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 29JUL2021	**Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia**	Guimarães P.O., *et al.* Brazil [gotopaper](#)	Therapeutics	**Aim**: to study the efficacy and safety of tofacitinib, a Janus kinase inhibitor, in patients who are hospitalized with Covid-19 pneumonia. Patients received either tofacitinib at a dose of 10 mg or placebo twice daily for up to 14 days or until hospital discharge. <u>Primary outcome</u>: occurrence of death or respiratory failure through day 28 as assessed with the use of an eight-level ordinal scale. **Results** > A total of 289 patients underwent randomization at 15 sites in Brazil. Overall, 89.3% of the patients received glucocorticoids during hospitalization. > The cumulative incidence of death or respiratory failure through day 28 was 18.1% in the tofacitinib group and 29.0% in the placebo group (risk ratio, 0.63; 95% CI, 0.41 to 0.97; P=0.04). > Death from any cause through day 28 occurred in 2.8% of the patients in the tofacitinib group and in 5.5% of those in the placebo group (hazard ratio, 0.49; 95% CI, 0.15 to 1.63). > The proportional odds of having a worse score on the eight-level ordinal scale with tofacitinib, as compared with placebo, was 0.60 (95% CI, 0.36 to 1.00) at day 14 and 0.54 (95% CI, 0.27 to 1.06) at day 28. > Serious adverse events occurred in 20 patients (14.1%) in the tofacitinib group and in 17 (12.0%) in the placebo group. **Conclusions** Among patients hospitalized with Covid-19 pneumonia, tofacitinib led to a lower risk of death or respiratory failure through day 28 than placebo.
NEJM 28JUL2021	**Covid-19 Breakthrough Infections in Vaccinated Health Care Workers**	Bergwerk M., *et al*. Israel [gotopaper](#)	Vaccines - Immunisation	**Aim**: to characterize breakthrough infections and define correlates of breakthrough and infectivity in healthcare workers (HCW) who received the BNT162b2 vaccine. - Full epidemiologic analysis of HCW who were symptomatic or had known infection exposures. - Correlates of breakthrough infection assessed in a case–control analysis, matching patients with breakthrough infection who had antibody titers obtained within a week before SARS-CoV-2 detection (peri-infection period) with 4-5 uninfected controls - Correlation between neutralizing antibody titers and N gene cycle threshold (Ct) values with respect to infectivity was assessed. **Results** > Among 1497 fully vaccinated HCW for whom RT-PCR data were available, 39 SARS-CoV-2 breakthrough infections were documented. > Neutralizing antibody titers in case patients during the peri-infection period were lower than those in matched uninfected controls (case-to-control ratio, 0.361; 95% CI, 0.165 to 0.787). > Higher peri-infection neutralizing antibody titers were associated with lower infectivity (higher Ct values). > Most breakthrough cases were mild or asymptomatic, although 19% had persistent symptoms (>6 weeks). > The B.1.1.7 (alpha) variant was found in 85% of samples tested. > A total of 74% of case patients had a high viral load (Ct value, <30) at some point during their infection; however, of these patients, only 17 (59%) had a positive result on concurrent Ag-RDT. > No secondary infections were documented. **Conclusions** Among fully vaccinated HCW, the occurrence of breakthrough infections with SARS-CoV-2 was correlated with neutralizing antibody titers during the peri-infection period. Most breakthrough infections were mild or asymptomatic, although persistent symptoms did occur.

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Nature 28JUL2021	**Rapid and stable mobilization of CD8+ T cells by SARS-CoV-2 mRNA vaccine**	Oberhardt V., *et al.* Germany [gotopaper](#)	Vaccines	**Aim**: to assess vaccine-induced CD8+ T cells response, compared to natural infection, and associated with other arms of vaccine-induced immunity. **Methods:** Continuous longitudinal analyses starting at baseline of prime vaccination until 3-4 months after boost on a single epitope level, to track the trajectories of bnt162b2 vaccine-elicited spike-specific CD8+ T cell responses in comparison to spike-specific CD4+ T cells, B cells, antibodies and their neutralizing activity. **Findings:** > On a single epitope level, a stable and fully functional CD8+ T cell response is vigorously mobilized one week after bnt162b2 prime vaccination when circulating CD4+ T cells and neutralizing antibodies are still weakly detectable. > Boost vaccination induced a robust expansion generating highly differentiated effector CD8+ T cells however, neither the functional capacity nor the memory precursor T cell pool was affected. > Compared to natural infection, vaccine-induced early memory T cells exhibited similar functional capacities but a different subset distribution. **CD8+ T cells are important effector cells, expanded in the early protection window after prime vaccination, precede maturation of other effector arms of vaccine-induced immunity and are stably maintained after boost vaccination.**
Blood 28JUL2021	**Aberrant glycosylation of anti-SARS-CoV-2 IgG is a pro-thrombotic stimulus for platelets**	Bye A.P., *et al.* Netherlands / UK [gotopaper](#)	Therapeutics	**Aim**: to investigate the effects of low fucosylation and high galactosylation of anti-75 spike IgG on platelet activation to find the significance of aberrant IgG glycosylation identified in critically-ill COVID-19 patients on platelet-mediated thrombus formation. **Findings:** > Immune complexes containing recombinant SARS-CoV-2 spike protein and anti-spike IgG enhanced platelet-mediated thrombosis on von Willebrand Factor in vitro, but only when the glycosylation state of the Fc domain was modified to correspond with the aberrant glycosylation previously identified in patients with severe COVID-19. > Activation was dependent on FcγRIIA and the authors provide in vitro evidence that this pathogenic platelet activation can be counteracted by therapeutic small molecules R406 (fostamatinib) and ibrutinib that inhibits tyrosine kinases Syk and Btk respectively or by the P2Y12 antagonist cangrelor. I**mmobilised immune complexes containing recombinant anti-spike IgG with low fucosylation and high galactosylation activate platelets to enhance thrombus formation on vWF, which is also elevated in severely ill COVID-19 patients.** **Potential COVID-19 therapies such as fostamatinib or acalabrutinib, targeting Syk or Btk respectively, may be effective in limiting the inflammatory response and reducing platelet-mediated thrombosis.**
Science Transl Med. 27JUL2021	**Intranasal ChAdOx1 nCoV-19/AZD1222 vaccination reduces viral shedding after SARS-CoV-2 D614G challenge in preclinical models**	van Doremalen N., *et al.* USA [gotopaper](#)	Vaccines	**Aim**: to investigate whether intranasally administered ChAdOx1 nCoV-19 reduces detection of virus in nasal swabs after challenging vaccinated macaques and hamsters with SARS-CoV-2 carrying a D614G mutation in the spike protein. **Results** > Viral loads in swabs obtained from intranasally vaccinated hamsters were decreased compared to control hamsters, and no viral RNA or infectious virus was found in lung tissue after a direct challenge. > Intranasal vaccination of hamsters protected against SARS-CoV-2 infection during direct contact with infected hamsters – no viral RNA or infectious virus was found in lung tissue after direct contact with infected hamsters. > Intranasal vaccination in rhesus macaques induced humoral and cellular immune responses and protected from infection. > Intranasal vaccination of rhesus macaques resulted in reduced virus concentrations in nasal swabs and a reduction in viral loads in bronchoalveolar lavage and lower respiratory tract tissue. **Intranasal vaccination with ChAdOx1 nCoV-19/AZD1222 reduced virus concentrations in nasal swabs in two different SARS-CoV-2 animal models, warranting further investigation as a potential vaccination route for COVID-19 vaccines.**

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BMJ 27JUL2021	**Diagnostic accuracy of rapid antigen tests in asymptomatic and presymptomatic close contacts of individuals with confirmed SARS-CoV-2 infection: cross sectional study**	Schuit E., *et al.* Netherlands gotopaper	Diagnostics	**Aim**: to assess the diagnostic test accuracy of two rapid antigen tests in asymptomatic and presymptomatic close contacts of people with SARS-CoV-2 infection on day 5 after exposure. > 4274 consecutively included close contacts (identified through test-and-trace programme or contact tracing app) aged 16 years or older and asymptomatic for covid-19 when requesting a test. >Main outcomes : Sensitivity, specificity, and positive and negative predictive values of Veritor System (Beckton Dickinson) and Biosensor (Roche Diagnostics) rapid antigen tests. **Findings:** > Of 2678 participants tested with Veritor, 233 (8.7%) had a RT-PCR confirmed SARS-CoV-2 infection of whom 149 were also detected by the rapid antigen test (sensitivity 63.9%). > Of 1596 participants tested with Biosensor, 132 (8.3%) had a RT-PCR confirmed SARS-CoV-2 infection of whom 83 were detected by the rapid antigen test (sensitivity 62.9%). > In those who were still asymptomatic at the time of sampling, sensitivity was 58.7% for Veritor (n=2317) and 59.4% for Biosensor (n=1414) > In those who developed symptoms were 84.2% (n=219) for Veritor and 73.3% (n=158) for Biosensor. > Specificities were >99%, and positive and negative predictive values were >90% and >95%, for both rapid antigen tests in all analyses. **The sensitivities of both rapid antigen tests in asymptomatic and presymptomatic close contacts tested on day 5 onwards after close contact with an index case were >60%, increasing to more than 85% after a viral load cut-off was applied as a proxy for infectiousness.**
Lancet Respir Med. 27JUL2021	**Doxycycline for community treatment of suspected COVID-19 in people at high risk of adverse outcomes in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial**	Butler C. C., *et al.* UK gotopaper	Therapeutics	**Aim**: to assess the efficacy of doxycycline to treat suspected COVID-19 in the community among people at high risk of adverse outcomes. **Methods** > People aged ≥65 years, or ≥50 years with comorbidities who had been unwell (for ≤14 days) with suspected COVID-19 or a positive PCR test for SARS-CoV-2 infection in the community > Coprimary endpoints: time to first self-reported recovery, and hospitalisation or death related to COVID-19, both measured over 28 days from randomisation and analysed by intention to treat. **Results** > 2689 participants were enrolled and randomised between April 2, 2020 to Dec 14, 2020 > Of these, 2508 (93·3%) participants contributed follow-up data and were included in the primary analysis: 780 (31·1%) in the usual care plus doxycycline group, 948 in the usual care only group (37·8%), and 780 (31·1%) in the usual care plus other interventions group. > Among the 1792 participants randomly assigned to the usual care plus doxycycline and usual care only groups, the mean age was 61·1 years (SD 7·9); 999 (55·7%) participants were female and 790 (44·1%) were male. > In the primary analysis model, there was little evidence of difference in median time to first self-reported recovery between the usual care plus doxycycline group and the usual care only group (9·6 [95% Bayesian Credible Interval [BCI] 8·3 to 11·0] days vs 10·1 [8·7 to 11·7] days, hazard ratio 1·04 [95% BCI 0·93 to 1·17]). The estimated benefit in median time to first self-reported recovery was 0·5 days [95% BCI −0·99 to 2·04] and the probability of a clinically meaningful benefit (defined as ≥1·5 days) was 0·10. > Hospitalisation or death related to COVID-19 occurred in 41 (crude percentage 5·3%) participants in the usual care plus doxycycline group and 43 (4·5%) in the usual care only group (estimated absolute percentage difference −0·5% [95% BCI −2·6 to 1·4]); there were five deaths (0·6%) in the usual care plus doxycycline group and two (0·2%) in the usual care only group. > **In patients with suspected COVID-19 in the community in the UK, who were at high risk of adverse outcomes, treatment with doxycycline was not associated with clinically meaningful reductions in time to recovery or hospital admissions or deaths related to COVID-19, and should not be used as a routine treatment for COVID-19.**

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Nature Commun. 27JUL2021	**Impact of tiered restrictions on human activities and the epidemiology of the second wave of COVID-19 in Italy**	Manica M., *et al.* Italy [gotopaper]	Public Health / Epidemiology	**Aim:** Evaluate the impact on human mobility and SARS-CoV-2 transmissibility of the three-tiered regional restriction system introduced by the Italian government in autumn 2020 **Context:** > In Italy, starting from November 6, 2020, a three-tiered restriction system was introduced > In each of the 21 regions and autonomous provinces, based on the combination of several quantitative indicators, restriction measures were applied according to three tiers (yellow, orange and red from the less to the most restrictive) > Restriction measures consist in limitations of retail, service activities and individual movement, and reinforced distance-learning in schools **Methods:** > Mobility data: Google community mobility reports at the provincial level from September 25 to November 25, 2020 > Estimation of the net reproduction number $R(t)$ from the epidemic curve of symptomatic cases, as the weekly moving average of the maximum a posteriori of a likelihood function where the serial interval is estimated from the analysis of contact tracing in Lombardy > The association between tiers and changes in human mobility and of $R(t)$ is modeled by linear mixed models > Several models are considered, with alternative choices of target variables, level of geographic aggregation, selection of regions and duration of the serial interval **Findings:** > Significant and progressive reduction of the time spent outside of home, especially in locations associated with recreational and retail activities, and public transport > The activity reduction in all locations outside of home was far from that observed during the nationwide lockdown imposed in Italy during the first wave > The reproduction numbers were close to 1 in the week November 19-25 in the yellow tier, and were significantly below 1 in orange and red tiers > The relative mean reduction of $R(t)$ between the week October 30-November 5 and the week November 19-25 is estimated to be of 13-19% in the yellow tier, 27-38% in the orange tier and 36-45% in the red tier, consistently across all models > The authors estimate that the reduction in transmissibility averted about 24 500 hospital admissions between November 6 and 25, 2020 **Conclusions:** > Stricter restrictions (orange and red tiers) were associated with a decreasing incidence and the most permissive tier (yellow) was sufficient to reduce the reproduction number to values close to the epidemic threshold > The tier system resulted in a much lower impact on human acticvites compared to lockdown and in large reduction in daily hospitalizations

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Nature Med. 26JUL2021	**Immunogenicity and reactogenicity of heterologous ChAdOx1 nCoV-19/mRNA vaccination**	Schmidt T., *et al.* Germany [gotopaper]	Vaccines	**Aim**: observational study on immunogenicity and reactogenicity of heterologous priming with the ChAdOx1 nCoV-19 vector vaccine followed by boosting with a messenger RNA vaccine (BNT162b2 or mRNA-1273). **Results** > In healthy adult individuals (n = 96), the heterologous vaccine regimen induced spike-specific IgG, neutralizing antibodies and spike-specific CD4 T cells, the levels of which were significantly higher than after homologous vector vaccine boost (n = 55) and higher or comparable in magnitude to homologous mRNA vaccine regimens (n = 62). > Spike-specific CD8 T cell levels after heterologous vaccination were significantly higher than after both homologous regimens. > Spike-specific T cells were predominantly polyfunctional with largely overlapping cytokine-producing phenotypes in all three regimens. > Recipients of both the homologous vector regimen and the heterologous vector/mRNA combination reported greater reactogenicity following the priming vector vaccination, whereas heterologous boosting was well tolerated and comparable to homologous mRNA boosting. **Heterologous vector/mRNA boosting induces strong humoral and cellular immune responses with acceptable reactogenicity profiles.**
Lancet Infect Dis. 26JUL2021	**Safety, tolerability, and immunogenicity of an aerosolised adenovirus type-5 vector-based COVID-19 vaccine (Ad5-nCoV) in adults: preliminary report of an open-label and randomised phase 1 clinical trial**	Wu S., *et al.* China [gotopaper]	Vaccines	**Aim**: Phase 1 trial to evaluate safety and immunogenicity of an aerosolised adenovirus type-5 vector-based COVID-19 vaccine (Ad5-nCoV) in adults without COVID-19 from China. - Participants were randomly assigned (1:1:1:1:1) into five groups to be vaccinated via intramuscular injection, aerosol inhalation, or both. - Aerosol groups received an initial high dose (2 × 10^{10} viral particles; HDmu group) or low dose (1 × 10^{10} viral particles; LDmu group) of Ad5-nCoV vaccine on day 0, followed by a booster on day 28. - Mixed vaccination group received an initial intramuscular (5 × 10^{10} viral particles) vaccine on day 0, followed by an aerosolised booster (2 × 10^{10} viral particles) vaccine on day 28 (MIX group). - Intramuscular groups received one dose (5 × 10^{10} viral particles; 1Dim group) or two doses (10 × 10^{10} viral particles; 2Dim group) of Ad5-nCoV on day 0. Primary safety outcome: adverse events 7 days after each vaccination Primary immunogenicity outcome: anti-SARS-CoV-2 S IgG antibody and SARS-CoV-2 neutralising antibody geometric mean titres at day 28 **Results** > 130 participants were enrolled into the trial and randomly assigned into one of the five groups (26 participants per group). > Within 7 days after vaccination, adverse events occurred in 18 (69%) in the HDmu group, 19 (73%) in the LDmu group, 19 (73%) in the MIX group, 19 (73%) in the 1Dim group, and 15 (58%) in the 2Dim group. > The most common adverse events reported 7 days after the first or booster vaccine were fever (62 [48%] of 130 participants), fatigue (40 [31%]), and headache (46 [35%]). > More adverse events were reported in participants who received intramuscular vaccination, including participants in the MIX group (49 [63%] of 78 participants), than those who received aerosol vaccine (13 [25%] of 52 participants) after the first vaccine vaccination. > No serious adverse events within 56 days after the first vaccine. > At days 28 after last vaccination, geometric mean titres of SARS-CoV-2 neutralising antibody was 107 (95% CI 47–245) in the HDmu group, 105 (47–232) in the LDmu group, 396 (207–758) in the MIX group, 95 (61–147) in the 1Dim group, and 180 (113–288) in the 2Dim group. > Geometric mean concentrations of RBD-binding IgG was 261 EU/mL (95% CI 121–563) in HDmu group, 289 EU/mL (138–606) in LDmu group, 2013 EU/mL (1180–3435) in MIX group, 915 EU/mL (588–1423) in the 1Dim group, and 1190 EU/mL (776–1824) in the 2Dim group. **Conclusions** - Aerosolised Ad5-nCoV is well tolerated, and two doses of aerosolised Ad5-nCoV elicited neutralising antibody responses, similar to one dose of intramuscular injection. - An aerosolised booster vaccination at 28 days after 1st intramuscular injection induced strong IgG and neutralising antibody responses.

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Cell 23JUL2021	**Memory B Cell Repertoire for Recognition of Evolving SARS-CoV-2 Spike**	Tong P., *et al.* USA gotopaper	Immunology	**Aim**: to chart memory B cell receptor-encoded antibodies from 19 COVID-19 convalescent subjects against SARS-CoV-2 spike (S) **Methods:** Global assessment of the distribution of memory B-cell encoded antibodies among cooperative and competitive recognition clusters on the SARS-CoV-2 S glycoprotein to examine features that direct their collaborative robustness against emerging SARS-CoV-2 variants.And a comprehensive competition analysis of 152 monoclonal antibodies (mAbs) from 19 subjects for binding with trimeric S ectodomain. **Findings:** > 7 major epitopic regions of SARS-CoV-2 spike are consistently targeted by human Abs > Ab group assignment correlates with CoV binding breadth and neutralization potency > SARS-CoV-2 variants tend to escape Abs from the groups with most potent neutralizers > Intra-group Ab binding redundancy confers robustness against emerging variants **The study furnish a global atlas of S-specific memory B cell repertoires and illustrate properties driving viral escape and conferring robustness against emerging variants.**
NEJM 22JUL2021	**Prevention and Attenuation of Covid-19 with the BNT162b2 and mRNA-1273 Vaccines**	Thompson M.G., *et al.* USA gotopaper	Vaccines - Immunisation	**Aim**: to study the effectiveness of the two-dose mRNA vaccines BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) in preventing infection with SARS-CoV-2 and in attenuating Covid-19 when administered in real-world conditions. **Methods** > Prospective cohort study involving 3975 health care personnel, first responders, and other essential and frontline workers. From December 14, 2020, to April 10, 2021, the participants completed weekly SARS-CoV-2 testing by providing mid-turbinate nasal swabs for qualitative and quantitative RT-PCR analysis **Results** > SARS-CoV-2 was detected in 204 participants (5%), of whom 5 were fully vaccinated ($\geq$14 days after dose 2), 11 partially vaccinated ($\geq$14 days after dose 1 and <14 days after dose 2), and 156 unvaccinated; the 32 participants with indeterminate vaccination status (<14 days after dose 1) were excluded. > Adjusted vaccine effectiveness was 91% (95% confidence interval [CI], 76 to 97) with full vaccination and 81% (95% CI, 64 to 90) with partial vaccination. > Among participants with SARS-CoV-2 infection, the mean viral RNA load was 40% lower (95% CI, 16 to 57) in partially or fully vaccinated participants than in unvaccinated participants. > In addition, the risk of febrile symptoms was 58% lower (relative risk, 0.42; 95% CI, 0.18 to 0.98) and the duration of illness was shorter, with 2.3 fewer days spent sick in bed (95% CI, 0.8 to 3.7). **> Authorized mRNA vaccines were highly effective among working-age adults in pre-venting SARS-CoV-2 infection when administered in real-world conditions, and the vaccines attenuated the viral RNA load, risk of febrile symptoms, and duration of illness among those who had breakthrough infection despite vaccination.**

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NEJM 21JUL2021	**Effectiveness of Covid-19 Vaccines against the B.1.617.2 (Delta) Variant**	Lopez Bernal J., *et al.* UK gotopaper	Vaccines - Immunisation	**Aim**: to determine the effectiveness of the BNT162b2 and ChAdOx1 nCoV-19 vaccines against symptomatic COVID-19 due to Delta variant in a real-world setting. **Results** > Effectiveness after one dose of vaccine (BNT162b2 or ChAdOx1 nCoV-19) was notably lower among persons with the delta variant (30.7%; 95% CI, 25.2-35.7) than among those with the alpha variant (48.7%; 95% CI, 45.5-51.7); the results were similar for both vaccines. > With the BNT162b2 vaccine, the effectiveness of two doses was 93.7% (95% CI, 91.6 to 95.3) among persons with the alpha variant and 88.0% (95% CI, 85.3 to 90.1) among those with the delta variant. > With the ChAdOx1 nCoV-19 vaccine, the effectiveness of two doses was 74.5% (95% CI, 68.4 to 79.4) among persons with the alpha variant and 67.0% (95% CI, 61.3 to 71.8) among those with the delta variant. **Conclusions** Only modest differences in vaccine effectiveness were noted with the delta variant as compared with the alpha variant after the receipt of two vaccine doses. Absolute differences in vaccine effectiveness were more marked after the receipt of the first dose.
JAMA 20JUL2021	**Effect of Canakinumab vs Placebo on Survival Without Invasive Mechanical Ventilation in Patients Hospitalized With Severe COVID-19 - A Randomized Clinical Trial**	Caricchio R., *et al.* USA gotopaper	Therapeutics	**Aim:** To evaluate the efficacy of canakinumab, an anti–interleukin-1β antibody, in patients hospitalized with severe COVID-19. **Methods:** Randomized, double-blind, placebo-controlled phase 3 trial. 454 hospitalized patients with COVID-19 pneumonia, hypoxia (no invasive mechanical ventilation [IMV]), systemic hyperinflammation. Patients were randomly assigned 1:1 to receive a single intravenous infusion of canakinumab (450 mg for body weight of 40-<60 kg, 600 mg for 60-80 kg, and 750 mg for >80 kg; n = 227) or placebo (n = 227). Primary outcome : survival without IMV from day 3 to day 29. **Findings :** >Among 454 patients who were randomized (median age, 59 years; 187 women [41.2%]), 417 (91.9%) completed day 29 of the trial. > Between days 3 and 29, 198 of 223 patients (88.8%) survived without requiring IMV in the canakinumab group and 191 of 223 (85.7%) in the placebo group, with a rate difference of 3.1% (95% CI, −3.1% to 9.3%) and an odds ratio of 1.39 (95% CI, 0.76 to 2.54; P = .29). > COVID-19–related mortality occurred in 11 of 223 patients (4.9%) in the canakinumab group vs 16 of 222 (7.2%) in the placebo group, with a rate difference of −2.3% (95% CI, −6.7% to 2.2%) and an odds ratio of 0.67 (95% CI, 0.30 to 1.50). > Serious adverse events were observed in 36 of 225 patients (16%) treated with canakinumab vs 46 of 223 (20.6%) who received placebo. **Among patients hospitalized with severe COVID-19, treatment with canakinumab, compared with placebo, did not significantly increase the likelihood of survival without IMV at day 29.**
Nature 19JUL2021	**Broad sarbecovirus neutralization by a human monoclonal antibody**	Tortorici M.A., *et al.* International gotopaper	Therapeutics	**Background** The recent emergence of SARS-CoV-2 VOC highlight the need for broadly neutralizing antibodies that are not affected by the ongoing antigenic drift and that can prevent or treat future zoonotic infections. **Findings** > S2X259 mAb identified from the memory B cells of a COVID-19 convalescent individual, > S2X259 recognizes a highly conserved cryptic RBD epitope and cross-reacting with spikes from all sarbecovirus clades. > S2X259 broadly neutralizes spike-mediated entry of SARS-CoV-2 including the B.1.1.7, B.1.351, P.1, B.1.427/B.1.429 VOC, as well as a wide spectrum of human and potentially zoonotic sarbecoviruses through inhibition of ACE2 binding to the RBD. > S2X259 possesses an escape profile limited to the single substitution G504D. > Prophylactic and therapeutic administration of S2X259 protects Syrian hamsters against challenge with the prototypic SARS-CoV-2 and the B.1.351 VOC **Conclusions** S2X259 is a promising candidate for the prevention and treatment of emergent variants and zoonotic infections.

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NEJM 15JUL2021	**Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents**	Frenck R.W., et al. USA gotopaper	Vaccines	**Background** Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) had not been authorized for emergency use in persons younger than 16 years of age. **Methods** > Multinational, placebo-controlled, observer-blinded trial, > Two injections, 21 days apart, of 30 µg of BNT162b2 or placebo. > Immunogenicity obectif: noninferiority of the immune response to BNT162b2 in 12-to-15-year-old participants as compared with that in 16-to-25-year-old participants > Safety endpoint : reactogenicity and adverse events and efficacy against confirmed coronavirus disease 2019 (Covid-19; onset, ≥7 days after dose 2) in the 12-to-15-year-old cohort **Findings** > 2260 adolescents 12 to 15 years of age received injections (1131 BNT162b2, 1129 placebo). > BNT162b2 had a favorable safety and side-effect profile, with mainly transient mild-to-moderate reactogenicity: - injection-site pain [in 79 to 86% of participants], - fatigue [in 60 to 66%], - headache [in 55 to 65%]) > No vaccine-related serious adverse events and few overall severe adverse events. > The geometric mean ratio of SARS-CoV-2 50% neutralizing titers after dose 2 in 12-to-15-year-old participants relative to 16-to-25-year-old participants was 1.76 (95% confidence interval [CI], 1.47 to 2.10), ((noninferiority criterion met > greater response in the 12-to-15-year-old cohort). > Among participants without evidence of previous SARS-CoV-2 infection, no Covid-19 cases with an onset of 7 or more days after dose 2 were noted among BNT162b2 recipients, and 16 cases occurred among placebo recipients. >The observed vaccine efficacy was 100% (95% CI, 75.3 to 100). **Conclusions** BNT162b2 vaccine in 12-to-15-year-old recipients had a favorable safety profile, produced a greater immune response than in young adults, and was highly effective against Covid-19.
Blood 15JUL2021	**Rate of thrombosis in children and adolescents hospitalized with COVID-19 or MIS-C**	Whitworth H., et al. USA gotopaper	Clinic	**Aim:** to determine the incidence of thrombosis in children hospitalized with COVID-19 or MIS-C and evaluate associated risk factors. **Methods:** Multicenter retrospective cohort study, the patients were classified into 1 of 3 groups for analysis: COVID-19, MIS-C, or asymptomatic SARS-CoV-2. Standard statistical methods were used to summarize the data: frequency and percentage for categorical variables, and median and interquartile range for continuous scaled variables. **Findings :** > Among a total of 853 admissions (COVID-19, n = 426; MIS-C, n = 138; and asymptomatic SARS-CoV-2, n = 289) in 814 patients, there were 20 patients with thrombotic events (TEs; including 1 stroke). > Patients with MIS-C had the highest incidence (9 [6.5%] of 138) vs COVID-19 (9 [2.1%] of 426) or asymptomatic SARS-CoV-2 (2 [0.7%] of 289). > In patients with COVID-19 or MIS-C, a majority of TEs (89%) occurred in patients age ≥12 years. Patients age ≥12 years with MIS-C had the highest rate of thrombosis at 19% (9 of 48). > Notably, 71% of TEs that were not present on admission occurred despite thromboprophylaxis. **Multivariable analysis identified the following as significantly associated with thrombosis: age ≥12 years, cancer, presence of a central venous catheter, and MIS-C. In patients with COVID-19 or MIS-C, hospital mortality was 2.3% (13 of 564), but it was 28% (5 of 18) in patients with TEs.**

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JAMA Netw Open 15JUL2021	**Association of Remdesivir Treatment With Survival and Length of Hospital Stay Among US Veterans Hospitalized With COVID-19**	Ohl M.E., *et al.* USA gotopaper	Therapeutics	**Aim**: To examine associations between remdesivir treatment and survival and length of hospital stay among people hospitalized with COVID-19 in routine care settings (May-Oct 2020) <u>Main Outcomes</u> time to death within 30 days of remdesivir treatment, time to hospital discharge with time to death as a competing event. **Results** > Analysis included 1172 remdesivir recipients and 1172 controls, for a final matched cohort of 2344 individuals. Remdesivir recipients and matched controls were similar with regard to age (mean [SD], 66.6 [14.2] vs 67.5 [14.1] years), sex (1101 [93.9%] vs 1101 men [93.9%]), dexamethasone use (559 [47.7%] vs 559 [47.7%]), admission to the intensive care unit (242 [20.7%] vs 234 [19.1%]), and mechanical ventilation use (69 [5.9%] vs 45 [3.8%]). > Remdesivir treatment was not associated with 30-day mortality (143 remdesivir recipients [12.2%] vs 124 controls [10.6%]; log rank P = .26; adjusted HR, 1.06; 95% CI, 0.83-1.36). > Similar results for people receiving vs not receiving dexamethasone at remdesivir initiation (dex. recipients: adjusted HR, 0.93; 95% CI, 0.64-1.35; nonrecipients: adjusted HR, 1.19; 95% CI, 0.84-1.69). > Remdesivir recipients had a longer median time to hospital discharge compared with matched controls (6 days [interquartile range, 4-12 days] vs 3 days [1-7 days]; P < .001). **Conclusions** In this cohort study, remdesivir treatment was not associated with improved survival but was associated with longer hospital stays.
Clin Infect Dis. 15JUL2021	**Clinical improvement, outcomes, antiviral activity, and costs associated with early treatment with remdesivir for patients with COVID-19**	Wong C.K.H., *et al*. China gotopaper	Therapeutics	**Aim**: to explore the disease progression, various clinical outcomes, changes in viral load, and costs associated with early remdesivir treatment among COVID-19 patients. **Results** > Median follow-up was 14 days for both remdesivir (n=352) and control (n=1,347) groups. COVID-19 patients were hospitalised between Jan 2020 and Jan 2021. > Time to clinical improvement was significantly shorter in the remdesivir group than that of control (HR(95%CI)=1.14(1.01-1.29), p=0.038), as well as for achieving low viral load (1.51(1.24-1.83), p<0.001) and positive IgG antibody (1.50(1.31-1.70), p<0.001). > Early remdesivir treatment was associated with a lower risk of in-hospital death (HR=0.58, 95%CI 0.34-0.99, p=0.045), in addition to a significantly shorter length of hospital stay (difference -2.56 days, 95%CI -4.86 to -0.26, p=0.029), without increasing the risks of composite outcomes for clinical deterioration. **Conclusions** Early remdesivir treatment could be extended to hospitalized patients with moderate COVID-19 not requiring oxygen therapy on admission.
Clin Infect Dis. 15JUL2021	**Detection of Severe Acute Respiratory Syndrome Coronavirus 2 on Self-Collected Saliva or Anterior Nasal Specimens Compared With Healthcare Personnel–Collected Nasopharyngeal Specimens**	Marx G.E., *et al.* USA gotopaper	Diagnostics	**Aim:** To evaluate whether testing of self-collected Anterio-Nasal Specimens (ANS) or Saliva Specimen (SS) might accurately and reliably detect SARS-CoV-2 in real-life settings. **Methods:** 730 adults undergoing SARS-CoV-2 testing at community testing events and homeless shelters. Specimens were tested by rRT-PCR; viral culture was performed on a subset of positive specimens. The sensitivity of SS and ANS for SARS-CoV-2 detection by rRT-PCR was measured against that of NPS. **Findings :** >Sensitivity for SARS-CoV-2 detection by rRT-PCR appeared higher for SS than for ANS (85% vs 80%) and higher among symptomatic participants than among those without symptoms (94% vs 29% for SS; 87% vs 50% for ANS). > Among participants with culture-positive SARS-CoV-2 by any specimen type, the sensitivities of SS and ANS by rRT-PCR were 94% and 100%, respectively. > SS and ANS were equally preferred by participants; most would undergo NPS collection despite this method being the least preferred. **Self-collected SS and ANS offer practical advantages, are preferred by patients, and might be most useful for testing people with coronavirus disease 2019 symptoms.**

