naranbhai V., *et al.* USA gotopaper	Variants	**Aim:** to assess the cross-reactivity of T-cell responses to the Omicron variant. **Methods:** anti-SARS-CoV-2 T-cell responses were studied in 76 ambulatory adult volunteers in Chelsea, Massachusetts sampled prior to vaccination, after primary series vaccination, and/or after receipt of additional 'booster' doses. **Findings:** > T-cell responses in individuals with prior infection, vaccination, both prior infection and vaccination, and boosted vaccination are largely preserved to Omicron spike and non-spike proteins. > A subset of individuals (~21%) with a >50% reduction in T-cell reactivity to the Omicron spike was identifyed. > Evaluation of functional CD4+ and CD8+ memory T cell responses confirmed these findings and reveal that reduced recognition to Omicron spike is primarily observed within the CD8+ T cell compartment potentially due to escape from HLA binding. > Booster vaccination enhanced T-cell responses to Omicron spike. **In contrast to neutralizing immunity, these findings suggest preservation of T-cell responses to the Omicron variant, although with reduced reactivity in some individuals.**
Lancet Respir Med. 03FEB2022	**Efficacy and safety of baricitinib plus standard of care for the treatment of critically ill hospitalised adults with COVID-19 on invasive mechanical ventilation or extracorporeal membrane oxygenation: an exploratory, randomised, placebo-controlled trial**	Ely E.W., *et al.* USA gotopaper	Therapeutics	**Aim:** to evaluate the efficacy and safety of baricitinib plus standard of care in critically ill hospitalised adults with COVID-19 requiring invasive mechanical ventilation or extracorporeal membrane oxygenation. **Methods:** exploratory trial followed the study design of COV-BARRIER in a critically ill cohort not included in the main phase 3 trial. Participants (aged ≥18 years) hospitalised with laboratory-confirmed SARS-CoV-2 infection on baseline invasive mechanical ventilation or extracorporeal membrane oxygenation. Prespecified endpoints included all-cause mortality through days 28 and 60, number of ventilator-free days, duration of hospitalisation, and time to recovery through day 28. **Findings:** > 101 participants were enrolled into the exploratory trial and assigned to baricitinib (n=51) or placebo (n=50) plus standard of care. Standard of care included baseline systemic corticosteroid use in 87 (86%) participants. > Treatment with baricitinib significantly reduced 28-day all-cause mortality compared with placebo (20 [39%] of 51 participants died in the baricitinib group vs 29 [58%] of 50 in the placebo group; hazard ratio [HR] 0·54 [95% CI 0·31–0·96]; 46% relative reduction; absolute risk reduction 19%). > A significant reduction in 60-day mortality was also observed in the baricitinib group compared with the placebo group (23 [45%] events vs 31 [62%]; HR 0·56 [95% CI 0·33–0·97]; 44% relative reduction; absolute risk reduction 17%). In every six baricitinib-treated participants, one additional death was prevented compared with placebo at days 28 and 60. > The number of ventilator-free days did not differ significantly between treatment groups (mean 8·1 days [SD 10·2] in the baricitinib group vs 5·5 days [8·4] in the placebo group). > The mean duration of hospitalisation in baricitinib-treated participants was not significantly shorter than in placebo-treated participants (23·7 days [SD 7·1] vs 26·1 days [3·9]). **In critically ill hospitalised patients with COVID-19 who were receiving invasive mechanical ventilation or extracorporeal membrane oxygenation, treatment with baricitinib compared with placebo (in combination with standard of care, including corticosteroids) reduced mortality.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 01FEB2022	**Pandemic preparedness and COVID-19: an exploratory analysis of infection and fatality rates, and contextual factors associated with preparedness in 177 countries, from Jan 1, 2020, to Sept 30, 2021**	COVID-19 National Preparedness Collaborators International gotopaper	Public Health / Epidemiology	**Aim**: to understand the conditions associated with cross-country variation in national rates of COVID-19 infection and fatality, to guide investment in more effective preparedness and response for future pandemics. **Methods** - Daily SARS-CoV-2 infections and COVID-19 deaths for 177 countries and territories and 181 subnational locations, Jan 1, 2020, and Sept 30, 2021. - Cumulative infection rate and infection-fatality ratio (IFR) were estimated and standardised for environmental, demographic, biological, and economic factors. - Standardised national cumulative infection rates and IFRs were tested for associations with 12 pandemic preparedness indices, seven health-care capacity indicators, and ten other demographic, social, and political conditions using linear regression. - Relationship between interpersonal and governmental trust and corruption and changes in mobility patterns and COVID-19 vaccination rates was also assessed. **Results** > The factors that explained the most variation in cumulative rates of SARS-CoV-2 infection included the proportion of the population living below 100 m (5·4% [4·0–7·9] of variation), GDP per capita (4·2% [1·8–6·6]), and the proportion of infections attributable to seasonality (2·1% [95% uncertainty interval 1·7–2·7]). > Most cross-country variation in cumulative infection rates could not be explained. > The factors that explained the most variation in COVID-19 IFR over the same period were the age profile of the country (46·7% [18·4–67·6] of variation), GDP per capita (3·1% [0·3–8·6]), and national mean BMI (1·1% [0·2–2·6]). > 44·4% (29·2–61·7) of cross-national variation in IFR could not be explained. > Pandemic-preparedness indices, which aim to measure health security capacity, were not meaningfully associated with standardised infection rates or IFRs. > Measures of trust in the government and interpersonal trust, as well as less government corruption, had larger, statistically significant associations with lower standardised infection rates. > High levels of government and interpersonal trust, as well as less government corruption, were also associated with higher COVID-19 vaccine coverage among middle-income and high-income countries where vaccine availability was more widespread, and lower corruption was associated with greater reductions in mobility. > If these modelled associations were to be causal, an increase in trust of governments such that all countries had societies that attained at least the amount of trust in government or interpersonal trust measured in Denmark (75th percentile across these spectrums) might have reduced global infections by 12·9% (5·7–17·8) for government trust and 40·3% (24·3–51·4) for interpersonal trust. > Similarly, if all countries had a national BMI equal to or less than that of the 25th percentile, our analysis suggests global standardised IFR would be reduced by 11·1%. **Efforts to improve pandemic preparedness and response might benefit from investment in risk communication and community engagement strategies to boost the confidence of individuals in public health guidance. in such a scenario, increasing health promotion for key modifiable risks associates with lower fatalities.**
Nature 01FEB2022	**Attenuated fusogenicity and pathogenicity of SARS-CoV-2 Omicron variant**	Suzuki R., *et al.* Japan gotopaper	Virology	**Findings** > Our statistical modelling suggests that Omicron has spread more rapidly than the Delta variant in several countries including South Africa > Cell culture experiments show that Omicron is less fusogenic than Delta and an ancestral SARS-CoV-2 strain. Although the spike (S) protein of Delta is efficiently cleaved into two subunits, which facilitates cell–cell fusion2,3, Omicron S is less efficiently cleaved compared to Delta S and ancestral SARS-CoV-2 S. > Furthermore, in a hamster model, Omicron shows decreased lung infectivity and is less pathogenic compared to Delta and ancestral SARS-CoV-2.

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Nature 01FEB2022	**Altered TMPRSS2 usage by SARS-CoV-2 Omicron impacts tropism and fusogenicity**	Meng B., *et al.* UK gotopaper	Virology	**Aim**: to show that Omicron spike has higher affinity for ACE2 compared to Delta as well as a marked change of antigenicity conferring significant evasion of therapeutic monoclonal and vaccine-elicited polyclonal neutralising antibodies after two doses. **Findings** > mRNA vaccination as a third vaccine dose rescues and broadens neutralisation. Importantly, antiviral drugs remdesivir and molnupiravir retain efficacy against Omicron BA.1 > Replication was similar for Omicron and Delta virus isolates in human nasal epithelial cultures. However, in lower airway organoids, lung cells and gut cells, Omicron demonstrated lower replication > Omicron spike protein was less efficiently cleaved compared to Delta. > The defect for Omicron pseudotyped virus (PV) to enter specific cell types effectively correlated with higher cellular RNA expression of TMPRSS2, and knock down of TMPRSS2 impacted Delta entry to a greater extent than Omicron > Drug inhibitors targeting specific entry pathways demonstrated that the Omicron spike inefficiently utilises the cellular protease TMPRSS2 that promotes cell entry via plasma membrane fusion, with greater dependency on cell entry via the endocytic pathway > Consistent with suboptimal S1/S2 cleavage and inability to utilise TMPRSS2, syncytium formation by the Omicron spike was markedly impaired compared to the Delta spike. Omicron's less efficient spike cleavage at S1/S2 is associated with shift in cellular tropism away from TMPRSS2 expressing cells, with implications for altered pathogenesis.
Science Transl Med. 01FEB2022	**Infection or a third dose of mRNA vaccine elicits neutralizing antibody responses against SARS-CoV-2 in kidney transplant recipients**	Charmetant X., *et al.* France gotopaper	Vaccines - Immunisation	**Background**: previous infection SARS-CoV-2, but not the standard two-dose regimen of vaccination, provide protection against symptomatic COVID-19 in kidney transplant recipients. **Aim**: to compare the cellular and humoral immune responses of these two groups of patients. **Findings** > Neutralizing anti-Receptor Binding Domain (RBD) IgG antibodies were identified as the primary correlate of protection for transplant recipients. > Analysis of virus-specific B and T cell responses suggested that the generation of neutralizing anti-RBD IgG may have depended upon cognate T-B cell interactions that took place in germinal center, potentially acting as a limiting checkpoint. > High dose mycophenolate mofetil, an immunosuppressive drug, was associated with fewer antigen-specific B and T follicular helper (Tfh) cells after vaccination; this was not observed in patients recently infected with SARS-CoV-2. > Finally, we observed that, in two independent prospective cohorts, administration of a third dose of SARS-CoV-2 mRNA vaccine restored neutralizing titers of anti-RBD IgG in about 40% of individuals who had not previously responded to two doses of vaccine. **These findings suggest that a third dose of SARS-CoV-2 mRNA vaccine improves the RBD-specific responses of transplant patients treated with immunosuppressive drugs.**
Nature 01FEB2022	**SARS-CoV-2 Omicron variant replication in human bronchus and lung ex vivo**	Hui K.P.I., *et al.* China gotopaper	Variants	**Aim**: to assess SARS-CoV-2 variants of concern (VOC) transmissibility in ex vivo explant cultures of human bronchus and lung. **Methods :** The replication competence and cellular tropism of the wild-type (WT) virus, D614G, Alpha, Beta, Delta and Omicron variants in ex vivo explant cultures of human bronchus and lung was compared. Dependence on TMPRSS2 for infection was also evaluated. **Findings:** > Omicron replicated faster than all other SARS-CoV-2 in the bronchus but less efficiently in the lung parenchyma. > All VOCs had similar cellular tropism as the WT. Omicron was more dependent on cathepsins than other VOC tested, suggesting that the omicron variant enters cells by a different route than other variants. > The lower replication competence of Omicron in human lung may explain the reduced severity of Omicron that is now being reported in epidemiological studies although determinants of severity are multifactorial.

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Nature 31JAN2022	**Vaccines Elicit Highly Conserved Cellular Immunity to SARS-CoV-2 Omicron**	Liu J., *et al.* USA gotopaper	Variants	**Aim**: to study cellular immune responses against omicron following Covid-19 vaccination, particularly CD8+ T cell responses, which likely contribute to protection against severe SARS-CoV-2 disease. **Results** > Cellular immunity induced by current SARS-CoV-2 vaccines is highly conserved to the SARS-CoV-2 Omicron Spike. > Individuals who received Ad26.COV2.S or BNT162b2 vaccines demonstrated durable Spike-specific CD8+ and CD4+ T cell responses, which showed extensive cross-reactivity against both the Delta and Omicron variants, including in central and effector memory cellular subpopulations. > Median Omicron Spike-specific CD8+ T cell responses were 82-84% of WA1/2020 Spike-specific CD8+ T cell responses. **These data provide immunologic context for the observation that current vaccines still show robust protection against severe disease with the SARS-CoV-2 Omicron variant despite the substantially reduced neutralizing antibody responses.**
Nature 31JAN2022	**T cell responses to SARS-CoV-2 spike cross-recognize Omicron**	Keeton R., *et al.* South Africa gotopaper	Variants	**Aim**: to evaluate the extent to which components of the adaptive response such as T cells may still target Omicron despite its immune escape and contribute to protection from severe outcomes. - Ability of T cells to react with Omicron spike was assessed in 70 participants who were vaccinated with Ad26.CoV2.S, BNT162b2, or unvaccinated convalescent COVID-19 patients. **Results** > 70-80% of the CD4+ and CD8+ T cell response to spike was maintained across study groups. > The magnitude of Omicron cross-reactive T cells was similar to Beta and Delta variants, despite Omicron harboring considerably more mutations. > In Omicron-infected hospitalized patients (n=19), there were comparable T cell responses to ancestral spike, nucleocapsid and membrane proteins to those patients hospitalized in previous waves dominated by the ancestral, Beta or Delta variants (n=49). **Despite Omicron's extensive mutations and reduced susceptibility to neutralizing antibodies, the majority of T cell responses, induced by vaccination or infection, cross-recognize the variant.**
Lancet Respir Med. 31JAN2022	**Safety and immunogenicity of a high-dose quadrivalent influenza vaccine administered concomitantly with a third dose of the mRNA-1273 SARS-CoV-2 vaccine in adults aged ≥65 years: a phase 2, randomised, open-label study**	Izikson R., *et al.* France / USA gotopaper	Vaccines	**Aim**: to assess the safety and immunogenicity of concomitant administration of high-dose quadrivalent influenza vaccine (QIV-HD) and a mRNA-1273 vaccine booster dose in older adults. - Ongoing, phase 2, multicentre, open-label, descriptive trial at six clinical research sites in the USA **Results** > Between July 16 and Aug 31, 2021, 306 participants were enrolled and randomly assigned, of whom 296 received at least one vaccine dose (100 in the coadministration group, 92 in the QIV-HD, and 104 in the mRNA-1273 group) > Reactogenicity profiles were similar between the coadministration and mRNA-1273 groups, with lower reactogenicity rates in the QIV-HD group (frequency of solicited injection site reactions 86·0% [95% CI 77·6–92·1], 91·3% [84·2–96·0], and 61·8% [50·9–71·9]; frequency of solicited systemic reactions 80·0%, [70·8–87·3], 83·7% [75·1–90·2], and 49·4% [38·7–60·2], respectively). > Up to day 22, unsolicited adverse events were reported for 17·0% (95% CI 10·2–25·8) of participants in the coadministration group and 14·4% (8·3–22·7) of participants in the mRNA-1273 group, and tended to be reported at a slightly lower rate (10·9% [5·3–19·1]) in participants in the QIV-HD group. > Seven participants each reported one medically attended adverse event (three in the coadministration group, one in the QIV-HD group, and three in the mRNA-1273 group). There were no serious adverse events, adverse events of special interest, or deaths. **No safety concerns or immune interference were observed for concomitant administration of QIV-HD with mRNA-1273 booster in adults aged 65 years and older, supporting co-administration recommendations.**

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Nature Immunol. 31JAN2022	**Recognition and inhibition of SARS-CoV-2 by humoral innate immunity pattern recognition molecules**	Stravalaci M., *et al.* Italy gotopaper	Immunology	**Aim**: to conduct a systematic investigation of the interaction of human humoral fluid-phase pattern recognition molecules (PRMs) with SARS-CoV-2. **Methods :** Genetic association analyses from 2,000 individuals, including 332 with severe COVID-19 (hospitalization with respiratory failure and a confirmed SARS-CoV-2 RNA PCR test from nasopharyngeal swabs). **Findings:** > Of 12 PRMs tested, the long pentraxin 3 (PTX3) and mannose-binding lectin (MBL) bound the viral nucleocapsid and spike proteins, respectively. > MBL bound trimeric spike protein, including that of variants of concern (VoC), in a glycan-dependent manner and inhibited SARS-CoV-2 in three in vitro models. > After binding to spike protein, MBL activated the lectin pathway of complement activation. > Based on retention of glycosylation sites and modeling, MBL was predicted to recognize the Omicron VoC. > Genetic polymorphisms at the MBL2 locus were associated with disease severity. **Selected humoral fluid-phase PRMs can play an important role in resistance to, and pathogenesis of, COVID-19, a finding with translational implications.**
Nature Med. 28JAN2022	**Three exposures to the spike protein of SARS-CoV-2 by either infection or vaccination elicit superior neutralizing immunity to all variants of concern**	Wratil, PR., *et al.* Germany gotopaper	Immunology	**Aim**: to study neutralizing antibody dynamics in a longitudinal cohort of COVID-19 convalescent and infection-naive individuals vaccinated with BNT162b2 by quantifying anti-SARS-CoV-2-spike antibodies and determining their avidity and neutralization capacity in serum. > Cohort of 171 individuals - (98 convalescente and 73 naive) **Findings** > In a direct comparison with all other VoCs, omicron displays the most pronounced humoral immune escape evading antibody neutralization at early and late time points after vaccination. > A "hybrid immunity" in convalescents after one mRNA vaccination is not further enhanced by a second vaccination after a short time frame of three weeks. > In contrast, a timely spaced, second vaccination after several months further increases neutralization capacity to combat VoCs such as omicron with an unprecedented ability of immune escape. > In a longitudinal analysis there is no direct association between anti-spike IgG titers and the infection-neutralization capacity. > A stepwise increase in the avidity of SARS-CoV-2 spike-specific antibodies after the first vaccination in convalescents and after the second and third vaccination in naive individuals was noted, consistent with the reported occurrence of affinity-matured memory B cells up to 6 months after infection highlighting that the quality rather than the mere quantity of antibodies is important. > Triple-vaccinated naive individuals reach almost the same level of neutralization capacity against the immune escape VoC omicron as vaccinated convalescents, as well as individuals who experienced a break-through infection with either the delta or the omicron VoC. > The more rapid induction of high-avidity antibodies in convalescents after vaccination can be compensated for by three mRNA vaccinations in infection-naive individuals, and also develops after a breakthrough infection in twice vaccinated individuals. **Conclusions** Data suggest that a superior infection-neutralization capacity against SARS-CoV-2 VoCs - including those with immune escape properties - needs to develop over time following a total of three spike antigen exposures. These results support the notion that a single infection with SARS-CoV-2 does not provide a similar level of protection as the combination of infection and vaccination. Importantly, the dynamics by which the infection neutralization capacity increased were paralleled by an enhanced avidity of SARS-CoV-2 spike-binding antibodies providing a critical refinement for predicting the efficacy of protective humoral responses against a range of different VoCs

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Nature 28JAN2022	**Memory B cell repertoire from triple vaccinees against diverse SARS-CoV-2 variants**	Wang K., *et al.* China gotopaper	Variants	**Aim**: to evaluate whether sera from individuals who received two or three doses of inactivated vaccine could neutralize authentic Omicron. **Results** > The seroconversion rates of neutralizing antibodies were 3.3% (2/60) and 95% (57/60) for 2- and 3-dose vaccinees, respectively. > For three-dose recipients, the geometric mean neutralization antibody titre (GMT) of Omicron was 16.5-fold lower than that of the ancestral virus (254). > 323 human monoclonal antibodies (mAbs) derived from memory B cells in 3-dose vaccinees were isolated, half of which recognize the receptor binding domain (RBD). A subset of these (24/163) neutralizes all SARS-CoV-2 variants of concern (VOCs), including Omicron, potently. > Therapeutic treatments with representative broadly neutralizing mAbs were highly protective against SARS-CoV-2 Beta and Omicron infections in mice. > Atomic structures of the Omicron Spike in complex with three types of all five VOC-reactive antibodies defined the binding and neutralizing determinants and revealed a key antibody escape site, G446S, that confers greater resistance to one major class of antibodies bound at the right shoulder of RBD through altering local conformation at the binding interface. **These results rationalize the use of 3-dose immunization regimens and suggest that the fundamental epitopes revealed by these broadly ultrapotent antibodies are a rational target for a universal sarbecovirus vaccine.**
Nature Med. 27JAN2022	**Heterologous AD5-nCOV plus CoronaVac versus homologous CoronaVac vaccination: a randomized phase 4 trial**	Li J., *et al.* China gotopaper	Vaccines	**Aim**: to evaluate the safety and immunogenicity of the recombinant adenovirus type 5 (AD5)-vectored COVID-19 vaccine Convidecia as a heterologous booster versus those of CoronaVac as homologous booster in adults previously vaccinated with CoronaVac in an ongoing, randomized, observer-blinded, parallel-controlled phase 4 trial Co-primary endpoints: the occurrence of adverse reactions within 28 d after vaccination and geometric mean titers (GMTs) of neutralizing antibodies against live wild-type SARS-CoV-2 virus at 14 d after booster vaccination. **Results** > Between May 25 and 26, 2021, 302 participants aged between 18 and 75 years were recruited, who had received one dose of CoronaVac in the past 1–3 months or two doses of CoronaVac in the past 3–6 months. > The heterologous prime–boost regimen with one dose of Convidecia administered at an interval of 3–6 months after two doses of CoronaVac was safe and highly immunogenic in healthy adults aged 18–59 years. > No thromboses, vaccine-related anaphylaxis or other serious adverse events were observed in any of the groups by day 28 after the booster. These data indicate that heterologous boosting with Convidecia following one or two doses of CoronaVac has a good and manageable safety profile, despite the higher reactogenicity than that resulting from homologous boosting with CoronaVac. > Significant increases in neutralizing antibody levels against wild-type SARS-CoV-2 were observed after booster dose vaccination in all groups > In line with the neutralizing antibody titers, both heterologous and homologous boosters induced significant increases in RBD-binding IgG levels at day 14 **These data suggest that heterologous boosting with Convidecia following initial vaccination with CoronaVac is safe and more immunogenic than homologous boosting.**

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Lancet Infect Dis. 27JAN2022	**Persistence of protection against SARS-CoV-2 clinical outcomes up to 9 months since vaccine completion: a retrospective observational analysis in Lombardy, Italy**	Corrao G., *et al.* Italy gotopaper	Clinic	**Aim**: to investigate the effect of time since vaccine completion on the SARS-CoV-2 infection and its severe forms. **Methods :** Retrospective observational analysis using the vaccination campaign integrated platform of the Italian region of Lombardy, 5 351 085 individuals aged 12 years or older who received complete vaccination from Jan 17 to July 31, 2021, were followed up from 14 days after vaccine completion until Oct 20, 2021. **Findings:** > Overall, 14 140 infections and 2450 severe illnesses were documented, corresponding to incidence rates of 6·7 and 1·2 cases per 10 000 person-months, respectively. > From the first to the ninth month since vaccine completion, rates increased from 4·6 to 10·2 infections, and from 1·0 to 1·7 severe illnesses every 10 000 person-months. These figures correspond to relative reduction of vaccine effectiveness of 54·9% for infection and of 40·0% for severe illness. > The increasing infection rate was greater for individuals aged 60 years or older who received adenovirus-vectored vaccines (from 4·0 to 23·5 cases every 10 000 person-months). > The increasing severe illness rates were similar for individuals receiving mRNA-based vaccines (from 1·1 to 1·5 every 10 000 person-months) and adenovirus-vectored vaccines (from 0·5 to 0·9 every 10 000 person-months).
Lancet 27JAN2022	**Hyperimmune immunoglobulin for hospitalised patients with COVID-19 (ITAC): a double-blind, placebo-controlled, phase 3, randomised trial**	Polizzotto M., *et al.* International gotopaper	Therapeutics	**Aim**: to evaluate the safety and clinical efficacy of anti-SARS-CoV-2 hIVIG in addition to standard of care including the antiviral remdesivir in individuals hospitalised with COVID-19 without end-organ failure **Results** > From Oct 8, 2020, to Feb 10, 2021, 593 participants (n=301 hIVIG, n=292 placebo) were enrolled at 63 sites in 11 countries; 579 patients were included in the mITT analysis. > Compared with placebo, the hIVIG group did not have significantly greater odds of a more favourable outcome at day 7; the adjusted OR was 1·06 (95% CI 0·77–1·45; p=0·72). Infusions were well tolerated, although infusion reactions were more common in the hIVIG group (18·6% vs 9·5% for placebo; p=0·002). > The percentage with the composite safety outcome at day 7 was similar for the hIVIG (24%) and placebo groups (25%; OR 0·98, 95% CI 0·66–1·46; p=0·91). > The ORs for the day 7 ordinal outcome did not vary for subgroups considered, but there was evidence of heterogeneity of the treatment effect for the day 7 composite safety outcome: risk was greater for hIVIG compared with placebo for patients who were antibody positive (OR 2·21, 95% CI 1·14–4·29); for patients who were antibody negative, the OR was 0·51 (0·29–0·90; pinteraction=0·001). **When administered with standard of care including remdesivir, SARS-CoV-2 hIVIG did not demonstrate efficacy among patients hospitalised with COVID-19 without end-organ failure. The safety of hIVIG might vary by the presence of endogenous neutralising antibodies at entry.**

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NEJM 26JAN2022	**Homologous and Heterologous Covid-19 Booster Vaccinations**	Atmar R.L., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: to gather data on the serial use of homologous boosters and heterologous boosters in fully vaccinated recipients. - Phase 1–2, open-label clinical trial conducted in the US on adults who had completed a Covid-19 vaccine regimen at least 12 weeks earlier and had no reported history of SARS-CoV-2 infection and received a booster injection with mRNA-1273 (Moderna) at a dose of 100 µg, Ad26.COV2.S (Janssen) at a dose of 5×1010 virus particles, or BNT162b2 (Pfizer–BioNTech) at a dose of 30 µg. Primary end point: safety, reactogenicity, and humoral immunogenicity on trial days 15 and 29. **Results** > Of the 458 participants who were enrolled in the trial, 154 received mRNA-1273, 150 received Ad26.COV2.S, and 153 received BNT162b2 as booster vaccines; 1 participant did not receive the assigned vaccine. > Reactogenicity was similar to that reported for the primary series. More than half the recipients reported having injection-site pain, malaise, headache, or myalgia. > For all combinations, antibody neutralizing titers against a SARS-CoV-2 D614G pseudovirus increased by a factor of 4 to 73, and binding titers increased by a factor of 5 to 55. > Homologous boosters increased neutralizing antibody titers by a factor of 4 to 20, whereas heterologous boosters increased titers by a factor of 6 to 73. > Spike-specific T-cell responses increased in all but the homologous Ad26.COV2.S-boosted subgroup. > CD8+ T-cell levels were more durable in the Ad26.COV2.S-primed recipients, and heterologous boosting with the Ad26.COV2.S vaccine substantially increased spike-specific CD8+ T cells in the mRNA vaccine recipients. **Homologous and heterologous booster vaccines had an acceptable safety profile and were immunogenic in adults who had completed a primary Covid-19 vaccine regimen at least 12 weeks earlier.**
NEJM 26JAN2022	**Myocarditis after BNT162b2 Vaccination in Israeli Adolescents**	Mevorach D., *et al.* Israel gotopaper	Clinic	**Aim**: to report the incidence of hospitalization for myocarditis (June 2-Oct 20, 2021), among adolescents (12-15 yo) within 21 days after receipt of the first vaccine dose and within 30 days after receipt of the second dose. **Results** > 404,407 adolescents (195,579 of whom were male) received the first dose of vaccine, 326,463 adolescents (157,153 of whom were male) received the second dose, and 16 cases of myocarditis correlated to vaccination and leading to hospitalization were reported. > 1 occurred in an unvaccinated adolescent and 15 occurred in vaccinated adolescents — 1 case within 21 days after receipt of the first vaccine dose, 12 cases within 1 week after receipt of the second dose, and 2 later cases (1 each at 46 days and 70 days after receipt of the second dose). > All the cases were clinically mild, involving a mean duration of hospitalization of 3.1 days (range, 1 to 6) and no readmissions during 30 days of follow-up. > The risk estimates of myocarditis among male recipients in the 21 days after the first and second doses were 0.56 cases per 100,000 after the first dose and 8.09 cases per 100,000 after the second dose; the risk estimates among female recipients were 0 cases per 100,000 after the first dose and 0.69 cases per 100,000 after the second dose. > The risk estimates per person in this study were lower than the previously reported risks among male recipients 16 to 24 years of age in Israel. **The incidence of myocarditis leading to hospitalization among adolescents who received the second dose of the BNT162b2 vaccine was low but was higher than among recipients of the first vaccine dose and proportionately numerically higher than in recent estimates of incidence among unvaccinated persons.**