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NEJM 14JUL2021	**Bamlanivimab plus Etesevimab in Mild or Moderate Covid-19**	Dougan M., *et al.* USA [gotopaper]	Therapeutics	**Phase 3 trial of bamlanivimab/etesevimab in a cohort of ambulatory patients with mild or moderate Covid-19 who were at high risk for progression to severe disease.** - Treatment: 2800 mg of bamlanivimab and 2800 mg of etesevimab (single IV infusion) or placebo within 3 days after a laboratory diagnosis of SARS-CoV-2 infection. - <u>Primary outcome</u>: overall clinical status of the patients, defined as Covid-19–related hospitalization or death from any cause by day 29. **Results** > A total of 1035 patients underwent randomization. The mean (±SD) age of the patients was 53.8±16.8 years, and 52.0% were adolescent girls or women. > By day 29, a total of 11 of 518 patients (2.1%) in the bamlanivimab–etesevimab group had a Covid-19–related hospitalization or death from any cause, as compared with 36 of 517 patients (7.0%) in the placebo group (absolute risk difference, −4.8 percentage points; 95% confidence interval [CI], −7.4 to −2.3; relative risk difference, 70%; P<0.001). > No deaths occurred in the bamlanivimab–etesevimab group; in the placebo group, 10 deaths occurred, 9 of which were designated by the trial investigators as Covid-19–related. > At day 7, a greater reduction from baseline in the log viral load was observed among patients who received bamlanivimab plus etesevimab than among those who received placebo (difference from placebo in the change from baseline, −1.20; 95% CI, −1.46 to −0.94; P<0.001). **Conclusions** Among high-risk ambulatory patients, bamlanivimab plus etesevimab led to a lower incidence of Covid-19–related hospitalization and death than did placebo and accelerated the decline in the SARS-CoV-2 viral load.
NEJM 14JUL2021	**Durable Humoral and Cellular Immune Responses 8 Months after Ad26.COV2.S Vaccination**	Barouch D.H., *et al.* Netherlands/USA [gotopaper]	Vaccines	**Aim**: to describe the 8-month durability of humoral and cellular immune responses in 20 participants who received the Ad26.COV2.S vaccine in one or two doses (either 5×1010 viral particles or 1011 viral particles) and in 5 participants who received placebo. **Results** > Antibody responses were detected in all vaccine recipients on day 239 (8 months after the single-shot vaccine regimen or 6 months after the two-shot vaccine regimen) > The median binding antibody titer against the WA1/2020 receptor-binding domain was 645 on day 29, 1772 on day 57, 1962 on day 71, and 1306 on day 239. > The median WA1/2020 pseudovirus neutralizing antibody titer was 272 on day 29, 169 on day 57, 340 on day 71, and 192 on day 239. Antibody responses were relatively stable during the 8-month period. > On day 29, the median neutralizing antibody titer against the B.1.351 variant was lower by a factor of 13 than the response against WA1/2020; however, by day 239, that factor difference had decreased to 3 > Vaccine recipients who received the single-shot regimen had a median neutralizing antibody titer of 184 against WA1/2020 strain, 158 against the D614G variant, 147 against the B.1.1.7 variant, 171 against the B.1.617.1 variant, 107 against the B.1.617.2 variant, 129 against the P.1 variant, 87 against the B.1.429 variant, and 62 against the B.1.351 variant on day 239. > Spike-specific interferon-γ CD8+ and CD4+ T-cell responses also showed durability and stability over the study period. **Conclusions** Ad26.COV2.S vaccine elicited durable humoral and cellular immune responses with minimal decreases for at least 8 months after immunization. An expansion of neutralizing antibody breadth against SARS-CoV-2 variants was observed over the study period, suggesting maturation of B-cell responses even without further boosting.

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Nature Med. 14JUL2021	**Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination**	Barros-Martins J., *et al.* Germany <u>gotopaper</u>	Vaccines - Immunisation	**Aim**: to monitor ChAd-primed immune responses before and 3 weeks after booster with ChAd (n = 32) or BioNTech/Pfizer's BNT162b2 (n = 55), using Hannover Medical School's COVID-19 Contact Study cohort of healthcare professionals. > Although both vaccines boosted prime-induced immunity, **BNT162b2 induced significantly higher frequencies of spike-specific CD4+ and CD8+ T cells**. > BNT162b2 induced high titers of neutralizing antibodies against the B.1.1.7, B.1.351 and P.1 variants of concern of severe acute respiratory syndrome coronavirus 2. > BNT/BNT-vaccinated and ChAd/BNT-vaccinated individuals develop neutralizing antibodies to similar degrees 2–3 weeks after booster vaccination. Likewise, immune responses of the ChAd/ChAd group were in the range of earlier reported results.
Science Transl Med. 13JUL2021	**A high-throughput cell- and virus-free assay shows reduced neutralization of SARS-CoV-2 variants by COVID-19 convalescent plasma**	Fenwick C., *et al.* Switzerland <u>gotopaper</u>	Diagnostics	**Background**: detection of SARS-CoV-2-specific antibodies in serum provides limited insight into the protective nature of the immune response. Neutralizing antibodies recognizing the viral spike protein are more revealing, yet their measurement more challenging. **Aim**: to present a cell-free quantitative neutralization assay based on the competitive inhibition of trimeric SARS-CoV-2 spike protein binding to the angiotensin converting enzyme 2 (ACE2) receptor. > This high-throughput method matches the performance of the gold standard live virus infection assay, as verified with a panel of 206 seropositive donors with varying degrees of infection severity and virus-specific IgG titers, achieving 96.7% sensitivity and 100% specificity. > It allows for the parallel assessment of neutralizing activities against multiple SARS-CoV-2 spike protein variants of concern. > This assay was used to profile serum samples from 59 patients hospitalized with coronavirus disease 2019 (COVID-19). Although most sera had high activity against the 2019-nCoV parental spike protein and, to a lesser extent, the α (B.1.1.7) variant, only 58% of serum samples could efficiently neutralize a spike protein derivative containing mutations present in the β (B.1.351) variant. **The presented assay can evaluate effective neutralizing antibody responses to SARS-CoV-2 spike protein variants of concern after natural infection and can be applied to characterize vaccine-induced antibody responses or to assess the potency of monoclonal antibodies.**

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JAMA Intern Med. 13JUL2021	**Association of BNT162b2 mRNA and mRNA-1273 Vaccines With COVID-19 Infection and Hospitalization Among Patients With Cirrhosis**	John B.V., *et al.* USA	Vaccines - Immunisations	**Aim**: to study the association of receipt of the Pfizer BNT162b2 mRNA or the Moderna mRNA-1273 vaccines in patients with cirrhosis compared with a propensity-matched control group of patients at similar risk of infection and severe disease from COVID-19. - Patients who received at least 1 dose of an mRNA vaccine (n = 20 037) were propensity matched with 20 037 controls to assess the associations of vaccination with new COVID-19 infection and COVID-19 hospitalization and death. **Results** > The median (interquartile range) age of the vaccinated individuals in the study cohort was 69.1 (8.4) years and 19 465 (97.2%) of the participants in each of the vaccinated and unvaccinated groups were male, consistent with a US veteran population. The mRNA-1273 vaccine was administered in 10 236 (51%) and the BNT162b2 mRNA in 9801 (49%) patients. > The number of COVID-19 infections in the vaccine recipients was similar to the control group in days 0 to 7, 7 to 14, 14 to 21, and 21 to 28 after the first dose. > After 28 days, receipt of 1 dose of an mRNA vaccine was associated with a 64.8% reduction in COVID-19 infections and 100% protection against hospitalization or death due to COVID-19 infection. > The association of reduced COVID-19 infections after the first dose was lower among patients with decompensated (50.3%) compared with compensated cirrhosis (66.8%). > Receipt of a second dose was associated with a 78.6% reduction in COVID-19 infections and 100% reduction in COVID-19–related hospitalization or death after 7 days. **Conclusions** This study found that mRNA vaccine administration was associated with a delayed but modest reduction in COVID-19 infection but an excellent reduction in COVID-19–related hospitalization or death in patients with cirrhosis.
JAMA 12JUL2021	**Association Between BNT162b2 Vaccination and Incidence of SARS-CoV-2 Infection in Pregnant Women**	Goldshtein I., *et al.* Israel	Vaccines	**Aim**: to assess the association between receipt of BNT162b2 mRNA vaccine and risk of SARS-CoV-2 infection among pregnant women. - Pregnant women vaccinated with a first dose from December 19, 2020, through February 28, 2021, were 1:1 matched to unvaccinated women by age, gestational age, residential area, population subgroup, parity, and influenza immunization status. - Primary outcome: PCR–validated SARS-CoV-2 infection at ≥28 days after the first vaccine dose. **Results** > The cohort included 7530 vaccinated and 7530 matched unvaccinated women, 46% and 33% in the second and third trimester, respectively, with a mean age of 31.1 years (SD, 4.9 years). The median follow-up for the primary outcome was 37 days (interquartile range, 21-54 days; range, 0-70). > There were 118 SARS-CoV-2 infections in the vaccinated group and 202 in the unvaccinated group. Among infected women, 88 of 105 (83.8%) were symptomatic in the vaccinated group vs 149 of 179 (83.2%) in the unvaccinated group (P ≥ .99). > During 28 to 70 days of follow-up, there were 10 infections in the vaccinated group and 46 in the unvaccinated group. > The hazards of infection were 0.33% vs 1.64% in the vaccinated and unvaccinated groups, respectively, representing an absolute difference of 1.31% (95% CI, 0.89%-1.74%), with an adjusted hazard ratio of 0.22 (95% CI, 0.11-0.43). > Vaccine-related adverse events were reported by 68 patients; none was severe. The most commonly reported symptoms were headache (n = 10, 0.1%), general weakness (n = 8, 0.1%), nonspecified pain (n = 6, <0.1%), and stomachache (n = 5, <0.1%). **Conclusions** In this study on pregnant women, BNT162b2 mRNA vaccination compared with no vaccination was associated with a significantly lower risk of SARS-CoV-2 infection.

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Lancet Public Health 09JUL2021	**Genomics-informed responses in the elimination of COVID-19 in Victoria, Australia: an observational, genomic epidemiological study**	Lane C.R., *et al.* Australia [gotopaper]	Public Health / Epidemiology	**Aim**: to describe the genomic findings that located the source of the second wave in Victoria, Australia, and show the role of genomic epidemiology in the successful elimination of COVID-19 for a second time. > Between Jan 25, 2020, and Jan 31, 2021, there were 20 451 laboratory-confirmed cases of COVID-19 in Victoria, Australia, of which 15 431 were submitted for sequencing, and 11 711 met all quality control metrics and were included in the analysis. > 595 genomic clusters were identified, with a median of 5 cases per cluster (IQR 2–11). > Samples from 11 503 (98·2%) of 11 711 cases clustered with another sample in Victoria, either within a genomic cluster or transmission network. > Genomic analysis revealed that 10 426 cases, including 10 416 (98·4%) of 10 584 locally acquired cases, diagnosed during the second wave (between June and October, 2020) were derived from a single incursion from hotel quarantine, with the outbreak lineage (transmission network G, lineage D.2) rapidly detected in other Australian states and territories. > Phylodynamic analyses indicated that the epidemic growth rate of the outbreak lineage in Victoria during the initial growth phase (samples collected between June 4 and July 9, 2020; 47·4 putative transmission events, per branch, per year [1/years; 95% credible interval 26·0–85·0]), was similar to that of other reported variants, such as B.1.1.7 in the UK (mean approximately 71·5 1/years). > Strict interventions were implemented, and the outbreak lineage has not been detected in Australia since Oct 29, 2020. Subsequent cases represented independent international or interstate introductions, with limited local spread. **This study highlights how rapid escalation of clonal outbreaks can occur from a single incursion, and effectiveness of public health responses. Real-time genomic surveillance can alter the way in which public health agencies view and respond to COVID-19 outbreaks.**
Nature Med. 09JUL2021	**mRNA-1273 COVID-19 vaccine effectiveness against the B.1.1.7 and B.1.351 variants and severe COVID-19 disease in Qatar**	Chemaitelly H., *et al.* Qatar [gotopaper]	Vaccines - Variants	**Aim**: to assess the real-world effectiveness of the mRNA-1273 vaccine against SARS-CoV-2 variants of concern, specifically B.1.1.7 (Alpha) and B.1.351 (Beta), in Qatar, a population that comprises mainly working-age adults, using a matched test-negative, case-control study design. > Vaccine effectiveness was negligible for 2 weeks after the first dose, but **increased rapidly in the third and fourth weeks** immediately before administration of a second dose. > Effectiveness against **B.1.1.7 infection was 88.1%** (95% confidence interval (CI): 83.7–91.5%) ≥14 days after the first dose but before the second dose, **and was 100%** (95% CI: 91.8–100.0%) ≥14 days after the second dose. > Analogous effectiveness against B.1.351 infection was 61.3% after the first dose (95% CI: 56.5–65.5%) and 96.4% after the second dose (95% CI: 91.9–98.7%). > Effectiveness against any severe, critical or fatal COVID-19 disease due to any SARS-CoV-2 infection (predominantly B.1.1.7 and B.1.351) was 81.6% (95% CI: 71.0–88.8%) and 95.7% (95% CI: 73.4–99.9%) after the first and second dose, respectively. **The mRNA-1273 vaccine is highly effective against B.1.1.7 and B.1.351 infections, whether symptomatic or asymptomatic, and against any COVID-19 hospitalization and death, even after a single dose.**

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Lancet Global Health 09JUL2021	**Difference in mortality among individuals admitted to hospital with COVID-19 during the first and second waves in South Africa: a cohort study**	Jassat W., *et al.* South Africa [gotopaper](link)	Public Health / Epidemiology	**Aim**: to compare in-hospital mortality and other patient characteristics between the COVID-19 first wave and second wave (SARS-CoV-2 501Y.V2 (Beta) lineage predominant) in South Africa. **Results** > Peak rates of COVID-19 cases, admissions, and in-hospital deaths in the second wave exceeded rates in the first wave: COVID-19 cases, 240·4 cases per 100 000 people vs 136·0 cases per 100 000 people; admissions, 27·9 admissions per 100 000 people vs 16·1 admissions per 100 000 people; deaths, 8·3 deaths per 100 000 people vs 3·6 deaths per 100 000 people. > The weekly average growth rate in hospital admissions was 20% in wave 1 and 43% in wave 2 (ratio of growth rate in wave 2 compared with wave 1 was 1·19, 95% CI 1·18–1·20). > Compared with the first wave, individuals admitted to hospital in the second wave were more likely to be age 40–64 years (adjusted odds ratio [aOR] 1·22, 95% CI 1·14–1·31), and ≥65 years (aOR 1·38, 1·25–1·52), compared with younger than 40 years; of Mixed race (aOR 1·21, 1·06–1·38) compared with White race; and admitted in the public sector (aOR 1·65, 1·41–1·92); and less likely to be Black (aOR 0·53, 0·47–0·60) and Indian (aOR 0·77, 0·66–0·91), compared with White; and have a comorbid condition (aOR 0·60, 0·55–0·67). > For multivariable analysis, after adjusting for weekly COVID-19 hospital admissions, there was a 31% increased risk of in-hospital mortality in the second wave (aOR 1·31, 95% CI 1·28–1·35). In-hospital case-fatality risk increased from 17·7% in weeks of low admission (<3500 admissions) to 26·9% in weeks of very high admission (>8000 admissions; aOR 1·24, 1·17–1·32). **Conclusions** In South Africa, the second wave was associated with higher incidence of COVID-19, more rapid increase in admissions to hospital, and increased in-hospital mortality. Part of the increase in mortality of patients admitted to hospital could be related to the new Beta lineage.
Lancet Rheumatol. 08JUL2021	**The effect of methotrexate and targeted immunosuppression on humoral and cellular immune responses to the COVID-19 vaccine BNT162b2: a cohort study**	Mahil S.K., *et al.* UK [gotopaper](link)	Vaccines - Immunisation	**Aim**: to evaluate humoral and cellular immune responses to COVID-19 vaccine BNT162b2 in patients taking methotrexate and targeted biological therapies. Given the roll-out of extended interval vaccination programmes to maximise population coverage, we present findings after the first dose. - Cohort of patients with psoriasis and receiving methotrexate or targeted biological monotherapy ([TNF inhibitors, IL-17 inhibitors, or IL-23 inhibitors). - Controls: volunteers without psoriasis and receiving vaccine. Primary outcomes: neutralising antibody responses to wild-type SARS-CoV-2, and spike-specific T-cell responses (including interferon-γ, IL-2, and IL-21) 28 days after vaccination. **Results** > Between Jan 14-April 4, 2021, 84 patients with psoriasis (17 on methotrexate, 27 on TNF inhibitors, 15 on IL-17 inhibitors, and 25 on IL-23 inhibitors) and 17 healthy controls were included. The study population had a median age of 43 years (IQR 31–52), with 56 (55%) males, 45 (45%) females, and 85 (84%) participants of White ethnicity. > Seroconversion rates were lower in patients receiving immunosuppressants (60 [78%; 95% CI 67–87] of 77) than in controls (17 [100%; 80–100] of 17), with the lowest rate in those receiving methotrexate (seven [47%; 21–73] of 15). > Neutralising activity against wild-type SARS-CoV-2 was significantly lower in patients receiving methotrexate (median 50% inhibitory dilution 129 [IQR 40–236]) than in controls (317 [213–487], p=0·0032), but was preserved in those receiving targeted biologics (269[141–418] > Neutralising titres against the B.1.1.7 variant were similarly low in all participants. > Cellular immune responses were induced in all groups, and were not attenuated in patients receiving methotrexate or targeted biologics compared with controls. **Conclusions** Functional humoral immunity to a single dose of BNT162b2 is impaired by methotrexate but not by targeted biologics, whereas cellular responses are preserved.

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Lancet 08JUL2021	**Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey**	Tanriover M.D., *et al.* Turkey [gotopaper]	Vaccines	**Interim efficacy and safety results of a phase 3 clinical trial of CoronaVac, an inactivated whole-virion SARS-CoV-2 vaccine, in Turkey.** - Double-blind, randomised, placebo-controlled phase 3 trial on volunteers aged 18–59 years with no history of COVID-19. - The K1 cohort consisted of health-care workers (randomised in a 1:1 ratio), and other individuals were also recruited into the K2 cohort (randomised in a 2:1 ratio). - The study vaccine was 3 µg inactivated SARS-CoV-2 virion adsorbed to aluminium hydroxide in a 0·5 mL aqueous suspension. Participants received either vaccine or placebo intramuscularly on days 0 and 14. <u>Primary efficacy outcome</u>: prevention of PCR-confirmed symptomatic COVID-19 at least 14 days after the second dose. **Results** > The intention-to-treat group consisted of 10 214 participants (6646 [65·1%] in the vaccine group and 3568 [34·9%] in the placebo group) and the per protocol group consisted of 10 029 participants (6559 [65·4%] and 3470 [34·6%]) who received two doses of vaccine or placebo, recruited between Sept 14, 2020, and Jan 5, 2021. > During a median follow-up period of 43 days (IQR 36–48), nine cases of PCR-confirmed symptomatic COVID-19 were reported in the vaccine group (31·7 cases [14·6–59·3] per 1000 person-years) and 32 cases were reported in the placebo group (192·3 cases [135·7–261·1] per 1000 person-years) ≥14 days after the second dose, yielding a **vaccine efficacy of 83·5%** (95% CI 65·4–92·1; p<0·0001). > The frequencies of any adverse events were 1259 (18·9%) in the vaccine group and 603 (16·9%) in the placebo group (p=0·0108) with no fatalities or grade 4 adverse events. > The most common systemic adverse event was fatigue (546 [8·2%] participants in the vaccine group and 248 [7·0%] the placebo group, p=0·0228). Injection-site pain was the most frequent local adverse event (157 [2·4%] in the vaccine group and 40 [1·1%] in the placebo group, p<0·0001). **Conclusions** CoronaVac has high efficacy against PCR-confirmed symptomatic COVID-19 with a good safety and tolerability profile.
Nature 08JUL2021	**Mapping the human genetic architecture of COVID-19**	COVID-19 Host Genetic Initiative International [gotopaper]	Public Health / Epidemiology	Identifying host-specific genetic factors may reveal biological mechanisms of therapeutic relevance and clarify causal relationships of modifiable environmental risk factors for SARS-CoV-2 infection and outcomes. **Aim**: to investigate the role of human genetics in SARS-CoV-2 infection and COVID-19 severity through three genome-wide association meta-analyses comprised of up to 49,562 COVID-19 patients from 46 studies across 19 countries. > We reported **13 genome-wide significant loci that are associated with SARS-CoV-2 infection or severe manifestations of COVID-19**. > Several of these loci correspond to **previously documented associations to lung or autoimmune and inflammatory diseases**. They also represent potentially actionable mechanisms in response to infection. > Mendelian Randomization analyses support a **causal role for smoking and body mass index** for severe COVID-19 although not for type II diabetes. The rapid identification of novel host genetic factors associated with COVID-19 was made possible by the community of human genetic researchers coming together to prioritize sharing of data, results, resources and analytical frameworks.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 08JUL2021	**Reduced sensitivity of SARS-CoV-2 variant Delta to antibody neutralization**	Planas D., *et al.* France gotopaper	Variants	**Background**: The B.1.617 lineage includes three main subtypes (B1.617.1, B.1.617.2 and B.1.617.3), harbouring diverse Spike mutations in the N-terminal domain (NTD) and the receptor binding domain (RBD) which may increase their immune evasion potential. **Aim**: to study the isolate of an infectious Delta (B.1.617.2) strain from a traveller returning from India, examining its sensitivity to monoclonal antibodies (mAbs) and to antibodies present in sera from COVID-19 convalescent individuals or vaccine recipients. **Results** > Variant Delta was resistant to neutralization by some anti-NTD and anti-RBD mAbs including Bamlanivimab, which were impaired in binding to the Spike > Sera from convalescent patients collected up to 12 months post symptoms were 4-fold less potent against variant Delta, relative to variant Alpha (B.1.1.7). > Sera from individuals having received one dose of Pfizer or AstraZeneca vaccines barely inhibited variant Delta. Administration of two doses generated a neutralizing response in 95% of individuals, with titers 3-to-5-fold lower against Delta than Alpha. **Variant Delta spread is associated with an escape to antibodies targeting non-RBD and RBD Spike epitopes.**
NEJM 07JUL2021	**Effectiveness of an Inactivated SARS-CoV-2 Vaccine in Chile**	Jara A., *et al.* Chile gotopaper	Vaccines - Immunisation	**Estimation of CoronaVac (inactivated SARS-CoV-2 vaccine) efficacy preventing Covid-19 and related hospitalization, admission to the intensive care unit (ICU), and death, in mass vaccination campaign in Chile** > The study was conducted from February 2 to May 1, 2021. The cohort included approximately 10.2 million persons. > Among persons who were fully immunized, the adjusted vaccine effectiveness was 65.9% (95% confidence interval [CI], 65.2 to 66.6) for the prevention of Covid-19 and 87.5% (95% CI, 86.7 to 88.2) for the prevention of hospitalization, 90.3% (95% CI, 89.1 to 91.4) for the prevention of ICU admission, and 86.3% (95% CI, 84.5 to 87.9) for the prevention of Covid-19–related death. **These results suggest that the inactivated SARS-CoV-2 vaccine effectively prevented Covid-19, including severe disease and death.**
Nature Commun. 05JUL2021	**Monocyte-driven atypical cytokine storm and aberrant neutrophil activation as key mediators of COVID-19 disease severity**	Vanderbeke L., *et al.* Belgium gotopaper	Clinic	**Aim**: to elucidate the immunopathology underlying COVID-19 severity, through cytokine and multiplex immune profiling in COVID-19 patients. > Hypercytokinemia in COVID-19 differs from the interferon-gamma-driven cytokine storm in macrophage activation syndrome, and is more pronounced in critical versus mild-moderate COVID-19. > Systems modelling of cytokine levels paired with deep-immune profiling shows that classical monocytes drive this hyper-inflammatory phenotype and that a reduction in T-lymphocytes correlates with disease severity, with CD8+ cells being disproportionately affected. > Antigen presenting machinery expression is also reduced in critical disease. > Neutrophils contribute to disease severity and local tissue damage by amplification of hypercytokinemia and the formation of neutrophil extracellular traps. **These findings suggest a myeloid-driven immunopathology, in which hyperactivated neutrophils and an ineffective adaptive immune system act as mediators of COVID-19 disease severity.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Clin Infect Dis 05JUL2021	**Persistent symptoms in adult patients one year after COVID-19: a prospective cohort study**	Seessle J., *et al.* Germany gotopaper	Long Covid	**Aim**: to better understand the long-term course and etiology of long term symptoms in a cohort of COVID-19 patients (n=96, 32.3% hospitalised, 55.2% females) followed up to 12 month after symptom onset. **Results** > At month 12, only 22.9% of patients were completely free of symptoms. > The most frequent symptoms were reduced exercise capacity (56.3%), fatigue (53.1%), dyspnoea (37.5%), concentration problems (39.6%), problems finding words (32.3%), and sleeping problems (26.0%). > Females showed significantly more neurocognitive symptoms than males. > Antinuclear antibodies (ANA) titres were ≥1:160 in 43.6% of patients at 12 months post COVID-19 symptom onset, and neurocognitive symptom frequency was significantly higher in the group with an ANA titre ≥1:160 compared to <1:160. > Compared to patients without symptoms, patients with at least one long COVID symptom at 12 months did not differ significantly in their SARS-CoV-2-antibody levels, but had a significantly reduced physical and mental life quality. **Conclusions** Neurocognitive long COVID symptoms can persist at least for one year after COVID-19 symptom onset. Several neurocognitive symptoms were associated with ANA titre elevations, which may indicate autoimmunity as cofactor in aetiology of long COVID.
Lancet Respir Med. 02JUL2021	**BNT162b2 COVID-19 vaccine and correlates of humoral immune responses and dynamics: a prospective, single-centre, longitudinal cohort study in health-care workers**	Lustig Y., *et al.* Israel gotopaper	Vaccines - Immunisation	**Aim**: to assess the early antibody responses and antibody kinetics after each BNT162b2 vaccine dose in health-care workers of different ages and sexes, and with different comorbidities. - Prospective, single-centre, longitudinal cohort study - Participants were followed up weekly for 5 weeks after the first vaccine dose; a second dose was given at week 3. **Results** > Between Dec 19, 2020, and Jan 30, 2021, 4026 serum samples from 2607 participants were obtained. 342 individuals were included in the enriched comorbidities subgroup. > The first vaccine dose elicited positive IgG and neutralising antibody responses at week 3 in 707 (88·0%) of 803 individuals, and 264 (71·0%) of 372 individuals, respectively, which were rapidly increased at week 4 (ie, 1 week after the second vaccine dose) in 1011 (98·4%) of 1027 and 357 (96·5%) of 370 individuals, respectively. > Over 4 weeks of follow-up after vaccination, a high correlation (r=0·92) was detected between IgG against the receptor-binding domain and neutralising antibody titres. > First-dose induced IgG response was significantly lower in individuals aged 66 years and older (ratio of means 0·25, 95% CI 0·19–0·31) and immunosuppressed individuals (0·21, 0·14–0·31) compared with individuals aged 18·00–45·99 years and individuals with no immunosuppression, respectively. This disparity was partly abrogated following the second dose. > Overall, endpoint regression analysis showed that lower antibody concentrations were consistently associated with male sex (ratio of means 0·84, 95% CI 0·80–0·89), older age (ie, ≥66 years; 0·64, 0·58–0·71), immunosuppression (0·44, 0·33–0·58), and other specific comorbidities: diabetes (0·88, 0·79–0·98), hypertension (0·90, 0·82–0·98), heart disease (0·86, 0·75–1·00), and autoimmune diseases (0·82, 0·73–0·92). **Conclusions** BNT162b2 vaccine induces a robust and rapid antibody response. The second vaccine dose is particularly important for older and immunosuppressed individuals, highlighting the need for timely second vaccinations and potentially a revaluation of the long gap between doses in some countries.