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NEJM 26JAN2022	**SARS-CoV-2 Omicron Variant Neutralization after mRNA-1273 Booster Vaccination**	Pajon R., *et al.* USA gotopaper	Variants	**Aim**: to assess the potential susceptibility of omicron variant to the mRNA-1273 vaccine Evaluation of omicron neutralization by serum samples obtained from participants who had received the primary two-dose regimen of the mRNA-1273 vaccine (100 µg in each dose) and who received one booster dose of either: - the mRNA-1273 vaccine (at a dose of either 50 or 100 µg) - the bivalent mRNA-1273.211 vaccine (a 1:1 mix of mRNA-1273 vaccine and beta variant messenger RNAs [mRNAs], for a total dose of either 50 or 100 µg) - the bivalent mRNA-1273.213 vaccine (a 1:1 mix of beta and delta variant mRNAs, for a total dose of 100 µg). **Results** > The primary two-dose regimen of the mRNA-1273 vaccine elicited detectable neutralizing antibodies against the omicron variant in 85% of the participants 1 month after the second dose. > The 50% inhibitory dilution (ID50) geometric mean titer was 35.0 times lower than that against the D614G variant. > Seven months after the second dose was administered (before the booster), neutralization of the omicron variant was detected in only 55% of the participants, and the ID50 geometric mean titers were 8.4 times lower than those against the D614G variant. > A booster dose of 50 µg of the mRNA-1273 vaccine was associated with ID50 geometric mean titers against the omicron variant that were 20.0 times higher than those assessed 1 month after the second vaccination; these titers were 2.9 times lower than those against the D614G variant. > Neutralization titers against the omicron variant 6 months after the third (booster) dose of vaccine were 6.3 times lower than the peak titers assessed 1 month after the booster injection, but titers remained detectable in all the participants. > Six months after the booster, neutralization titers against the omicron variant declined faster than those against the D614G variant; however, this decline in titers against the omicron variant was similar to the decline observed in titers against the D614G variant after a second dose of the mRNA-1273 vaccine (by a factor of 7.8 from 1 month to 7 months). > The booster dose was associated with improved durability of neutralization of the D614G variant, which was 2.3 times lower 6 months after the booster injection than 1 month after the booster injection. > The 100-µg booster doses of the mRNA-1273, mRNA-1273.211, and mRNA-1273.213 vaccines all generated nearly identical ID50 geometric mean titers against the omicron variant (range, 2115 to 2228); these titers were 2.5 to 2.6 times higher than those assessed after the 50-µg booster dose of the mRNA-1273 vaccine and 1.4 to 1.5 times higher than the peak titers against the D614G variant 1 month after the second dose in the COVE trial. > The strong boosting of neutralization of the omicron variant was similar to the strong boosting of neutralization of the delta and beta variants. **After the primary two-dose series of the mRNA-1273 vaccine, neutralization titers against the omicron variant were 35.0 times lower than those against the D614G variant. However, a booster dose of mRNA-1273 vaccine substantially increased neutralization titers against the omicron variant, which may reduce the risk of breakthrough infection.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 26JAN2022	**Efficacy of Antibodies and Antiviral Drugs against Covid-19 Omicron Variant**	Takashita E., *et al.* Japan gotopaper	Variants	**Aim**: to examine the neutralizing ability of FDA-approved and investigational therapeutic monoclonal antibodies against omicron and other variants using a live-virus focus reduction neutralization assay (FRNT) - Tested monoclonal antibodies: LY-CoV016 estevimab, LY-CoV555 bamlanivimab, estevimab/bamlanivimab, REGN10987 imdevimab, REGN10933 casirivimab, imdevimab/casirivimab, COV2-2196 tixageimab, COV-2130 cilgavimab, tixageimab/cilgavimab, S209 sotrovimab precursor - Tested drugs: GS-4415224 (remdesivir), EIDD-1931 (molnupiravir), PF-00835231 (protease inhibitor) - Neutralisation assays against omicron (NC928 - isolated from a traveler), NC002 (an early SARS-CoV-2 strain from February 2020), alpha (HP127), beta (HP01542), gamma (TY7-503), delta (UW5250) **Results** > Monoclonal antibodies neutralized the early strain (NC002) and the alpha (HP127) and delta (UW5250) variants with a low FRNT50 value (1.34 to 150.38 ng per milliliter), except for LY-CoV555 (bamlanivimab), which showed markedly higher FRNT50 values against the delta variant than against the early strain and the alpha variant. > Etesevimab did not neutralize the omicron (NC928), beta (HP01542), or gamma (TY7-503) variants even at the highest FRNT50 value (>50,000 ng per milliliter) that was tested. > Bamlanivimab showed reduced neutralizing activity against the beta and gamma variants and did not neutralize omicron. > Imdevimab had high neutralizing activity against the beta and gamma variants but lost activity against omicron. > Casirivimab neutralized beta, gamma, and omicron with a high FRNT50 value (187.69 to 14,110.70 ng per milliliter); however, the FRNT50 value for omicron was higher by a factor of 18.6 than that for beta and higher by a factor of 75.2 than that for gamma. > COV2-2196 (tixagevimab), COV2-2130 (cilgavimab), and S309 (precursor of sotrovimab) also retained neutralizing activity against beta, gamma, and omicron; however, the FRNT50 values were higher by a factor of 3.7 to 198.2 for omicron than for beta or gamma. > All the combinations of monoclonal antibodies that were tested neutralized the early strain and the alpha and delta variants. > The combination of etesevimab plus bamlanivimab showed remarkably reduced neutralizing activity against gamma and lost neutralizing activity against omicron and beta. > The imdevimab–casirivimab combination retained activity against beta and gamma but lost inhibitory capability against omicron. > The tixagevimab–cilgavimab combination inhibited beta, gamma, and omicron; however, the FRNT50 values of this combination were higher by a factor of 24.8 to 142.9 for omicron than for beta or gamma, respectively. > The susceptibilities of omicron to the antiviral compounds tested were similar to those of the early strain (i.e., IC50 values for remdesivir, molnupiravir, and PF-07304814 that differed by factors of 1.2, 0.8, and 0.7, respectively). > These results suggest that all three of these compounds may show efficacy for treating patients infected with the omicron variant. **Therapeutic options may be available to combat the omicron variant; however, some therapeutic monoclonal antibodies may not be effective against this variant.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 26JAN2022	**Effects of a Prolonged Booster Interval on Neutralization of Omicron Variant**	Zhao X., *et al.* China gotopaper	Variants	**Aim**: to analyze the binding and neutralizing antibodies elicited by three doses (two priming doses and one booster dose) of an inactivated vaccine (CoronaVac and BBIBP-CorV) or a protein subunit vaccine (ZF2001), and those in persons who had recovered from Covid-19 (the convalescent group). Serum samples from the ZF2001 recipients were grouped according to the interval between the second and third dose: - short-interval ZF2001 group: second priming dose 1 month after the first dose and then the third dose 1 month after the second dose - prolonged-interval ZF2001 group: second priming dose 1 month after the first dose and then the third dose 4 months after the second dose. **Results** > The decreases in the titers of antibodies binding to the omicron variant were greater in the serum samples from both ZF2001 groups than in those from the inactivated-vaccine group or the convalescent group > In the convalescent group, 15 of 16 serum samples were negative for neutralizing antibodies against the omicron variant. > Among the persons who received three doses of either vaccine, 10 of 16 samples (62%) in the inactivated-vaccine group, 9 of 16 samples (56%) in the short-interval ZF2001 group, and 16 of 16 samples (100%) in the prolonged-interval ZF2001 group were positive for neutralizing antibodies against the omicron variant. > In a fifth group of persons who also had a prolonged 4-month interval between the second and third dose of ZF2001 but whose serum samples were collected 4 to 6 months after the third dose, 9 of 13 serum samples (69%) were positive for neutralizing antibodies against the omicron variant. > The titer of neutralizing antibodies against the omicron variant was lower than that against the prototype SARS-CoV-2 strain by a factor of 17.4 in the convalescent group, of 5.1 in the inactivated-vaccine group, of 10.6 in the short-interval ZF2001 group, and of 3.1 in the prolonged-interval ZF2001 group. **These findings support the use of multiple vaccine boosts and prolonged intervals between vaccine doses to protect against highly mutated variants such as omicron in persons who had previously received two priming doses of vaccine or who had previously recovered from SARS-CoV-2.**
Cell 25JAN2022	**Multiple Early Factors Anticipate Post-Acute COVID-19 Sequelae**	Su Y., *et al.* USA gotopaper	Long Covid	**Aim**: to assess quantifiable risk-factors for post-acute sequelae of COVID-19 (PASC) and their biological associations **Methods**: Deep multi-omic, longitudinal investigation of 309 COVID-19 patients from initial diagnosis to convalescence (2-3 months later), integrated with clinical data, and patient-reported symptoms. Aythors resolved four PASC-anticipating risk factors at the time of initial COVID-19 diagnosis: type 2 diabetes, SARS-CoV-2 RNAemia, Epstein-Barr virus viremia, and specific autoantibodies. **Findings**: > In patients with gastrointestinal PASC, SARS-CoV-2-specific and CMV-specific CD8+ T cells exhibited unique dynamics during recovery from COVID-19. > Analysis of symptom-associated immunological signatures revealed coordinated immunity polarization into four endotypes exhibiting divergent acute severity and PASC. > Immunological associations between PASC factors diminish over time leading to distinct convalescent immune states. **Detectability of most PASC factors at COVID-19 diagnosis emphasizes the importance of early disease measurements for understanding emergent chronic conditions and suggests PASC treatment strategies.** **These analyses provided a framework to understand the heterogeneity of "long COVID" and a rich resource for interrogating the biological factors that contribute to PASC**

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Science Immunol. 25JAN2022	**Vaccination before or after SARS-CoV-2 infection leads to robust humoral response and antibodies that effectively neutralize variants**	Bates T. A., *et al.* USA gotopaper	Vaccines - Immunsation	**Aim**: to assess the impact of breakthrough infection on the neutralizing antibody response and how this compares to the response elicited by hybrid immunity. **Methods**: Measurement of the neutralizing antibody responses from 104 vaccinated individuals, including those with breakthrough infections, hybrid immunity, and no infection history. **Findings**: > Human immune sera following breakthrough infection and vaccination following natural infection, broadly neutralize SARS-CoV-2 variants to a similar degree. > Hybrid immunity was associated with a remarkable improvement in the proportion of spike-specific antibodies that were also neutralizing. > While age negatively correlates with antibody response after vaccination alone, no correlation with age was found in breakthrough or hybrid immune groups. **The additional antigen exposure from natural infection substantially boosts the quantity, quality, and breadth of humoral immune response regardless of whether it occurs before or after vaccination.**
Cell 25JAN2022	**Immune imprinting, breadth of variant recognition and germinal center response in human SARS-CoV-2 infection and vaccination**	Röltgen K., *et al.* USA gotopaper	Vaccines - Immunsation	**Aim**: to investigate whether antibodies stimulated by mRNA vaccination (BNT162b2), including 3rd dose boosting, differ from those generated by infection or adenoviral (ChAdOx1-S and Gam-COVID-Vac) or inactivated viral (BBIBP-CorV) vaccines. **Methods**: Analysis of human lymph nodes after infection or mRNA vaccination for correlates of serological differences. **Findings**: > Antibody breadth against viral variants is less after infection compared to all vaccines evaluated, but improves over several months. > Viral variant infection elicits variant-specific antibodies, but prior mRNA vaccination imprints serological responses toward Wuhan-Hu-1 rather than variant antigens. > In contrast to disrupted germinal centers (GCs) in lymph nodes during infection, mRNA vaccination stimulates robust GCs containing vaccine mRNA and spike antigen up to 8 weeks post-vaccination in some cases. **SARS-CoV-2 antibody specificity, breadth and maturation are affected by imprinting from exposure history, and distinct histological and antigenic contexts in infection compared to vaccination.**
Science 25JAN2022	**SARS-CoV-2 Beta variant infection elicits potent lineage-specific and cross-reactive antibodies**	Reincke S.M., *et al.* Germany / USA gotopaper	Immunology	**Background**: SARS-CoV-2 Beta variant of concern (VOC) resists neutralization by major classes of antibodies from COVID-19 patients and vaccinated individuals. **Object of the study**: serum of Beta-infected patients revealed reduced cross-neutralization of wildtype virus. - Beta-specific and cross-reactive receptor-binding domain (RBD) antibodies were isolated from From these patients. > The Beta-specificity results from recruitment of VOC-specific clonotypes and accommodation of mutations present in Beta and Omicron into a major antibody class that is normally sensitive to these mutations. > The Beta-elicited cross-reactive antibodies share genetic and structural features with wildtype-elicited antibodies, including a public VH1-58 clonotype targeting the RBD ridge. **These findings advance our understanding of the antibody response to SARS-CoV-2 shaped by antigenic drift with implications for design of next-generation vaccines and therapeutics.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Infect Dis. 25JAN2022	**Safety and immunogenicity of an AS03-adjuvanted SARS-CoV-2 recombinant protein vaccine (CoV2 preS dTM) in healthy adults: interim findings from a phase 2, randomised, dose-finding, multicentre study**	Sridhar S., *et al.* UK / USA gotopaper	Vaccines	**Aim**: to evaluate the safety and immunogenicity of an optimised formulation of CoV2 preS dTM adjuvanted with AS03 (Sanofi Pasteur) to inform progression to phase 3 clinical trial. **Methods** - Phase 2 trial in adults (≥18 years old), including those with pre-existing medical conditions, immunocompromised (except recent organ transplant or chemotherapy) and at potentially increased risk for severe COVID-19. - Randomisation (1:1:1) with stratification by age (18–59 years and ≥60 years), rapid serodiagnostic test result, and high-risk medical conditions (yes or no), to receive two injections (day 1 and day 22) of 5 µg(low dose), 10 µg (medium dose), or 15 µg (high dose) CoV2 preS dTM antigen with fixed AS03 content. - Safety endpoints were evaluated for all randomised participants who received at least one dose of the study vaccine (safety analysis set), and are presented here for the interim study period (up to day 43). - Primary immunogenicity objective: to describe neutralising antibody titres to the D614G variant 14 days after the second vaccination (day 36) in participants who were SARS-CoV-2 naive who received both injections, provided samples at day 1 and day 36, did not have protocol deviations, and did not receive an authorised COVID-19 vaccine before day 36. - Neutralising antibodies were measured using a pseudovirus neutralisation assay and are presented here up to 14 days after the second dose. - Secondary immunogenicity objective: assessment of neutralising antibodies in non-naive participants. **Findings** > 722 participants enrolled and randomly assigned between Feb 24, 2021, and March 8, 2021, 721 received at least one injection (low dose=240, medium dose=239, and high dose=242). > The proportion of participants reporting at least one solicited adverse reaction (injection site or systemic) in the first 7 days after any vaccination was similar between treatment groups (217 [91%] of 238 in the low-dose group, 213 [90%] of 237 in the medium-dose group, and 218 [91%] of 239 in the high-dose group); these adverse reactions were transient, mostly mild to moderate in intensity, and occurred at a higher frequency and intensity after the second vaccination. > 4 participants reported immediate unsolicited adverse events; 2 (one each in the low-dose group and medium-dose group) were considered to be vaccine related. > 5 participants reported 7 vaccine-related medically attended adverse events (2 in the low-dose group, 1 in the medium-dose group, and 4 in the high-dose group). > No vaccine-related serious adverse events and no adverse events of special interest were reported. > Among participants naive to SARS-CoV-2 at day 36, 158 (98%) of 162 in the low-dose group, 166 (99%) of 168 in the medium-dose group, and 163 (98%) of 166 in the high-dose group had at least a two-fold increase in neutralising antibody titres to the D614G variant from baseline. > Neutralising antibody geometric mean titres (GMTs) at day 36 for participants who were naive were 2189 (95% CI 1744–2746) for the low-dose group, 2269 (1792–2873) for the medium-dose group, and 2895 (2294–3654) for the high-dose group. GMT ratios (day 36: day 1) were 107 (95% CI 85–135) in the low-dose group, 110 (87–140) in the medium-dose group, and 141 (111–179) in the high-dose group. > Neutralising antibody titres in non-naive adults 21 days after one injection tended to be higher than titres after two injections in adults who were naive, with GMTs 21 days after one injection for participants who were non-naive being 3143 (95% CI 836–11 815) in the low-dose group, 2338 (593–9226) in the medium-dose group, and 7069 (1361–36 725) in the high-dose group. **Two injections of CoV2 preS dTM-AS03 showed acceptable safety and reactogenicity, and robust immunogenicity in adults who were SARS-CoV-2 naive and non-naive. These results supported progression to phase 3 evaluation of the 10 µg antigen dose for primary vaccination and a 5 µg antigen dose for booster vaccination.**