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Science 01JUL2021	**Ultrapotent antibodies against diverse and highly transmissible SARS-CoV-2 variants**	Wang L., *et al.* USA gotopaper	Therapeutics	The emergence of highly transmissible SARS-CoV-2 variants of concern (VOC) that are resistant to therapeutic antibodies highlights the need for continuing discovery of broadly reactive antibodies. > We identify **four receptor-binding domain targeting antibodies from three early-outbreak convalescent donors with potent neutralizing activity** against 23 variants including the B.1.1.7, B.1.351, P.1, B.1.429, B.1.526 and B.1.617 VOCs. > **Two antibodies are ultrapotent**, with sub-nanomolar neutralization titers (IC50 0.3 to 11.1 ng/mL; IC80 1.5 to 34.5 ng/mL). > We define the **structural and functional determinants** of binding for all four VOC-targeting antibodies, and how these enable neutralisation of escaping mutants. > We show that **combinations of two antibodies decrease the in vitro generation of escape mutants**, suggesting their potential in mitigating resistance development.
Nature Commun. 30JUN2021	**SARS-CoV-2-specific T cell memory is sustained in COVID-19 convalescent patients for 10 months with successful development of stem cell-like memory T cells**	Jung J.H., *et al.* Republic of Korea gotopaper	Immunology	**Aim**: to evaluate SARS-CoV-2-specific CD4+ and CD8+ T cell responses in COVID-19 convalescent patients up to 317 days post-symptom onset (DPSO) through ex vivo assays. > **Memory T cell responses are maintained during the study period regardless of the severity of COVID-19**. Sustained polyfunctionality and proliferation capacity of SARS-CoV-2-specific T cells was observed. > Among SARS-CoV-2-specific CD4+ and CD8+ T cells detected by activation-induced markers, the proportion of **stem cell-like memory T (TSCM) cells is increased**, peaking at approximately 120 DPSO. > Development of TSCM cells is confirmed by SARS-CoV-2-specific MHC-I multimer staining. **Considering the self-renewal capacity and multipotency of TSCM cells, our data suggest that SARS-CoV-2-specific T cells are long-lasting after recovery from COVID-19.**
PNAS 30JUN2021	**Scalable live-attenuated SARS-CoV-2 vaccine candidate demonstrates preclinical safety and efficacy**	Wang Y., *et al.* USA gotopaper	Vaccines	**Aim**: to describe COVI-VAC, the only live attenuated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine currently in clinical development. > COVI-VAC was developed by recoding a segment of the viral spike protein with synonymous suboptimal codon pairs (codon-pair deoptimization), introducing 283 silent (point) mutations. Furin cleavage site within the spike protein was deleted from the viral genome for added safety. Except for the furin cleavage site deletion, the COVI-VAC and parental SARS-CoV-2 amino acid sequences are identical. > COVI-VAC was temperature sensitive in vitro yet grew robustly (>107 plaque forming units/mL) at the permissive temperature. > Tissue viral loads were consistently lower, lung pathology milder, and weight loss reduced in Syrian golden hamsters (Mesocricetus auratus) vaccinated intranasally with COVI-VAC compared to those inoculated with wild-type (WT) virus. > COVI-VAC inoculation generated spike IgG antibody levels and plaque reduction neutralization titers similar to those in hamsters inoculated with WT virus. > Upon challenge with WT virus, COVI-VAC vaccination reduced lung challenge viral titers, resulted in undetectable virus in the brain, and protected hamsters from almost all SARS-CoV-2–associated weight loss. > Highly attenuated COVI-VAC is protective at a single intranasal dose in a relevant in vivo model. **These results, coupled with its large-scale manufacturing potential, supports COVI-VAC potential use in mass vaccination programs.**

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NEJM 30JUN2021	**Prevention and Attenuation of Covid-19 with the BNT162b2 and mRNA-1273 Vaccines**	Thompson M.G., *et al.* USA gotopaper	Vaccines - Immunisation	Effectiveness of the two-dose messenger RNA (mRNA) vaccines BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna) in preventing infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and in attenuating coronavirus disease 2019 (Covid-19) when administered in real-world conditions. **Methods** > Prospective cohort study. 3975 HCW , first responders, and other essential and frontline workers. > Weekly SARS-CoV-2 testing by providing mid-turbinate nasal swabs for qualitative and quantitative RT-PCR analysis. **Findings** > SARS-CoV-2 was detected in 204 participants (5%) - 5 were fully vaccinated (≥14 days after dose 2), - 11 partially vaccinated (≥14 days after dose and <14 days after dose 2), -156 unvaccinated; - 32 participants with indeterminate vaccination status were excluded. > Adjusted vaccine effectiveness was 91% with full vaccination and 81% (95% CI, 64 to 90) with partial vaccination. > Among participants with SARS-CoV-2 infection, the mean viral RNA load was 40% lower (95% CI, 16 to 57) in partially or fully vaccinated participants than in unvaccinated participants. > The risk of febrile symptoms was 58% lower and the duration of illness was shorter, with 2.3 fewer days spent sick in bed **Conclusions** Authorized mRNA vaccines were highly effective among working-age adults in preventing SARS-CoV-2 infection when administered in real-world conditions, and the vaccines attenuated the viral RNA load, risk of febrile symptoms, and duration of illness among those who had breakthrough infection despite vaccination.
NEJM 30JUN2021	**Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine**	Heath P.T., *el al.* UK gotopaper	Vaccines	NVX-CoV2373 vaccine (Novavax) is a recombinant nanoparticle vaccine against SARS-CoV-2 that contains the full-length spike glycoprotein of the prototype strain plus Matrix-M adjuvant **Methods** > Phase 3, randomized, observer-blinded, placebo-controlled trial > 33 sites in the United Kingdom. Adults between the ages of 18 and 84 years in a 1:1 ratio to receive two intramuscular 5-µg doses of NVX-CoV2373 or placebo administered 21 days apart. Efficacy end point: was virologically confirmed mild, moderate, or severe SARS-CoV-2 infection with an onset at least 7 days after the second injection in participants who were serologically negative at baseline. **Findings** > 14,039 participants included - 27.9% were 65 years of age or older - 44.6% had coexisting illnesses. > Infections reported in 10 participants in the vaccine group and in 96 in the placebo group, with a symptom onset of at least 7 days after the second injection, for a vaccine efficacy of 89.7% (95% confidence interval [CI], 80.2 to 94.6). >No hospitalizations or deaths reported among the 10 cases in the vaccine group. > Five cases of severe infection reported, all of which were in the placebo group. > Efficacy of 86.3% (95% CI, 71.3 to 93.5) against the B.1.1.7 (or alpha) variant and 96.4% (95% CI, 73.8 to 99.5) against non-B.1.1.7 variants. > Reactogenicity was generally mild and transient. The incidence of serious adverse events was low and similar in the two groups. **Conclusions** A two-dose regimen of the NVX-CoV2373 vaccine administered to adult participants conferred 89.7% protection against SARS-CoV-2 infection and showed high efficacy against the B.1.1.7 variant. (

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 30JUN2021	**SARS-CoV-2-specific T cell memory is sustained in COVID-19 convalescent patients for 10 months with successful development of stem cell-like memory T cells**	Jung J.H., *et al.* Republic of Korea <u>gotopaper</u>	Immunology	**Aim**: to evaluate SARS-CoV-2-specific CD4+ and CD8+ T cell responses in COVID-19 convalescent patients up to 317 days post-symptom onset (DPSO) and find that memory T cell responses are maintained during the study period regardless of the severity of COVID-19. **Methods:** Cohort of 101 individuals with SARS-CoV-2 infection. The peak disease severity was evaluated according to the NIH severity of illness categories19: asymptomatic (n = 7), mild (n = 46), moderate (n = 25), severe (n = 14), and critical (n = 9). Whole blood samples were obtained longitudinally (2–4 time points) from 56 patients or at a single time point from 45 patients. Whole blood was collected 1–317 days post-symptom onset (DPSO). **Findings:** > SARS-CoV-2-specific TSCM cells were successfully developed, indicating that SARS-CoV-2-specific T cell memory may be long-lasting in COVID-19 convalescent patients. > T cells from PBMCs obtained after 200 DPSO exhibiting sustained polyfunctionality and proliferation capacity. > PD-1 and TIGIT are rarely expressed in SARS-CoV-2-specific TSCM cells, indicating that SARS-CoV-2-specific TSCM cells are not exhausted-like progenitors, but bona fide stem-like memory cells. **SARS-CoV-2-specific memory T cell responses are maintained 10 months after the infection.**
Nature 30JUN2021	**Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2**	Collier D.A., *et al.* UK <u>gotopaper</u>	Immunology	Analysis of immune responses following vaccination with mRNA vaccine BNT162b2 in elderly participants and younger health care workers. > Serum neutralisation and binding **IgG/IgA after the first vaccine dose diminished with increasing age**, with a marked drop in participants > 80 years old. > Sera from participants **> 80 showed significantly lower neutralisation potency against B.1.1.7, B.1.351 and P.1**. variants of concern as compared to wild type and were more likely to lack any neutralisation against VOC following the first dose. However, following the second dose, neutralisation against VOC was detectable regardless of age. > Frequency of **SARS-CoV-2 Spike specific B-memory cells** was higher in elderly responders versus non-responders after first dose. Elderly participants demonstrated clear reduction in somatic hypermutation of class switched cells. > **SARS-CoV-2 Spike specific T- cell IFNγ and IL-2 responses** decreased with increasing age, and both cytokines were secreted primarily by CD4 T cells. **We conclude that the elderly are a high risk population that warrant specific measures to boost vaccine responses, particularly where variants of concern are circulating.**
Nature Med. 29JUN2021	**Reduction in life expectancy in Brazil after COVID-19**	Castro M. J., *et al.* USA <u>gotopaper</u>	Public Health / Epidemiology	In this study, we used data on reported total deaths in 2020 and in January–April 2021 to measure and compare the death toll across states **Findings** > We estimate a decline in 2020 life expectancy at birth (e0) of 1.3 years, a mortality level not seen since 2014. > The reduction in life expectancy at age 65 (e65) in 2020 was 0.9 years, setting Brazil back to 2012 levels > The decline was larger for males, widening by 9.1% the female–male gap in e0. Among states, Amazonas lost 60.4% of the improvements in e0 since 2000 > In the first 4 months of 2021, COVID-19 deaths represented 107% of the total 2020 figures > **Assuming that death rates would have been equal to 2019 all-cause rates in the absence of COVID-19, COVID-19 deaths in 2021 have already reduced e0 in 2021 by 1.8 years, which is slightly larger than the reduction estimated for 2020 under similar assumptions.**

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Clin Infect Dis. 29JUN2021	**Rapidly increasing SARS-CoV-2 seroprevalence and limited clinical disease in three Malian communities: a prospective cohort study**	Sagara I., *et al.* International [gotopaper](#)	Public Health / Epidemiology	Estimation of the cumulative incidence of SARS-CoV-2 in three communities in Mali , and understand factors associated with infection. **Methods** > blood samples collection and demographic, social, medical, and self-reported symptoms information from residents aged 6 months and older over two study visits. > SARS-CoV-2 antibodies were measured using a highly specific two-antigen ELISA optimized for use in Mali. **Findings** > 94.8% (2533/2672) of participants completed both study visits. > A total of 31.3% (837/2672) were aged <10 years, 27.6% (737/2672) were aged 10-17 years, and 41.1% (1098/2572) were aged ≥18 years. > The cumulative SARS-CoV-2 exposure rate was 58.5% (95% CI: 47.5 to 69.4). This varied between sites and was 73.4% in the urban community of Sotuba, 53.2% in the rural town of Bancoumana, and 37.1% in the rural village of Donéguébougou. > Study site and increased age were associated with serostatus at both study visits. >Minimal difference in reported symptoms based on serostatus. **Conclusion** The true extent of SARS-CoV-2 exposure in Mali is greater than previously reported and may now approach hypothetical 'herd immunity' in urban areas. The epidemiology of the pandemic in the region may be primarily subclinical and within background illness rates.
Nature 28JUN2021	**SARS-CoV-2 mRNA vaccines induce persistent human germinal centre responses**	Turner J.S., *et al.* USA [gotopaper](#)	Immunology	The dynamics of antibody secreting plasmablasts (PBs) and germinal centre (GC) B cells induced by SARS-CoV-2 mRNA vaccines in humans remain unclear. **Aim**: to examine antigen-specific B cell responses in peripheral blood (n=41) and draining lymph nodes (LNs) in 14 individuals who received two doses of BNT162b2. > Circulating **IgG- and IgA-secreting PBs** targeting the S protein peaked one week after the second immunization then declined, becoming undetectable three weeks later. > These PB responses preceded maximal levels of serum anti-S binding and neutralizing antibodies to an **early circulating SARS-CoV-2 strain as well as emerging variants**, especially in individuals previously infected with SARS-CoV-2, who produced the most robust serologic responses. > By examining fine needle aspirates (FNAs) of draining axillary LNs, we identified **GC B cells that bound S protein** in all participants sampled after primary immunization. > High frequencies of **S-binding GC B cells and PBs were sustained in these draining LNs for at least twelve weeks after the booster immunization**. > S-binding GC B cell-derived monoclonal antibodies predominantly targeted the RBD of the S protein, with fewer clones binding to the NTD or to epitopes shared with the S proteins of the human betacoronaviruses OC43 and HKU1. > The latter cross-reactive B cell clones had higher levels of somatic hypermutation compared to those that only recognized SARS-CoV-2 S protein, suggesting a memory B cell origin. **Our studies demonstrate that SARS-CoV-2 mRNA-based vaccination of humans induces a persistent GC B cell response, enabling the generation of robust humoral immunity.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Infect Dis. 28JUN2021	**Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy children and adolescents: a double-blind, randomised, controlled, phase 1/2 clinical trial**	Han B., *et al.* China [gotopaper]	Vaccines	Safety, tolerability, and immunogenicity of a candidate COVID-19 vaccine, CoronaVac, containing inactivated SARS-CoV-2, in children and adolescents aged 3–17 years. NCT04551547. **Methods** > Double-blind, randomised, controlled, phase 1/2 clinical trial. Healthy children and adolescents aged 3–17 years old. > vaccine (in 0·5 mL aluminum hydroxide adjuvant) or aluminum hydroxide only (alum only, control). Two doses (day 0 and day 28). > Dose-escalation in two blocks (1·5 µg or 3·0 µg per injection). Primary safety endpoint: adverse reactions within 28 days after each injection in all participants who received at least one dose. Primary immunogenicity endpoint: seroconversion rate of neutralising antibody to live SARS-CoV-2 at 28 days after the second injection. **Findings** > 550 participants received at least one dose of vaccine or alum only (n=71 for phase 1 and n=479 for phase 2; safety population). > In the combined safety profile of phase 1 and phase 2, any adverse reactions within 28 days after injection occurred in 56 (26%) of 219 participants in the 1·5 µg group, 63 (29%) of 217 in the 3·0 µg group, and 27 (24%) of 114 in the alum-only group, without significant difference (p=0·55). > In phase 1, seroconversion of neutralising antibody after the second dose was observed in 27 of 27 participants (100·0% [95% CI 87·2–100·0]) in the 1·5 µg group and 26 of 26 participants (100·0% [86·8–100·0]) in the 3·0 µg group, with the geometric mean titres of 55·0 (95% CI 38·9–77·9) and 117·4 (87·8–157·0). > In phase 2, seroconversion was seen in 180 of 186 participants (96·8% [93·1–98·8]) in the 1·5 µg group and 180 of 180 participants (100·0% [98·0–100·0]) in the 3·0 µg group, with the geometric mean titres of 86·4 (73·9–101·0) and 142·2 (124·7–162·1). There were no detectable antibody responses in the alum-only groups. **Conclusion** CoronaVac was well tolerated and safe and induced humoral responses in children and adolescents aged 3–17 years. Neutralising antibody titres induced by the 3·0 µg dose were higher than those of the 1·5 µg dose. The results support the use of 3·0 µg dose with a two-immunisation schedule for further studies in this population.
Lancet 25JUN2021	**Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial**	Borobia A.M., *et al.* Spain [gotopaper]	Vaccines	**Aim**: to assess the immunogenicity and reactogenicity of BNT162b2 (Comirnaty, BioNTech, Mainz, Germany) administered as second dose in participants primed with ChAdOx1-S (Vaxzevria, AstraZeneca, Oxford, UK). **Methods:** Phase 2, open-label, randomised, controlled trial on adults aged 18–60 years, vaccinated with a single dose of ChAdOx1-S 8–12 weeks before screening, and no history of SARS-CoV-2 infection. The primary outcome was 14-day immunogenicity, measured by immunoassays for SARS-CoV-2 trimeric spike protein and receptor binding domain (RBD). Individuals were enrolled and randomly assigned to either the intervention group (n=450) or control group (n=226) at five university hospitals in Spain (mean age 44 years; 382 [57%] women and 294 [43%] men). **Findings:** > In the intervention group, geometric mean titres of RBD antibodies increased from 71·46 BAU/mL at baseline to 7756·68 BAU/mL at D 14 > IgG against trimeric spike protein increased from 98·40 BAU/mL to 3684·87 BAU/mL. > The interventional: control ratio was 77·69 for RBD protein and 36·41 for trimeric spike protein IgG. > Reactions were mild (n=1210 [68%]) or moderate (n=530 [30%]), with injection site pain (n=395 [88%]), induration (n=159 [35%]), headache (n=199 [44%]), and myalgia (n=194 [43%]) the most commonly reported adverse events. No serious adverse events were reported. **BNT162b2 given as a second dose in individuals prime vaccinated with ChAdOx1-S induced a robust immune response, with an acceptable and manageable reactogenicity profile.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
BMJ 24JUN2021	**Effect of the covid-19 pandemic in 2020 on life expectancy across populations in the USA and other high income countries: simulations of provisional mortality data**	Woolf S. H., *et al.* USA [gotopaper](#)	Public Health / Epidemiology	**Aim**: to estimate changes in life expectancy in 2010-18 and during 2020 Covid pandemic in 2020 across population groups in the United States and to compare outcomes with peer nations. **Findings** > Between 2010 and 2018, the gap in life expectancy between the US and the peer country average increased from 1.88 years (78.66 v 80.54 years, respectively) to 3.05 years (78.74 v 81.78 years) > Between 2018 and 2020, life expectancy in the US decreased by 1.87 years (to 76.87 years), 8.5 times the average decrease in peer countries (0.22 years), widening the gap to 4.69 years > Life expectancy in the US decreased disproportionately among racial and ethnic minority groups between 2018 and 2020, declining by 3.88, 3.25, and 1.36 years in Hispanic, non-Hispanic Black, and non-Hispanic White populations, respectively. > In Hispanic and non-Hispanic Black populations, reductions in life expectancy were average 18 and 15 times the average in peer countries, respectively. > Progress since 2010 in reducing the gap in life expectancy in the US between Black and White people was erased in 2018-20; life expectancy in Black men reached its lowest level since 1998 (67.73 years), and the longstanding Hispanic life expectancy advantage almost disappeared. **The US had a much larger decrease in life expectancy between 2018 and 2020 than other high income nations, with pronounced losses among the Hispanic and non-Hispanic Black populations. Health disadvantage, high death rates in 2020 and inequality of minority groups are likely the products of policy choices and systemic racism.**
Clin Infect Dis. 24JUN2021	**Neutralizing Monoclonal Antibody Treatment Reduces Hospitalization for Mild and Moderate COVID-19: A Real-World Experience**	Verderese J.P., *et al.* USA [gotopaper](#)	Therapeutics	**Aim**: to assess the impact of NmAb treatment given in the outpatient clinical practice setting on hospital utilization. - 707 confirmed COVID-19 patients received NmAb and 1709 historic COVID-19 controls were included; 553 (78%) received BAM, 154 (22%) received REGN-COV2. Post-index hospitalization rates were compared. **Findings:** > Patients receiving NmAb infusion had significantly lower hospitalization rate (5.8% vs. 11.4%), a shorter length of stay if hospitalized (mean 5.2 days vs. 7.4 days), and fewer ED visits within 30 days post-index (8.1% vs 12.3%) than controls. > Hospitalization-free survival was significantly longer in NmAb patients compared to controls. > There was a trend towards a lower hospitalization rate among patients who received NmAb within 2-4 days after symptom onset. > In multivariate analysis, having received a NmAb transfusion was independently associated with a lower risk of hospitalization after adjustment for age, sex, race, BMI and referral source: adjusted hazard ratio (95% CI) = 0.54 (0.38 – 0.79), p=0.0012. > Overall mortality was not different between the two groups. **NmAb treatment reduced hospital utilization especially when received within a few days of symptom onset.**
Clin Infect Dis. 24JUN2021	**Poor Antibody Response after Two Doses of SARS-CoV-2 vaccine in Transplant Recipients**	Mazzola A., *et al.* France [gotopaper](#)	Vaccines - Immunisation	**Assessment of vaccine immunogenicity and safety** 28 days after two doses of mRNA-vaccine BNT162b2 (Pfizer/BioNTech) in a cohort of **liver, kidney and heart transplant recipients** (SOT). > 143 patients and 25 HCWs included, 45% liver, 41.2 % kidney and 18.1% (n=26) heart transplant recipients. Median time from transplantation to the first BNT162b2 injection was 45.0 months > Seroconversion rate after the second dose was significantly lower among SOT recipients than among HCWs (28.6% vs. 100.0%, p<0.0001) > Positive anti-S1 IgG among all SOT-recipients with previous COVID19 > 4 patients developed severe COVID-19 between and after the two doses and one with negative anti-S1 > Vaccine response seems to be dramatically low in kidney and heart transplant-recipients (16.6% and 34.8%). Kidney transplantation and time from transplantation to the first vaccination <2 years were risk factors related to a negative serological response (OR: 4.01 and 2.87) **Poor humoral response to BNT162b2 in vaccine SOT-recipients, and defined kidney transplant-recipients, transplantation time and diabetes were risk factors for negative response to the vaccine**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Infect Dis. 23JUN2021	**Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort study**	Shrotri M., *et al.* UK [gotopaper](#)	Vaccines - Immunisation	**Aim**: to investigate the protective effect of the first dose of ChAdOx1 nCoV-19 and BNT162b2 in residents of long-term care facilities in terms of PCR-confirmed SARS-CoV-2 infection over time since vaccination. **Results** > 10 412 care home residents aged 65 years and older from 310 LTCFs were included. Median participant age was 86 years (IQR 80–91), 7247 (69·6%) of 10 412 residents were female, and 1155 residents (11·1%) had evidence of previous SARS-CoV-2 infection. 9160 (88·0%) residents received at least one vaccine dose, of whom 6138 (67·0%) received ChAdOx1 and 3022 (33·0%) received BNT162b2. > Between Dec 8, 2020, and March 15, 2021, there were 36 352 PCR results in 670 628 person-days, and 1335 PCR-positive infections (713 in unvaccinated residents and 612 in vaccinated residents) were included. > Adjusted hazard ratios (HRs) for PCR-positive infection relative to unvaccinated residents declined from 28 days after the first vaccine dose to 0·44 (95% CI 0·24–0·81) at 28–34 days and 0·38 (0·19–0·77) at 35–48 days. > Similar effect sizes were seen for ChAdOx1 (adjusted HR 0·32, 95% CI 0·15–0·66) and BNT162b2 (0·35, 0·17–0·71) vaccines at 35–48 days. > Mean PCR Ct values were higher for infections that occurred at least 28 days after vaccination than for those occurring before vaccination (31·3 [SD 8·7] in 107 PCR-positive tests vs 26·6 [6·6] in 552 PCR-positive tests; p<0·0001). **Single-dose vaccination with BNT162b2 and ChAdOx1 vaccines provides substantial protection against infection in older adults >65yo from 4–7 weeks after vaccination and might reduce SARS-CoV-2 transmission.**
Lancet Infect Dis. 23JUN2021	**Effectiveness of BNT162b2 and ChAdOx1 nCoV-19 COVID-19 vaccination at preventing hospitalisations in people aged at least 80 years: a test-negative, case-control study**	Hyams C., *et al.* UK [gotopaper](#)	Vaccines - Immunisation	**Aim**: to evaluate effectiveness of one dose of ChAdOx1 nCoV-19 and BNT162b2 COVID-19 vaccine in reducing COVID-19-related admissions to hospital in people > 80 yo. > Between Dec 18, 2020, and Feb 26, 2021, 466 adults were eligible (144 test-positive and 322 test-negative). > 18 (13%) of 135 people with SARS-CoV-2 infection and 90 (34%) of 269 controls received one dose of BNT162b2. > The adjusted vaccine effectiveness was 71·4% (95% CI 46·5–90·6). Nine (25%) of 36 people with COVID-19 infection and 53 (59%) of 90 controls received one dose of ChAdOx1 nCoV-19. The adjusted vaccine effectiveness was 80·4% (95% CI 36·4–94·5). When BNT162b2 effectiveness analysis was restricted to the period covered by ChAdOx1 nCoV-19, the estimate was 79·3% (95% CI 47·0–92·5). **One dose of either BNT162b2 or ChAdOx1 nCoV-19 resulted in substantial risk reductions of COVID-19-related hospitalisation in people aged > 80 years.**
Nature Med. 23JUN2021	**Long COVID in a prospective cohort of home-isolated patients**	Blomberg B., *et al.* Norway [gotopaper](#)	Public Health / Epidemiology	We conducted a long-term follow-up in a prospective cohort study of 312 patients—247 home-isolated and 65 hospitalized—comprising 82% of total cases in Bergen during the first pandemic wave in Norway. **Findings** > At 6 months, 61% (189/312) of all patients had persistent symptoms, which were independently associated with severity of initial illness, increased convalescent antibody titers and pre-existing chronic lung disease > We found that 52% (32/61) of home-isolated young adults, aged 16–30 years, had symptoms at 6 months, including loss of taste and/or smell (28%, 17/61), fatigue (21%, 13/61), dyspnea (13%, 8/61), impaired concentration (13%, 8/61) and memory problems (11%, 7/61) **Our findings that young, home-isolated adults with mild COVID-19 are at risk of long-lasting dyspnea and cognitive symptoms highlight the importance of infection control measures, such as vaccination**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 23JUN2021	**Protective efficacy of Ad26.COV2.S against SARS-CoV-2 B.1.351 in macaques**	Yu J., *et al.* USA [gotopaper](#)	Vaccines	Demonstration that Ad26.COV2.S elicits humoral and cellular immune responses that cross-react with the B.1.351 variant and protects against B.1.351 challenge in rhesus macaques. > Ad26.COV2.S induced **lower binding and neutralizing antibodies against B.1.351** as compared with WA1/2020 but elicited **CD8 and CD4 T cell responses that were comparable against WA1/2020, B.1.351, B.1.1.7, P.1, and CAL.20C** variants. > B.1.351 infection of sham control rhesus macaques resulted in higher levels of virus replication in bronchoalveolar lavage and nasal swabs than did WA1/2020 infection. > Ad26.COV2.S provided robust protection against both WA1/2020 and B.1.351, although we observed **higher levels of virus in vaccinated animals following B.1.351 challenge**. **These data demonstrate that Ad26.COV2.S provided robust protection against B.1.351 challenge in rhesus macaques.**
Science 22JUN2021	**Drug-induced phospholipidosis confounds drug repurposing for SARS-CoV-2**	Tummino T.A., *et al.* France / USA [gotopaper](#)	Therapeutics	Hypothesis that phospholipidosis was a shared mechanism underlying the antiviral activity of many repurposed drugs. Testing of 23 cationic amphiphilic drugs tested, including hydroxychloroquine, azithromycin, amiodarone, and four others already in clinical trials: > **Phospholipidosis was monotonically correlated with antiviral efficacy**. Conversely, drugs active against the same targets **that did not induce phospholipidosis were not antiviral**. > Phospholipidosis depends on the physicochemical properties of drugs, and **does not reflect specific target-based activities**, rather it may be considered a toxic confound in early drug discovery. Early detection of phospholipidosis could eliminate these artifacts, enabling a focus on molecules with therapeutic potential.
Lancet Infect Dis 22JUN21	**Risk of hospitalisation associated with infection with SARS-CoV-2 lineage B.1.1.7 in Denmark: an observational cohort study**	Bager P., *et al.* Denmark [gotopaper](#)	Public Health / Epidemiology	**Aim:** to assess the risk of hospitalisation associated with B.1.1.7 using individual-level data from national registers in Denmark **Methods:** Observational cohort study of all SARS-CoV-2-positive cases confirmed by RT-PCR, sampled between Jan 1 and March 24, 2021, with 14 days of follow-up for COVID-19 hospitalisation. Among all cases, COVID-19 hospitalisation was defined as first admission lasting longer than 12 h within 14 days of a sample with a positive RT-PCR result. **Findings:** > Between Jan 1 and March 24, 2021, 50 958 individuals with a positive SARS-CoV-2 test and at least 14 days of follow-up for hospitalisation were identified. > 30 572 individuals (60·0%) had genome data, of whom 10 544 (34·5%) were infected with B.1.1.7. 1944 (6·4%) individuals had a COVID-19 hospitalisation and of these, 571 (29·4%) had a B.1.1.7 infection and 1373 (70·6%) had an infection with other SARS-CoV-2 lineages. > Although the overall number of hospitalisations decreased during the study period, the proportion of individuals infected with B.1.1.7 increased from 3·5% to 92·1% per week. > B.1.1.7 was associated with a crude RR of hospital admission of 0·79 (95% CI 0·72–0·87; p<0·0001) and an adjusted RR of 1·42 (95% CI 1·25–1·60; p<0·0001). > The adjusted RR was increased in all strata of age and calendar period—the two covariates with the largest contribution to confounding of the crude RR. **Infection with SARS-CoV-2 lineage B.1.1.7 was associated with an increased risk of hospitalisation compared with that of other lineages in an analysis adjusted for covariates.**

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Lancet Infect Dis. 22JUN2021	**Mortality and critical care unit admission associated with the SARS-CoV-2 lineage B.1.1.7 in England: an observational cohort study**	Patone M., *et al.* UK [gotopaper](link)	Public Health / Epidemiology	**Aim:** to estimate the risk of critical care admission, mortality in patients who are critically ill, and overall mortality associated with lineage B.1.1.7 compared with non-B.1.1.7. Also, to compare clinical outcomes between the two groups. **Methods:** Observational cohort study, the authors linked large primary care (QResearch), national critical care (Intensive Care National Audit & Research Centre Case Mix Programme), and national COVID-19 testing (Public Health England) databases. SARS-CoV-2 positive samples with S-gene molecular diagnostic assay failure (SGTF) as a proxy for the presence of lineage B.1.1.7 were used. Two cohorts were extracted from the data: the primary care cohort, comprising patients in primary care with a positive community COVID-19 test and known SGTF status; and the critical care cohort, comprising patients admitted for critical care with a positive community COVID-19 test and known SGTF status. **Findings:** > The primary care cohort included 198 420 patients with SARS-CoV-2 infection. Of these, 117 926 (59·4%) had lineage B.1.1.7, 836 (0·4%) were admitted to CCU, and 899 (0·4%) died within 28 days. >The critical care cohort included 4272 patients admitted to CCU. Of these, 2685 (62·8%) had lineage B.1.1.7 and 662 (15·5%) died at the end of critical care. > In the primary care cohort, we estimated adjusted hazard ratios (HRs) of 2·15 (95% CI 1·75–2·65) for CCU admission and 1·65 (1·36–2·01) for 28-day mortality for patients with lineage B.1.1.7 compared with the non-B.1.1.7 group. > The adjusted HR for mortality in critical care, estimated with the critical care cohort, was 0·91 (0·76–1·09) for patients with lineage B.1.1.7 compared with those with non-B.1.1.7 infection. **Patients with lineage B.1.1.7 were at increased risk of CCU admission and 28-day mortality compared with patients with non-B.1.1.7 SARS-CoV-2. For patients receiving critical care, mortality appeared to be independent of virus strain.**
Science 22JUN2021	**Chimeric spike mRNA vaccines protect against Sarbecovirus challenge in mice**	Martinez, D.R, *et al.* USA [gotopaper](link)	Vaccines	The emergence of SARS-CoV in 2003 and SARS-CoV-2 in 2019 highlights the need to develop universal vaccination strategies against the broader *Sarbecovirus* subgenus. **Findings** > Chimeric spikes encoding NTD, RBD, and S2 domains into "bivalent" and "trivalent" vaccine immunogens -> protection against challenge from SARS-CoV, SARS-CoV-2, SARS-CoV-2 B.1.351, bat CoV (Bt-CoV) RsSHC014, and a heterologous Bt-CoV WIV-1 in vulnerable aged mice. > Chimeric spike mRNAs induced high levels of broadly protective neutralizing antibodies against high-risk Sarbecoviruses. > SARS-CoV-2 mRNA vaccination not only showed a marked reduction in neutralizing titers against heterologous Sarbecoviruses, but SARS-CoV and WIV-1 challenge in mice resulted in breakthrough infections. > Chimeric spike mRNA vaccines efficiently neutralized D614G, mink cluster five, and the UK B.1.1.7., and South African B.1.351 variants of concern. **Conclusions** > Multiplexed-chimeric spikes can prevent SARS-like zoonotic coronavirus infections with pandemic potential.