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Immunity 25JAN2022	**Immuno-proteomic profiling reveals aberrant immune cell regulation in the airways of individuals with ongoing post-COVD-19 respiratory disease**	Vijayakumar B., *et al.* UK gotopaper	Long Covid	**Aim**: to assess the immunological landscape of the human respiratory tract after recovery from acute viral infection. **Methods**: The immune cell and proteomic composition of the airways and peripheral blood were analyzed in a group of previously hospitalized COVID19 patients with persistent radiological abnormalities in their lungs more than 3 months post discharge. **Findings**: > Post-COVID-19 patients showed abnormal airway (but not plasma) proteomes, with elevated concentration of proteins associated with apoptosis, tissue repair and epithelial injury versus healthy individuals. > Increased numbers of cytotoxic lymphocytes were observed in individuals with greater airway dysfunction, while increased B cell numbers and altered monocyte subsets were associated with more widespread lung abnormalities. > One year follow-up of some post-COVID-19 patients indicated that these abnormalities resolved over time. In summary, COVID-19 causes a prolonged change to the airway immune landscape in those with persistent lung disease, with evidence of cell death and tissue repair linked to ongoing activation of cytotoxic T cells. **Distinct immune-protein signatures associated with different pathophysiological changes in the post-COVID19 lung. These changes, and lung pathology, do however appear to resolve over the longer (> 1 year) term.**
Nature Commun. 25JAN2022	**Immunoglobulin signature predicts risk of post-acute COVID-19 syndrome**	Cervia C., *et al.* Switzerland gotopaper	Long Covid	**Aim**: to study COVID-19 patients during primary infection and up to one year later, compared to healthy subjects. **Methods**: Characterisation of a prospective cohort of 215 individuals by clinical visits and laboratory analyses up to one year of follow-up. **Findings**: > The development of PACS correlates with a distinct Ig signature as well as patient age, history of asthma bronchiale, and a number of symptoms, all measured during primary infection. > The authors discover an immunoglobulin (Ig) signature, based on total IgM and IgG3 levels, which – combined with age, history of asthma bronchiale, and five symptoms during primary infection – is able to predict the risk of PACS independently of timepoint of blood sampling. > **These findings highlight the benefit of measuring Igs for the early identification of patients at high risk for PACS, whichwhich in turn is crucial for understanding the pathomechanisms of PACS and identification of preventive measures for treatment and care.**
Cell 24JAN2022	**SARS-CoV-2 vaccination induces immunological T cell memory able to cross-recognize variants from Alpha to Omicron**	Tarke A., *et al.* Italy / USA gotopaper	Immunology	**Aim**: to address whether T cell responses induced by different vaccine platforms (mRNA-1273, BNT162b2, Ad26.COV2.S, NVX-CoV2373) cross-recognize early SARS-CoV-2 variants. **Results** > T cell responses to early variants were preserved across vaccine platforms. > By contrast, significant overall decreases were observed for memory B cells and neutralizing antibodies. > In subjects ~6 months post-vaccination, 90% (CD4+) and 87% (CD8+) of memory T cell responses were preserved against variants on average by AIM assay, and 84% (CD4+) and 85% (CD8+) preserved against Omicron. > Omicron RBD memory B cell recognition was substantially reduced to 42% compared to other variants. > T cell epitope repertoire analysis revealed a median of 11 and 10 spike epitopes recognized by CD4+ and CD8+ T cells, with average preservation > 80% for Omicron. **Functional preservation of the majority of T cell responses may play an important role as second-level defenses against diverse variants.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Cell 25JAN2022	**Structural and functional characterizations of infectivity and immune evasion of SARS-CoV-2 Omicron**	Cui Z., *et al.* China gotopaper	Variants	**Analysis of cryo-EM structures of the Spike (S) from Omicron** **Findings** > Amino acid substitutions forge interactions that stably maintain an active conformation for receptor recognition. > The relatively more compact domain organization confers improved stability and enhances attachment but compromises the efficiency of the viral fusion step. > Alterations in local conformation, charge and hydrophobic microenvironments underpin the modulation of the epitopes such that they are not recognized by most NTD- and RBD-antibodies, facilitating viral immune escape. Structure of the Omicron S bound with human ACE2, the analysis of sequence conservation in ACE2 binding region of 25 sarbecovirus members, and heatmaps of the immunogenic sites and their corresponding mutational frequencies **sheds light on conserved and structurally restrained regions that can be used for the development of broad-spectrum vaccines and therapeutics.**
Lancet Respir Med. 24JAN2022	**SARS-CoV-2 infection and vaccine effectiveness in England (REACT-1): a series of cross-sectional random community surveys**	Chadeau-Hyam M., *et al.* UK gotopaper	Vaccines - Immunisation	**Aim**: to analyse the underlying dynamics driving patterns in SARS-CoV-2 prevalence during September, 2021, in England (REACT-1 study) - Using RT-PCR swab positivity data from 100 527 participants in round 14 of REACT-1 (Sept 9–27, 2021), community-based prevalence of SARS-CoV-2 and vaccine effectiveness against infection were estimated by combining round 14 data with data from round 13 (June 24 to July 12, 2021; n=172 862). **Results** > During September, 2021, we estimated a mean RT-PCR positivity rate of 0·83% (95% CrI 0,76–0,89), with a reproduction number (R) overall of 1,03 (95% CrI 0,94–1,14). > Among the 475 (62,2%) of 764 sequenced positive swabs, all were of the delta variant; 22 (4,63%; 95% CI 3,07–6,91) included the Tyr145His mutation in the spike protein associated with the AY.4 sublineage, and there was one Glu484Lys mutation. > Age, region, key worker status, and household size jointly contributed to the risk of swab positivity. > The highest weighted prevalence was observed among children aged 5–12 years, at 2,32% (95% CrI 1,96–2,73) and those aged 13–17 years, at 2,55% (2,11–3,08). > The SARS-CoV-2 epidemic grew in those aged 5–11 years, with an R of 1,42 (95% CrI 1,18–1,68), but declined in those aged 18–54 years, with an R of 0,81 (0,68–0,97). > At ages 18–64 years, the adjusted vaccine effectiveness against infection was 62,8% (95% CI 49,3–72,7) after two doses compared to unvaccinated people, for all vaccines combined, 44,8% (22,5–60,7) for the ChAdOx1 nCov-19 vaccine, and 71,3% (56,6–81,0) for the BNT162b2 vaccine. > In individuals aged 18 years and older, the weighted prevalence of swab positivity was 0,35% (95% CrI 0,31–0,40) if the second dose was administered up to 3 months before their swab but 0,55% (0,50–0,61) for those who received their second dose 3–6 months before their swab, compared to 1,76% (1·60–1·95) among unvaccinated individuals. **In September, 2021, infections were increasing exponentially in children aged 5–17 years, at a time when vaccination rates were low in this age group. In adults, compared to those who received their second dose <3 months ago, the higher prevalence of swab positivity at 3–6 months following two doses of the COVID-19 vaccine suggests an increased risk of breakthrough infections during this period.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Microbe 24JAN2022	**Safety and immunogenicity of the SARS-CoV-2 ARCoV mRNA vaccine in Chinese adults: a randomised, double-blind, placebo-controlled, phase 1 trial**	Chen G.L., *et al.* China gotopaper	Vaccines	**Aim**: to assess the preliminary safety, tolerability, and immunogenicity of an mRNA vaccine ARCoV, which encodes the SARS-CoV-2 spike protein receptor-binding domain (RBD). **Methods** - Phase 1 trial of ARCoV on healthy adults aged 18–59 years negative for SARS-CoV-2 infection randomised to receive an intramuscular injection of vaccine (5 μg, 10 μg, 15 μg, 20 μg, or 25 μg) or placebo. Primary safety outcome: incidence of adverse events or adverse reactions within 60 min, and at days 7, 14, and 28 after each vaccine dose. Secondary safety outcome: abnormal changes detected by laboratory tests at days 1, 4, 7, and 28 after each vaccine dose. Secondary immunogenicity outcome – humoral immune responses: titres of neutralising antibodies to live SARS-CoV-2, neutralising antibodies to pseudovirus, and RBD-specific IgG at baseline and 28 days after first vaccination and at days 7, 15, and 28 after second vaccination. Exploratory outcome: SARS-CoV-2-specific T-cell responses at 7 days after the first vaccination and at days 7 and 15 after the second vaccination. **Results** > 120 eligible participants were randomly assigned to receive five-dose levels of ARCoV or a placebo (20 per group) – 30 Oct-02Dec 2020. All participants received the first vaccination and 118 received the second dose. > No serious adverse events were reported within 56 days after vaccination and the majority of adverse events were mild or moderate. > Fever was the most common systemic adverse reaction (one [5%] of 20 in the 5 μg group, 13 [65%] of 20 in the 10 μg group, 17 [85%] of 20 in the 15 μg group, 19 [95%] of 20 in the 20 μg group, 16 [100%] of 16 in the 25 μg group; p<0·0001). > The incidence of grade 3 systemic adverse events were none (0%) of 20 in the 5 μg group, three (15%) of 20 in the 10 μg group, six (30%) of 20 in the 15 μg group, seven (35%) of 20 in the 20 μg group, five (31%) of 16 in the 25 μg group, and none (0%) of 20 in the placebo group (p=0·0013). > The majority of fever resolved in the first 2 days after vaccination for all groups. The incidence of solicited systemic adverse events was similar after administration of ARCoV as a first or second vaccination. > Humoral immune responses including anti-RBD IgG and neutralising antibodies increased significantly 7 days after the second dose and peaked between 14 and 28 days thereafter. > Specific T-cell response peaked between 7 and 14 days after full vaccination. 15 μg induced the highest titre of neutralising antibodies, which was about twofold more than the antibody titre of convalescent patients with COVID-19. **ARCoV was safe and well tolerated at all five doses. The acceptable safety profile, together with the induction of strong humoral and cellular immune responses, support further clinical testing of ARCoV at a large scale.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 21JAN2022	**Association Between 3 Doses of mRNA COVID-19 Vaccine and Symptomatic Infection Caused by the SARS-CoV-2 Omicron and Delta Variants**	Accorsi E. K., *et al.* USA gotopaper	Vaccines - Immunsation	**Aim**: to estimate the association between receipt of 3 doses of Pfizer-BioNTech BNT162b2 or Moderna mRNA-1273 and symptomatic SARS-CoV-2 infection, stratified by variant (Omicron and Delta). **Methods**: A test-negative case-control analysis among adults 18 years or older with COVID-like illness tested December 10, 2021, through January 1, 2022, by a national pharmacy-based testing program (4666 COVID-19 testing sites across 49 US states). 23 391 cases (13 098 Omicron; 10 293 Delta) and 46 764 controls were included (mean age, 40.3 years; 42 050 [60.1%] women). **Findings**: > Prior receipt of 3 mRNA vaccine doses was reported for 18.6% (n = 2441) of Omicron cases, 6.6% (n = 679) of Delta cases, and 39.7% (n = 18 587) of controls. > Prior receipt of 2 mRNA vaccine doses was reported for 55.3% (n = 7245), 44.4% (n = 4570), and 41.6% (n = 19 456), respectively; and being unvaccinated was reported for 26.0% (n = 3412), 49.0% (n = 5044), and 18.6% (n = 8721), respectively. > The adjusted odds ratio for 3 doses vs unvaccinated was 0.33 for Omicron and 0.065 for Delta; for 3 vaccine doses vs 2 doses the adjusted odds ratio was 0.34 for Omicron and 0.16 for Delta. > Median cycle threshold values were significantly higher in cases with 3 doses vs 2 doses for both Omicron and Delta (Omicron N gene: 19.35 vs 18.52; Omicron ORF1ab gene: 19.25 vs 18.40; Delta N gene: 19.07 vs 17.52; Delta ORF1ab gene: 18.70 vs 17.28; Delta S gene: 23.62 vs 20.24). **These findings suggest that receipt of 3 doses of mRNA vaccine, relative to being unvaccinated and to receipt of 2 doses, was associated with protection against both the Omicron and Delta variants, although the higher odds ratios for Omicron suggest less protection for Omicron than for Delta.**
Lancet 21JAN2022	**Heterologous versus homologous COVID-19 booster vaccination in previous recipients of two doses of CoronaVac COVID-19 vaccine in Brazil (RHH-001): a phase 4, non-inferiority, single blind, randomised study**	Costa Clemens S.A., *et al.* International gotopaper	Vaccines	**Aim**: to assess whether a third dose of the homologous or a different vaccine could boost immune responses. **Methods** > RHH-001 is a phase 4, participant masked, two centre, safety and immunogenicity study of Brazilian adults (≥18 yo) in São Paulo or Salvador who had received two doses of CoronaVac 6 months earlier. > The third heterologous dose was of either Ad26.COV2-S (Janssen), BNT162b2 (Pfizer–BioNTech), or ChAdOx1 nCoV-19 (AZD1222, AstraZeneca), compared with a third homologous dose of CoronaVac. **Findings** > Between Aug 16, and Sept 1, 2021, 1240 participants were randomly assigned to one of the four groups, of whom 1239 were vaccinated and 1205 were eligible for inclusion in the primary analysis > Antibody concentrations were low before administration of a booster dose with detectable neutralising antibodies of 20·4% (95% CI 12·8–30·1) in adults aged 18–60 years and 8·9% (4·2–16·2) in adults 61 years or older. > All heterologous regimens had anti-spike IgG responses at day 28 that were superior to homologous booster responses: geometric mean ratios (heterologous vs homologous) were 6·7 (95% CI 5·8–7·7) for Ad26.COV2-S, 13·4 (11·6–15·3) for BNT162b2, and 7·0 (6·1–8·1) for ChAdOx1 nCoV-19 > At day 28, all groups except for the homologous boost in the older adults reached 100% seropositivity: geometric mean ratios (heterologous vs homologous) were 8·7 (95% CI 5·9–12·9) for Ad26.COV2-S vaccine, 21·5 (14·5–31·9) for BNT162b2, and 10·6 (7·2–15·6) for ChAdOx1 nCoV-19. Live virus neutralising antibodies were also boosted against delta (B.1.617.2) and omicron variants (B.1.1.529) > There were 4 serious adverse events, 3 considered possibly related to the vaccine received: one in the BNT162b2 group and two in the Ad26.COV2-S group. Antibody concentrations were low at 6 months after previous immunisation with two doses of CoronaVac. However, **all four vaccines administered as a third dose induced a significant increase in binding and neutralising antibodies. Heterologous boosting resulted in more robust immune responses than homologous.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 20JAN2022	**Efficacy of the adjuvanted subunit protein COVID-19 vaccine, SCB-2019: a phase 2 and 3 multicentre, double-blind, randomised, placebo-controlled trial**	Bravo L., *et al.* International gotopaper	Vaccines	**Aim**: to assess the safety and efficacy of the COVID-19 vaccine SCB-2019 (Clover Biopharmaceuticals) - Ongoing phase 2 and 3 trial in adults ≥18 years who were in good health or with a stable chronic health condition, randomly assigned 1:1 to receive two 0,5 mL intramuscular doses of SCB-2019 (30 µg, adjuvanted with 1,50 mg CpG-1018 and 0,75 mg alum) or placebo (0·9% sodium chloride for injection supplied in 10 mL ampoules) 21 days apart. Primary endpoints: vaccine efficacy, safety and solicited local and systemic adverse events in the phase 2 subset. **Results** > 30 174 participants were enrolled from March 24, 2021, until the cutoff date of Aug 10, 2021, of whom > 30 128 subjects receiving their first assigned vaccine (n=15 064) or a placebo injection (n=15 064) – March 24-1ug 10 2021. The per-protocol population consisted of 12 355 baseline SARS-CoV-2-naive participants (6251 vaccinees and 6104 placebo recipients). Most exclusions (13 389 [44·4%]) were because of seropositivity at baseline. > There were 207 confirmed per-protocol cases of COVID-19 at 14 days after the second dose, 52 vaccinees versus 155 placebo recipients, and an overall vaccine efficacy against any severity COVID-19 of 67,2% (95,72% CI 54,3–76,8), 83,7% (97,86% CI 55,9–95,4) against moderate-to-severe COVID-19, and 100% (97,86% CI 25,3–100,0) against severe COVID-19. > All COVID-19 cases were due to virus variants; vaccine efficacy against any severity COVID-19 due to the three predominant variants was 78,7% (95% CI 57,3–90,4) for delta, 91,8% (44,9–99,8) for gamma, and 58,6% (13,3–81,5) for mu. > No safety issues emerged in the follow-up period for the efficacy analysis (median of 82 days [IQR 63–103]). The vaccine elicited higher rates of mainly mild-to-moderate injection site pain than the placebo after the first (35,7% [287 of 803] vs 10,3% [81 of 786]) and second (26,9% [189 of 702] vs 7,4% [52 of 699]) doses, but the rates of other solicited local and systemic adverse events were similar between the groups. **Two doses of SCB-2019 vaccine plus CpG and alum provides notable protection against the entire severity spectrum of COVID-19 caused by SAR-CoV-2 viruses circulating at the time of study.**