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Science Tansl Med. 22JUN2021	**Key epidemiological drivers and impact of interventions in the 2020 SARS-CoV-2 epidemic in England**	Knock E.S., *et al.* UK [gotopaper]	Public Health / Epidemiology	**Aim:** Propose a model of SARS-CoV-2 transmission to reproduce the first two waves of the epidemic in England and fit it using multiple surveillance data streams **Methods:** > Age-structured stochastic compartmental SEIR-like transmission model of SARS-CoV-2, representing care homes, hospital clinical pathways, and the wider community > Bayesian approach integrating multiple data streams to estimate model parameters and to reconstruct regional epidemics > Data of daily recorded deaths, PCR testing, hospital admissions, hospital bed occupancy, individual patient outcomes, contact surveys, and serological surveys > Examination of counterfactual epidemic scenarios, varying the date and duration of the first national lockdown and the effectiveness of restricting care home visits, to quantify the impact on mortality **Findings:** > Among the control measures implemented, only national lockdown brought the reproduction number below 1 consistently; if introduced one week earlier it could have reduced deaths in the first wave from an estimated 48,600 to 25,600 (95% credible interval [95%CrI]: 15,900–38,400) > The infection fatality ratio decreased from 1.00% (95%CrI: 0.85%–1.21%) to 0.79% (95%CrI: 0.63%–0.99%), suggesting improved clinical care > The infection fatality ratio was higher in the elderly residing in care homes (23.3%, 95%CrI: 14.7%–35.2%) than those residing in the community (7.9%, 95%CrI: 5.9%–10.3%) **Conclusions:** > The model integrates multiple data sources and provides a balanced overview of transmission, hospitalisation, and mortality patterns of SARS-CoV-2 in the first and second waves in England (up to 2nd December) > This study suggests that any vaccination campaign will need to achieve high coverage and a high degree of protection in vaccinated individuals to allow non-pharmaceutical interventions to be lifted without a resurgence of transmission
JAMA Pediatr. 21JUN2021	**Association Between Race and COVID-19 Outcomes Among 2.6 Million Children in England**	Saatci D., et al. UK [gotopaper]	Public Health / Epidemiology	**Aim**: to investigate the association between race and childhood COVID-19 testing and hospital outcomes. Primary outcome: hospital admission with confirmed COVID-19. Secondary outcomes: SARS-CoV-2–positive test result and any hospital attendance with confirmed COVID-19 and intensive care admission. **Results** > Of 2 576 353 children (mean [SD] age, 9.23 [5.24] years; 48.8% female), 410 726 (15.9%) were tested for SARS-CoV-2 and 26 322 (6.4%) tested positive. > A total of 1853 children (0.07%) with confirmed COVID-19 attended hospital, 343 (0.01%) were admitted to the hospital, and 73 (0.002%) required intensive care. > Testing varied across race. White children had the highest proportion of SARS-CoV-2 tests (223 701/1 311 041 [17.1%]), whereas Asian children (33 213/243 545 [13.6%]), Black children (7727/93 620 [8.3%]), and children of mixed or other races (18 971/147 529 [12.9%]) had lower proportions. > Compared with White children, Asian children were more likely to have COVID-19 hospital admissions (adjusted odds ratio [OR], 1.62; 95% CI, 1.12-2.36), whereas Black children (adjusted OR, 1.44; 95% CI, 0.90-2.31) and children of mixed or other races (adjusted OR, 1.40; 95% CI, 0.93-2.10) had comparable hospital admissions. > Asian children were more likely to be admitted to intensive care (adjusted OR, 2.11; 95% CI, 1.07-4.14), and Black children (adjusted OR, 2.31; 95% CI, 1.08-4.94) and children of mixed or other races (adjusted OR, 2.14; 95% CI, 1.25-3.65) had longer hospital admissions (≥36 hours). In this large population-based study, **several race-specific disparities were observed in severe COVID-19 outcomes**. However, **ascertainment bias and residual confounding should be considered** before drawing conclusions.

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Nature 21JUN2021	**In vivo monoclonal antibody efficacy against SARS-CoV-2 variant strains**	Chen, R.E., *et al.* USA gotopaper	Therapeutics	Rapidly-emerging variants jeopardize antibody-based countermeasures against SARS-CoV-. While cell culture experiments have demonstrated loss of potency of several anti-spike neutralizing antibodies against SARS-CoV-2 variant strains, the in vivo significance of theseresults remains uncertain. **Methods** > Panel of infectious SARS-CoV-2 strains including B.1.1.7, B.1.429, B.1.617.1 and B.1.526 isolates, as well as a SARS-CoV-2 strain with a D614G substitution, a N501Y and D614G substitutions and chimeric SARS-CoV-2 strains > Panel of (mAbs) corresponding to many in advanced clinical development: 2B04/47D11 (AbbVie), S309/S2E12 (Vir Biotechnology), COV2-2130/COV2-2196 (Vanderbilt University Medical Center with derivatives being evaluated by AstraZeneca), REGN10933/REGN10987 (synthesized based on casirivimab and imdevimab sequences from Regeneron), and LY-CoV555 (synthesized based on bamlanivimab sequences from Lilly) **Findings** > All individual mAbs efficiently neutralized chimeric SARS-CoV-2 strains, and B.1.1.7 strains, and several mAbs. Several mAbs (COV2-2130, COV2-2196, S309, S2E12, and 47D11) B.1.429, and B.1.526 strains > Impact of SARS-CoV-2 spike variation on antibody neutralization: REGN10987 or LY-CoV555 respectively show a 10-fold or complete loss in inhibitory activity against the B.1.429 and B.1.617.1 > Some individual mAbs showed reduced or abrogated neutralizing activity in cell culture against B.1.351, B.1.1.28, B.1.617.1, and B.1.526 viruses with E484 spike protein mutations, low prophylactic doses of mAb combinations protected against infection by many variants in K18-hACE2 transgenic mice, 129S2 immunocompetent mice, and hamsters without emergence of resistance. Exceptions were mAb LY-CoV555 and LY-CoV555/LY-CoV016 mono- and combination therapy, which lost all protective activity, and AbbVie 2B04/47D11, which showed partial loss of activity. > Higher doses of several mAb cocktails protected in vivo against viruses with a B.1.351 spike gene. **Conclusion** Many but not all combination therapies with neutralizing mAbs should retain efficacy against emerging SARS-CoV-2 variant
Cell 18JUN2021	**In vitro and in vivo functions of SARS-CoV-2 infection-enhancing and neutralizing antibodies**	Li D., et al. USA gotopaper	Immunology	A concern regarding SARS-CoV-2 antibodies is whether they mediate disease enhancement. Here, we isolated neutralising antibodies (Nabs) against the receptor-binding domain (RBD) and the N-terminal domain (NTD) of SARS-CoV-2 spike from individuals with acute or convalescent SARS-CoV-2 or a history of SARS-CoV infection. > Cryo-electron microscopy of RBD and NTD antibodies demonstrated function-specific modes of binding. **Neutralizing or infection-enhancing NTD antibodies bound distinct epitopes**. > **RBD or NTD antibodies exhibited infection enhancement in vitro**: select RBD NAbs demonstrated Fc receptor-γ (FcγR)-mediated enhancement of virus infection in vitro, while 5 non-neutralizing NTD antibodies mediated FcγR-independent in vitro infection enhancement. > However, **both types of infection-enhancing antibodies protected from SARS-CoV-2 replication in monkeys and mice**. 3 of 46 monkeys infused with enhancing antibodies had higher lung inflammation scores compared to controls. One monkey had alveolar edema and elevated bronchoalveolar lavage inflammatory cytokines. Cross-reactive RBD neutralizing antibodies were protective--most potent, DH1047. Thus, while **in vitro antibody-enhanced infection does not necessarily herald enhanced infection in vivo, increased lung inflammation can rarely occur in** SARS-CoV-2 antibody-infused macaques.

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Lancet HIV 18JUN2021	**Safety and immunogenicity of the ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 in HIV infection: a single-arm substudy of a phase 2/3 clinical trial**	Frater J., *et al.* UK [gotopaper](#)	Vaccines - Immunisation	**Methods** > Single-arm open-label vaccination substudy within the protocol of the larger phase 2/3 trial COV002 Adults aged 18–55 years with HIV on antiretroviral therapy (ART), with undetectable plasma HIV viral loads were enrolled >Prime-boost regimen of ChAdOx1 nCoV-19, with two doses was 4–6 weeks apart. Primary outcomes safety and reactogenicity of the vaccine. Outcomes were compared with an HIV-uninfected group from the main COV002 study within the same age group **Findings** > 54 participants with HIV (all male, median age 42·5 years [IQR 37·2–49·8]) enrolled, receiving two doses of ChAdOx1 nCoV-19. > Median CD4 count at enrolment: 694·0 cells/µL (IQR 573·5–859·5). > No serious adverse events occurred. Local and systemic reactions occurring during the first 7 days after prime vaccination included pain at the injection site (26 [49%] of 53 participants with available data), fatigue (25 [47%]), headache (25 [47%]), malaise (18 [34%]), chills (12 [23%]), muscle ache (19 [36%]), joint pain (five [9%]), and nausea (four [8%]), the frequencies of which were similar to the HIV-negative participants. > Anti-spike IgG responses by ELISA peaked at day 42 (median 1440 ELISA units [EUs; IQR 704–2728]; n=50) and were sustained until day 56 (median 941 EUs [531–1445]; n=49). No correlation between the magnitude of the anti-spike IgG response at day 56 and CD4 cell count (p=0·93) or age (p=0·48). > ELISpot and T-cell proliferative responses peaked at day 14 and 28 after prime dose and were sustained to day 56. > Compared with participants without HIV no difference in magnitude or persistence of SARS-CoV-2 spike-specific humoral or cellular responses (p>0·05 for all analyses). **Conclusions** In this study, ChAdOx1 nCoV-19 was safe and immunogenic in people with HIV, supporting vaccination for those well controlled on ART.
JAMA Oncol. 17JUN2021	**Association of Convalescent Plasma Therapy With Survival in Patients With Hematologic Cancers and COVID-19**	Thompson M. A., *et al.* USA [gotopaper](#)	Therapeutics	Is convalescent plasma therapy associated with improved outcomes of hospitalized patients with COVID-19 and hematologic cancer? **Findings** > In this cohort study of 966 patients with hematologic cancer and COVID-19, after adjustment for potential confounding factors, convalescent plasma treatment was associated with a significantly improved 30-day mortality in the 143 individuals who received it > This association remained significant after propensity score matching **These findings suggest a potential survival benefit in the administration of convalescent plasma to patients with hematologic cancers and COVID-19.**
Nature Commun. 17JUN2021	**Multianalyte serology in home-sampled blood enables an unbiased assessment of the immune response against SARS-CoV-2**	Roxhed N., *et al.* Sweden [gotopaper](#)	Diagnostics	We establish a multianalyte and multiplexed approach to reliably profile IgG and IgM levels against several versions of SARS-CoV-2 proteins (S, RBD, N) in home-sampled driedblood spots (DBS) **Findings** > We analyse DBS collected during spring of 2020 from 878 random and undiagnosed individuals from the population in Stockholm, Sweden, and use classification approaches to estimate an accumulated seroprevalence of 12.5% (95% CI: 10.3%–14.7%). > This includes 5.4% of the samples being IgG+ IgM+ against several SARS-CoV-2 proteins, as well as 2.1% being IgG– IgM+ and 5.0% being IgG+IgM–for the virus'S protein. > Subjects classified as IgG+ for several SARS-CoV-2 proteins report influenza-like symptoms more frequently than those being IgG+ for only the S protein (OR=6.1;p< 0.001) > Among all seropositive cases, 30% are asymptomatic. **Our strategy enables an accurate individual-level and multiplexed assessment of antibodies in home-sampled blood, assisting our under-standing about the undiagnosed seroprevalence and diversity of the immune response against the coronavirus.**

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Clin Infect Dis. 17JUN2021	**Post-vaccination SARS-CoV-2 infections and incidence of presumptive B.1.427/B.1.429 variant among healthcare personnel at a northern California academic medical center**	Jacobson K. B., *et al.* USA gotopaper	Vaccines - Variants	**Aim:** to compare the mutation prevalence among unvaccinated, early post-vaccinated (<=14 days after dose 1), partially vaccinated (positive test >14 days after dose 1 and ≤14 days after dose 2) and fully vaccinated (>14 days after dose 2) post-vaccine SARS-CoV-2 cases (PVSCs). **Methods:** > **D**emographic and clinical information from PVSCs, defined as health care personnel (HCP) with positive SARS-CoV-2 NAAT after receiving ≥1 vaccine dose. Available specimens were tested for L452R, N501Y and E484K mutations by RT-PCR. **Findings:** > From December 2020-April 2021, ≥23,090 HCPS received at least1 dose of an mRNA-based SARS-CoV-2 vaccine, and 660 HCP cases of SARS-CoV-2 occurred of which 189 were PVSCs. > Among the PVSCs, 114 (60.3%), 49 (25.9%) and 26 (13.8%) were early post-vaccination, partially vaccinated, and fully vaccinated, respectively. > Of 261 available samples from vaccinated and unvaccinated HCP, 103 (39.5%), including 42 PVSCs (36.5%), had L452R mutation presumed to be B.1.427/B.1.429,. >When adjusted for community prevalence of B.1.427/B.1.429, PVSCs did not have significantly elevated risk for infection with B.1.427/B.1.429 compared with unvaccinated HCP. **Most PVSCs occurred prior to expected onset of full, vaccine-derived immunity. Presumptive B.1.427/B.1.429 was not more prevalent in post-vaccine cases than in unvaccinated SARS-CoV-2 HCP.**
Cell 17JUN2021	**Reduced neutralization of SARS-CoV-2 B.1.617 by vaccine and convalescent serum**	Liu C., *et al.* UK gotopaper	Variants	Here we study the ability of monoclonal antibodies, convalescent and vaccine sera to neutralize B.1.617.1 and B.1.617.2 and complement this with structural analyses of Fab/RBD complexes and map the antigenic space of current variants. **Findings** > Neutralization of both viruses is reduced when compared with ancestral Wuhan related strains but there is no evidence of widespread antibody escape as seen with B.1.351 > However, B.1.351 and P.1 sera showed markedly more reduction in neutralization of B.1.617.2 suggesting that individuals previously infected by these variant may be more susceptible to reinfection by B.617.2. **This observation provides important new insight for immunisation policy with future variant vaccines in non-immune populations.**
Clin Infect Dis. 16JUN2021	**Humoral and cellular immune responses against SARS-CoV-2 variants and human coronaviruses after single BNT162b2 vaccination**	Stankov M. V., *et al.* UK gotopaper	Immunology	**Aim:** to assess humoral and T cell responses against SARS-CoV-2 WT, variants of concern (VOC) and endemic human coronaviruses (hCoV) that were induced after single and double vaccination with BNT162b2 were analysed. **Methods:** Anti-SARS-CoV-2 S IgG and IgA levels were determined in individuals early (mean 8.7 days, range 2 to 14 days) and late (mean 20.6 days, range 17-27 days) after immunization with a single 30 µg dose of BNT162b2 (n=124) **Findings:** > Despite readily detectable IgG against the receptor-binding domain (RBD) of the SARS-CoV-2 S protein at day 14 after a single vaccination, inhibition of SARS-CoV-2 S-driven host cell entry was weak and particularly low for the B.1.351 variant. > Frequencies of SARS-CoV-2 WT and VOC specific T cells were low in many vaccinees after application of a single dose and influenced by immunity against endemic hCoV. > The second vaccination significantly boosted T cell frequencies reactive for WT, B.1.1.7 and B.1.351 variants. **These results call into question whether neutralizing antibodies significantly contribute to protection against COVID-19 upon single vaccination and suggest that cellular immunity is central for the early defenses against COVID-19.**

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NEJM 16JUN2021	**Tofacitinib in Patients Hospitalized with Covid-19 Pneumonia**	Guimarães P.O., *et al.* Brazil [gotopaper]	Therapeutics	**Aim**: to evaluate efficacy and safety of tofacitinib, a Janus kinase inhibitor, in patients who are hospitalized with Covid-19 pneumonia. <u>Regimens:</u> 10 mg tofacitinib or placebo twice daily for up to 14 days or until hospital discharge. <u>Primary outcome:</u> occurrence of death or respiratory failure through day 28 (assessment with 8-level ordinal scale. All-cause mortality and safety were also assessed. **Results** > A total of 289 patients underwent randomization at 15 sites in Brazil. Overall, 89.3% of the patients received glucocorticoids during hospitalization. > The cumulative incidence of death or respiratory failure through day 28 was 18.1% in the tofacitinib group and 29.0% in the placebo group (risk ratio, 0.63; 95%CI, 0.41-0.97; P=0.04). > Death from any cause through day 28 occurred in 2.8% of the patients in the tofacitinib group and in 5.5% of those in the placebo group (hazard ratio, 0.49; 95% CI, 0.15-1.63). > The proportional odds of having a worse score on the 8-level ordinal scale with tofacitinib, as compared with placebo, was 0.60 (95% CI, 0.36-1.00) at day 14 and 0.54 (95% CI, 0.27-1.06) at day 28. > Serious adverse events occurred in 20 patients (14.1%) in the tofacitinib group and in 17 (12.0%) in the placebo group. **Among patients hospitalized with Covid-19 pneumonia, tofacitinib led to a lower risk of death or respiratory failure through day 28 than placebo**.
Nature Commun 16JUN2021	**Modeling the effectiveness of olfactory testing to limit SARS-CoV-2 transmission**	Larremore D.B., *et al.* USA [gotopaper]	Diagnostics	**Aim:** Analyzing how screening for olfactory dysfunction could impact COVID-19 spread depending on the prevalence of olfactory dysfunction among infected individuals, its duration, the timing of onset, and the frequency of testing **Methods:** > Olfactory dysfunction is a symptom identified in 76–83% of SARS-CoV-2 infections, including those with no other symptoms, when a standardized olfaction test is used > Simulations using a stochastic SIR model with susceptible, infected, recovered, isolated and self-isolated compartments > Individual viral loads were simulated for each infection based on key features of latency, proliferation, peak, and clearance identified in the literature > Individuals who scored positive for olfactory dysfunction are tested by RT-PCR and isolated if positive > 35% of individuals are assumed to have viral load trajectories with prolonged clearance times and self isolate within 0–2 days of peak viral load > 80% of the population is assumed to participate in the screening protocol, with olfactory testing either daily, every third day, or weekly **Findings:** > Screening for olfactory dysfunction daily or every third day limits viral spread in simulations, provided symptom prevalence was larger than 50% > When symptom prevalence is 75% or higher, olfactory screening every third day has comparable effectiveness than weekly RT-PCR or antigen testing > Estimating the reproductive number R shows that daily, or every 3 days, olfactory testing is sufficient to keep viral infections from developing into an outbreak, provided that olfactory dysfunction typically occurs within 2 days of positivity by RT-PCR > Cost estimates were performed and show a reduction of cost by a factor of 16 to 31 **Conclusions:** > The study suggests that screening for olfactory dysfunction could be a high impact and cost-effective method for broad COVID-19 screening and surveillance > It can be also useful as a point-of-entry screening tool, such as screening of airline passengers

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BMJ 15JUN2021	**Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: cohort analysis**	Nyberg T., *et al.* UK [gotopaper](#)	Public Health / Epidemiology - Variants	Retrospective cohort analysis to evaluate the relation between diagnosis of covid-19 with SARS-CoV-2 variant B.1.1.7 and the risk of hospital admission compared with diagnosis with wild-type SARS-CoV-2 variants. Participants: 839 278 patients with laboratory confirmed covid-19, of whom 36 233 had been admitted to hospital within 14 days, tested between 23 Nov 2020 and 31 Jan 2021 and assessed for S-gene target failure (SGTF), a proxy test for the B.1.1.7 variant. Patient data were stratified by age, sex, ethnicity, deprivation, region of residence, and date of positive test. Main outcome: hospital admission 1-14 days after the first positive SARS-CoV-2 test. **Results** > 27 710 (4.7%) of 592 409 patients with SGTF variants and 8523 (3.5%) of 246 869 patients without SGTF variants had been admitted to hospital within 1-14 days. The stratum adjusted **hazard ratio of hospital admission was 1.52** (95%CI, 1.47-1.57) for patients with covid-19 infected with SGTF variants, compared with those infected with non-SGTF variants. > The **effect was modified by age** (P<0.001), with hazard ratios of 0.93-1.21 in patients younger than 20 years with versus without SGTF variants, 1.29 in those aged 20-29, and 1.45-1.65 in those aged ≥30 years. > The adjusted absolute risk of hospital admission within 14 days was 4.7% (95%CI, 4.6%-4.7%) for patients with SGTF variants and 3.5% (3.4% to 3.5%) for those with non-SGTF variants. **Risk of hospital admission is higher for people infected with the B.1.1.7 variant compared with wild-type SARS-CoV-2, likely reflecting a more severe disease. The higher severity may be specific to adults older than 30 years.**
Ann Intern Med. 15JUN21	**Safety and Immunogenicity of a Third Dose of SARS-CoV-2 Vaccine in Solid Organ Transplant Recipients: A Case Series**	Werbel W.A., *et al.* USA [gotopaper](#)	Vaccines - Immunisation	Description of antibody responses and vaccine reactions in recipients of solid organ transplants who had a suboptimal response to standard vaccination and subsequently received a third dose of vaccine between 20 March 2021 and 10 May 2021. **Findings** > Thirty patients (median age 57 years, 17 women, and 1 non-White. None of the patients were exposed to SARS CoV 2. In 25 patients, maintenance immunosuppression included tacrolimus or cyclosporine plus mycophenolate. In addition, corticosteroids were used for 24 patients, sirolimus for 1, and belatacept for 1. The median time between transplantation and initial vaccination was 4.5 years. During the initial vaccination, 57% of the 30 patients received 2 doses of the 162b2 vaccine (Pfizer/BioNTech), and 43% received 2 doses of the mRNA-1273 vaccine (Moderna). > Before 3rd dose 24 patients had negative antibody titers, and 6 patients had low-positive antibody titers > Patients received the third dose of vaccine a median of 67 days (IQR, 54 to 81 days) after the second dose of their initial vaccine series; 15 patients received the Ad26.COV2.S vaccine (Johnson & Johnson/Janssen), 9 received the mRNA-1273 vaccine (Moderna), and 6 received the 162b2 vaccine (Pfizer/BioNTech). > Of the 6 patients with low-positive antibody titers before the third dose, all had high-positive antibody titers after the third dose. > Of the 24 patients with negative antibody titers before the third dose, only 6 (25%) had high-positive antibody titers after the third dose. Two (8%) had low-positive antibody titers, and 16 (67%) remained negative. >Safety: Fifteen patients reported mild or moderate local reactions, and 1 reported severe arm pain **Conclusions** These observations support the use of clinical trials to determine whether booster doses to prevent COVID-19 in transplant patients can be incorporated into clinical practice.

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Science Immunol. 15JUN21	**Impaired humoral immunity to SARS-CoV-2 BNT162b2 vaccine in kidney transplant recipients and dialysis patients**	Rincon-Arevalo H., *et al.* International [gotopaper](#)	Vaccines - Immunisation	It is not known how well mRNA vaccines induce B and plasma cell responses in dialysis patients (DP) or kidney transplant recipients (KTR) compared to healthy controls (HC) > Study of humoral and B cell responses of 35 HC, 44 DP and 40 KTR. **Findings** **>** Markedly impaired anti-BNT162b2 responses among KTR and DP compared to HC. > In DP, the response was delayed (3-4 weeks after boost) and reduced with anti-S1 IgG and IgA positivity in 70.5% and 68.2%, respectively. >KTR did not develop IgG responses except one patient who had a prior unrecognized infection and developed anti-S1 IgG. >The majority of antigen-specific B cells (RBD+) were identified in the plasmablast or post-switch memory B cell compartments in HC, whereas RBD+ B cells were enriched among pre-switch and naïve B cells from DP and KTR. >The frequency and absolute number of antigen-specific circulating plasmablasts in the cohort correlated with the Ig response, a characteristic not reported for other vaccinations. **Conclusions** **I**mmunosuppression resulted in impaired protective immunity after mRNA vaccination, including Ig induction with corresponding generation of plasmablasts and memory B cells.
Nature Commun. 15JUN2021	**Molecular benchmarks of a SARS-CoV-2 epidemic**	Jonsson H., *et al.* Iceland [gotopaper](#)	Public Health / Epidemiology	Assessing epidemic control with molecular information during a well characterized epidemic in Iceland. **Findings** > We demonstrate how the viral concentration decreased in those newly diagnosed as the epidemic transitioned from exponential growth phase to containment phase. > The viral concentration in the cases identified in population screening decreased faster than in those symptomatic and considered at high risk and that were targeted by the healthcare system. > The viral concentration persists in recovering individuals as we found that half of the cases are still positive after two weeks > We demonstrate that accumulation of mutations in SARS-CoV-2 genome can be exploited to track the rate of new viral generations throughout the different phases of the epidemic, where the accumulation of mutations decreases as the transmission rate decreases in the containment phase **Overall, the molecular signatures of SARS-CoV-2 infections contain valuable epidemiological information that can be used to assess the effectiveness of containment measures.**
Nature 14JUN2021	**Naturally enhanced neutralizing breadth against SARS-CoV-2 one year after infection**	Wang Z., *et al.* USA [gotopaper](#)	Immunology	Report on immunological status of a cohort of 63 COVID-19-convalescent individuals assessed at 1.3, 6.2 and 12 months after infection, 41% of whom also received mRNA vaccines. > In the absence of vaccination antibody reactivity to the receptor binding domain (RBD) of SARS-CoV-2, neutralizing activity and the number of RBD-specific memory B cells remain **relatively stable from 6 to 12 months**. > **Vaccination increases all components of the humoral response**, and as expected, results in serum **neutralizing activities against variants of concern that are comparable to or greater than neutralizing activity against the original Wuhan Hu-1** achieved by vaccination of naive individuals. > The mechanism underlying these broad-based responses involves **ongoing antibody somatic mutation, memory B cell clonal turnover, and development of monoclonal antibodies** that are exceptionally resistant to SARS-CoV-2 RBD mutations, including those found in variants of concern. > B cell clones expressing broad and potent antibodies are selectively **retained in the repertoire over time and expand dramatically after vaccination**. The data suggest that immunity in convalescent individuals will be very long lasting and that convalescent individuals who receive available mRNA vaccines will produce antibodies and memory B cells that should be protective against circulating SARS-CoV-2 variants.