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Cell 20JAN2022	**SARS-CoV-2 breakthrough infections elicit potent, broad and durable neutralizing antibody responses**	Walls A. C., *et al.* USA gotopaper	Immunology	**Findings** > Breakthrough infections induce potent neutralizing antibody responses > Number of exposures (infection or vaccination) correlate with potency and breadth > Three-dose vaccination improves neutralization of the SARS-CoV-2 Omicron variant > SARS-CoV-2 infection or vaccination elicit moderate neutralization of SARS-CoV **Here, we demonstrate that breakthrough infections induce serum binding and neutralizing antibody responses that are markedly more potent, durable and resilient to spike mutations observed in variants than those in subjects who received only two doses of vaccine. However, we show that breakthrough cases, subjects who were vaccinated after infection and individuals vaccinated three times have serum neutralizing activity of comparable magnitude and breadth, indicating that increased number of exposures to SARS-CoV-2 antigen(s) enhance the quality of antibody responses. Neutralization of SARS-CoV was moderate, however, underscoring the importance of developing vaccines eliciting broad sarbecovirus immunity for pandemic preparedness.**
Nature Med. 20JAN2022	**Neutralizing antibodies against the SARS-CoV-2 Omicron variant following homologous and heterologous CoronaVac or BNT162b2 vaccination**	Cheng S M.S., *et al.* China gotopaper	Vaccines - Immunisation	**Findings** > We have previously established that a 50% plaque reduction neutralization (PRNT50) antibody titre ≥25.6 in our live virus assay corresponded to the threshold for 50% protection from infection against wild-type (WT) SARS-CoV-2. > Here we show markedly reduced serum antibody titres against the Omicron variant (geometric mean titre (GMT) <10) as compared to wild-type virus 3-5 weeks after two doses of BNT162b2 (GMT 218.8) or CoronaVac vaccines (GMT 32.5). > A BNT162b2 booster dose elicited Omicron PRNT50 titres ≥25.6 in 88% of individuals (22 of 25) who previously received 2 doses of BNT162b2 and 80% of individuals (24 of 30) who previously received CoronaVac. > However, few (3%) previously infected individuals (1 of 30) or those vaccinated with three doses of CoronaVac (1 of 30) met this threshold. **Our findings suggest that countries primarily using CoronaVac vaccines should consider mRNA vaccine boosters in response to the spread of Omicron. Studies evaluating the effectiveness of different vaccines against the Omicron variant are urgently needed.**
Nature Med. 20JAN2022	**Neutralizing antibodies against the SARS-CoV-2 Delta and Omicron variants following heterologous CoronaVac plus BNT162b2 booster vaccination**	Pérez-Then E., *et al.* Dominican Republic/USA gotopaper	Vaccines - Immunisation	**Aim**: to evaluate the effects of a heterologous BNT162b2 mRNA vaccine booster on the humoral immunity of participants that had received a two-dose regimen of CoronaVac **Findings** > We found that heterologous CoronaVac prime followed by BNT162b2 booster regimen induces elevated virus-specific antibody levels and potent neutralization activity against the ancestral virus and Delta variant, resembling the titers obtained after two-doses of mRNA vaccines. > While neutralization of Omicron was undetectable in participants that had received a two-dose regimen of CoronaVac vaccine, BNT162b2 booster resulted in a 1.4-fold increase in neutralization activity against Omicron, compared to two-dose mRNA vaccine > Despite this increase, neutralizing antibody titers were reduced by 7.1-fold and 3.6-fold for Omicron compared to ancestral and Delta variant, respectively. **Our findings have immediate implications for multiples countries that previously used a CoronaVac regimen and reinforce the notion that the Omicron variant is associated with immune escape from vaccines or infection-induced immunity, highlighting the global need for vaccine boosters to combat the impact of emerging variants.**

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JAMA Pediatrics 19JAN2022	**Assessment of Clinical Outcomes Among Children and Adolescents Hospitalized With COVID-19 in 6 Sub-Saharan African Countries**	Nachega J.B., *et al.* International gotopaper	Clinic	**Aim**: to assess the clinical outcomes and factors associated with outcomes among children and adolescents hospitalized with COVID-19 in 6 countries in sub-Saharan Africa. **Methods** > Retrospective record review of data from 25 hospitals in the Democratic Republic of the Congo, Ghana, Kenya, Nigeria, South Africa, and Uganda (March 1 to December 31, 2020), and included 469 hospitalized patients aged 0 to 19 years with SARS-CoV-2 infection. **Findings** > Morbidity and mortality were substantially higher than reported among those in non-African settings and were independently associated with age younger than 1 year and select noncommunicable disease comorbidities. > Among 469 hospitalized children and adolescents, the median age was 5.9 years (IQR, 1.6-11.1 years); 245 patients (52.4%) were male, and 115 (24.5%) had comorbidities. A total of 39 patients (8.3%) were from central Africa, 172 (36.7%) from eastern Africa, 208 (44.3%) from southern Africa, and 50 (10.7%) from western Africa. > Thirty-nine patients (8.3%) died, including 22 of 69 patients (31.9%) who required intensive care unit admission and 4 of 18 patients (22.2%) with suspected or confirmed multisystem inflammatory syndrome in children. > Age younger than 1 year (adjusted subdistribution hazard ratio [asHR], 0.48; 95% CI, 0.27-0.87), the presence of 1 comorbidity (asHR, 0.54; 95% CI, 0.40-0.72), and the presence of 2 or more comorbidities (asHR, 0.26; 95% CI, 0.18-0.38) were associated with reduced rates of hospital discharge. **In this cohort study of children and adolescents hospitalized with COVID-19 in sub-Saharan Africa, high rates of morbidity and mortality were observed among infants and patients with noncommunicable disease comorbidities, suggesting that COVID-19 vaccination and therapeutic interventions are needed for young populations in this region.**
Lancet 19JANV2022	**Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study**	Wolter N., *et al.* South Africa gotopaper	Clinic	**Aim**: to assess the clinical severity of infections with the omicron variant using S gene target failure (SGTF) on the PCR test as a proxy. **Methods** > Data linkages for national, South African COVID-19 case data, SARS-CoV-2 laboratory test data, SARS-CoV-2 genome data, and COVID-19 hospital admissions data. **Findings** > From Oct 1 (week 39), 2021, to Dec 6 (week 49), 2021, 161 328 cases of COVID-19 were reported in South Africa. 38 282 people were diagnosed via TaqPath PCR tests and 29 721 SGTF infections and 1412 non-SGTF infections were identified. > The proportion of SGTF infections increased from two (3·2%) of 63 in week 39 to 21 978 (97·9%) of 22 455 in week 48. After controlling for factors associated with hospitalisation, individuals with SGTF infections had significantly lower odds of admission than did those with non-SGTF infections (256 [2·4%] of 10 547 vs 121 [12·8%] of 948; adjusted odds ratio [aOR] 0·2, 95% CI 0·1–0·3). > After controlling for factors associated with disease severity, the odds of severe disease were similar between hospitalised individuals with SGTF versus non-SGTF infections (42 [21%] of 204 vs 45 [40%] of 113; aOR 0·7, 95% CI 0·3–1·4). > Compared with individuals with earlier delta variant infections, SGTF-infected individuals had a significantly lower odds of severe disease (496 [62·5%] of 793 vs 57 [23·4%] of 244; aOR 0·3, 95% CI 0·2–0·5), after controlling for factors associated with disease severity. **Odds of hospitalisation among individuals with SGTF versus non-SGTF infections diagnosed during the same time period was significantly reduced . SGTF-infected individuals had a significantly reduced odds of severe disease compared with individuals infected earlier with the delta variant. Some of this reduced severity is probably a result of previous immunity.**