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JAMA Neurol. 11JUN2021	**Association Between SARS-CoV-2 Infection and Immune-Mediated Myopathy in Patients Who Have Died**	Aschman T., *et al.* Germany [gotopaper](#)	Clinics	**Aim:** To study skeletal muscle and myocardial inflammation in patients with COVID-19 who had died. **Methods** Case-control autopsy series were conducted in a university hospital as a multidisciplinary postmortem investigation. Patients with COVID-19 or other critical illnesses who had died between March 2020 and February 2021 and on whom an autopsy was performed were included. **Findings** > Skeletal muscle samples from the patients who died with COVID-19 showed a higher overall pathology score (mean [SD], 3.4 [1.8] vs 1.5 [1.0]) and a higher inflammation score (mean [SD], 3.5 [2.1] vs 1.0 [0.6]) > Relevant expression of MHC class I antigens on the sarcolemma was present in 23 of 42 specimens from patients with COVID-19 (55%) and upregulation of MHC class II antigens in 7 of 42 specimens from patients with COVID-19 (17%), but neither were found in any of the controls. > Increased numbers of NK cells (median [interquartile range], 8 [8] vs 3 [4] cells per 10 high-power fields, 1-10 cells per 10 high-power fields) were found. > Skeletal muscles showed more inflammatory features than cardiac muscles, and inflammation was most pronounced in patients with COVID-19 with chronic courses. > In some muscle specimens, SARS-CoV-2 RNA was detected by reverse transcription–polymerase chain reaction, but no evidence for a direct viral infection of myofibers was found by immunohistochemistry and electron microscopy. **Most individuals with severe COVID-19 showed signs of myositis ranging from mild to severe. Inflammation of skeletal muscles was associated with the duration of illness and was more pronounced than cardiac inflammation. SARS-CoV-2 may be associated with a postinfectious, immune-mediated myopathy.**
JAMA Pediatrics 11JUN2021	**Comparison of Symptoms and RNA Levels in Children and Adults With SARS-CoV-2 Infection in the Community Setting**	Chung E., *et al.* USA [gotopaper](#)	Virology	**Aim**: to characterize symptoms of pediatric COVID-19 in the community and analyze the association between symptoms and SARS-CoV-2 RNA levels, as approximated by cycle threshold (Ct) values, in children and adults. <u>Sample</u>: population-based convenience sample of children <18 years and adults in Washington, who enrolled for home self-collection of upper respiratory samples for SARS-CoV-2 testing, Mar-Nov 2020. <u>Main Outcomes</u>: RT-PCR–confirmed SARS-CoV-2 infection, with Ct values stratified by age and symptoms. **Results** > Among 555 SARS-CoV-2–positive participants (mean [SD] age, 33.7 [20.1] years; 320 were female [57.7%]), 47 of 123 children (38.2%) were asymptomatic compared with 31 of 432 adults (7.2%). > When symptomatic, fewer symptoms were reported in children compared with adults (mean [SD], 1.6 [2.0] vs 4.5 [3.1]). > Symptomatic individuals had lower Ct values (higher viral RNA levels) than asymptomatic individuals (adjusted estimate for children, −3.0; 95% CI, −5.5 to −0.6; P = .02; adjusted estimate for adults, −2.9; 95% CI, −5.2 to −0.6; P = .01). > The difference in mean Ct values was neither statistically significant between symptomatic children and symptomatic adults (adjusted estimate, −0.7; 95% CI, −2.2 to 0.9; P = .41) nor between asymptomatic children and asymptomatic adults (adjusted estimate, −0.6; 95% CI, −4.0 to 2.8; P = .74). **SARS-CoV-2 RNA levels were significantly higher in symptomatic individuals than in asymptomatic individuals and no significant age-related differences were found.**

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JAMA Netw Open 11JUN2021	**Trends in Venous Thromboembolism Anticoagulation in Patients Hospitalized With COVID-19**	Vaughn V. M., *et al.* USA gotopaper	Clinics	To characterize frequency, variation across hospitals, and change over time in VTE prophylaxis and treatment-dose anticoagulation in patients hospitalized for COVID-19, as well as the association of anticoagulation strategies with in-hospital and 60-day mortality. **Methods** > This cohort study of adults hospitalized with COVID-19 used a pseudorandom sample from 30 US hospitals in the state of Michigan participating in a collaborative quality initiative > Data analyzed were from patients hospitalized between March 7, 2020, and June 17, 2020. Data were analyzed through March 2021 **Findings** > Of a total 1351 patients with COVID-19 included, only 18 (1.3%) had a confirmed VTE, and 219 (16.2%) received treatment-dose anticoagulation > Use of treatment-dose anticoagulation without imaging ranged from 0% to 29% across hospitals and increased over time > Of 1127 patients who ever received anticoagulation, 392 (34.8%) missed 2 or more days of prophylaxis. Missed prophylaxis varied from 11% to 61% across hospitals and decreased markedly over time (aOR, 0.89; 95% CI, 0.82-0.97 per week). > VTE nonadherence was associated with higher 60-day but not in-hospital mortality. Receiving any dose of anticoagulation (vs no anticoagulation) was associated with lower in-hospital mortality (only prophylactic dose: aHR, 0.36; 95% CI, 0.26-0.52; any treatment dose: aHR, 0.38; 95% CI, 0.25-0.58) > However, only the prophylactic dose of anticoagulation remained associated with lower mortality at 60 days (prophylactic dose: aHR, 0.71; 95% CI, 0.51-0.90; treatment dose: aHR, 0.92; 95% CI, 0.63-1.35). **This large, multicenter cohort of patients hospitalized with COVID-19, found evidence of rapid dissemination and implementation of anticoagulation strategies, including use of treatment-dose anticoagulation. As only prophylactic-dose anticoagulation was associated with lower 60-day mortality, prophylactic dosing strategies may be optimal for patients hospitalized with COVID-19.**
Lancet Child Adolesc Health 10JUN2021	**Clinical characteristics and risk factors for death among hospitalised children and adolescents with COVID-19 in Brazil: an analysis of a nationwide database**	Oliveira E.A.., *et al.* Brazil gotopaper	Clinics	**Aim:** to characterise the clinical features of children and adolescents hospitalised with laboratory-confirmed SARS-CoV-2 infection and to evaluate risk factors for COVID-19-related death in this population. **Methods** Analysis of all patients <20 years who had qRT-PCR-confirmed COVID-19 and were registered in a nationwide surveillance database of patients admitted to hospital with severe acute respiratory disease in Brazil (SIVEP-Gripe). Primary outcome: time to recovery (discharge) or in-hospital death, evaluated by competing risks analysis (cumulative incidence function). **Findings** > Of the 82 055 patients younger than 20 years reported to SIVEP-Gripe during the study period, 11 613 (14·2%) had available data > Among these patients, 886 (7·6%) died in hospital (median 6 days [IQR 3–15] after hospital admission), 10 041 (86·5%) patients were discharged from the hospital, 369 (3·2%) were in hospital at the time of analysis, and 317 (2·7%) were missing information on outcome. > **The estimated probability of death was 4·8% during the first 10 days after hospital admission, 6·7% during the first 20 days, and 8·1% at the end of follow-up**. > The competing risks multivariate survival analysis showed that risk of death was increased in infants <2 years (hazard ratio 2·36) or adolescents aged 12–19 years (2·23) relative to children aged 2–11 years; those of Indigenous ethnicity (3·36) relative to those of White ethnicity **Death from COVID-19 was associated with age, Indigenous ethnicity, poor geopolitical region, and pre-existing medical conditions. Disparities in health care, poverty, and comorbidities can contribute to magnifying the burden of COVID-19 in more vulnerable and socioeconomically disadvantaged children and adolescents in Brazil.**

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Blood 10JUN2021	**Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with chronic lymphocytic leukemia**	Herishanu Y., *et al.* International gotopaper	Vaccines - Immunisation	Evaluation of humoral immune responses to the BNT162b2 COVID-19 vaccine in patients with chronic lymphocytic leukemia (CLL), compared with age-matched healthy control subjects. **Methods** > Patients received 2 vaccine doses, 21 days apart > Antibody titers were measured by using the Elecsys Anti-SARS-CoV-2 S assay after administration of the second dose. **Findings** > 167 patients with CLL: antibody response rate- 39.5%. > Comparison between 52 patients with CLL and 52 sex- and aged-matched healthy control subjects revealed a significantly reduced response rate among patients (52% vs 100%, respectively; adjusted odds ratio, 0.010; 95% confidence interval, 0.001-0.162; P < .001). > The response rate was highest in patients who obtained clinical remission after treatment (79.2%), followed by 55.2% in treatment-naive patients and 16.0% in patients under treatment at the time of vaccination. > Patients treated with either Bruton's tyrosine kinase inhibitors or venetoclax ± anti-CD20 antibody, response rates were considerably low (16.0% and 13.6%). > None of the patients exposed to anti-CD20 antibodies <12 months before vaccination responded. > In a multivariate analysis, independent predictors of response were younger age, female sex, lack of currently active treatment, IgG levels ≥550 mg/dL, and immunoglobulin M levels ≥40 mg/dL. **Conclusions** Antibody-mediated response to the BNT162b2 mRNA COVID-19 vaccine in patients with CLL is markedly impaired and affected by disease activity and treatment.
Nature Med. 10JUN2021	**Community-level evidence for SARS-CoV-2 vaccine protection of unvaccinated individuals**	Milman O., *et al.* Israel gotopaper	Vaccines - Immunisation	**Aim:** to analyse whether and to what extent the fraction of patients vaccinated in each community affects the risk of infection in an unvaccinated cohort of individuals <16 years old in same community. **Methods** Analysis on the vaccination rates and test results of 177 distinct communities with a presumed low rate of natural immunization as inferred by a low fraction of individuals infected with SARS-CoV-2. The vaccination dates and test results were retrieved of members of Maccabi Healthcare Services (MHS), Israel's second largest healthcare maintenance organization (Dec 2020-Mar 2021). The study population is representative of only part of the overall population for each community. **Findings** > Rates of vaccination in each community are associated with a substantial later decline in infections among a cohort of individuals aged under 16 years, who are unvaccinated. > On average, for each 20 percentage points of individuals who are vaccinated in a given population, the positive test fraction for the unvaccinated population decreased approximately twofold. **These results provide observational evidence that vaccination not only protects individuals who have been vaccinated but also provides cross-protection to unvaccinated individuals in the community.**
Nature 10JUN2021	**BNT162b2-elicited neutralization of B.1.617 and other SARS-CoV-2 variants**	Liu J., *et al.* USA gotopaper	Vaccines	Report on effects against variants of 20 human sera, drawn 2 or 4 weeks after two doses of BNT162b2. > **Sera neutralize** engineered SARS-CoV-2 with a USA-WA1/2020 genetic background (a virus strain isolated in January 2020) and spike glycoproteins from the newly emerged **B.1.617.1, B.1.617.2, B.1.618** (all first identified in India) **or B.1.525** (first identified in Nigeria) lineages. > Geometric mean plaque reduction neutralization titers against the variant viruses, particularly the B.1.617.1 variant, appear **lower than the titer against USA-WA1/2020 virus, but all sera tested neutralize the variant viruses at titers of at least 40**. The susceptibility of these newly emerged variants to BNT162b2 vaccine-elicited neutralization supports mass immunization strategies.

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Nature Med. 09JUN2021	**First-dose ChAdOx1 and BNT162b2 COVID-19 vaccines and thrombocytopenic, thromboembolic and hemorrhagic events in Scotland**	Simpson C.R., *et al.* UK [gotopaper]	Vaccines	Estimation of the associations between exposure to first-dose ChAdOx1 or BNT162b2 vaccination and hematological and vascular adverse events **Methods** > Nested incident-matched case-control study and a confirmatory self-controlled case series (SCCS) analysis. **Findings** > Association was between ChAdOx1 vaccination and idiopathic thrombocytopenic purpura (ITP) (0–27 d after vaccination; adjusted rate ratio (aRR) = 5.77, 95% confidence interval (CI), 2.41–13.83), with an estimated incidence of 1.13 (0.62–1.63) cases per 100,000 doses. An SCCS analysis confirmed that this was unlikely due to bias (RR = 1.98 (1.29–3.02)). > Increased risk for arterial thromboembolic events (aRR = 1.22, 1.12–1.34) 0–27 d after vaccination, with an SCCS RR of 0.97 (0.93–1.02). > For hemorrhagic events 0–27 d after vaccination, the aRR was 1.48 (1.12–1.96), with an SCCS RR of 0.95 (0.82–1.11). > A first dose of ChAdOx1 was found to be associated with small increased risks of ITP, with suggestive evidence of an increased risk of arterial thromboembolic and hemorrhagic events. The attenuation of effect found in the SCCS analysis means that there is the potential for overestimation of the reported results, which might indicate the presence of some residual confounding or confounding by indication. **Conclusions** Public health authorities should inform their jurisdictions of these relatively small increased risks associated with ChAdOx1. No positive associations were seen between BNT162b2 and thrombocytopenic, thromboembolic and hemorrhagic events.
Nature Med. 09JUN2021	**Impact of vaccination on new SARS-CoV-2 infections in the United Kingdom**	Pritchard E., *et al.* UK [gotopaper]	Public Health / Epidemiology	**Methods** > We used the Office for National Statistics COVID-19 Infection Survey—a large community-based survey of individuals living in randomly selected private households across the United Kingdom—to assess the effectiveness of the BNT162b2 (Pfizer–BioNTech) and ChAdOx1 nCoV-19 (Oxford–AstraZeneca; ChAdOx1) vaccines against any new SARS-CoV-2 PCR-positive tests, split according to self-reported symptoms, cycle threshold value (<30 versus ≥30; as a surrogate for viral load) and gene positivity pattern (compatible with B.1.1.7 or not) **Results** > Using 1,945,071 real-time PCR results from nose and throat swabs taken from 383,812 participants between 1 December 2020 and 8 May 2021 > Vaccination with the ChAdOx1 or BNT162b2 vaccines already reduced SARS-CoV-2 infections ≥21 d after the first dose (61% (95% confidence interval (CI) = 54–68%) versus 66% (95% CI = 60–71%), respectively), with greater reductions observed after a second dose (79% (95% CI = 65–88%) versus 80% (95% CI = 73–85%), respectively) > The largest reductions were observed for symptomatic infections and/or infections with a higher viral burden. **Overall, COVID-19 vaccination reduced the number of new SARS-CoV-2 infections, with the largest benefit received after two vaccinations and against symptomatic and high viral burden infections, and with no evidence of a difference between the BNT162b2 and ChAdOx1 vaccines.**

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Nature 09JUN2021	**Immunogenicity of Ad26.COV2.S vaccine against SARS-CoV-2 variants in humans**	Alter G., *et al.* International <u>gotopaper</u>	Vaccines	**Aim** Study of the humoral and cellular immune responses induced by Ad26.COV2.S against the original SARS-CoV-2 strain WA1/2020 as well as against the B.1.1.7, CAL.20C, P.1., and B.1.351 variants (Population enroled at COV1001 phase 1/2 clinical trial) **Findings** > Ad26.COV2.S induced median pseudovirus neutralizing antibody titers 5.0- and 3.3-fold lower against the B.1.351 and P.1 variants, respectively, as compared with WA1/2020 on day 71 following vaccination. > Median binding antibody titers were 2.9- and 2.7-fold lower against the B.1.351 and P.1 variants, respectively, as compared with WA1/2020. > Antibody-dependent cellular phagocytosis, complement deposition, and NK cell activation responses were largely preserved against the B.1.351 variant. > CD8 and CD4 T cell responses, including central and effector memory responses, were comparable among the WA1/2020, B.1.1.7, B.1.351, P.1, and CAL.20C variants. **Conclusions** These data show that neutralizing antibody responses induced by Ad26.COV2.S are reduced against the B.1.351 and P.1 variants, but functional non-neutralizing antibody responses and T cell responses are largely preserved against SARS-CoV-2 variants.
Cell 08JUN2021	**SARS-CoV-2 mRNA vaccination induces functionally diverse antibodies to NTD, RBD and S2**	Amanat F., *et al.* USA <u>gotopaper</u>	Vaccines	**Aim:** to study the unbiased plasmablast response to SARS-CoV-2 mRNA-based vaccination. **Results:** > Polyclonal antibody responses in vaccinees were robust and comparable to or exceeded those seen after natural infection. > The ratio of binding to neutralizing antibodies after vaccination was greater after natural infection. > At the monoclonal level, the majority of vaccine-induced antibodies did not have neutralizing activity. > A co-dominance of mAbs targeting the NTD and RBD of SARS-CoV-2 spike and an original antigenic-sin like backboost to seasonal human coronaviruses OC43 and HKU1 was found. > Neutralizing activity of NTD mAbs but not RBD mAbs against a clinical viral isolate carrying E484K as well as extensive changes in the NTD was abolished, suggesting that a proportion of vaccine induced RBD binding antibodies may provide substantial protection against viral variants carrying single E484K RBD mutations. > Data from plasmablasts suggest that, at least, some of the vaccine-induced response is biased by pre-existing immunity to human β-coronaviruses.

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Lancet Rheumatol. 08JUN2021	**Inflammatory biomarkers in COVID-19-associated multisystem inflammatory syndrome in children, Kawasaki disease, and macrophage activation syndrome: a cohort study**	Rodriguez-Smith J. J., *et al*. USA [gotopaper](#)	Clinics	The pathogenesis of Multisystem inflammatory syndrome in children (MIS-C) remains undefined, and whether specific inflammatory biomarker patterns can distinguish MIS-C from other hyperinflammatory syndromes, including Kawasaki disease and macrophage activation syndrome (MAS), is unknown. Therefore, we aimed to investigate whether inflammatory biomarkers could be used to distinguish between these conditions. **Methods** > Clinical and laboratory features as well as S100A8/A9, S100A12, interleukin (IL)-18, chemokine (C-X-C motif) ligand 9 (CXCL9), and IL-6 concentrations were assessed by ELISA and compared using parametric and non-parametric tests and receiver operating characteristic curve analysis. **Results** > Between April 30, 2019, and Dec 14, 2020, we enrolled 19 patients with MIS-C and nine patients with Kawasaki disease > Patients with MIS-C and Kawasaki disease had similar S100 proteins and IL-18 concentrations but patients with MIS-C were distinguished by significantly higher median concentrations of the IFNy-induced CXCL9 (1730 pg/mL [IQR 604–6300] vs 278 pg/mL [54–477]; p=0·038) > Stratifying patients with MIS-C by CXCL9 concentrations (high vs low) revealed differential severity of clinical and laboratory presentation > Compared with patients with MIS-C and low CXCL9 concentrations, more patients with high CXCL9 concentrations had acute kidney injury, altered mental status, shock, and myocardial dysfunction; these patients also had higher concentrations of systemic inflammatory markers and increased severity of cytopenia and coagulopathy > By contrast, patients with MIS-C and low CXCL9 concentrations resembled patients with Kawasaki disease, including the frequency of coronary involvement > Elevated concentrations of S100A8/A9, S100A12, and IL-18 were also useful in distinguishing systemic JIA from Kawasaki disease with high sensitivity and specificity **Our findings show MIS-C is distinguishable from Kawasaki disease primarily by elevated CXCL9 concentrations. The stratification of patients with MIS-C by high or low CXCL9 concentrations provides support for MAS-like pathophysiology in patients with severe MIS-C, suggesting new approaches for diagnosis and management.**
Science Transl Med. 08JUN2021	**Antibodies elicited by mRNA-1273 vaccination bind more broadly to the receptor binding domain than do those from SARS-CoV-2 infection**	Greaney A.J., *et al*. USA [gotopaper](#)	Vaccines	The susceptibility of immunity to viral evolution is shaped in part by the breadth of epitopes targeted by antibodies elicited by vaccination or natural infection. **Aim**: to investigate how human antibody responses to vaccines are influenced by viral mutations through deep mutational scanning to compare the specificity of polyclonal antibodies elicited by either two doses of the mRNA-1273 COVID-19 vaccine or natural infection with SARS-CoV-2. > The neutralizing activity of vaccine-elicited antibodies was more targeted to the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein compared to antibodies elicited by natural infection. > Within the RBD, binding of vaccine-elicited antibodies was more broadly distributed across epitopes compared to infection-elicited antibodies. > This greater binding breadth means that single RBD mutations have less impact on neutralization by vaccine sera compared to convalescent sera. **Antibody immunity acquired by natural infection or different modes of vaccination may have a differing susceptibility to erosion by SARS-CoV-2 evolution.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 07JUNE2021	**Spread of a SARS-CoV-2 variant through Europe in the summer of 2020**	Hodcroft E., *et al.* Switzerland [gotopaer](#)	Public Health / Epidemiology – Variants	**Aim**: Describing and interpreting the spread of the EU1 variant in Europe in the summer 2020. **Methods**: > Phylogenetic and phylogeographic analysis of genomic sequences shared on GISAID; identification of the EU1 variant (B.1.177 and its sublineages in Pango nomenclature) > Estimation of travel volumes and fluxes using mobile phone data > Phylodynamic analysis of transmission chains in Switzerland > Characterisation of the S:A222V mutation in the spike through its effect on antibody binding, and through production of lentiviral particles pseudotyped with spike with or without the mutation. > Analysis of a model estimating the number of variant imports in various European countries, and estimation of the local spread of the variant **Findings**: > The EU1 variant likely appeared in Spain and was detected in late June 2020; probably initially among agricultural workers in Aragon and Catalonia > It carries spike mutation A222V, which does not seem to have a major phenotypic effect > The EU1 variant was multiply introduced to different European countries once traveled resumed; it then spread locally and became dominant in some countries > There is no detection of a particular transmission advantage of the EU1 variant; the rise in frequency is associated with epidemic rebound (EU1 spread because it was at the right place at the right time). **Conclusion**: > The study underlines the importance of coordinated and systematic sequencing efforts, and of multi-country genomic surveillance and data sharing to track variants across countries. > The EU1 variant does not seem to be associated to neither increased transmissibility, immune escape nor different clinical consequences. > The EU1 variant spread thanks to travel and regional differences in prevalence. This result should encourage policy makers to take social and geographic heterogeneities into account when designing policies for mitigating Covid-19 and reopening > The study indicates that the summer travel guidelines and restrictions in 2020 were generally not sufficient to prevent onward transmission of introductions. The authors stress the importance of identifying ways of reducing the risk of introducing variants, and of monitoring and controlling the spread of introduced ones.
Nature 07JUNE2021	**Nanobodies from camelid mice and llamas neutralize SARS-CoV-2 variants**	Xu, J., *et al.* USA [gotopaper](#)	Therapeutics	One potential alternative to avert viral escape is the use of camelid VHHs or nanobodies, which can recognize epitopes often inaccessible to conventional antibodies **Methods** > We isolate anti-RBD nanobodies from llamas and "nanomice" we engineered to produce VHHs cloned from alpacas, dromedaries and camels **Findings** > We identified two sets of highly neutralizing nanobodies - Group 1 circumvents antigenic drift by recognizing an RBD region that is highly conserved in coronaviruses but rarely targeted by human antibodies. - Group 2 is almost exclusively focused to the RBD-ACE2 interface and fails to neutralize variants carrying E484K or N501Y substitutions. Notably however, group 2 nanobodies retain full neutralization activity against variants when expressed as homotrimers, rivaling the most potent antibodies produced to date against SARS-CoV-2. These findings suggest that multivalent nanobodies overcome SARS-CoV-2 mutations through two separate mechanisms: enhanced avidity for the ACE2 binding domain, and recognition of conserved epitopes largely inaccessible to human antibodies. **Therefore, while new SARS-CoV-2 mutants will continue to emerge, nanobodies represent promising tools to prevent COVID-19 mortality when vaccines are compromised.**

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JAMA Netw Open 07JUN2021	**Assessment of Effectiveness of 1 Dose of BNT162b2 Vaccine for SARS-CoV-2 Infection 13 to 24 Days After Immunization**	Chodick G., *et al.* Israel gotopaper	Vaccines - Immunisation	**Aim**: to assess the short-term effectiveness of the first dose of the BNT162b2-vaccine against SARS-CoV-2 infection 13-24 days after immunization in a real-world setting. By comparing daily and cumulative infection rates in days 13-24 and in days 1-12 after one dose. **Results** > Data for 503 875 individuals (mean [SD] age, 59.7 [14.7] years; 263 228 [52.4%] women) were analyzed, of whom 351 897 had follow-up data for days 13 to 24. > The cumulative incidence of SARS-CoV-2 infection was 2484 individuals (0.57%) during days 1 through 12 and 614 individuals (0.27%) in days 13 through 24. > The weighted mean (SE) daily incidence of SARS-CoV-2 infection in days 1 through 12 was 43.41 (12.07) infections per 100 000 population and 21.08 (6.16) infections per 100 000 population in days 13 through 24, a relative risk reduction (RRR) of 51.4% (95% CI, 16.3%-71.8%). > The decrease in incidence was evident from day 18 after the first dose. > Similar RRRs were calculated in individuals aged 60 years or older (44.5%; 95% CI, 4.1%-67.9%), those younger than 60 years (50.2%; 95% CI, 14.1%-71.2%), women (50.0%; 95% CI, 13.5%-71.0%), and men (52.1%; 95% CI, 17.3%-72.2%). > Findings were similar in subpopulations (eg, ultraorthodox Jewish: RRR, 53.5% [95% CI, 19.2%-73.2%]) and patients with various comorbidities (eg, cardiovascular diseases: RRR, 47.2% [95% CI, 7.8%-69.8%]). > Vaccine effectiveness against symptomatic COVID-19 was 54.4% (95% CI, 21.4%-73.6%). **In this comparative effectiveness study of a single dose of the BNT162b2 vaccine, results were comparable to that of the phase III randomized clinical trial.**
Cell 05JUN2021	**The monoclonal antibody combination REGEN-COV protects against SARS-CoV-2 mutational escape in preclinical and human studies**	Copin R., *et al.* USA gotopaper	Therapeutics	**Aim:** to investigate the sequence diversity of the spike protein and monitored emergence of virus variants in SARS-COV-2 isolates found in COVID-19 patients treated with the two-antibody combination REGEN-COV, as well as in preclinical in vitro studies using single, dual, or triple antibody combinations, and in hamster in vivo studies using REGEN-COV or single monoclonal antibody treatments. **Methods:** REGEN-COV (previously known as REGN-COV2) is a cocktail of two fully-human non-competing, neutralizing antibodies — casirivimab (REGN10933) and imdevimab (REGN10987) — that target the receptor binding domain (RBD) on the SARS-CoV-2 spike protein and thereby prevent viral entry into the host cell. **Results:** > While only one to two passages led to complete virus resistance against all mAbs used as monotherapy, seven consecutive passages were needed to reach complete resistance to the REGEN-COV combination, requiring selection of multiple simultaneous mutations impacting each antibody. > The three-antibody combination has similar neutralization potency as REGEN-COV. The addition of the third non-competing RBD mAb further increased protection against viral escape, with no loss of antiviral potency observed through eleven consecutive passages > Selection of resistance variants in almost half (18/40) of monotherapy treated animals versus none (0/20) of the animals treated with the REGEN-COV combination. > The REGEN-COV combination retained full neutralization potency, thereby providing its full antiviral activity in treated individuals and limiting any potential selection of resistant variants. **The combination of non-competing antibodies in REGEN-COV provides protection against all current SARS-CoV-2 variants of concern/interest and also protects against emergence of new variants and their potential seeding into the population in a clinical setting.**

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Science 03JUN2021	**Fe-S cofactors in the SARS-CoV-2 RNA-dependent RNA polymerase are potential antiviral targets**	Maio N., *et al.* USA gotopaper	Therapeutics	**Context** : Fe-S clusters, inorganic cofactors often associated with biological redox reactions, have been identified in numerous proteins involved in DNA and RNA metabolism, where they play a variety of critical functional roles. **Aim:** To analyse the primary sequences of SARS-CoV-2 proteins to investigate whether any might incorporate Fe-S clusters and to investigate whether nsp12 coordinated a Fe-S cluster. Additionally, to exploit the sensitivity of Fe-S clusters to oxidative degradation to prevent coronavirus replication in cell culture models. **Results:** > The catalytic subunit of the RdRp, nsp12, ligates two iron-sulfur metal cofactors in sites that were modeled as zinc centers in the available cryo-electron microscopy structures of the RdRp complex. These metal binding sites are essential for replication and for interaction with the viral helicase. >>These iron-sulfur clusters thus serve as cofactors for the SARS-CoV-2 RdRp and are targets for therapy of COVID-19. > Oxidation of the clusters by the stable nitroxide TEMPOL caused their disassembly, potently inhibited the RdRp, and blocked SARS-CoV-2 replication in cell culture. > TEMPOL exhibited a strong antiviral activity at concentrations above 0.2 mM. Viral titers were reduced by more than 5 log10 in the presence of 0.4 mM TEMPOL, which is reported to have a CC50 greater than 100 mM **The study presents a molecular basis for pursuing TEMPOL and other related stable nitroxides as potential SARS-CoV-2 therapies during active viral infection.**
JAMA 03JUN2021	**Effect of Bamlanivimab vs Placebo on Incidence of COVID-19 Among Residents and Staff of Skilled Nursing and Assisted Living FacilitiesA Randomized Clinical Trial**	Cohen M.S., *et al.* USA gotoper	Therapeutics	**Aim:** to determine the effect of bamlanivimab on the incidence of COVID-19 among residents and staff of skilled nursing and assisted living facilities. **Methods:** >Randomized, double-blind, single-dose, phase 3 trial that enrolled residents and staff of 74 skilled nursing and assisted living facilities in the United States with at least 1 confirmed SARS-CoV-2 index case. >Participants were randomized to receive a single intravenous infusion of bamlanivimab, 4200 mg (n = 588), or placebo (n = 587). **Results:** > The prevention population comprised a total of 966 participants (666 staff and 300 residents) who were negative at baseline for SARS-CoV-2 infection and serology (mean age, 53.0 [range, 18-104] years; 722 [74.7%] women). > Bamlanivimab significantly reduced the incidence of COVID-19 in the prevention population compared with placebo (8.5% vs 15.2%; odds ratio, 0.43 ; absolute risk difference, −6.6 percentage points). > Five deaths attributed to COVID-19 were reported by day 57; all occurred in the placebo group. > Among 1175 participants who received study product (safety population), the rate of participants with adverse events was 20.1% in the bamlanivimab group and 18.9% in the placebo group. > The most common adverse events were urinary tract infection (reported by 12 participants [2%] who received bamlanivimab and 14 [2.4%] who received placebo) and hypertension (reported by 7 participants [1.2%] who received bamlanivimab and 10 [1.7%] who received placebo). **Among residents and staff in skilled nursing and assisted living facilities, treatment with bamlanivimab monotherapy reduced the incidence of COVID-19 infection.**

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NEJM 02JUN2021	**Thromboembolic Events in the South African Ad26.COV2.S Vaccine Study**	Takuva, S., *et al.* International [gotopaper](#)	Vaccines	Interim safety data from the first 288,368 participants vaccinated with Ad26.COV2.S in the Sisonke study (open label, single-group, phase 3b implementation study to monitor the effectiveness of the single-dose Ad26.COV2.S vaccine among 500,000 health care workers in South Africa) **Findings** > Five arterial, venous thrombotic, or embolic events reported in 5 health care workers with known risk factors for thromboembolism (1.7 events per 100,000 participants) > One case of pulmonary embolus occurred 23 days after vaccination in a 63-year-old woman on overweight, with hypertension, diabetes mellitus, and a history of venous thrombosis(fatal issue) > A second case occurred in a 64-year-old woman who received a diagnosis of cor pulmonale 17 days after vaccination; this case had features consistent with chronic and recurrent pulmonary emboli. > Two cerebrovascular accidents (infarcts on imaging) were reported — 45-year-old woman with rheumatic heart disease and a history of human immunodeficiency virus infection, cerebrovascular accident, and aortic valve replacement, in whom left-sided weakness developed the day after vaccination, — 38-year-old woman who had given birth to twins 9 months before vaccination and presented with features of transient ischemic attack 8 days after vaccination. > A 65-year-old woman with chronic diabetes mellitus had deterioration and blurring of vision 8 days after vaccination and received a diagnosis of retinal vein occlusion and macular hemorrhage. > To date, no case of vaccine-induced immune thrombotic thrombocytopenia has been documented. **Conclusions** The rate of adverse events following Ad26.COV2.S vaccination is low, and thromboembolic events have occurred mainly in persons with risk factors for thromboembolism.
NEJM 02JUN2021	**Cross-Reactive Neutralizing Antibody Responses Elicited by SARS-CoV-2 501Y.V2 (B.1.351)**	Moyo-Gwete, T., *et al.* South Africa [gotopaper](#)	Vaccines	Study of immune response to B1.531 and of the ability of antibodies elicited by the variant to cross-react with other variants **Methods** > Characterization of the SARS-CoV-2 infections in a cohort of hospitalized patients with COVID19 in South Africa > Blood sample colection 89 patients at the time when the epidemic in South Africa as a whole was dominated by B1.531 which accounted for more than 90% of infections - 28 (31%) were randomly selected for SARS-CoV-2 sequencing, all of whom were shown by phylogenetic analysis to be infected with B1.531. **Findings** > Binding and neutralizing antibody responses of infected patients to the B1.531 spike protein: high-titer binding and neutralizing antibody responses > Titration of a subset of 46 samples revealed that plasma samples had higher titers to the spike protein of B1.531 than to the spike protein of the original variant (mean of 1.7 times as high), but high-level binding to the original variant remained > assesement of nautralisation capacity of sera B1.531 infected patients agains P1 ou original variant: - 53 of 57 samples maintained neutralization activity against the original variant (GMT 203), approximately one third of the titer against the B1.531 variant - 10 samples tested against P1 variant: high levels of neutralization of this variant, with some samples showing higher potency against P.1 than against B1.531 **Conslusions** B1.531 elicits robust neutralizing antibody responses against both the original variant and P.1, which indicates high levels of cross-reactivity.

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Lancet Microbe 02JUN2021	**Co-infections, secondary infections, and antimicrobial use in patients hospitalised with COVID-19 during the first pandemic wave from the ISARIC WHO CCP-UK study: a multicentre, prospective cohort study**	Russel C.D., *et al*. UK [gotopaper](#)	Clinic	**Aim**: to describe microbiologically confirmed co-infections and secondary infections, and antimicrobial use, in patients admitted to hospital with COVID-19 (ISARIC, CCP-UK study). **Results** > Analysis of data from 48 902 patients admitted to hospital (Feb 6 and June 8, 2020). Median age 74 years (IQR 59–84), 20 786 (42·6%) of 48 765 women. Microbiological investigations were recorded for 8649 (17·7%) of 48 902 patients, with clinically significant COVID-19-related respiratory or bloodstream culture results recorded for 1107 patients. > 762 (70·6%) of 1080 infections were secondary, occurring more than 2 days after hospital admission. > **Staphylococcus aureus** and **Haemophilus influenzae** were the most common pathogens causing respiratory co-infections (diagnosed ≤2 days after admission), with **Enterobacteriaceae** and **S aureus** most common in secondary respiratory infections. > Bloodstream infections were most frequently caused by **Escherichia coli** and **S aureus**. > Among patients with available data, 13 390 (**37·0%**) of 36 145 had received antimicrobials **in the community** for this illness episode before hospital admission. > 39 258 (**85·2%**) of 46 061 patients with inpatient antimicrobial data received one or more antimicrobials at some point **during their admission** (highest for patients in critical care). > Frequent use of broad-spectrum agents and use of carbapenems rather than carbapenem-sparing alternatives was identified. **In patients admitted to hospital with COVID-19, bacterial infections are rare, and more likely to be secondary infections. The frequency and nature of antimicrobial use are concerning.**
Clin Infect Dis. 29MAY2021	**Neutralization heterogeneity of United Kingdom and South-African SARS-CoV-2 variants in BNT162b2-vaccinated or convalescent COVID-19 healthcare workers**	Marot S., *et al*. France [gotopaper](#)	Vaccines - Immunisation	Neutralizing antibodies (NAbs) potency against SARS-CoV-2 variants **Findings:** > Despite decreased NAb titers elicited by BNT162b2-vaccine against VOC202012/01 and 501Y.V2 strains, 28/29 healthcare workers (HCW) had a NAb titer ≥1:10. Although immune protection correlates need to be defined, our findings suggests a certain humoral protection activity either on UK or SA variants after two doses of mRNA-vaccine. > In contrast, six months after COVID-19 mild-forms, only 9/15 (60%) of HCW displayed detectable NAbs against 501Y.V2 strain **This result supports a strong recommendation for SARS-CoV-2 vaccination of previously infected subjects.**
JAMA Intern Med. 28MAY2021	**Assessment of SARS-CoV-2 Reinfection 1 Year After Primary Infection in a Population in Lombardy, Italy**	Vitale J., *et al*. Italy [gotopaper](#)	Public Health / Epidemiology	**Aim**: to investigate the one-year incidence (Feb 2021) of SARS-CoV-2 primary infection and reinfection among individuals who underwent diagnostic RT-PCR between Feb-July 2020 in Lombardy, Italy. Reinfections were defined by a second RT-PCR positivity beyond 90 days after complete resolution of the first infection and with at least 2 consecutive negative test results between episodes. **Results** > Demographic characteristics: Median age 59 (IQR 40-78) years, positive cases were older and geographically distributed more in the industrial area of Legnano. > During follow-up (mean [SD], 280 [41] days) 5 reinfections (0.31%; 95% CI, 0.03%-0.58%) were confirmed among 1579 positive patients. > Most of reinfected patients were evaluated, treated, and followed in hospitals or dedicated COVID-19 ambulatories. One was hospitalized, and 4 had a close relationship with health facilities. Mean (SD) interval between primary infection and reinfection was >230 (90) days. > Of 13 496 persons initially not infected with SARS-CoV-2, 528 (3.9%; 95% CI, 3.5%-4.2%) subsequently developed a primary infection. > The incidence density per 100 000 person days was **1.0 (95% CI, 0.5-1.5) for reinfections compared with 15.1 (95% CI, 14.5-15.7) for new infections**, while the incidence rate ratio adjusted for age, sex, ethnicity, and the sanitarian area was 0.07 (95% CI, 0.06-0.08). **The study results suggest that reinfections are rare events and patients who have recovered from COVID-19 have a lower risk of reinfection 1 year later. Observation ended before SARS-CoV-2 variant spread.**

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JAMA Oncol. 28MAY2021	**Evaluation of Seropositivity Following BNT162b2 Messenger RNA Vaccination for SARS-CoV-2 in Patients Undergoing Treatment for Cancer**	Massarweh A., *et al.* Israel gotopaper	Vaccines - Immunisation	**Aim**: To evaluate rates of antispike (anti-S) antibody response to a BNT162b2 vaccine in patients with cancer who are undergoing systemic treatment vs healthy controls. **Methods:** Prospective cohort study included 102 adult patients with solid tumors undergoing active intravenous anticancer treatment and 78 controls who received the second dose of the BNT162b2 vaccine at least 12 days before enrollment. Serum samples were analyzed and the titers of the IgG antibodies against SARS-CoV-2 spike receptor–binding domain **Results:** >The analysis included 180 participants, which comprised 102 patients with cancer (median [interquartile range (IQR)] age, 66 years; 58 men [57%]) and 78 healthy controls (median [IQR] age, 62 [49-70] years; 25 men [32%]). >The most common tumor type was gastrointestinal (29 [28%]). In the patient group, 92 (90%) were seropositive for SARS-CoV 2 antispike IgG antibodies after the second vaccine dose, whereas in the control group, all were seropositive. >The median IgG titer in the patients with cancer was significantly lower than that in the controls (1931 [IQR, 509-4386] AU/ml vs 7160 [IQR, 3129-11 241] AU/m). >In a multivariable analysis, the only variable that was significantly associated with lower IgG titers was treatment with chemotherapy plus immunotherapy (β, −3.5; 95% CI, −5.6 to −1.5).
JAMA Oncol. 28MAY2021	**Difference in SARS-CoV-2 Antibody Status Between Patients With Cancer and Health Care Workers During the COVID-19 Pandemic in Japan**	Yazaki S., *et al.* Japan gotopaper	Vaccines - Immunisation	**Aim**: To evaluate serum SARS-CoV-2 antibody status in patients with cancer and health care workers (HCWs) during the COVID-19 pandemic in Japan. **Methods:** Participants were enrolled for this prospective cross-sectional study between August 3 and October 30, 2020, from 2 comprehensive cancer centers in the epidemic area around Tokyo, Japan. **Results:** > A total of 500 patients with cancer (median age, 62.5 years [range, 21-88 years]; 265 men [55.4%]) and 1190 HCWs (median age, 40 years [range, 20-70 years]; 382 men [25.4%]) were enrolled. >The seroprevalence was 1.0% (95% CI, 0.33%-2.32%) in patients and 0.67% (95% CI, 0.29%-1.32%) in HCWs (P = .48). >The N-IgG and S-IgG antibody levels were significantly lower in patients than in HCWs (N-IgG: β, −0.38; 95% CI, −0.55 to −0.21; P < .001; and S-IgG: β, −0.39; 95% CI, −0.54 to −0.23; P < .001). >Additionally, among patients, N-IgG levels were significantly lower in those who received chemotherapy than in those who did not (median N-IgG levels, 0.1 [interquartile range (IQR), 0-0.3] vs 0.1 [IQR, 0-0.4], P = .04). >In contrast, N-IgG and S-IgG levels were significantly higher in patients who received immune checkpoint inhibitors than in those who did not (median N-IgG levels: 0.2 [IQR, 0.1-0.5] vs 0.1 [IQR, 0-0.3], P = .02; S-IgG levels: 0.15 [IQR, 0-0.3] vs 0.1[IQR, 0-0.2], P = .02). **The seroprevalence of SARS-CoV-2 antibodies did not differ between the 2 groups; however, findings suggest that comorbid cancer and treatment with systemic therapy, including chemotherapy and immune checkpoint inhibitors, may influence the immune response to SARS-CoV-2.**

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PNAS 28MAY2021	**Intracounty modeling of COVID-19 infection with human mobility: Assessing spatial heterogeneity with business traffic, age, and race**	Hou X., *et al*. USA [gotopaper](#)	Public Health / Epidemiology	**Aim:** To develop models incorporating spatial heterogeneity and mobility flows to make predictions on the effect of nonpharmaceutical interventions **Methods:** > SEIR epidemic model capturing social and geographic heterogeneity within a small geographic region (a single county), with stochastic transmission rate and heterogeneous local mobility > Unsupervised machine learning to partition a county into local clusters using human mobility flow data from SafeGraph, giving smartphone coordinates over time > Other data: test results (Public Health Offices of City of Madison & Dane County and Milwaukee County) between March 11-August 14, 2020; demographic and socioeconomic attributes (US Census Bureau) > Online data assimilation and the ensemble Kalman filter method are used to update the model parameters along time > Study of several scenarii of reopening policies **Findings:** > The spatial clustering constructed from mobility data is strongly correlated with demographic heterogeneity (e.g. in terms of race and ethnicity composition, age structure) > There is a strong heterogeneity of the estimated effective reproduction number across clusters > In a college town (Dane County), the most important heterogeneity is age structure > In a large city area (Milwaukee County), racial and ethnic heterogeneity becomes more apparent > Scenario studies indicate a strong response of the spread rate to various reopening policies **Conclusion:** Policy makers may need to take social and geographic heterogeneities into account very carefully when designing policies for mitigating the ongoing spread of of Covid-19 and reopening
NEJM 27MAY2021	**Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents**	Frenck R.W., *et al*. International [gotopaper](#)	Vaccines	Safe, effective vaccines are needed to protect adolescents, facilitate in-person learning and socialization, and contribute to herd immunity **Methods** > Ongoing multinational, placebo-controlled, observer-blinded trial > Participants randomly assigned in a 1:1 ratio to receive two injections, 21 days apart, of 30 µg of BNT162b2 or placebo. > Immunogenicity objective: noninferiority of the immune response to BNT162b2 in 12-to-15-year-old participants as compared with that in 16-to-25-year-old participants >Safety (reactogenicity and adverse events) and efficacy against confirmed Covid-19 (onset ≥7 days after dose 2) in 12-15-yo cohort. **Findings** > 1131 adolescents 12 to 15 years of age received BNT162b2; 1129 received placebo. > BNT162b2 had a favorable safety and side-effect profile, with mainly transient mild-to-moderate reactogenicity (mainly injection-site pain [79-86% of participants], fatigue [60-66%], headache [55-65%]). > No vaccine-related serious adverse events and few overall severe adverse events. > The GMT of SARS-CoV-2 50% neutralizing titers after dose 2 in 12-to-15-year-old participants relative to 16-to-25-year-old participants was 1.76 (95% confidence interval [CI], 1.47 to 2.10), which met the noninferiority criterion of a lower boundary of the two-sided 95% confidence interval greater than 0.67 and indicated a greater response in the 12-to-15-year-old cohort. > Among participants without evidence of previous SARS-CoV-2 infection, no Covid-19 cases with an onset of 7 or more days after dose 2 were noted among BNT162b2 recipients, and 16 cases occurred among placebo recipients. > The observed VE was 100% (95% CI, 75.3 to 100). **Conclusions** The BNT162b2 vaccine in 12-to-15-year-old recipients had a favorable safety profile, produced a greater immune response than in young adults, and was highly effective against Covid-19.

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Lancet Respir Med. 27MAY2021	**Colchicine for community-treated patients with COVID-19 (COLCORONA): a phase 3, randomised, double-blinded, adaptive, placebo-controlled, multicentre trial**	Tardif J., et al. Canada [gotopaper]	Therapeutics	**Aim**: to investigate the effect of colchicine (oral anti-inflammatory) on the composite of COVID-19-related death or hospital admission. - Phase 3, 1:1 randomised, double-blind, adaptive, placebo-controlled, international multicentre trial. - Patients with COVID-19 diagnosed by PCR testing or clinical criteria who were not being treated in hospital, ≥40-year-old and who had at least one high-risk characteristic. - Treatment: orally administered colchicine (0·5 mg twice/day for 3 days, then once/day for 27 days thereafter) or matching placebo. Primary efficacy endpoint: composite of death or hospital admission for COVID-19. **Results** > Trial enrolment: March 23, 2020 - Dec 22, 2020. 4488 patients included (53·9% women; median age 54·0 years, IQR 47·0–61·0), 2235 were randomly assigned to colchicine and 2253 to placebo. > Overall, he primary endpoint occurred in 104 (4·7%) of 2235 patients in the colchicine group and 131 (5·8%) of 2253 patients in the placebo group (odds ratio [OR] 0·79, 95·1% CI 0·61–1·03; p=0·081). > Among the 4159 patients with PCR-confirmed COVID-19, the primary endpoint occurred in 96 (4·6%) of 2075 patients in the colchicine group and 126 (6·0%) of 2084 patients in the placebo group (OR 0·75, 0·57–0·99; p=0·042). > Serious adverse events were reported in 108 (4·9%) of 2195 patients in the colchicine group and 139 (6·3%) of 2217 patients in the placebo group (p=0·051); pneumonia occurred in 63 (2·9%) of 2195 patients in the colchicine group and 92 (4·1%) of 2217 patients in the placebo group (p=0·021). Diarrhoea was reported in 300 (13·7%) of 2195 patients in the colchicine group and 161 (7·3%) of 2217 patients in the placebo group (p<0·0001). **In community-treated patients** including those without diagnostic test, the **effect of colchicine on COVID-19-related clinical events was not statistically significant. Among patients with PCR-confirmed COVID-19, colchicine led to a lower rate of the composite of death or hospital admission** than placebo.
Lancet Infect Dis. 27MAY2021	**Same-day SARS-CoV-2 antigen test screening in an indoor mass-gathering live music event: a randomised controlled trial**	Revollo B., et al. Spain [gotopaper]	Public Health / Epidemiology	> Randomised controlled open-label trial to assess effectiveness of a comprehensive preventive intervention for a mass-gathering indoor event (live concert) based on systematic same-day screening of attendees with Ag-RDTs, use of facial masks, and adequate air ventilation in Barcelona (Spain) (NCT04668625.) > Adults 18–59-yo, Ag-RDT negative result from a nasopharyngeal swab collected immediately before entering the event. > Randomisation 1:1 to either attend the indoor event for 5 hours or go home. > Nasopharyngeal specimens analysed by RT-PCR and cell culture > 8 days after the event, a nasopharyngeal swab was collected and analysed by Ag-RDT, RT-PCR, and a transcription-mediated amplification test (TMA). Primary outcome: difference in incidence of RT-PCR-confirmed SARS-CoV-2 infection at 8 days, control vs. intervention groups. **Findings** > 1047 people randomized. 465 were finally included in the final analysis for the experimental group and 49 5in the control group . > At baseline, 15 (3%) of 495 individuals in the control group and 13 (3%) of 465 in the experimental group tested positive on TMA despite a negative Ag-RDT result. > The RT-PCR test was positive in one case in each group and cell viral culture was negative in all cases. > 8 days after the event, two (<1%) individuals in the control arm had a positive Ag-RDT and PCR result, whereas no Ag-RDT nor RT-PCR positive results were found in the intervention arm. > The Bayesian estimate for the incidence between the experimental and control groups was −0·15% (95% CI −0·72 to 0·44). **Conclusions** Preliminary evidence on indoor mass-gathering event safety during a COVID-19 outbreak under a comprehensive preventive intervention.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Clin Infect Dis. 27MAY2021	**Risk Factors for Death Among the First 80 543 COVID-19 Cases in China: Relationships Between Age, Underlying Disease, Case Severity, and Region**	Zhang Y., *et al.* China [gotopaper]	Public Health / Epidemiology	Examining risk factors for COVID-19 death **Methods** > A total of 80 543 COVID-19 cases reported in China, nationwide, through April 8, 2020 were included **Findings** > Overall national case fatality ratio (CFR) was 5.64% > Risk factors for death were **older age, presence of underlying disease**, **worse case severity**, and **near-epicenter region** > CFR increased from 0.35% (30-39 years) to 18.21% (≥70 years) without underlying disease > Regardless of age, CFR increased from 2.50% for no underlying disease to 7.72% for 1, 13.99% for 2, and 21.99% for ≥3 > CFR increased with worse case severity from 2.80% (mild), to 12.51% (severe) and 48.60% (critical) regardless of region > Compared to other regions, CFR was much higher in Wuhan regardless of case severity (mild: 3.83% versus 0.14% in Hubei and 0.03% elsewhere; moderate: 4.60% versus 0.21% and 0.06%; severe: 15.92% versus 5.84% and 1.86%; and critical: 58.57% versus 49.80% and 18.39%). **Older patients regardless of underlying disease and patients with underlying disease regardless of age were at elevated risk of death. Higher death rates near the outbreak epicenter and during the surge of cases reflect the deleterious effects of allowing health systems to become overwhelmed.**
JAMA 26MAY2021	**Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults**	Kaabi N.A., *et al.* International [gotopaper]	Vaccines	**Evaluation of the efficacy and adverse events of 2 inactivated COVID-19 vaccines.** **Methods** Randomized, double-blind, phase 3 trial. United Arab Emirates and Bahrain. > 18 yearsof age without history of COVID-19. Participants rendomized to receive 1 of 2 inactivated vaccines developed from SARS-CoV-2 WIV04 (5 µg/dose; n = 13 459) and HB02 (4 µg/dose; n = 13 465) strains or an aluminum hydroxide (alum)–only control (n = 13 458). 2 IM injections 21 days apart. Primary outcome: efficacy against laboratory-confirmed symptomatic COVID-19 14 days following a second vaccine dose among participants who had no virologic evidence of SARS-CoV-2 infection at randomization. Secondary outcome: efficacy against severe COVID-19. **Findings** > 40 382 participants randomized (mean age, 36.1 years; 32 261 [84.4%] men), > 38 206 (94.6%) who received 2 doses were included in the primary efficacy analysis. >Symptomatic COVID-19 was identified in 26 participants in the WIV04 group (12.1 [95% CI, 8.3-17.8] per 1000 person-years), 21 in the HB02 group (9.8 [95% CI, 6.4-15.0] per 1000 person-years), and 95 in the alum-only group (44.7 [95% CI, 36.6-54.6] per 1000 person-years). VE: 72.8% (95% CI, 58.1%-82.4%) for WIV04 and 78.1% (95% CI, 64.8%-86.3%) for HB02 (P < .001 for both). > Two severe cases of COVID-19 occurred in the alum-only group and none occurred in the vaccine groups. > Adverse reactions 7 days after each injection occurred in 41.7% to 46.5% of participants in the 3 groups; serious adverse events were rare and similar in the 3 groups (WIV04: 64 [0.5%]; HB02: 59 [0.4%]; alum-only: 78 [0.6%]). **Conclusions** **T**reatment of adults with either of 2 inactivated SARS-CoV-2 vaccines significantly reduced the risk of symptomatic COVID-19, and serious adverse events were rare.

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Nature 27MAY2021	**BNT162b2 vaccine induces neutralizing antibodies and poly-specific T cells in humans**	Sahin U., *et al.* Germany [gotopaper](#)	Vaccines	**Background** BNT162b2, a lipid nanoparticle (LNP) formulated nucleoside-modified messenger RNA (mRNA) that encodes the SARS-CoV-2 spike glycoprotein (S) stabilized in the prefusion conformation, has demonstrated 95% efficacy in preventing COVID-19. **Aim**: to extend the previous phase 1/2 trial report and present BNT162b2 prime/boost induced immune response data from a second phase 1/2 trial in healthy adults (18-55 years of age). **Results** > BNT162b2 elicited strong antibody responses, with SARS-CoV-2 serum 50% neutralizing geometric mean titers up to 3.3-fold above those observed in COVID-19 human convalescent samples (HCS) one-week post-boost. > BNT162b2-elicited sera neutralized 22 pseudoviruses bearing SARS-CoV-2 S variants. > Most participants had a strong IFNγ- or IL-2-positive CD8+ and CD4+ T helper type 1 (TH1) T cell response, detectable throughout the full observation period of nine weeks following the boost. > pMHC multimer technology identified several BNT162b2-induced epitopes that were presented by frequent MHC alleles and conserved in mutant strains. > One-week post-boost, epitope-specific CD8+ T cells of the early differentiated effector-memory phenotype comprised 0.02-2.92% of total circulating CD8+ T cells and were detectable (0.01-0.28%) eight weeks later. B**NT162b2 elicits an adaptive humoral and poly-specific cellular immune response against epitopes conserved in a broad range of variants at well tolerated doses.**
JAMA 26MAY2021	**Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults**	Al Kaabi N., *et al.* International [gotopaper](#)	Vaccines - Immunization	**Efficacy and adverse events of 2 inactivated COVID-19 vaccines.** **Methods** **>** Prespecified interim analysis of an ongoing randomized, double-blind, phase 3 trial in the United Arab Emirates and Bahrain among adults 18 years and older without known history of COVID-19. ClinicalTrials.gov Identifier: NCT04510207; > Participants were randomized to receive 1 of 2 inactivated vaccines developed from SARS-CoV-2 WIV04 (5 µg/dose; n = 13 459) and HB02 (4 µg/dose; n = 13 465) strains or an aluminum hydroxide (alum)–only control (n = 13 458) (2 intramuscular injections 21 days apart) Outcomes: efficacy against laboratory-confirmed symptomatic COVID-19 14 days following a second vaccine dose among participants who had no virologic evidence of SARS-CoV-2 infection at randomization. Efficacy against severe COVID-19. Incidence of adverse events and reactions was collected in participants who received at least 1 dose. **Findings:** > 40 382 participants (mean age 36.1 yrs; 32 261 [84.4%] men) > 38 206 (94.6%) received 2 doses > During a median (range) follow-up duration of 77 (1-121) days, symptomatic COVID-19 was identified in 26 participants in the WIV04 group (12.1 [95% CI, 8.3-17.8] per 1000 person-years), 21 in the HB02 group (9.8 [95% CI, 6.4-15.0] per 1000 person-years), and 95 in the alum-only group (44.7 [95% CI, 36.6-54.6] per 1000 person-years), resulting in a vaccine efficacy, compared with alum-only, of 72.8% (95% CI, 58.1%-82.4%) for WIV04 and 78.1% (95% CI, 64.8%-86.3%) for HB02 (P < .001 for both). > Two severe cases of COVID-19 occurred in the alum-only group and none occurred in the vaccine groups. > Adverse reactions 7 days after each injection occurred in 41.7% to 46.5% of participants in the 3 groups; serious adverse events were rare and similar in the 3 groups (WIV04: 64 [0.5%]; HB02: 59 [0.4%]; alum-only: 78 [0.6%]). **Conclusion** Treatment of adults with either of 2 inactivated SARS-CoV-2 vaccines significantly reduced the risk of symptomatic COVID-19, and serious adverse events were rare.

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PNAS 25MAY2021	**Just 2% of SARS-CoV-2–positive individuals carry 90% of the virus circulating in communities**	Yang Q., et al. USA <u>gotopaper</u>	Public Health / Epidemiology	**Aim:** Describing the estimated distribution of viral loads among SARS-CoV-2-positive asymptomatic individuals detected through random surveillance **Methods:** > Surveillance through repeated testing of asymptomatic individuals on the University of Colorado Boulder campus (72500 saliva samples; 1405 positive, mostly from unique individuals). > Detection by qRT-PCR of saliva samples > Estimation of viral loads from Ct values > Comparison to datasets of symptomatic individuals **Findings:** > Distributions of viral loads are similar between asymptomatic and symptomatic populations > Large heterogeneity of Ct values (hence viral loads): at a given time point 2% of positive individuals host 90% of the circulated virions **Limitations:** The authors interpret the difference in viral loads as exclusively due to individual variation in peak viral load. However, the authors do control for the time since infection, and therefore should not dismiss the fact that viral loads changes over the course of infection, which mechanically leads to a whole range of Ct values in a population sampled at a given point in time. **Conclusions:** At a given point in time, the vast majority of circulating virions in communities are found within the bodies of a small number of individuals.
JAMA Netw Open 25MAY2021	**Association of Circulating Sex Hormones With Inflammation and Disease Severity in Patients With COVID-19**	Dhindsa S., *et al*. USA <u>gotopaper</u>	Clinic	**Contribution of sex hormones to severe COVID-19 illness in men: association of concentrations of serum testosterone, estradiol, and insulinlike growth factor 1 (IGF-1, concentrations of which are regulated by sex hormone signaling) with COVID-19 severity.** **Methods** > Prospective cohort study > Collection of serum samples from patients with COVID-19 (diagnosed using nasopharyngeal swabs). > Testosterone, estradiol, and IGF-1 concentrations measured at the time of presentation (day 0) and at day 3, 7, 14, 28 after admission <u>Main Outcomes</u> Baseline hormone concentrations compared among patients who had severe COVID-19 vs those with mild COVID-19. **Findings** > Among 152 patients (90 [59.2%] men; 62 [40.8%] women; mean [SD] age, 63 [16] years), 143 patients (94.1%) were hospitalized. > Among 66 men with severe COVID-19, median testosterone concentrations were lower at day 0 (53 [18 to 114] ng/dL vs 151 [95 to 217] ng/dL; P = .01) and day 3 (19 [6 to 68] ng/dL vs 111 [49 to 274] ng/dL; P = .006) compared with 24 men with milder disease. > Testosterone concentrations were inversely associated with concentrations of interleukin 6 (β = −0.43; 95% CI, −0.52 to −0.17; P < .001), C-reactive protein (β = −0.38; 95% CI, −0.78 to −0.16; P = .004), interleukin 1 receptor antagonist (β = −0.29; 95% CI, −0.64 to −0.06; P = .02), hepatocyte growth factor (β = −0.46; 95% CI, −0.69 to −0.25; P < .001), and interferon γ–inducible protein 10 (β = −0.32; 95% CI, −0.62 to −0.10; P = .007). > Estradiol and IGF-1 concentrations were not associated with COVID-19 severity in men. > Testosterone, estradiol, and IGF-1 concentrations were similar in women with and without severe COVID-19. > Gene set enrichment analysis revealed upregulated hormone signaling pathways in CD14+CD16− (ie, classical) monocytes and CD14−CD16+ (ie, nonclassical) monocytes in male patients with COVID-19 who needed intensive care unit treatment vs those who did not. **Conclusion** Lower testosterone concentrations during hospitalization were associated with increased disease severity and inflammation in men.

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Clin Microbiol Infect. 25MAY2021	**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**	Ader F., et al. France [gotopaper]	Therapeutics	**Aim**: to evaluate clinical, virological and safety outcomes of lopinavir/ritonavir, lopinavir/ritonavir-interferon (IFN)-β-1a, hydroxychloroquine or remdesivir in comparison to standard of care (control) in COVID-19 inpatients requiring oxygen and/or ventilatory support. - Phase 3 multi-centre open-label, randomized 1:1:1:1:1, adaptive, controlled trial (DisCoVeRy). - Results for the lopinavir/ritonavir-containing arms and for the hydroxychloroquine arm, stopped prematurely, are reported. Primary outcome: clinical status at day 15, measured by the WHO 7-point ordinal scale. Secondary outcomes included SARS-CoV-2 quantification in respiratory specimens, pharmacokinetic and safety analyses. **Results** > 583 participants (lopinavir/ritonavir, n=145; lopinavir/ritonavir-IFN-β-1a, n=145; hydroxychloroquine, n=145; control, n=148). 418 (71.7%) males, median age 63yrs (IQR, 54-71), 211 (36.2%) had severe disease. > The day-15 clinical status was not improved with investigational treatments: lopinavir/ritonavir vs. control, adjusted odds ratio (aOR) 0.83, (95%CI 0.55-1.26, P=0.39); lopinavir/ritonavir-IFN-β-1a vs. control, aOR 0.69 (95%CI 0.45-1.04, P=0.08); hydroxychloroquine vs. control, aOR 0.93 (95%CI 0.62-1.41, P=0.75). > No significant effect of investigational treatment was observed on SARS-CoV-2 clearance. > Trough plasma concentrations of lopinavir and ritonavir were higher than those expected, while those of hydroxychloroquine were those expected with the dosing regimen. > The occurrence of Serious Adverse Events was significantly higher in participants allocated to the lopinavir/ritonavir-containing arms. **Conclusions** In adults hospitalized for COVID-19, lopinavir/ritonavir, lopinavir/ritonavir-IFN-ß-1a and hydroxychloroquine did not improve the clinical status at day 15, nor SARS-CoV-2 clearance in respiratory tract specimens.
Ann Intern Med. 25MAY2021	**Safety and Immunogenicity of Anti–SARS-CoV-2 Messenger RNA Vaccines in Recipients of Solid Organ Transplants**	Marion O., *et al*. France [gotopaper]	Vaccines - Immunisation	**Assessement of the humoral response to messenger RNA (mRNA)–based vaccination in recipients of solid organ transplant (SOT) (COVID-19 Mortality within this group: 20%).** - Vaccinees with heart, kidney, liver, or pancreas transplants. - Spike protein antibodies monitored before and after vaccination. **Findings** > 950 patients of the 2666 within receiving at least 1 dose of an mRNA vaccine (BNT162b2 vaccine [Pfizer-BioNTech], n = 942; mRNA-1273 vaccine [Moderna], n = 8) and had anti–SARS-CoV-2 antibodies monitored. Fifty patients had vaccination without monitoring of antibodies, 80 patients were are planned to be vaccinated within the month , and 257 patients declined the vaccine. No feedback from the remaining 1329 patients. > 895 of the 950 patients had an available serologic screening just before the first injection. Prevalence of anti–SARS-CoV-2 antibodies: 2.1% (95% CI, 1.3% to 3.3%; n = 19 of 895). Only 5 of the 19 patients who were seropositive previously had symptomatic COVID-19. > A total of 576 patients benefited from a second injection at day 28. The prevalence of anti–SARS-CoV-2 antibodies before the second injection was 6.4% (CI, 4.6% to 8.8%; n = 37 of 576). > In 367 patients who had a 4-week follow-up after the second dose, the prevalence of anti–SARS-CoV-2 antibodies increased from 1.4% (CI, 0.4% to 3.2%; n = 5 of 367) at baseline to 6.3% (CI, 4.0% to 9.3%; n = 23 of 367) at day 28 and 33.8% (CI, 29.0% to 38.9%; n = 124 of 367) 1 month after the second dose > The tolerance of mRNA vaccines was excellent, with no serious adverse events reported, except in 1 patient with a liver transplant who developed paresthesia of the lower limb. **Conclusion** > In immunocompromised patients, such as recipients of SOT, a weak humoral response to mRNA vaccines is reported > Recipients of liver transplant showed a better humoral response than recipients of other organs.