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NEJM 19JAN2022	**Effectiveness of mRNA-1273 and BNT162b2 Vaccines in Qatar**	Abu-Raddad L.J., *et al.* Qatar gotopaper	Vaccines - Immunsation	**Aim**: to compare the protection afforded by the mRNA-1273 vaccine with that of the BNT162b2 vaccine in Qatar. - Two matched retrospective cohort studies to assess the incidence of documented SARS-CoV-2 infection after the first and second doses of the mRNA-1273 and BNT162b2 vaccines. - Same population of persons who had received the mRNA-1273 or BNT162b2 vaccines between December 21, 2020, and October 20, 2021. **Results** > 192,123 persons who had received two doses of mRNA-1273 matched with the same number of persons who had received two doses of BNT162b2. > Among the mRNA-1273–vaccinated persons, 878 breakthrough infections were recorded after the second dose at a median follow-up of 89 days. Of these, 3 progressed to severe Covid-19 (acute-care hospitalization), but none progressed to critical disease (hospitalization in an intensive care unit) or death. > Among BNT162b2-vaccinated persons, 1262 breakthrough infections were recorded after the second dose at a median follow-up of 86 days. Of these, 7 progressed to severe Covid-19, none to critical disease, and 1 to death. > In both vaccinated cohorts, breakthrough infections tended to occur among persons with a longer interval since the time of vaccination. The divergence between the two vaccine cohorts in the incidence of documented infection started during the third week after the first dose. > The incidences of SARS-CoV-2 infection and severe Covid-19 were lower among mRNA-1273–vaccinated persons than among BNT162b2-vaccinated persons after only one dose. > At 6 months of follow-up after the second dose, the estimated cumulative incidence of breakthrough infection was 0.59% (95% CI, 0.55 to 0.64) among persons who received the mRNA-1273 vaccine and 0.84% (95% CI, 0.79 to 0.89) among those who received the BNT162b2 vaccine. > The estimated overall adjusted hazard ratio for infection after the second dose of mRNA-1273 vaccine, as compared with the second dose of BNT162b2 vaccine, was 0.69 (95% CI, 0.63 to 0.75). > The estimated overall adjusted hazard ratio for severe, critical, or fatal Covid-19 after the second dose was 0.37 (95% CI, 0.10 to 1.41). **Vaccination with mRNA-1273 was associated with a lower incidence of SARS-CoV-2 breakthrough infection than vaccination with BNT162b2; this finding is consistent with the differences in neutralizing antibody titers. However, both vaccines elicited strong protection against Covid-19–related hospitalization and death.**
NEJM 19JAN2022	**Immunogenicity and Reactogenicity of Vaccine Boosters after Ad26.COV2.S Priming**	Sablerolles R.S.G., *et al.* Netherlands gotopaper	Vaccines	**Aim**: to evaluate the immunogenicity and reactogenicity of a homologous or heterologous booster at day 28 in persons who have received an Ad26.COV2.S priming dose. Primary end point: level of S-specific binding antibodies Secondary end points: levels of neutralizing antibodies, S-specific T-cell responses, and reactogenicity. **Results** > Homologous or heterologous booster vaccination in 434 participants resulted in higher levels of S-specific binding antibodies, neutralizing antibodies, and T-cell responses than a single Ad26.COV2.S vaccination. > The increase in binding antibodies was significantly larger with heterologous regimens that included mRNA-based vaccines than with the homologous booster. > The mRNA-1273 booster was most immunogenic and was associated with higher reactogenicity than the BNT162b2 and Ad26.COV2.S boosters. Local and systemic reactions were generally mild to moderate in the first 2 days after booster administration. **The Ad26.COV2.S and mRNA boosters had an acceptable safety profile and were immunogenic in health care workers who had received a priming dose of Ad26.COV2.S vaccine. The strongest responses occurred after boosting with mRNA-based vaccines. Boosting with any available vaccine was better than not boosting.**

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Science Transl Med. 18JAN2022	**Early non-neutralizing, afucosylated antibody responses are associated with COVID-19 severity**	Chakraborty S., *et al.* USA gotopaper	Clinic	**Aim :** To study the effect of afucosylated antibody signaling in the lungs. **Methods:** A model system in which human immune complexes (ICs) of defined composition are intratracheally administered to mice that express human FcγRs was developed. Molecular and cellular changes that were triggered in the lung by distinct antibody signaling pathways were then assessed by characterization of bronchoalveolar lavage (BAL) fluid collected after IC administration. **Findings** > human IgG-Fc gamma receptor (FcγR) interactions could regulate inflammation in the lung. > Afucosylated IgG immune complexes isolated from COVID-19 patients induced inflammatory cytokine production and robust infiltration of the lung by immune cells. > By contrast, vaccine-elicited IgG did not promote an inflammatory lung response. **IgG-FcγR interactions are able to regulate inflammation in the lung and may define distinct lung activities associated with the IgG that are associated with severe COVID-19 and protection against infection with SARS-CoV-2.**
Science 18JAN2022	**Neutralization of SARS-CoV-2 Omicron by BNT162b2 mRNA vaccine–elicited human sera**	Muik A., *et al.* Germany / USA gotopaper	Variants	**Aim:** to understand the effect of the new mutations in Omicron on recognition by neutralizing antibodies in vaccinated individuals. **Methods:** Wuhan, Beta, Delta, or Omicron pseudoviruses were tested with sera of 51 participants that received two or three doses of the mRNA-based COVID-19 vaccine BNT162b2. **Findings** > Following two doses, sera had >22-fold reduced neutralizing titers against Omicron compared to Wuhan pseudovirus. > One month after the third vaccine dose, Omicron-neutralizing titers were increased 23-fold compared to two doses, with titers similar to Wuhan-neutralizing titers after two doses. > The requirement of a third vaccine dose to effectively neutralize Omicron was confirmed using live SARS-CoV-2 in a subset of participants. **These data suggest that three doses of the mRNA vaccine BNT162b2 may protect against Omicron-mediated COVID-19.**
Nature Med. 14JAN2022	**Ancestral SARS-CoV-2-specific T cells cross-recognize the Omicron variant**	Gao Y., *et al.* Sweden gotopaper	Variants	**Findings** > We report here that SARS-CoV-2 spike-specific CD4+ and CD8+ T cells induced by prior infection or BNT162b2 vaccination provide extensive immune coverage against B.1.1.529. > The median relative frequencies of SARS-CoV-2 spike-specific CD4+ T cells that cross-recognized B.1.1.529 in previously infected or BNT162b2-vaccinated individuals were 84% and 91%, respectively, and the corresponding median relative frequencies for SARS-CoV-2 spike-specific CD8+ T cells were 70% and 92%, respectively > Pairwise comparisons across groups further revealed that SARS-CoV-2 spike-reactive CD4+ and CD8+ T cells were functionally and phenotypically similar in response to the ancestral strain or B.1.1.529 **Collectively, our data indicate that established SARS-CoV-2 spike-specific CD4+ and CD8+ T cell responses, especially after BNT162b2 vaccination, remain largely intact against B.1.1.529.**

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JAMA 14JAN2022	**Effect of Subcutaneous Casirivimab and Imdevimab Antibody Combination vs Placebo on Development of Symptomatic COVID-19 in Early Asymptomatic SARS-CoV-2 Infection**	O'Brien M.P., *et al.* USA gotopaper	Therapeutics	**Aim**: to evaluate the effect of combination subcutaneous casirivimab and imdevimab on progression from early asymptomatic SARS-CoV-2 infection to symptomatic COVID-19. - Phase 3 trial of close household contacts of a SARS-CoV-2–infected index case (enrolment July 2020–Jan 2021; follow-up until March 2021). Asymptomatic individuals (aged ≥12 years) were eligible if identified within 96 hours of index case positive test collection. - Interventions: 1 dose of subcutaneous casirivimab and imdevimab, 1200 mg (600 mg of each; n = 158), or placebo (n = 156). Primary end point: proportion of seronegative participants who developed symptomatic COVID-19 during the 28-day efficacy assessment period. **Results** > 204 participants asymptomatic and seronegative at baseline included in the primary efficacy analysis. > Subcutaneous casirivimab and imdevimab, 1200 mg, significantly prevented progression to symptomatic disease (29/100 [29.0%] vs 44/104 [42.3%] with placebo; odds ratio, 0.54 [95% CI, 0.30-0.97]; P = .04; absolute risk difference, −13.3% [95% CI, −26.3% to −0.3%]). > Casirivimab and imdevimab reduced the number of symptomatic weeks per 1000 participants (895.7 weeks vs 1637.4 weeks with placebo; P = .03), an approximately 5.6-day reduction in symptom duration per symptomatic participant. > Treatment with casirivimab and imdevimab also reduced the number of high viral load weeks per 1000 participants (489.8 weeks vs 811.9 weeks with placebo; P = .001). > The proportion of participants receiving casirivimab and imdevimab who had 1 or more treatment-emergent adverse event was 33.5% vs 48.1% for placebo, including events related (25.8% vs 39.7%) or not related (11.0% vs 16.0%) to COVID-19. **Among asymptomatic SARS-CoV-2–positive individuals living with an infected household contact, treatment with subcutaneous casirivimab and imdevimab antibody combination vs placebo significantly reduced the incidence of symptomatic COVID-19 at 28d.**
Nature Immunol. 13JAN2022	**Immunological dysfunction persists for 8 months following initial mild-to-moderate SARS-CoV-2 infection**	Phetsouphanh C., *et al.* Australia gotopaper	Immunology	**Aim**: to study individuals with Long COVID (LC) compared to age- and gender-matched recovered individuals without LC, unexposed donors and individuals infected with other coronaviruses. **Findings** > Patients with LC had highly activated innate immune cells, lacked naive T and B cells and showed elevated expression of type I IFN (IFN-β) and type III IFN (IFN-λ1) that remained persistently high at 8 months after infection > Using a log-linear classification model, we defined an optimal set of analytes that had the strongest association with LC among the 28 analytes measured > Combinations of the inflammatory mediators IFN-β, PTX3, IFN-γ, IFN-λ2/3 and IL-6 associated with LC with 78.5–81.6% accuracy. **This work defines immunological parameters associated with LC and suggests future opportunities for prevention and treatment.**
Science Transl Med. 13JAN2022	**Antibodies elicited by SARS-CoV-2 infection or mRNA vaccines have reduced neutralizing activity against Beta and Omicron pseudoviruses**	Sievers B.L., *et al.* USA gotopaper	Variants	**Aim**: to evaluate the magnitude and breadth of the neutralizing antibody response over time in individuals after infection and in mRNA-vaccinated individuals, using pseudoparticles expressing the spike protein of several SARS-CoV-2 variants. **Results** > Boosting increases the magnitude of the antibody response to wildtype (D614), Beta, Delta, and Omicron variants; however, the Omicron variant was the most resistant to neutralization. > We further observed that vaccinated healthy adults had robust and broad antibody responses whereas responses may have been reduced in vaccinated pregnant women, underscoring the importance of learning how to maximize mRNA vaccine responses in pregnant populations. **Findings show substantial heterogeneity in the magnitude and breadth of responses after infection and mRNA vaccination and may support addition of conserved viral antigens to existing vaccines.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Med. 13JAN2021	**SARS-CoV-2 infection and COVID-19 vaccination rates in pregnant women in Scotland**	Stock S.J., *et al.* UK gotopaper	Public Health / Epidemiology	**Aim**: to obtain data on population-level data on COVID-19 vaccine uptake in pregnancy and SARS-CoV-2 infection outcomes. **Results** > Between 8 Dec 2020 and 31 Oct 2021 in Scotland, 25,917 COVID-19 vaccinations were given to 18,457 pregnant women. > Vaccine coverage was substantially lower in pregnant women than in the general female population of 18–44 years; 32.3% of women giving birth in October 2021 had two doses of vaccine compared to 77.4% in all women. > The extended perinatal mortality rate for women who gave birth within 28 d of a COVID-19 diagnosis was 22.6 per 1,000 births (95% CI 12.9–38.5; pandemic background rate 5.6 per 1,000 births; 452 out of 80,456; 95% CI 5.1–6.2). > Overall, 77.4% (3,833 out of 4,950; 95% CI 76.2–78.6) of SARS-CoV-2 infections, 90.9% (748 out of 823; 95% CI 88.7–92.7) of SARS-CoV-2 associated with hospital admission and 98% (102 out of 104; 95% CI 92.5–99.7) of SARS-CoV-2 associated with critical care admission, as well as all baby deaths, occurred in pregnant women who were unvaccinated at the time of COVID-19 diagnosis. **Addressing low vaccine uptake rates in pregnant women is imperative to protect the health of women and babies in the ongoing pandemic.**
Clin Infect Dis. 13JAN2022	**Necessity of COVID-19 Vaccination in Persons Who Have Already Had COVID-19**	Shrestha N. K., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim :** to evaluate the necessity of COVID-19 vaccination in persons with prior COVID-19. **Methods:** Employees of Cleveland Clinic working in Ohio were included. Anyone who tested positive for COVID-19 at least once before the study start date was considered previously infected. One was considered vaccinated 14 days after receiving the second dose of a COVID-19 mRNA vaccine. The cumulative incidence of COVID-19, symptomatic COVID-19, and hospitalizations for COVID-19, were examined over the next year. **Findings** > Among 52238 employees, 4718 (9%) were previously infected, and 36922 (71%) were vaccinated by the study's end. > Cumulative incidence of COVID-19 was substantially higher throughout for those previously uninfected who remained unvaccinated than for all other groups, lower for the vaccinated than unvaccinated, and lower for those previously infected than those not. > Incidence of COVID-19 increased dramatically in all groups after the Omicron variant emerged. > In multivariable Cox proportional hazards regression, both prior COVID-19 and vaccination were independently associated with significantly lower risk of COVID-19. > Among previously infected subjects, a lower risk of COVID-19 overall was not demonstrated, but vaccination was associated with a significantly lower risk of symptomatic COVID-19 in both the pre-Omicron (HR 0.60, 95% CI 0.40–0.90) and Omicron (HR 0.36, 95% CI 0.23–0.57) phases. **Both previous infection and vaccination provide substantial protection against COVID-19. Vaccination of previously infected individuals does not provide additional protection against COVID-19 for several months, but after that provides significant protection at least against symptomatic COVID-19.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 12JAN2022	**SARS-CoV-2 Omicron Variant Neutralization in Serum from Vaccinated and Convalescent Persons**	Rössler A., *et al.* Austria gotopaper	Variants	**Aim**: to study whether serum samples obtained from persons who had been vaccinated against SARS-CoV-2 or who had recovered from SARS-CoV-2 infection (i.e., convalescent) would be able to neutralize the omicron variant. Serum samples: - 10 participants infected with alpha variant, 8 with beta, and 7 with delta. - 10 participants had received two doses of the mRNA-1273 vaccine, 10 the ChAdOx1-S vaccine, and 20 the BNT162b2 vaccine; 20 participants received heterologous ChAdOx1-S/BNT162b2. - 5 participants had been infected and subsequently received one or two doses of BNT162b2, and 5 had been vaccinated with two doses of mRNA-1273, ChAdOx1-S, or BNT162b2 and subsequently had breakthrough infection. **Results** > Serum samples from vaccinated persons neutralized the omicron variant to a much lesser extent than any other variant analyzed (alpha, beta, or delta). > Some cross-neutralization of the omicron variant in samples obtained from persons who had received either homologous BNT162b2 vaccination or heterologous ChAdOx1-S–BNT162b2 vaccination was observed, but not in samples from persons who had received homologous ChAdOx1-S vaccination. > We did not find neutralizing antibodies against the omicron variant in serum samples obtained 4 to 6 months after receipt of the second dose of the mRNA-1273 vaccine (however, in this group, the interval between receipt of the second dose and sampling was longer than for the other groups). > Serum samples that were obtained from convalescent participants largely did not neutralize the omicron variant, although cross-neutralization was observed against other variants. > 9 of the 10 serum samples obtained from convalescent–vaccinated or vaccinated–convalescent participants were able to neutralize the omicron variant, although to a lesser degree than the delta variant. **The omicron variant shows immune escape. Although receipt of a third dose of BNT162b2 may increase the level of cross-neutralizing antibodies, the rapid development of new, variant-adapted vaccines is warranted.**
Ann Intern Med. 11JAN2022	**Antibody Response to a Fourth Messenger RNA COVID-19 Vaccine Dose in Kidney Transplant Recipients: A Case Series**	Caillard S., *et al.* France gotopaper	Vaccines - Immunisation	**Aim**: to investigate whether a fourth dose of an mRNA-based anti–SARS-CoV-2 vaccine would increase antispike IgG titers in kidney transplant recipients who showed a weak serologic response after 3 doses. **Methods** > A fourth dose of mRNA vaccine (BNT162b2 [Pfizer], n = 34; mRNA-1273 [Moderna], n = 58) was given to 92 kidney transplant recipients from 3 independent French university hospitals (Strasbourg, Lyon, and Nantes) who had antispike IgG titers less than 143 BAU/mL 1 month after a third dose. **Findings** > There were no safety concerns with the fourth vaccine dose. > After a median of 29 days, median antispike IgG levels increased from 16.4 BAU/mL (interquartile range, 5.9 to 62.3 BAU/mL) to 145 BAU/mL (interquartile range, 27.6 to 243 BAU/mL) (Figure) and 50% of patients reached the threshold of 143 BAU/mL. Patients who reached this threshold had a longer interval between their transplant and fourth vaccine dose and were less frequently treated with steroids. > The percentage of patients who had antispike IgG titers above 143 BAU/mL after the fourth dose was 48% for the BNT162b2 vaccine and 52% for the mRNA-1273 vaccine, and patients who received the mRNA-1273 vaccine had higher IgG titers (median, 150 vs. 122 BAU/mL). **Our study indicates that a fourth dose of an mRNA-based vaccine produces a satisfactory antibody response in some kidney transplant recipients who did not respond adequately after 3 previous doses, and it supports the use of a fourth vaccine dose for these patients.**

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NEJM 12JAN2022	**Effectiveness of BNT162b2 Vaccine against Critical Covid-19 in Adolescents**	Olson S.M., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: to assess the real-world effectiveness of the BNT162b2 vaccine in adolescents between 12 and 18 years of age against the delta variant. - Case patients (hospitalised for Covid-19) were compared to two hospital-based control groups: patients who had Covid-19–like symptoms but negative for SARS-CoV-2 (test-negative) and patients who did not have Covid-19–like symptoms (syndrome-negative). **Results** > A total of 445 case patients and 777 controls were enrolled. Overall, 17 case patients (4%) and 282 controls (36%) had been fully vaccinated. > Of the case patients, 180 (40%) were admitted to the ICU, and 127 (29%) required life support; only 2 patients in the ICU had been fully vaccinated. > The overall effectiveness of the BNT162b2 vaccine against hospitalization for Covid-19 was 94% (95% CI, 90 to 96); the effectiveness was 95% (95% CI, 91 to 97) among test-negative controls and 94% (95% CI, 89 to 96) among syndrome-negative controls. > The effectiveness was 98% against ICU admission and 98% against Covid-19 resulting in the receipt of life support. > All 7 deaths occurred in patients who were unvaccinated. **Among hospitalized adolescent patients, two doses of the BNT162b2 vaccine were highly effective against Covid-19–related hospitalization and ICU admission or the receipt of life support.**
NEJM 12JAN2022	**Duration of Protection against Mild and Severe Disease by Covid-19 Vaccines**	Andrews N., *et al.* UK gotopaper	Vaccines - Immunisation	**Aim**: to estimate ChAdOx1-S (ChAdOx1 nCoV-19) and BNT162b2 vaccine effectiveness against symptomatic Covid-19 and related hospitalization and death in England. - Effectiveness was assessed according to participant age and status with regard to coexisting conditions and over time since receipt of the second vaccine dose to investigate waning of effectiveness separately for the B.1.1.7 (alpha) and B.1.617.2 (delta) variants. **Results** > Vaccine effectiveness against symptomatic Covid-19 with the delta variant peaked in the early weeks after receipt of the second dose and then decreased by 20 weeks to 44.3% (95% CI, 43.2 to 45.4) with the ChAdOx1-S vaccine and to 66.3% (95% CI, 65.7 to 66.9) with the BNT162b2 vaccine. > Waning of vaccine effectiveness was greater in persons 65 years of age or older than in those 40 to 64 years of age. > At 20 weeks or more after vaccination, vaccine effectiveness decreased less against both hospitalization, to 80.0% (95% CI, 76.8 to 82.7) with the ChAdOx1-S vaccine and 91.7% (95% CI, 90.2 to 93.0) with the BNT162b2 vaccine, and death, to 84.8% (95% CI, 76.2 to 90.3) and 91.9% (95% CI, 88.5 to 94.3), respectively. > Greater waning in vaccine effectiveness against hospitalization was observed in persons 65 years of age or older in a clinically extremely vulnerable group and in persons 40 to 64 years of age with underlying medical conditions than in healthy adults. **We observed limited waning in vaccine effectiveness against Covid-19–related hospitalization and death at 20 weeks or more after vaccination with two doses of the ChAdOx1-S or BNT162b2 vaccine. Waning was greater in older adults and in those in a clinical risk group.**

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NEJM 12JAN2022	**Effectiveness of Covid-19 Vaccines over a 9-Month Period in North Carolina**	Lin D.Y., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: to estimate the effectiveness of the BNT162b2 (Pfizer–BioNTech), mRNA-1273 (Moderna), and Ad26.COV2.S (Johnson & Johnson–Janssen) vaccines in reducing the current risks of Covid-19, hospitalization, and death, as a function of time elapsed since vaccination (Dec 2020-Sept 2021) **Results** > For the two-dose regimens of mRNA vaccines BNT162b2 (30 µg per dose) and mRNA-1273 (100 µg per dose), vaccine effectiveness against Covid-19 was 94.5% (95% CI, 94.1 to 94.9) and 95.9% (95% CI, 95.5 to 96.2), respectively, at 2 months after the first dose and decreased to 66.6% (95% CI, 65.2 to 67.8) and 80.3% (95% CI, 79.3 to 81.2), respectively, at 7 months. > Among early recipients of BNT162b2 and mRNA-1273, effectiveness decreased by approximately 15 and 10 percentage points, respectively, from mid-June to mid-July, when the delta variant became dominant. > For the one-dose regimen of Ad26.COV2.S (5×1010 viral particles), effectiveness against Covid-19 was 74.8% (95% CI, 72.5 to 76.9) at 1 month and decreased to 59.4% (95% CI, 57.2 to 61.5) at 5 months. > All three vaccines maintained better effectiveness in preventing hospitalization and death than in preventing infection over time, although the two mRNA vaccines provided higher levels of protection than Ad26.COV2.S. **All three Covid-19 vaccines had durable effectiveness in reducing the risks of hospitalization and death. Waning protection against infection over time was due to both declining immunity and the emergence of the delta variant.**
JAMA Netw Open 11JAN2022	**Outcomes of SARS-CoV-2–Positive Youths Tested in Emergency Departments**	Funk A.L., *et al.* International gotopaper	Clinics	**Aim**: to estimate the proportion of children with severe outcomes within 14 days of testing positive for SARS-CoV-2 in an emergency department (ED). - Youth <18 years SARS-CoV-2 positive, 14-day follow-up, March 2020-June 2021 **Results** > Among 3222 patients enrolled, 3221 (>99.9%) had index visit outcome data available, 2007 (62.3%) were from the United States, 1694 (52.6%) were male, and 484 (15.0%) had a self-reported chronic illness; the median (IQR) age was 3 (0-10) years. > After 14 days of follow-up, 735 children (22.8% [95% CI, 21.4%-24.3%]) were hospitalized, 107 (3.3% [95% CI, 2.7%-4.0%]) had severe outcomes, and 4 children (0.12% [95% CI, 0.03%-0.32%]) died. > Characteristics associated with severe outcomes included being aged 5 to 18 years (age 5 to <10 years vs <1 year: odds ratio [OR], 1.60 [95% CI, 1.09-2.34]; age 10 to <18 years vs <1 year: OR, 2.39 [95% CI 1.38-4.14]), having a self-reported chronic illness (OR, 2.34 [95% CI, 1.59-3.44]), prior episode of pneumonia (OR, 3.15 [95% CI, 1.83-5.42]), symptoms starting 4 to 7 days prior to seeking ED care (vs starting 0-3 days before seeking care: OR, 2.22 [95% CI, 1.29-3.82]), and country (eg, Canada vs US: OR, 0.11 [95% CI, 0.05-0.23]; Costa Rica vs US: OR, 1.76 [95% CI, 1.05-2.96]; Spain vs US: OR, 0.51 [95% CI, 0.27-0.98]). > Among a subgroup of 2510 participants discharged home from the ED after initial testing and who had complete follow-up, 50 (2.0%; 95% CI, 1.5%-2.6%) were eventually hospitalized and 12 (0.5%; 95% CI, 0.3%-0.8%) had severe outcomes. > Compared with hospitalized SARS-CoV-2–negative youths, the risk of severe outcomes was higher among hospitalized SARS-CoV-2–positive youths (risk difference, 3.9%; 95% CI, 1.1%-6.9%). **Approximately 3% of SARS-CoV-2–positive youths tested in EDs experienced severe outcomes within 2 weeks of their ED visit. Among children discharged home from the ED, the risk was much lower.**

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Nature Commun. 11JAN2022	**Rapid antigen testing as a reactive response to surges in nosocomial SARS-CoV-2 outbreak risk**	Smith D.R.M., *et al.* France gotopaper	Public health / Epidemiology	We simulate SARS-CoV-2 transmission in a long-term care hospital with varying COVID-19 containment measures in place (social distancing, face masks, vaccination) **Findings** > Across scenarios, nosocomial incidence is reduced by up to 40-47% (range of means) with routine symptomatic RT-PCR testing, 59-63% with the addition of a timely round of Ag-RDT screening, and 69-75% with well-timed two-round screening. > For the latter, a delay of 4-5 days between the two screening rounds is optimal for transmission prevention. > Screening efficacy varies depending on test sensitivity, test type, subpopulations targeted, and community incidence **Efficiency, however, varies primarily depending on underlying outbreak risk, with health-economic benefits scaling by orders of magnitude depending on the COVID-19 containment measures in place.**
Clin Microbiol Infect. 10JAN2022	**Efficacy of favipiravir in adults with mild COVID-19: a randomized, double-blind, multicenter, placebo-controlled trial clinical trial**	Bosaeed M., *et al.* Saudi Arabia gotopaper	Therapeutics	**Aim**: to evaluate whether favipiravir reduces the time to viral clearance as documented by negative SARS-CoV-2 RT-PCR in mild COVID-19 cases compared to placebo. **Methods** > In this randomized, double-blinded, multicenter, and placebo-controlled trial, adults with PCR confirmed mild COVID-19 were recruited in an outpatient setting at seven medical facilities across Saudi Arabia. > Participants were randomized in a 1:1 ratio to receive either favipiravir 1800 mg by mouth twice daily on day one followed by 800 mg twice daily (n=112) or a matching placebo (n=119), for a total of 5 to 7 days. **Findings** > 231 patients were randomized and began the study (median age, 37 [interquartile range: 32-44] years; 155 [67%] men), and 112 (48.5%) were assigned to the treatment group and 119 (51.5%) into the placebo group. > The data and safety monitoring board (DSMB) recommended stopping enrollment because of futility at the interim analysis. > The median time to viral clearance was 10 (IQR: 6-12) days in the favipiravir group and 8 (IQR: 6-12) days in the placebo group, with a hazard ratio of 0.87 for the favipiravir group (95% CI 0.571 to 1.326; p-value =0.51). > The median time to clinical recovery was 7 days (IQR: 4-11) in the favipiravir group and 7 days (IQR: 5-10) in the placebo group. There was no difference between the two groups on the secondary outcome of hospital admission. > There were no drug-related severe adverse events. **In this clinical trial, favipiravir therapy in mild COVID-19 patients did not reduce the time to viral clearance within 15 days of starting the treatment.**

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Nature Commun. 10JAN2022	**Dynamics of spike-and nucleocapsid specific immunity during long-term follow-up and vaccination of SARS-CoV-2 convalescents**	Koerber N., *et al.* Germany gotopaper	Immunology	**Aim** Characterization of the dynamics of anti-viral immunity during long-term follow-up and after BNT162b2 mRNA-vaccination in convalescents after asymptomatic or mild SARS-CoV-2 infection. **Findings** > Virus-specific and virus-neutralizing antibody titers rapidly declined in convalescents over 9 months after infection > Virus-specific cytokine-producing polyfunctional T cells persisted, among which IL-2-producing T cells correlated with virus-neutralizing antibody titers. > Among convalescents, 5% of individuals failed to mount long-lasting immunity after infection and showed a delayed response to vaccination compared to 1% of naïve vaccinees, but successfully responded to prime/boost vaccination. This lack of induction of long-lasting adaptive immunity might have resulted either from infection with too few viruses or contact with the poorly infectious virus, where innate immunity in the upper respiratory tract might have sufficed to achieve early control of infection but may have failed to induce lasting adaptive immunity. > 8% of convalescents showed a selective increase in virus-neutralizing antibody titers without accompanying increased frequencies of circulating SARS-CoV-2-specific T cells. > The same convalescents, responded to vaccination with simultaneous increase in antibody and T cell immunity revealing the strength of mRNA-vaccination to increase virus-specific immunity in convalescents. **Conclusions** These results advocate for the use of vaccination in individuals with prior mild SARS-CoV-2 infection to further enhance immune protection for the prevention of re-infection.
Nature Commun. 10JAN2022	**Robust and durable serological response following pediatric SARS-CoV-2 infection**	Renk H., *et al.* Germany gotopaper	Immunology	**Methods** > we examine 548 children and 717 adults within 328 households with at least one member with a previous laboratory-confirmed SARS-CoV-2 infection > we assess serological response at 3–4 months and 11–12 months after infection using a bead-based multiplex immunoassay for 23 human coronavirus antigens including SARS-CoV-2 and its Variants of Concern (VOC) and endemic human coronaviruses (HCoVs), and additionally by three commercial SARS-CoV-2 antibody assays. > Neutralization against wild type SARS-CoV-2 and the Delta VOC are analysed in a pseudotyped virus assay **Findings** > Children, compared to adults, are five times more likely to be asymptomatic, and have higher specific antibody levels which persist longer (96.2% versus 82.9% still seropositive 11–12 months post infection) > Of note, symptomatic and asymptomatic infections induce similar humoral responses in all age groups > SARS-CoV-2 infection occurs independent of HCoV serostatus > Neutralization responses of children and adults are similar, although neutralization is reduced for both against the Delta VOC. **Overall, the long-term humoral immune response to SARS-CoV-2 infection in children is of longer duration than in adults even after asymptomatic infection.**