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Science Immunol. 25MAY2021	**SARS-CoV-2 variants of concern partially escape humoral but not T-cell responses in COVID-19 convalescent donors and vaccinees**	Geers D., et al. Netherlands gotopaper	Immunology	**Aim**: to study humoral and cellular immune responses to wild type SARS-CoV-2 and the B.1.1.7 and B.1.351 variants of concern in a cohort of 121 BNT162b2 mRNA-vaccinated health care workers (HCW) > Twenty-three HCW recovered from mild COVID-19 disease and exhibited a recall response with high levels of SARS-CoV-2-specific functional antibodies and virus-specific T cells after a single vaccination. > Specific immune responses were also detected in seronegative HCW after one vaccination, but a second dose was required to reach high levels of functional antibodies and cellular immune responses in all individuals. > Vaccination-induced **antibodies cross-neutralized the variants B.1.1.7 and B.1.351**, but the neutralizing capacity and Fc-mediated **functionality against B.1.351 was consistently 2- to 4-fold lower** than to the homologous virus. > Peripheral blood mononuclear cells were stimulated with peptide pools spanning the mutated S regions of B.1.1.7 and B.1.351 to detect cross-reactivity of SARS-CoV-2-specific T cells with variants. **No differences in CD4+ T-cell activation in response to variant antigens was observed**, indicating that the B.1.1.7 and B.1.351 S proteins do not escape T-cell-mediated immunity elicited by wild type S protein. **Some variants can partially escape humoral immunity induced by SARS-CoV-2 infection or BNT162b2 vaccination, but S-specific CD4+ T-cell activation is not affected by the mutations in the B.1.1.7 and B.1.351 variants.**
Science 25MAY2021	**Estimating infectiousness throughout SARS-CoV-2 infection course**	Jones T.C., *et al.* Germany / USA gotopaper	Virology	**Aim**: to analyse viral load and whether samples yield a replicating virus isolate in cell culture (parameters for quantifying viral infection and shedding). Sample: 25,381 German SARS-CoV-2 cases, including 6110 from test centres attended by pre-symptomatic, asymptomatic, and mildly-symptomatic (PAMS) subjects, 9519 who were hospitalised, and 1533 B.1.1.7 lineage infections. > The youngest had mean log10 viral load 0.5 (or less) lower than older subjects and an estimated ~78% of the peak cell culture replication probability, due to smaller swab sizes, unlikely to be clinically relevant. > Viral loads above 109 copies per swab were found in 8% of subjects, one-third of whom were PAMS, with mean age 37.6. > PAMS subjects in apparently-healthy groups can be expected to be as infectious as hospitalised patients at the time of detection. > Estimate of 4.3 days from onset of shedding to peak viral load (8.1) and cell culture isolation probability (0.75). > B.1.1.7 subjects had mean log10 viral load 1.05 higher than non-B.1.1.7, with estimated cell culture replication probability 2.6 times higher. **Accurate estimations can be directly obtained from two easily-measured virological parameters, viral load and sample cell culture infectivity.**
Cell 24MAY2021	**An infectivity-enhancing site on the SARS-CoV-2 spike protein targeted by antibodies**	Liu Y., et al. Japan gotopaper	Virology	The effects of antibodies against spike protein domains other than the RBD are largely unknown. > Screening of a series of anti-spike monoclonal antibodies from COVID-19 patients showed that some of antibodies against the N-terminal-domain (NTD) **induced the open conformation of receptor binding domain (RBD) and thus enhanced the binding capacity of the spike protein to ACE2** and infectivity of SARS-CoV-2. > Mutational analysis revealed that all the infectivity-enhancing antibodies recognized a specific site on the NTD. > Structural analysis demonstrated that all the infectivity-enhancing antibodies bound to NTD in a similar manner. > Divalent bridging of spikes is required to induce RBD-up sate. > The antibodies against this infectivity-enhancing site were **detected at high levels in severe patients**. > Antibodies against the infectivity-enhancing site were **identified in uninfected donors**, albeit at a lower frequency. **These findings demonstrate that not only neutralizing antibodies but also enhancing antibodies are produced during SARS-CoV-2 infection.**

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Nature 24MAY2021	**SARS-CoV-2 infection induces long-lived bone marrow plasma cells in humans**	Turner J.S., *et al.* USA [gotopaper](link)	Immunology	**Aim:** to determine whether SARS-CoV-2 infection induces antigen-specific long-lived bone marrow plasma cells (BMPCs) in humans. **Methods:** Blood samples were collected approximately 1 month after onset of symptoms from 77 SARS-CoV-2 convalescent volunteers(49% female, 51% male, median age 49), the majority of whom had expe-rienced mild illness (7.8% hospitalized). Follow-up blood samples were collected three times at approximately 3-month intervals. Additionally, bone marrow aspirates were collected from 18 of the participants 7 to 8 months after infection and from 11 healthy volunteers with no history of SARS-CoV-2 infection or vaccination. **Findings:** > In patients who experienced mild infections (n=77), serum anti-SARS-CoV-2 spike (S) antibodies decline rapidly in the first 4 months after infection and then more gradually over the following 7 months, remaining detectable at least 11 months after infection. > Anti-S antibody titers correlated with the frequency of S-specific BMPCs obtained from bone marrow aspirates of 18 SARS-CoV-2 convalescent patients 7 to 8 months after infection. S-specific BMPCs were not detected in aspirates from 11 healthy subjects with no history of SARS-CoV-2 infection. > S-binding BMPCs are quiescent, indicating that they are part of a long-lived compartment. Consistently, circulating resting memory B cells directed against the S protein were detected in the convalescent individuals. **SARS-CoV-2 infection induces a robust antigen-specific, long-lived humoral immune response in humans.**
Clin Microbiol Infect. 23MAY2021	**Clinical outcomes in COVID-19 patients infected with different SARS-cov-2 variants in marseille, France**	Dao T.L., *et al.* France [gotopaper](link)	Virology	**Clinical and epidemiological aspects associated with different predominant lineages circulating in Marseille from March 2020 to January 2021.** **Methods** > Single-center retrospective cohort study > Characteristics of patients infected with four different SARS-CoV-2 variants were documented from medical files. Outcome: occurrence of clinical failure, defined as hospitalization (for outpatients), transfer to the intensive-care unit (inpatients), death (all) **Findings** > 254 patients were infected with clade 20A (20AS), 85 with Marseille-1 (M1V), 190 with Marseille-4 (M4V) and 211 with N501Y (N501YV) variants. (i) 20AS presented a bell-shaped epidemiological curve and nearly disappeared around May 2020. (ii) M1V reached a very weak peak, then disappeared after a month-and-a-half. (iii) M4V appeared in July presented an atypical wave form during seven months. (iv) N501YV was only recently appeared. > As compared to 20AS, patients infected with M1V were less likely to report dyspnoea (aOR=0.50, p=0.04), rhinitis (aOR=0.57, p=0.04) and to be hospitalised (aOR=0.22, p=0.002). > Patients infected with M4V were more likely to report fever than those with 20AS and M1V (aOR=2.49, p<0.0001 and aOR=2.30, p=0.007, respectively) and to be hospitalised than those with M1V (aOR=4.81, p=0.003). > Patients infected with N501YV reported lower rate of rhinitis (aOR=0.50, p=0.001) and anosmia (aOR=0.57, p=0.02), as compared to those infected with 20AS. > A lower rate of hospitalisation associated with N501YV infection as compared to 20AS and M4V (aOR=0.33, p<0.0001 and aOR=0.27, p<0.0001, respectively). **Conclusions** The four lineages have presentations which differ from one other, epidemiologically and clinically. This supports SARS-CoV-2 genomic surveillance through next-generation sequencing.

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Lancet 22MAY2021	**Patient care and clinical outcomes for patients with COVID-19 infection admitted to African high-care or intensive care units (ACCCOS): a multicentre, prospective, observational cohort study**	ACCCOS Investigators Group International gotopaper	Public Health / Epidemiology	**Resources, comorbidities, and critical care interventions are associated with mortality incritically ill African patients due to COVID-19** **Methods** > Multicentre, prospective, observational cohort study in adults (aged 18 years or older) with suspected or confirmed COVID-19 infection referred to intensive care or high-care units in 64 hospitals in ten African countries (ie, Egypt, Ethiopia, Ghana, Kenya, Libya, Malawi, Mozambique, Niger, Nigeria, and South Africa). ClinicalTrials.gov, NCT04367207. Primary outcome: in-hospital mortality censored at 30 days. **Findings** > 6779 patients referred to critical care. > Of these, 3752 (55·3%) patients were admitted and 3140 (83·7%) patients from 64 hospitals in ten countries participated (mean age 55·6 years; 1890 [60·6%] of 3118 participants were male). > In-hospital mortality within 30 days of admission was 48·2% (95% CI 46·4–50·0; 1483 of 3077 patients). > Factors that were independently associated with mortality were (i) increasing age per year (odds ratio 1·03; 1·02–1·04); (ii) HIV/AIDS (1·91; 1·31–2·79); (iii) diabetes (1·25; 1·01–1·56); (iv)chronic liver disease (3·48; 1·48–8·18); (v) chronic kidney disease (1·89; 1·28–2·78); (vi) delay in admission due to a shortage of resources (2·14; 1·42–3·22); (vii) quick sequential organ failure assessment score at admission (for one factor [1·44; 1·01–2·04], for two factors [2·0; 1·33–2·99], and for three factors [3·66, 2·12–6·33]); (viii) respiratory support (high flow oxygenation [2·72; 1·46–5·08]; continuous positive airway pressure [3·93; 2·13–7·26]; invasive mechanical ventilation [15·27; 8·51–27·37]); (ix) cardiorespiratory arrest within 24 h of admission (4·43; 2·25–8·73); (x) vasopressor requirements (3·67; 2·77–4·86). > Steroid therapy was associated with survival (0·55; 0·37–0·81). **Conclusion** Increased mortality was associated with insufficient critical care resources, as well as the comorbidities of HIV/AIDS, diabetes, chronic liver disease, and kidney disease, and severity of organ dysfunction at admission.
Clin Infect Dis. 20MAY2021	**Factors Associated with Readmission in the US Following Hospitalization with COVID-19**	Verna E.C., *et al.* USA gotopaper	Clinic	**Aim:** to estimate the rate and risk factors associated with COVID-19-related readmission and inpatient mortality. **Methods:** Retrospective cohort study utilizing deidentified chargemaster data from 297 hospitals across 40 US states on patients hospitalized with COVID-19 February 15-June 09, 2020. Mulitvariable logistic regression was used to measure risk factor associations with 30-day readmission and in-hospital mortality. **Findings:** > Among 29,659 patients, 1,070 (3.6%) were readmitted. > Readmitted patients were more likely to have diabetes, hypertension, cardiovascular disease (CVD), chronic kidney disease (CKD) vs those not readmitted and to present on first admission with acute kidney injury (15.6% vs. 9.2%), congestive heart failure (6.4% vs. 2.4%), and cardiomyopathy (2.1% vs. 0.8%). > Higher odds of readmission were observed in patients age >60 vs. 1840 (odds ratio [OR]=1.92), and admitted in the Northeast vs. West (OR=1.43) or South (OR=1.28). > Comorbidities including diabetes (OR=1.34), CVD (OR=1.46), CKD stage 1-5 (OR=1.51) and stage 5 (OR=2.27) were associated with higher odds of readmission. > **12.3% of readmitted patients died during second hospitalization. Readmission was associated with certain comorbidities and acute conditions during first hospitalization.**

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Science 20MAY2021	**Face masks effectively limit the probability of SARS-CoV-2 transmission**	Cheng Y., *et al.* USA [gotopaper]	Public Health / Epidemiology	**Aim:** to develop a quantitative model of airborne virus exposure that can explain these contrasting results and provide a basis for quantifying the efficacy of face masks. **Methods:** The analysis was focused on respiratory particles and droplets with diameters smaller than 100 µm (traditional physical definition of aerosols). **Findings:** > **M**ask efficacy strongly depends on airborne virus abundance. Based on direct measurements of SARS-CoV-2 in air samples and population-level infection probabilities, the authors find that the virus abundance in most environments is sufficiently low for masks to be effective in reducing airborne transmission. > A person typically emits a total number of about 3×10^6 particles during a 30 min period. This very large number implies that indoor environments are usually in a respiratory particle-rich regime. Surgical masks with particle collection efficiencies around ~50% cannot prevent the release of millions of particles per person and their inhalation by others. > For SARS-CoV-2, the viral load of infectious individuals can vary by orders of magnitude. The authors find that most environments and contacts are under conditions of low virus abundance (virus-limited) where surgical masks are effective at preventing virus spread. > **More advanced masks and other protective equipment are required in potentially virus-rich indoor environments including medical centers and hospitals.** > Masks are particularly effective in combination with other preventive measures like ventilation and distancing.
Nature 19MAY2021	**Diverse Functional Autoantibodies in Patients with COVID-19**	Wang E.Y., *et al.* USA [gotopaper]	Immunology	**Aim:** to screen a cohort of 194 SARS-CoV-2 infected COVID-19 patients and healthcare workers for autoantibodies against 2,770 extracellular and secreted proteins (the "exoproteome"). Exoproteome-targeting autoantibodies can exert a wide range of functional effects such as perturbation of cell signaling (as with the case of anti-IFN-I autoantibodies[11,12]) and targeted killing of specific cell populations via Fc receptors (FcR) and/or complement. **Methods:** A high-throughput autoantibody (AAb) discovery technique called Rapid Extracellular Antigen Profiling (REAP)[7] was used to screen the cohort. **Findings:** > COVID-19 patients exhibit dramatic increases in autoantibody reactivities compared to uninfected controls, with a high prevalence of autoantibodies against immunomodulatory proteins including cytokines, chemokines, complement components, and cell surface proteins. > These autoantibodies perturb immune function and impair virological control by inhibiting immunoreceptor signaling and by altering peripheral immune cell composition. > Murine surrogates of these autoantibodies exacerbate disease severity in a mouse model of SARS-CoV-2 infection. > Analysis of autoantibodies against tissue-associated antigens revealed associations with specific clinical characteristics and disease severity. **These findings implicate a pathological role for exoproteome-directed autoantibodies in COVID-19 with diverse impacts on immune functionality and associations with clinical outcomes.**

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BMJ 19MAY2021	**Risk of clinical sequelae after the acute phase of SARS-CoV-2 infection: retrospective cohort study**	Daugherty S.E., *et al.* USA gotopaper	Clinic	**Aim:** to evaluate the excess risk and relative hazards for developing incident clinical sequelae after the acute phase of SARS-CoV-2 infection in adults aged 18-65 **Methods:** Retrospective cohort study from individuals aged 18-65 with continuous enrollment in the health plan from January 2019 to the date of a diagnosis of SARS-CoV-2 infection. Three merged data sources from a large United States health plan: a large national administrative claims database, an outpatient laboratory testing database, and an inpatient hospital admissions database. **Findings:** > 14% of adults aged ≤65 who were infected with SARS-CoV-2 (27 074 of 193 113) had at least one new type of clinical sequelae that required medical care after the acute phase of the illness, which was 4.95% higher than in the 2020 comparator group. > The risk for specific new sequelae attributable to SARS-Cov-2 infection after the acute phase, including chronic respiratory failure, cardiac arrythmia, hypercoagulability, encephalopathy, peripheral neuropathy, amnesia (memory difficulty), diabetes, liver test abnormalities, myocarditis, anxiety, and fatigue, was significantly greater than in the three comparator groups (2020, 2019, and viral lower respiratory tract illness groups). > Significant risk differences because of SARS-CoV-2 infection ranged from 0.02 to 2.26 per 100 people, and hazard ratios ranged from 1.24 to 25.65 compared with the 2020 comparator group. >**Individuals who were older, had pre-existing conditions, and were admitted to hospital because of covid-19 were at greatest excess risk.** > Younger adults (aged ≤50), those with no pre-existing conditions, or those not admitted to hospital for covid-19 also had an increased risk of developing new clinical sequelae.
JAMA Netw Open 19MAY2021	**Assessment of the Association of Vitamin D Level With SARS-CoV-2 Seropositivity Among Working-Age Adults**	Li Y., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim**: to examine whether low levels of vitamin D (<20 ng/mL or < 30 ng/mL.) are associated with SARS-CoV-2 seropositivity, an indicator of previous infection. **Results** > The 18 148 individuals included in this study had test results for SARS-CoV-2 IgG in 2020 and vitamin D levels from the prepandemic and pandemic periods. Median (interquartile range) age was 47 (37-56) years, 12 170 (67.1%) were women, 900 (5.0%) were seropositive, 4498 (24.8%) had a vitamin D level <20 ng/mL, and 10 876 (59.9%) had a vitamin D level <30 ng/mL before the pandemic. > In multivariable models adjusting for age, sex, race/ethnicity, education, body mass index, blood pressure, smoking status, and geographical location, SARS-CoV-2 seropositivity was not associated with having a vitamin D level <20 ng/mL before (odds ratio [OR], 1.04; 95% CI, 0.88-1.22) or during (OR, 0.93; 95% CI, 0.79-1.09) the pandemic; it was also not associated with having a vitamin D level <30 ng/mL before (OR, 1.09; 95% CI, 0.93-1.27) or during (OR, 1.05; 95% CI, 0.91-1.23) the pandemic. Similar results were observed in propensity score analyses. > SARS-CoV-2 seropositivity was associated with obesity (OR, 1.26; 95% CI, 1.08-1.46), not having a college degree (OR, 1.40; 95% CI, 1.21-1.62), and Asian (OR, 1.46; 95% CI, 1.13-1.87), Black (OR, 2.74; 95% CI, 2.25-3.34), Hispanic (OR, 2.65; 95% CI, 2.15-3.27), American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander (OR, 2.01; OR, 1.54-2.62) race/ethnicity, and was inversely associated with high blood pressure (OR, 0.82; 95% CI, 0.70-0.96), smoking (OR, 0.60; 95% CI, 0.47-0.78), and residing in the US Northeast (OR, 0.75; 95% CI, 0.62-0.92) and West (OR, 0.54; 95% CI, 0.44-0.67). **Conclusions** In this cohort study, SARS-CoV-2 seropositivity was not associated with low levels of vitamin D independently of other risk factors.

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Nature Med. 18MAY2021	**Phase 1 randomized trial of a plant-derived virus-like particle vaccine for COVID-19**	Ward B.J., *et al.* Canada [gotopaper]	Vaccines	Safety and immunogenicity data from the virus-like particle vaccine candidate produced by MEDICAGO. (CoVLP: NCT04450004). **Methods** > Phase 1 blinded, dose escalation, randomized controlled study of a virus-like particle vaccine candidate produced in plants that displays the SARS-CoV-2 spike glycoprotein > Adults (18–55 years, n = 180) receiving two intramuscular doses of CoVLP (3.75 μg, 7.5 μg, and 15 μg) 21 d apart, alone or adjuvanted with AS03 or CpG1018 or placebo. <u>Primary outcomes:</u> short-term tolerability/safety and immunogenicity of CoVLP formulations assessed by neutralizing antibody (NAb) and cellular responses. **Findings** > All formulations were well tolerated, and adverse events after vaccination were generally mild to moderate, transient and highest in the adjuvanted groups. > No CoVLP dose effect on serum NAbs, but titers increased significantly with both adjuvants > After the second dose, NAbs in the CoVLP + AS03 groups were more than tenfold higher than titers in Coronavirus 2019 convalescent sera. > Spike protein-specific interferon-γ and interleukin-4 cellular responses were also induced.
Nature Med. 18MAY2021	**Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection**	Khoury D.S., *et al.* Australia [gotopaper]	Immunology	Analysis of the relationship between *in vitro* neutralization levels and observed protection from SARS-CoV-2 infection (data from seven current vaccines and from convalescent cohorts) **Findings** > The neutralization level for 50% protection against detectable SARS-CoV-2 infection to be 20.2% of the mean convalescent level (95% confidence interval (CI) = 14.4–28.4%). > Estimated neutralization level required for 50% protection from severe infection was significantly lower (3% of the mean convalescent level; 95% CI = 0.7–13%, $P = 0.0004$). > Modeling of the decay of the neutralization titer over the first 250 d after immunization predicts that a significant loss in protection from SARS-CoV-2 infection will occur, although protection from severe disease should be largely retained. > Neutralization titers against some SARS-CoV-2 variants of concern are reduced compared with the vaccine strain **Conclusion** Neutralization level is highly predictive of immune protection, and provide an evidence-based model of SARS-CoV-2 immune protection that will assist in developing vaccine strategies to control the future trajectory of the pandemic.
Science Immunol. 18MAY2021	**Pharmacological activation of STING blocks SARS-CoV-2 infection**	Minghua L., *et al.* USA [gotopaper]	Therapeutics	Since pretreatment with IFNs can block viral infection, we reasoned that pharmacological activation of innate immune pathways could control SARS-CoV-2 infection **Methods** > To identify potent antiviral innate immune agonists, we screened a panel of 75 microbial ligands that activate diverse signaling pathways and identified cyclic dinucleotides (CDNs), canonical STING agonists, as antiviral. **Findings** > SARS-CoV-2 evades interferon (IFN) activation in respiratory epithelial cells, resulting in a delayed response in bystander cells > Since CDNs have poor bioavailability, we tested the small molecule STING agonist diABZI, and found that it potently inhibits SARS-CoV-2 infection of diverse strains including variants of concern (B.1.351) by transiently stimulating IFN signaling > Importantly, diABZI restricts viral replication in primary human bronchial epithelial cells and in mice in vivo. Our study provides evidence that activation of STING may represent a promising therapeutic strategy to control SARS-CoV-2.

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Science Immunol. 18MAY2021	**A diamidobenzimidazole STING agonist protects against SARS-CoV-2 infection**	Humphries F., *et al.* USA gotopaper	Therapeutics	Describe a diamidobenzimidazole compound: diABZI-4 **Findings** > diABZ-4 activates STING and is highly effective in limiting SARS-CoV-2 replication in cells and animals. > diABZI-4 inhibited SARS-CoV-2 replication in lung epithelial cells. > Administration of diABZI-4 intranasally before or even after virus infection conferred complete protection from severe respiratory disease in K18-ACE2-transgenic mice infected with SARS-CoV-2. > Intranasal delivery of diABZI-4 induced a rapid short-lived activation of STING, leading to transient proinflammatory cytokine production and lymphocyte activation in the lung associated with inhibition of viral replication. **Our study supports the use of diABZI-4 as a host-directed therapy which mobilizes antiviral defenses for the treatment and prevention of COVID-19.**
Clin Infect Dis. 17MAY2021	**The effectiveness of the TWO-DOSE BNT162b2 vaccine: analysis of real-world data**	Chodick G., *et al.* Israel gotopaper	Vaccines - Immunisations	**Aim**: to evaluate the effectiveness of BNT162b2 vaccine in preventing SARS-CoV-2 infection and COVID-19-related hospitalization and mortality. Primary outcome: incidence rate of a SARS-CoV-2 infection confirmed with rt-PCR, between 7 to 27 days after second dose (protection-period), as compared to days 1 to 7 after the first dose, where no protection by the vaccine is assumed (reference-period). **Results** > Data of 1,178,597 individuals vaccinated with BNT162b2 were analyzed (mean age 47.7 years [SD=18.1], 48.4% males) of whom 872,454 (74.0%) reached the protection period. > Overall, 4514 infections occurred during the reference period compared to 728 during the protection period, yielding a weighted mean daily incidence of 54.8 per 100,000 (95%CI: 26.1-115.0 per 100,000) and 5.4 per 100,000 (95%CI: 3.5-8.4 per 100,000), respectively. > The vaccine effectiveness in preventing infection was 90% (95%CI:79%- 95%) and 94% (95%CI:88%-97%) against COVID-19. > Among immunosuppressed patients, vaccine effectiveness against infection was 71% (95%CI:37%-87%). > The adjusted hazard ratios for hospitalization in those infected were 0.82 (95%CI:0.36-1.88), 0.45 (95%CI:0.23-0.90), and 0.56 (95%CI:0.36-0.89) in the age groups 16-44, 45-64 and ≥75 , respectively. **The effectiveness of the BNT162b2 vaccine is comparable to the one reported in the phase III clinical trial.**
Blood 14MAY2021	**Frequency of positive anti-PF4/polyanion antibody tests after COVID-19 vaccination with ChAdOx1 nCoV-19 and BNT162b2**	Thiele T., *et al.* Germany gotopaper	Vaccines	- Vaccination with COVID-19 vaccine ChAdOx1 nCoV-19 (AstraZeneca) has been associated with rare vaccine-induced immune thrombotic thrombocytopenia (VITT). - Affected patients test strongly positive in PF4/polyanion enzyme immunoassays (EIAs) and serum-induced platelet activation is maximal in the presence of PF4. **Aim**: to determine the frequency of anti-PF4/polyanion antibodies in healthy vaccinees and to assess if PF4/polyanion EIA-positive sera exhibit platelet-activating properties after vaccination with ChAdOx1 nCoV-19 (n=138) or BNT162b2 (BioNTech/Pfizer; n=143). > 19 of 281 participants tested positive for anti-PF4/polyanion antibodies post-vaccination (All: 6.8% [95%CI, 4.4-10.3]; BNT162b2: 5.6% [95%CI, 2.9-10.7]; ChAdOx1 nCoV-19: 8.0% [95%CI, 4.5-13.7%]). > Optical densities were mostly low (between 0.5-1.0 units; reference range, <0.50) and none of the PF4/polyanion EIA-positive samples induced platelet activation in the presence of PF4. **Positive PF4/polyanion EIAs can occur after SARS-CoV-2 vaccination with both mRNA- and adenoviral vector-based vaccines, but the majority of these antibodies likely have minor (if any) clinical relevance**. Pathogenic platelet-activating antibodies that cause VITT do not occur commonly following vaccination.

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Lancet Resp Med. 14MAY2021	**Changes in in-hospital mortality in the first wave of COVID-19: a multicentre prospective observational cohort study using the WHO Clinical Characterisation Protocol UK**	Docherty A.B., *et al.* UK [gotopaper](#)	Clinics	**Aim :** to quantify potential drivers of mortality rates in in-hospital patients and to identify groups of patients who remain at high risk of dying in hospital. **Methods :** > multicentre prospective observational cohort study of patients with COVID-19 admitted to 247 acute hospitals in England, Scotland, and Wales during the first wave of the pandemic (between March 9 and Aug 2, 2020). > A three-way decomposition mediation analysis using natural effects models to explore associations between week of admission and in-hospital mortality was performed. >The primary outcome was weekly in-hospital mortality at 28 days. **Findings :** > 80 713 patients were recruited, of whom 63 972 were eligible and included in the study. >Unadjusted weekly in-hospital mortality declined from 32·3% in March 9 to April 26, 2020, to 16·4% in June 15 to Aug 2, 2020. >Reductions in mortality were observed in all age groups, in all ethnic groups, for both sexes, and in patients with and without comorbidities. >After adjustment, there was a 32% reduction in the risk of mortality per 7-week period (odds ratio [OR] 0·68). >The higher proportions of patients with severe disease and comorbidities earlier in the first wave (March and April) than in June and July accounted for 10·2% of this reduction. >Changes in respiratory support and use of steroids accounted for 22·2%, OR 0·95 (0·94–0·95) of the reduction in in-hospital mortality. **A significant reduction in in-hospital mortality was associated with differences in respiratory support and critical care use, which could partly reflect accrual of clinical knowledge**.
Lancet 14MAY2021	**Convalescent plasma 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 safety and efficacy of convalescent plasma therapy in patients admitted to hospital with COVID-19. Primary outcome: 28-day mortality, analysed on an intention-to-treat basis. **Findings** > 11558 (71%) of 16287 patients enrolled in RECOVERY were assigned to either the convalescent plasma group or the usual care group (May 28, 2020, and Jan 15, 2021). > There was no significant difference in 28-day mortality between the two groups: 1399 (24%) of 5795 patients in the convalescent plasma group and 1408 (24%) of 5763 patients in the usual care group died within 28 days (rate ratio 1·00, 95% CI 0·93–1·07; p=0·95). > The 28-day mortality rate ratio was similar in all prespecified subgroups of patients, including in those patients without detectable SARS-CoV-2 antibodies at randomisation. > Allocation to convalescent plasma had no significant effect on the proportion of patients discharged from hospital within 28 days (3832 [66%] patients in the convalescent plasma group vs 3822 [66%] patients in the usual care group; rate ratio 0·99, 95% CI 0·94–1·03; p=0·57). > Among those not on invasive mechanical ventilation at randomisation, there was no significant difference in the proportion of patients meeting the composite endpoint of progression to invasive mechanical ventilation or death (1568 [29%] of 5493 patients in the convalescent plasma group vs 1568 [29%] of 5448 patients in the usual care group; rate ratio 0·99, 95% CI 0·93–1·05; p=0·79). **In patients hospitalised with COVID-19, high-titre convalescent plasma did not improve survival or other prespecified clinical outcomes.**

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BMJ 13MAY2021	**Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study**	Lopez-Bernal, J., *et al.* UK https://doi.org/10.1136/bmj.n1088	Vaccines - Immunisations	Real world effectiveness of the Pfizer-BioNTech BNT162b2 and Oxford-AstraZeneca ChAdOx1-S vaccines against confirmed covid-19 symptoms (including the UK variant of concern B.1.1.7), admissions to hospital, and deaths. **Methods** > Case-control study. > 156 930 adults aged 70 years and older who reported symptoms of covid-19 between 8 December 2020 and 19 February 2021 and were successfully linked to vaccination data in the National Immunisation Management System. > Interventions! Vaccination with BNT162b2 or ChAdOx1-S. <u>Main outcome</u> PCR confirmed symptomatic SARS-CoV-2 infections, admissions to hospital for covid-19, and deaths with covid-19. **Findings** **>** Participants aged 80 years and older vaccinated with BNT162b2 before 4 January 2021 had a higher odds of testing positive for covid-19 in the first nine days after vaccination (odds ratio up to 1.48, 95% confidence interval 1.23 to 1.77). Vaccine effects were noted 10 to 13 days after vaccination, reaching a vaccine effectiveness of 70% (95% confidence interval 59% to 78%). From 14 days after the second dose the vaccination effectiveness was estimated to 89% (85% to 93%). Vaccine effectiveness reached 61% (51% to 69%) from 28 to 34 days after vaccination, then plateaued. > With ChAdOx1-S, effects were seen from 14 to 20 days after vaccination, reaching an effectiveness of 60% (41% to 73%) from 28 to 34 days, increasing to 73% (27% to 90%) from day 35 onwards. > Further 43% (33% to 52%) reduced risk of emergency hospital admission and 51% (37% to 62%) reduced risk of death was observed in those who had received one dose of BNT162b2. > Participants who had received one dose of ChAdOx1-S had a further 37% (3% to 59%) reduced risk of emergency hospital admission. Follow-up was insufficient to assess the effect of ChAdOx1-S on mortality. > Combined with the effect against symptomatic disease, a single dose of either vaccine was about 80% effective at preventing admission to hospital with covid-19 and a single dose of BNT162b2 was 85% effective at preventing death with covid-19. **Conclusion** Vaccination with either one dose of BNT162b2 or ChAdOx1-S was associated with a significant reduction in symptomatic covid-19 in older adults, and with further protection against severe disease. Both vaccines showed similar effects. Protection was maintained for the duration of follow-up (>6 weeks). A second dose of BNT162b2 was associated with further protection against symptomatic disease. A clear effect of the vaccines against the B.1.1.7 variant was found.