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Nature Microbiol. 10JAN2022	**Induction of robust cellular and humoral immunity against SARS-CoV-2 after a third dose of BNT162b2 vaccine in previously unresponsive older adults**	Romero-Olmedo A.J., *et al.* Germany gotopaper	Immunology	**Aim**: to compare SARS-CoV-2-specific antibody and T-cell responses between older and younger audults after receiving two doses of BNT162b2. - Older adults (>80 years old, n = 51), younger control group (20–53 years old, n = 46) - Analysis of spike-specific IgG, neutralization capacity against SARS-CoV-2 and SARS-CoV-2-reactive CD4 T cells (CD40L+ and IFNγ+) in peripheral blood **Results** > Two doses of BNT162b2 increased neutralization capacity against wild-type and also Delta, although at a lower level. Young and older groups demonstrated a further increase (10-fold average) between first and second dose of spike-specific CD4 T cells. > Overall antibody and CD4 T-cell response was lower in older vaccinees at a high level of significance. 10% of older adults were identifies as low-/non-responders. > After receiving a third vaccination with BNT162b2, 4 out of 5 low-/non-responders showed antibody and T-cell responses similar to those of responders after two vaccinations. **Overall, immune responses against SARS-CoV-2 are lower in aged versus young vaccinees, although most of them mount adaptive SARS-CoV-2-specific immunity after two doses of BNT162b2. Those who are initially hardly responding to two doses can mount a virus-specific adaptive immune response after a third BNT162b2 dose.**
BMJ 07JAN2022	**Atorvastatin versus placebo in patients with covid-19 in intensive care: randomized controlled trial**	Sadeghipour P., *et al.* Iran gotopaper	Therapeutics	**Aim**: to assess the effect of statin treatment versus placebo on clinical outcomes in Covid-19 patients admitted to intensive care unit (ICU). **Methods** > a multicenter, randomized controlled trial with a 2×2 factorial design in 11 hospitals in Iran. > Atorvastatin 20 mg orally once daily versus placebo, continued for 30 days from randomization irrespective of hospital discharge status. > The primary efficacy outcome was a composite of venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or all cause mortality within 30 days from randomization. Prespecified safety outcomes included increase in liver enzyme levels more than three times the upper limit of normal and clinically diagnosed myopathy. **Findings** > Of 605 patients randomized between 29 July 2020 and 4 April 2021 for statin randomization in the INSPIRATION-S trial, 343 were co-randomized to intermediate dose versus standard dose prophylactic anticoagulation with heparin based regimens, whereas 262 were randomized after completion of the anticoagulation study. 587 of the 605 participants were included in the primary analysis of INSPIRATION-S, reported here: 290 were assigned to atorvastatin and 297 to placebo (median age 57 years (interquartile range 45-68 years); 256 (44%) women). > The primary outcome occurred in 95 (33%) patients assigned to atorvastatin and 108 (36%) assigned to placebo (odds ratio 0.84, 95% confidence interval 0.58 to 1.21). > Death occurred in 90 (31%) patients in the atorvastatin group and 103 (35%) in the placebo group (odds ratio 0.84, 95% confidence interval 0.58 to 1.22). > Rates for venous thromboembolism were 2% (n=6) in the atorvastatin group and 3% (n=9) in the placebo group (odds ratio 0.71, 95% confidence interval 0.24 to 2.06). > Myopathy was not clinically diagnosed in either group. Liver enzyme levels were increased in five (2%) patients assigned to atorvastatin and six (2%) assigned to placebo (odds ratio 0.85, 95% confidence interval 0.25 to 2.81). **In adults with covid-19 admitted to the ICU, atorvastatin was not associated with a significant reduction in the composite of venous or arterial thrombosis, treatment with extracorporeal membrane oxygenation, or all cause mortality compared with placebo. Treatment was, however, found to be safe. As the overall event rates were lower than expected, a clinically important treatment effect cannot be excluded.**

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JAMA Netw Open 07JAN2022	**SARS-CoV-2 Reinfection Rate and Estimated Effectiveness of the Inactivated Whole Virion Vaccine BBV152 Against Reinfection Among Health Care Workers in New Delhi, India**	Malhotra S., *et al.* India gotopaper	Vaccines - Immunisation	**Aim:** to assess the incidence density of reinfection among a cohort of HCWs and estimate the effectiveness of the inactivated whole virion vaccine BBV152 against reinfection in New Delhi, India - Vaccination with 0, 1, or 2 doses of BBV152. **Methods** **>** HCWs were categorized as: - fully vaccinated (with 2 doses and ≥15 days after the second dose), - partially vaccinated (with 1 dose or 2 doses with <15 days after the second dose), - or unvaccinated. > Incidence density of COVID-19 reinfection per 100 person-years was computedand included for analysis. **Findings** **>** Among 15 244 HCWs who participated in the study, 4978 (32.7%) were diagnosed with COVID-19. > The reinfection incidence density was 7.26 (95% CI: 6.09-8.66) per 100 person-years (124 HCWs [2.5%]). > Fully vaccinated HCWs had lower risk of reinfection (HR, 0.14 [95% CI, 0.08-0.23]), symptomatic reinfection (HR, 0.13 [95% CI, 0.07-0.24]), and asymptomatic reinfection (HR, 0.16 [95% CI, 0.05-0.53]) compared with unvaccinated HCWs. > Among the 3 vaccine categories, reinfection was observed in 60 of 472 (12.7%) of unvaccinated (incidence density, 18.05 per 100 person-years; 95% CI, 14.02-23.25), 39 of 356 (11.0%) of partially vaccinated (incidence density 15.62 per 100 person-years; 95% CI, 11.42-21.38), and 17 of 1089 (1.6%) fully vaccinated (incidence density 2.18 per 100 person-years; 95% CI, 1.35-3.51) HCWs. > The estimated effectiveness of BBV152 against reinfection was 86% (95% CI, 77%-92%); symptomatic reinfection, 87% (95% CI, 76%-93%); and asymptomatic reinfection, 84% (95% CI, 47%-95%) among fully vaccinated HCWs. > Partial vaccination was not associated with reduced risk of reinfection. **Conclusions** These findings suggest that BBV152 was associated with protection against both symptomatic and asymptomatic reinfection in HCWs after a complete vaccination schedule, when the predominant circulating variant was B.1.617.2.
Cell 06JAN2022	**mRNA-based COVID-19 vaccine boosters induce neutralizing immunity against SARS-CoV-2 Omicron variant**	Garcia-Beltran W.F., *et al.* USA gotopaper	Variants	**Aim**: to measure the neutralization potency of sera from 88 mRNA-1273, 111 BNT162b, and 40 Ad26.COV2.S vaccine recipients against wild-type, Delta, and Omicron SARS-CoV-2 pseudoviruses. - Individuals that received their primary series recently (<3 months), distantly (6–12 months), or an additional "booster" dose were included, while accounting for prior SARS-CoV-2 infection. **Results** > Neutralization of Omicron was undetectable in most vaccinees. > However, individuals boosted with mRNA vaccines exhibited potent neutralization of Omicron, only 4–6-fold lower than wild type, suggesting enhanced cross-reactivity of neutralizing antibody responses. > Omicron pseudovirus infects more efficiently than other variants tested. **This study highlights the importance of additional mRNA doses to broaden neutralizing antibody responses against highly divergent SARS-CoV-2 variants.**

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JAMA Oncol. 07JAN2022	**SARS-CoV-2 Antibody Response to 2 or 3 Doses of the BNT162b2 Vaccine in Patients Treated With Anticancer Agents**	Fenioux C., *et al.* France gotopaper	Vaccines - Immunisation	**Aim**: to assess the immune humoral response to 2 or 3 doses of the BNT162b2 vaccine in patients treated with anticancer agents. - Observational cohort study of adults treated with anticancer agents who received 2 or 3 doses of vaccine (Feb 1-May 31, 2021) - individuals with a weak humoral response 1 month after the second dose received a third injection. - Humoral response was evaluated with a threshold of anti–SARS-CoV-2 spike protein antibody levels at 1000 arbitrary units (AU)/mL to neutralize less-sensitive COVID-19 variants. **Results** > Among 163 patients (median age, 66 [27-89] years, 86 men [53%]) with solid tumors who received 2 or 3 doses of vaccine, 122 individuals (75%) were treated with chemotherapy, 15 with immunotherapy (9%), and 26 with targeted therapies (16%). > The proportions of patients with an anti-S immunoglobulin G titer greater than 1000 AU/mL were 15% (22 of 145) at the time of the second vaccination and 65% (92 of 142) 28 days after the second vaccination. > Humoral response decreased 3 months after the second dose. > Treatment type was associated with humoral response; in particular, time between vaccine and chemotherapy did not interfere with the humoral response. > Among 36 patients receiving a third dose of vaccine, a serologic response greater than 1000 AU/mL occurred in 27 individuals (75%). **This study supports the use of a third vaccine dose among patients with active cancer treatment for solid tumors.**
Science 06JAN2022	**Antibody-mediated broad sarbecovirus neutralization through ACE2 molecular mimicry**	Park Y.J., *et al.* International gotopaper	Therapeutics	**Understanding broadly neutralizing sarbecovirus antibody responses is key to developing countermeasures against SARS-CoV-2 variants and future zoonotic sarbecoviruses**. **Findings** > Isolation and characterization of a human monoclonal antibody, designated S2K146, broadly neutralizing viruses belonging to SARS-CoV- and SARS-CoV-2-related sarbecovirus clades (using ACE2 as an entry receptor) > S2K146 potently neutralized VSV pseudotypes harboring SARS-CoV-2 S glycoproteins from VOCs including Alpha, Beta, Gamma, Delta plus (AY.1/AY.2), Epsilon and Lambda > S2K146 also weakly neutralized VSV pseudotyped harboring the K493Y/T498W mutations, which enable human ACE2-mediated entry > S2K146 neutralized as well authentic SARS-CoV-2 and SARS-CoV-2 VOC > Structural and functional studies show that most of the virus residues that directly bind S2K146 are also involved in binding to ACE2. > S2K146 protects against SARS-CoV-2 Beta challenge in hamsters > Viral passaging experiments reveal a high barrier for emergence of escape mutants, making it a good candidate for clinical development. **Conclusion** The conserved ACE2-binding residues present a site of vulnerability that might be leveraged for developing vaccines eliciting broad sarbecovirus immunity.

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Immunity 05JAN2022	**mRNA-1273 vaccine-induced antibodies maintain Fc-effector functions across SARS-CoV-2 Variants of Concern**	Kaplonek P., *et al.* USA gotopaper	Immunology	**Aim**: to study SARS-CoV-2 antibody effector functions that go beyond neutralisation. - Profiling of the binding and functional capacity of convalescent antibodies and Moderna mRNA-1273 COVID-19 vaccine-induced antibodies across SARS-CoV-2 variants of concern (VOCs). **Results** > While neutralizing responses to VOCs decreased in both groups, Fc-mediated responses were distinct. > In convalescent individuals, while antibodies exhibited robust binding to VOCs, they showed compromised interactions with Fc-receptors. > Conversely, vaccine-induced antibodies also bound robustly to VOCs but continued interacting with Fc-receptors and mediated antibody effector functions. **These data point to a resilience in the mRNA vaccine-induced humoral immune response that may continue to protect from SARS-CoV-2 VOCs independent of neutralization.**
NEJM 05JAN2021	**Effect of Covid-19 Vaccination on Transmission of Alpha and Delta Variants**	Eyre D.W., et *al.* UK gotopaper	Vaccines - Immunisation	**Background** Before Delta variant: vaccination reduced transmission of SARS-CoV-2 from infected vaccinated persons, potentially by reducing viral loads. With Delta: vaccination still lowers the risk of infection, but similar viral loads in vaccinated and unvaccinated persons questions the degree to which vaccination prevents transmission. **Methods** Contact-testing to perform a retrospective observational cohort study involving adult contacts of SARS-CoV-2–infected adult index patients. **Findings** > Among 146,243 tested contacts of 108,498 index patients - 54,667 (37%) had positive SARS-CoV-2 polymerase-chain-reaction (PCR) tests. > In index patients who became infected with the alpha variant, two vaccinations with either BNT162b2 or ChAdOx1 nCoV-19, were independently associated with reduced PCR positivity in contacts > Vaccine-associated reductions in transmission of the delta variant were smaller than those with the alpha variant > Reductions in transmission of the delta variant after two BNT162b2 vaccinations were greater > Variation in Ct values in index patients explained 7 to 23% of vaccine-associated reductions in transmission of the two variants. > The reductions in transmission of the delta variant declined over time after the second vaccination, reaching levels that were similar to those in unvaccinated persons by 12 weeks in index patients who had received ChAdOx1 nCoV-19 and attenuating substantially in those who had received BNT162b2. > Protection in contacts also declined in the 3-month period after the second vaccination. **Conclusions** Vaccination was associated with a smaller reduction in transmission of the delta variant than of the alpha variant, and the effects of vaccination decreased over time.

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Cell 04JAN2022	**SARS-CoV-2 Omicron-B.1.1.529 leads to widespread escape from neutralizing antibody responses**	Dejnirattisai W., *et al.* UK gotopaper	Variants	**Findings** > Neutralization titres of Omicron by sera from vaccinees and convalescent subjects infected with early pandemic as well as Alpha, Beta, Gamma, Delta are substantially reduced or fail to neutralize. > Titres against Omicron are boosted by third vaccine doses and are high in cases both vaccinated and infected by Delta. > Mutations in Omicron knock out or substantially reduce neutralization by most of a large panel of potent monoclonal antibodies and antibodies under commercial development. > Omicron S has structural changes from earlier viruses, combining mutations conferring tight binding to ACE2 to unleash evolution driven by immune escape, leading to a large number of mutations in the ACE2 binding site which rebalance receptor affinity to that of early pandemic viruses.