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Nature 12MAY2021	**The epidemiological impacts of the NHS COVID-19 App**	Wymant C., *et al.* UK [gotopaper]	Public Health / Epidemiology	**Aim**: Investigate the impact of the NHS COVID-19 app for England and Wales, from its launch on 24 September 2020 through to the end of December 2020, using data aggregated at the level of local authorities. **Methods**: > Estimation of the secondary attack rate (SAR) in app-notified individuals based on a probabilistic model for how many positive test results would be expected among those recently notified. > Evaluation of the number of cases averted by the app based on notifications and SAR, using a mechanistic probabilistic modelling approach. > Evaluation of the number of cases averted by the app using a stratified statistical approach, allowing to address confounding factors. **Findings**: 16.5 million users (28% of the total population) sent approximately 1.7 million exposure notifications, 4.4 per index case consenting to contact tracing. > SAR was estimated at 6.0%, comparable to the SAR for manually traced close contacts. > Modelling based on the notifications and SAR gave 284,000 (108,000- 450,000) cases averted by the app. > Statistical comparison of matched neighbouring local authorities gave 594,000 (317,000-914,000) cases averted by the app. > For every percentage point increase in app users, the number of cases can be reduced by 0.8% (modelling) or 2.3% (statistical analysis). **Limitation**: > It is an observational study: no randomized or systematic experiment resulted in different app uptake in different places. **Conclusion**: > These findings provide evidence for continued development and deployment of privacy-preserving contact tracing apps in populations that are awaiting full protection from vaccines. > Digital tracing is best understood as part of a system of non-pharmaceutical interventions, not in isolation. Also, it is not a substitute for manual tracing, both being valuable.
BMJ 11MAY2021	**Use of repurposed and adjuvant drugs in hospital patients with covid-19: multinational network cohort study**	Prats-Uribe A., *et al.* UK / USA [gotopaper]	Therapeutics	**Aim :** to investigate the use of repurposed and adjuvant drugs in patients admitted to hospital with covid-19 across three continents. **Methods :** >Multinational network cohort study. > Data collected from Hospital electronic health records from the United States, Spain, and China, and nationwide claims data from South Korea. >303 264 patients admitted to hospital with covid-19 from January 2020 to December 2020 **Findings :** > Of the 303 264 patients included, 290 131 were from the US, 7599 from South Korea, 5230 from Spain, and 304 from China. > 3455 drugs were identified. > Common repurposed drugs were hydroxychloroquine (used in from <5 (<2%) patients in China to 2165 (85.1%) in Spain), azithromycin (from 15 (4.9%) in China to 1473 (57.9%) in Spain), combined lopinavir and ritonavir (from 156 (<2%) in the VA-OMOP US to 2,652 (34.9%) in South Korea and 1285 (50.5%) in Spain), and umifenovir (0% in the US, South Korea, and Spain and 238 (78.3%) in China). > Use of adjunctive drugs varied greatly, with the five most used treatments being enoxaparin, fluoroquinolones, ceftriaxone, vitamin D, and corticosteroids. > Hydroxychloroquine use increased rapidly from March to April 2020 but declined steeply in May to June and remained low for the rest of the year. > The use of dexamethasone and corticosteroids increased steadily during 2020.

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Jama Netw. Open 11MAY2021	**Global Incidence of Neurological Manifestations Among Patients Hospitalized With COVID-19—A Report for the GCS-NeuroCOVID Consortium and the ENERGY Consortium**	Chou S.H.Y., *et al.* USA gotopaper	Clinic	**Aim**: To determine the neurological phenotypes, incidence, and outcomes among adults hospitalized with COVID-19. 3 cohorts: - GCS-NeuroCOVID all COVID-19 – hospitalized patients with COVID-19 with and without neurological manifestations (n = 3055; 57% men, mean age 59.9 years [95% CI, 59.3-60.6]). - GCS-NeuroCOVID COVID-19 neurological cohort – patients hospitalized with COVID-19 who had confirmed neurological manifestations (n = 475; 55% men, and the mean age 62.6 [61.1-64.1]). - ENERGY cohort – patients with COVID-19 who received formal neurological consultation. (n = 214; 62% men, mean age 67 years [52-78]). **Results** > A total of 3083 of 3743 patients (82%) across cohorts had any neurological manifestation (self-reported neurological symptoms and/or clinically captured neurological sign and/or syndrome). > The most common self-reported symptoms included headache (1385 of 3732 patients [37%]) and anosmia or ageusia (977 of 3700 patients [26%]). > The most prevalent neurological signs and/or syndromes were acute encephalopathy (1845 of 3740 patients [49%]), coma (649 of 3737 patients [17%]), and stroke (222 of 3737 patients [6%]), while meningitis and/or encephalitis were rare (19 of 3741 patients [0.5%]). > Presence of clinically captured neurologic signs and/or syndromes was associated with increased risk of in-hospital death (adjusted odds ratio [aOR], 5.99; 95% CI, 4.33-8.28) after adjusting for study site, age, sex, race, and ethnicity. > Presence of preexisting neurological disorders (aOR, 2.23; 95% CI, 1.80-2.75) was associated with increased risk of developing neurological signs and/or syndromes with COVID-19. **Conclusions** In this multicohort study, neurological manifestations were prevalent among patients hospitalized with COVID-19 and were associated with higher in-hospital mortality.
Nature Med. 11MAY2021	**Neutralizing antibody responses to SARS-CoV-2 in symptomatic COVID-19 is persistent and critical for survival**	Dispinseri S., *et al.* Italy gotopaper	Immunology	Antibody responses of 162 COVID-19 symptomatic patients in the COVID-BioB cohort followed longitudinally for up to eight months from symptom onset to find SARS-CoV-2 neutralization, as well as antibodies either recognizing SARS-CoV-2 spike antigens and nucleoprotein, or specific for S2 antigen of seasonal beta-coronaviruses and hemagglutinin of the H1N1 flu virus. **Findings** > The presence of neutralizing antibodies within the first weeks from symptoms onset correlates with time to a negative swab result (p = 0.002). The lack of neutralizing capacity correlates with an increased risk of a fatal outcome (p = 0.008). > Neutralizing antibody titers progressively drop after 5–8 weeks but are still detectable up to 8 months in the majority of recovered patients regardless of age or co-morbidities, with IgG to spike antigens providing the best correlate of neutralization. >Antibody responses to seasonal coronaviruses are temporarily boosted, and parallel those to SARS-CoV-2 without dampening the specific response or worsening disease progression. **Conclusions** Compromised immune responses to the SARS-CoV-2 spike to be a major trait of COVID-19 patients with critical conditions, and thereby inform on the planning of COVID-19 patient care and therapy prioritization.

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Clin Infect Dis. 11MAY2021	**Trends over time in the risk of adverse outcomes among patients with SARS-CoV-2 infection**	Loannou G.N., *et al.* USA [gotopaper](#)	Public Health / Epidemiology	We aimed to describe trends in adverse outcomes among patients who tested positive for SARS-CoV-2 between February and September 2020 within a national healthcare system. **Methods** > Identified enrollees in the national U.S. Veterans Affairs healthcare system who tested positive for SARS-CoV-2 between 2/28/2020 and 9/30/2020 (n=55,952), with follow-up extending to 11/19/2020 > Determined trends over time in incidence of the following outcomes that occurred within 30 days of testing positive: hospitalization, intensive care unit (ICU) admission, mechanical ventilation and death. **Findings** > Between February and July 2020, there were marked **downward trends in the 30-day incidence** of hospitalization (44.2% to 15.8%), ICU admission (20.3% to 5.3%), mechanical ventilation (12.7% to 2.2%), and death (12.5% to 4.4%), which subsequently plateaued between July and September 2020. > These trends persisted after adjustment for sociodemographic characteristics, comorbid conditions, documented symptoms and laboratory tests, including among subgroups of patients hospitalized, admitted to the ICU or treated with mechanical ventilation. > From February to September, there were decreases in the use of hydroxychloroquine (56.5% to 0%), azithromycin (48.3% to 16.6%) vasopressors (20.6% to 8.7%), and dialysis (11.6% to 3.8%) and increases in the use of dexamethasone (3.4% to 53.1%), other corticosteroids (4.9% to 29.0%) and remdesivir (1.7% to 45.4%) among hospitalized patients. **The risk of adverse outcomes in SARS-CoV-2-positive patients decreased markedly between February and July, with subsequent stabilization from July to September. These trends were not explained by changes in measured baseline patient characteristics and may reflect changing treatment practices or viral pathogenicity.**
Clin Microbiol Infect. 10MAY2021	**Persistent COVID-19 symptoms are highly prevalent 6 months after hospitalization: results from a large prospective cohort**	Ghosn J., *et al.* France [gotopaper](#)	Public Health / Epidemiology	We have assessed, in the longitudinal prospective French COVID-19 cohort, symptoms that persisted 6 months after admission for COVID-19. **Findings** > M6 data were available for 1137 participants (Hospitalized patients with virologically confirmed COVID-19). Median age was 61 years (IQR 51–71) and 288 (29%, 95% CI 26–32%) were admitted to intensive care unit (ICU) during the acute phase. > 650 (68%, 95% CI 65–71%) and 639 (60%, 95% CI 57–63%) participants had at least one symptom at M3 and M6 visit, respectively, mostly fatigue, dyspnoea, joint pain and myalgia. > At M6, 255 (24%, 95% CI 21–27%) of participants had three or more persistent symptoms. > The presence of three or more symptoms at M6 was independently associated with female gender (adjusted odds ratio (aOR) 2.40, 95% CI 1.75–3.30), having three or more symptoms at admission (aOR 2.04, 95% CI 1.45–2.89) and ICU admission/transfer during acute phase (aOR 1.55, 95% CI 1.09–2.18), but not significantly with age or having two or more comorbidities. > 125 (29%, 95% CI 25–34%) of those who initially had a professional occupation were not back to work at M6. **A fourth of individuals admitted to hospital for COVID-19 still had three or more persistent symptoms at M6. Longitudinal follow-up of individuals with severe COVID-19 is warranted to better understand the pathophysiology underlying this long-term persistence.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Infect Dis. 10MAY2021	**Post-acute effects of SARS-CoV-2 infection in individuals not requiring hospital admission: a Danish population-based cohort study**	Lund L.C., *et al*. Denmark [gotopaper](#)	Long Covid	**Aim:** to analyze the risk of delayed complications in individuals not requiring hospital admission for COVID-19. **Methods:** Population-based cohort study using the Danish prescription, patient, and health insurance registries. All individuals with a positive or negative RT-PCR test for SARS-CoV-2 in Denmark between Feb 27 and May 31, 2020. The outcomes of interest were delayed acute complications, chronic disease, hospital visits due to persisting symptoms, and prescription drug use. **Findings:** > 10 498 eligible individuals tested positive for SARS-CoV-2 in Denmark from Feb 27 to May 31, 2020, of whom 8983 (85·6%) were alive and not admitted to hospital 2 weeks after their positive test.The matched SARS-CoV-2-negative reference population not admitted to hospital consisted of 80 894 individuals. > Compared with SARS-CoV-2-negative individuals, SARS-CoV-2-positive individuals were not at an increased risk of initiating new drugs (RD <0·1%) except bronchodilating agents, specifically short-acting β2-agonists (117 [1·7%] of 6935 positive individuals vs 743 [1·3%] of 57 206 negative individuals. And triptans (33 [0·4%] of 8292 vs 198 [0·3%] of 72 828. > There was an increased risk of receiving hospital diagnoses of dyspnoea (103 [1·2%] of 8676 vs 499 [0·7%] of 76 728; RD +0·6%; RR 2·00) and venous thromboembolism (20 [0·2%] of 8785 vs 110 [0·1%] of 78 872; RD +0·1%; RR 1·77) for SARS-CoV-2-positive individuals compared with negative individuals. > Prior event rate ratio-adjusted rate ratios of overall general practitioner visits (1·18) and outpatient hospital visits (1·10), but not hospital admission, showed increases among SARS-CoV-2-positive individuals compared with SARS-CoV-2-negative individuals. **The absolute risk of severe post-acute complications after SARS-CoV-2 infection not requiring hospital admission is low**.
Clin Microbiol Infect. 09MAY2021	**Outbreak investigation of symptomatic SARS-COV-2 VOC 202012/01-lineage B.1.1.7 infection in healthcare workers, Italy**	Loconsole D., *et al*. Italy [gotopaper](#)	Public Health / Epidemiology - Variants	**Aim**: to describe an outbreak of SARS-CoV-2 lineage B.1.1.7 infection in three HCWs in a hospital setting; two of the HCWs were fully vaccinated (i.e., had received two doses). **Methods:** Two physicians and one nurse working on the same shift on February 20, 2021, were involved in the outbreak. Real-time PCR, antigen tests, and serological tests for the IgG anti-spike protein of SARS-CoV-2 were performed, along with whole-genome sequencing (WGS). **Findings:** >SARS-CoV-2 infection was confirmed in all three HCWs; all presented with mild symptoms of COVID-19. >The two physicians were fully vaccinated with BNT162b2 vaccine, with the second dose administered 1 month before symptom onset. Both had high titres of IgG anti-spike antibodies at the time of diagnosis. >WGS confirmed that all virus strains were VOC 202012/01-lineage B.1.1.7, suggesting a common source of exposure. >Epidemiological investigation revealed that the suspected source was a SARS-CoV-2-positive patient who required endotracheal intubation due to severe COVID-19. All procedures were carried out using a full suite of personal protective equipment (PPE). **This mini-outbreak highlights some important issues about the efficacy of vaccines against transmission of SARS-CoV-2 variants,** the high risk of exposure among HCWs, and the need for optimized implementation of PPE in hospitals.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Clin Microbiol Infect. 08MAY2021	**SARS-COV-2 antibody dynamics and B-cell memory response over-time in COVID-19 convalescent subjects**	Achiron A., *et al.* Israel gotopaper	Immunology	**Aim**: to evaluate long-term IgG (antiS1) SARS-CoV-2 antibody response and B-cell memory response in COVID-19 convalescent subjects. **Results** > Antibody response was **not detected** in 26 of 392 (6.6%) COVID-19 convalescent subjects. > Over 9 months, the level of antibodies decreased by 50% but **stabilized at 6 months and prevailed a protective level up to 9 months**. > No differences were found regarding IgG SARS-COV-2 antibody levels for age, gender, and major blood types, over-time. > COVID-19 asymptomatic subjects **did not differ in antibody level** overtime from subjects with mild to severe disease. > Repeated paired IgG SARS-COV-2 antibody level analyses disclosed that over 6 and 9 months, 15.3% (9 of 59) and 15.8% (3 of 19) of subjects **became SARS-COV-2 IgG seronegative**, respectively, all with low antibody level at 3 months. Rate of antibody decline was not affected by age, gender, or clinical symptomatology. > In a subgroup of recovering subjects, **memory B-cell response up to 9-months post infection** was undetectable in 31.8% (14/44) of subjects with no correlation to age, SARS-COV-2 antibody level, or time post-infection. **Conclusions** Majority of COVID-19 convalescent subjects develop IgG SARS-COV-2 antibody response that prevails a protective level over a period of up to 9-months.
Lancet Rheumatol. 07MAY2021	**Non-steroidal anti-inflammatory drug use and outcomes of COVID-19 in the ISARIC Clinical Characterisation Protocol UK cohort: a matched, prospective cohort study**	Drake T.M., *et al.* UK gotopaper	Therapeutics	We aimed to characterise the safety of NSAIDs and identify whether pre-existing NSAID use was associated with increased severity of COVID-19 disease. **Methods** **>** Prospective, multicentre cohort study included patients of any age admitted to hospital with a confirmed or highly suspected SARS-CoV-2 infection leading to COVID-19 > We used propensity score matching to further estimate effects of NSAIDS while accounting for covariate differences in populations. **Findings** > Jan 17 and Aug 10, 2020, we enrolled 78 674 patients across 255 health-care facilities in England, Scotland, and Wales. 72 179 patients had death outcomes available for matching. 40 406 (56·2%) of 71 915 were men, 31 509 (43·8%) were women. > In this cohort, 4211 (5·8%) patients were recorded as taking systemic NSAIDs before admission to hospital. > At hospital admission, we observed no significant differences in severity between exposure groups. > After adjusting for explanatory variables, **NSAID use was not associated with worse in-hospital mortality** (matched OR 0·95, 95% CI 0·84–1·07; p=0·35), critical care admission (1·01, 0·87–1·17; p=0·89), requirement for invasive ventilation (0·96, 0·80–1·17; p=0·69), requirement for non-invasive ventilation (1·12, 0·96–1·32; p=0·14), requirement for oxygen (1·00, 0·89–1·12; p=0·97), or occurrence of acute kidney injury (1·08, 0·92–1·26; p=0·33). **NSAID use is not associated with higher mortality or increased severity of COVID-19. Policy makers should consider reviewing issued advice around NSAID prescribing and COVID-19 severity.**

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Sci Rep. 07MAY2021	**Incorporating false negative tests in epidemiological models for SARS-CoV-2 transmission and reconciling with seroprevalence estimates**	Bhattacharyya R., *et al.* India gotopaper	Public Health / Epidemiology	**Aims:** Estimate the number of unreported COVID-19 cases and deaths by taking into account the false negative rate of RT-PCR tests in the Delhi area. **Methods:** > Modelisation of the epidemic dynamic by an age-structured SEIR model taking into account the tests and false negatives. > Estimation of the model parameters by a well-known stochastic algorithm. > Model-based results are compared with data form serological surveys. **Findings:** The number of Covid-19 cases and deaths in the Delhi area is dramatically underestimated. > In July 2020, the underreporting factor was (34-53) for the number of cases, and (8-13) for the number of deaths. > In Janary 2021, the underreporting factor remains (13-22) for the number of cases, and (3-7) for the number of deaths. **Limits:** > The model does not take into account false positive of PCR tests. > Estimation of the false negative rate of PCR tests has a large impact on the estimation of the underreporting factors, limiting their accuracy. **Conclusion:** > Epidemic modeling can provide a less expensive method, with similar accuracy to large serological surveys, for estimating underreporting of Covid-19 cases. > This model predicts a very large number of unreported deaths due to Covid-19, making the cost of achieving herd immunity by letting the epidemics run its course even higher than previously expected.
Clin Infect Dis. 06MAY2021	**Interacting Epidemics in Amazonian Brazil: Prior Dengue Infection Associated with Increased COVID-19 Risk in a Population-Based Cohort Study**	Nicolete V.C., *et al.* International gotopaper	Public Health / Epidemiology	**Immunity after dengue virus (DENV) infection has been suggested to cross-protect from severe SARS-CoV-2 infection and mortality.** **Methods** > Serological surveys in proven prior DENV infection diagnosed subjects before the coronavirus 2019 (COVID-19) pandemic > Outcome: reduced the risk of SARS-CoV-2 infection and clinically apparent COVID-19 over the next 13 months **Findings** > Anti-DENV IgG was found in 37.0% of 1,285 cohort participants in 2019 > In 2020, 35.2% of the participants had anti-SARS-CoV-2 IgG and 57.1% of the 448 SARS-CoV-2 seropositives reported clinical manifestations at the time of infection. > Participants aged >60 were twice more likely to have symptomatic COVID-19 than under-five children. > Locally circulating SARS-CoV-2 isolates were assigned to the B.1.1.33 lineage. **Conclusion** Contrary to the cross-protection hypothesis, prior DENV infection was associated with twice the risk of clinically apparent COVID-19 upon SARS-CoV-2 infection

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JAMA 06MAY2021	**Association Between Vaccination With BNT162b2 and Incidence of Symptomatic and Asymptomatic SARS-CoV-2 Infections Among Health Care Workers**	Angel Y., *et al.* Israel gotopaper	Vaccines	Importance Randomized clinical trials have provided estimates of the effectiveness of the BNT162b2 vaccine against symptomatic SARS-CoV-2 infection, but its effect on asymptomatic infections remains unclear. **Association of vaccination with the Pfizer-BioNTech BNT162b2 vaccine with symptomatic and asymptomatic SARS-CoV-2 infections among health care workers.** **Methods** > Single-center, retrospective cohort study (Tel Aviv, Israel). > Data collected on symptomatic and asymptomatic SARS-CoV-2 infections confirmed via PCR tests in HCW undergoing regular screening with nasopharyngeal swabs > Comparision of the incidence of infection between fully vaccinated and unvaccinated participants Primary outcome IRR for symptomatic and asymptomatic SARS-CoV-2 infection of fully vaccinated vs unvaccinated HCW **Findings** > 6710 health care workers followed up for a median period of 63 days > 5953 health care workers (88.7%) received at least 1 dose of the BNT162b2 vaccine, 5517 (82.2%) received 2 doses, and 757 (11.3%) were not vaccinated > Symptomatic SARS-CoV-2 infection occurred in 8 fully vaccinated HCW and 38 unvaccinated HCW (incidence rate, 4.7 vs 149.8 per 100 000 person-days) >Asymptomatic SARS-CoV-2 infection occurred in 19 fully vaccinated HCW and 17 unvaccinated HCW (incidence rate, 11.3 vs 67.0 per 100 000 person-days, respectively) **Conclusions** Receipt of the BNT162b2 vaccine compared with no vaccine was associated with a significantly lower incidence of symptomatic and asymptomatic SARS-CoV-2 infection more than 7 days after the second dose.
Clin Infect Dis. 05MAY2021	**SARS-CoV-2 RNAemia predicts clinical deterioration and extrapulmonary complications from COVID-19**	Ram-Mohan N., *et al.* USA gotopaper	Clinic	**Aim**: to characterise relationships between SARS-CoV-2 RNAemia and disease severity, clinical deterioration, and specific extrapulmonary complications (EPCs). RNAemia was quantified by quantitative (qPCR) and digital (dPCR) PCR. > 23.0% (44/191) of SARS-CoV-2 positive patients had viral RNA detected in plasma by dPCR, compared to 1.4% (2/147) by qPCR. > Most patients with serial measurements had undetectable RNAemia within 10 days of symptom onset, reached maximum clinical severity within 16 days, and symptom resolution within 33 days. > Initially RNAaemic patients were more likely to manifest severe disease (OR 6.72 [95% CI, 2.45 – 19.79]), worsening of disease severity (OR 2.43 [95% CI, 1.07 – 5.38]), and EPCs (OR 2.81 [95% CI, 1.26 – 6.36]). RNA load correlated with maximum severity (r = 0.47 [95% CI, 0.20 – 0.67]). **dPCR is more sensitive than qPCR for the detection of SARS-CoV-2 RNAemia, which is a robust predictor of eventual COVID-19 severity and oxygen requirements, as well as EPCs.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 05MAY2021	**Antibody Response to 2-Dose SARS-CoV-2 mRNA Vaccine Series in Solid Organ Transplant Recipients**	Boyarsky B.J., *et al.* USA [gotopaper]	Vaccines	In this study, we assessed antibody response after the second dose. **Methods** > Transplant recipients without prior polymerase chain reaction–confirmed COVID-19 were recruited from across the US to participate in this prospective cohort > Those who completed the 2-dose SARS-CoV-2 mRNA vaccine series between December 16, 2020, and March 13, 2021, were included and followed up through April 13, 2021 **Findings** > Overall, of the 658 participants, 98 (15%) had measurable antibody response after dose 1 and dose 2; 301 (46%) had no antibody response after dose 1 or dose 2; and 259 (39%) had no antibody response after dose 1 but subsequent antibody response after dose 2 > Among all 658 participants, median (IQR) antibody levels after dose 2 were 2.14 U/mL (<0.4-245.8) (Roche) and 1.23 arbitrary units (0.13-6.38) (EUROIMMUN) > Among the 357 with detectable antibody after dose 2, median (IQR) antibody levels were 142.1 U/mL (9.44->250) (Roche) and 6.48 arbitrary units (3.75-8.72) (EUROIMMUN) overall; > Among the 473 receiving antimetabolites, 38 participants (8%) had antibody response after dose 1 and dose 2; 268 (57%) had no antibody response after dose 1 or dose 2; and 167 (35%) had no antibody response after dose 1 but subsequent antibody after dose 2. **In this study of the humoral response to 2 doses of mRNA SARS-CoV-2 vaccine among solid organ transplant recipients, the majority had detectable antibody responses after the second dose, although participants without a response after dose 1 had generally low antibody levels. Poor humoral response was persistently associated with use of antimetabolite immunosuppression.** **Although this study demonstrates an improvement in antispike antibody responses in transplant recipients after dose 2 compared with dose 1, these data suggest that a substantial proportion of transplant recipients likely remain at risk for COVID-19 after 2 doses of mRNA vaccine.**
Lancet Resp Med. 05MAY2021	**3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalisation: a prospective study**	Wu X., *et al.* China/UK [gotopaper]	Clinic	**Aim:** to describe the temporal trends in respiratory outcomes over 12 months in patients hospitalised for severe COVID-19 and to investigate the associated risk factors. **Methods:** Prospective, longitudinal, cohort study, patients admitted to hospital for severe COVID-19 who did not require mechanical ventilation were prospectively followed up at 3 months, 6 months, 9 months, and 12 months after discharge from Renmin Hospital of Wuhan University, Wuhan, China. Patients with a history of hypertension; diabetes; cardiovascular disease; cancer; and chronic lung disease, including asthma or chronic obstructive pulmonary disease; or a history of smoking were excluded. >135 eligible patients, 83 (61%) patients participated in this study. **Findings:** >The median age of participants was 60 years (IQR 52–66). Temporal improvement in pulmonary physiology and exercise capacity was observed in most patients; however, persistent physiological and radiographic abnormalities remained in some patients with COVID-19 at 12 months after discharge. > A significant reduction in DLCO over the study period was observed, with a median of 77% of predicted (IQR 67–87) at 3 months, 76% of predicted (68–90) at 6 months, and 88% of predicted (78–101) at 12 months after discharge. >**At 12 months after discharge, radiological changes persisted in 20 (24%) patients.** >Multivariate logistic regression showed increasing odds of impaired DLCO associated with female sex (odds ratio 8·61) and radiological abnormalities were associated with peak HRCT pneumonia scores during hospitalisation (1·36). **In most patients who recovered from severe COVID-19, dyspnoea scores and exercise capacity improved over time.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Med. 05MAY2021	**Delayed production of neutralizing antibodies correlates with fatal COVID-19**	Lucas C., *et al.* USA gotopaper	Immunology	**Aim**: to study the exact features of antibody responses that govern COVID-19 disease outcomes, analysing the nature of antibody responses in disease severity and mortality in 229 Covid-19 patients. > A correlation between anti-spike (S) IgG levels, length of hospitalization and clinical parameters associated with worse clinical progression was observed. Although high anti-S IgG levels correlated with worse disease severity, such **correlation was time dependent**. > Deceased patients did not have higher overall humoral response than discharged patients. However, they mounted **a robust, yet delayed, response**, measured by anti-S, anti-receptor-binding domain IgG and neutralizing antibody (NAb) levels compared to survivors. > Delayed seroconversion kinetics **correlated with impaired viral control** in deceased patients. > Sera from 85% of patients displayed some neutralization capacity during their disease course, but **NAb generation before 14 d of disease onset emerged as a key factor for recovery**. These data indicate that COVID-19 mortality does not correlate with the cross-sectional antiviral antibody levels per se but rather with the delayed kinetics of NAb production.
Lancet 05MAY2021	**Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data**	Haas E.J., *et al.* Israel gotopaper	Vaccines	**Real-world effectiveness of two doses of BNT162b2 against a range of SARS-CoV-2 outcomes and to evaluate the nationwide public-health impact following the widespread introduction of the vaccine.** **Methods** > National surveillance data from the first 4 months of the nationwide vaccination campaign to ascertain: (i) incident cases of laboratory-confirmed SARS-CoV-2 infections (ii) vaccine uptake in residents of Israel aged 16 years and older. > Vaccine effectiveness against SARS-CoV-2 outcomes was calculated on the basis of incidence rates in fully vaccinated individuals compared with rates in unvaccinated individuals **Findings** > Jan 24 to April 3, 2021: 232 268 SARS-CoV-2 infections, 7694 COVID-19 hospitalisations, 4481 severe or critical COVID-19 hospitalisations, and 1113 COVID-19 deaths in people aged 16 years or older. > By April 3, 2021, 4 714 932 (72·1%) of 6 538 911 people aged 16 years and older were fully vaccinated with two doses of BNT162b2. > Vaccine effectiveness at 7 days or longer after the second dose were 95·3% > Adjusted estimates of vaccine effectiveness at 7 days or longer after the second dose were: (i) 95·3% against SARS-CoV-2 infection, (ii) 91·5% against asymptomatic SARS-CoV-2 infection, (iii) 97·0% against symptomatic COVID-19, (iv) 97·2% against COVID-19-related hospitalisation (v),97·5% against severe or critical COVID-19-related hospitalisation (vi) 96·7% against COVID-19-related death. > In all age groups, as vaccine coverage increased, the incidence of SARS-CoV-2 outcomes declined. > 8006 of 8472 samples tested showed a spike gene target failure, giving an estimated prevalence of the B.1.1.7 variant of 94·5% among SARS-CoV-2 infections. **Conslusions** Two doses of BNT162b2 are highly effective across all age groups in preventing symptomatic and asymptomatic SARS-CoV-2 infections and COVID-19-related hospitalisations, severe disease, and death, including those caused by the B.1.1.7 SARS-CoV-2 variant. There were marked and sustained declines in SARS-CoV-2 incidence corresponding to increasing vaccine coverage.

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 05MAY2021	**Efficacy of NVX-CoV2373 Covid-19 Vaccine against the B.1.351 Variant**	Shinde V., *et al.* South Africa <u>gotopaper</u>	Vaccines	**Aim:** Evaluation of vaccine efficacy in a setting of ongoing SARS-CoV-2 transmission including high prevalence of B1.351 viral variant. **Methods** > Phase 2a–b trial (South Africa), > Population: HIV– or HIV + in a stable condition. Radomization 1:1 ratio, two doses of either NVX-CoV2373 vaccine (5 µg of recombinant spike protein with 50 µg of Matrix-M1 adjuvant) or placebo. <u>Primary end points:</u> Safety and vaccine efficacy against laboratory-confirmed symptomatic Covid-19 at ≥7 days after the second dose **Findings** > 4387 participants receiving at least 1 injection of vaccine or placebo. > 30% of the participants were seropositive for SARS-CoV-2 at baseline. > Among 2684 baseline seronegative participants (94% HIV-negative and 6% HIV-positive), predominantly mild-to-moderate Covid-19 developed in 15 participants in the vaccine group and in 29 in the placebo group (vaccine efficacy, 49.4%; 95% CI, 6.1 to 72.8). > Vaccine efficacy among HIV-negative participants was 60.1% (95% CI, 19.9 to 80.1). > Of 41 sequenced isolates, 38 (92.7%) were the B.1.351 variant. >Post hoc vaccine efficacy against B.1.351 was 51.0% (95% CI, −0.6 to 76.2) among the HIV-negative participants. >Preliminary local and systemic reactogenicity events were more common in the vaccine group; serious adverse events were rare in both groups. **Conclusions** The NVX-CoV2373 vaccine was efficacious in preventing Covid-19, with higher vaccine efficacy observed among HIV-negative participants. Most infections were caused by the B.1.351 variant.
NEJM 05MAY2021	**Effectiveness of the BNT162b2 Covid-19 Vaccine against the B.1.1.7 and B.1.351 Variants**	Abu-Raddad L.J., Chemaitelly H. Qatar <u>gotopaper</u>	Vaccines	**Context** Qatar launched a mass immunization campaign with BNT16b2 vaccine on December 21, 2020. Vaccination scale-up occurred during Qatar's 2nd and 3rd waves of SARS-CoV-2 infections, triggered by expansion of B.1.1.7 and B.1.351 variants. Viral genome sequencing (Feb 23 to March 18) indicated that 50.0% of cases of Covid-19 in Qatar were caused by B.1.351 and 44.5% by B.1.1.7. Nearly all cases in which virus was sequenced after March 7 were caused by either B.1.351 or B.1.1.7. **Aim:** Evaluation of BNT162b2 vaccine effectiveness **Methodology** (i) Test-negative case–control study design (ii) Cohort study design by comparing the incidence of infection among vaccinated persons with the incidence in the national cohort of persons who were antibody-negative **Findings** > Effectiveness of the vaccine against any documented infection with B.1.1.7 variant: 89.5% (95% [CI], 85.9 to 92.3) at ≥14 days after dose 2 > Effectiveness against any documented infection with the B.1.351 variant: 75.0% (95% CI, 70.5 to 78.9). > Vaccine effectiveness against severe, critical, or fatal disease due to infection with any SARS-CoV-2 (with B.1.1.7 and B.1.351 variants being predominant within Qatar): 97.4% (95% CI, 92.2 to 99.5) > Vaccine effectiveness within the cohort 87.0% (95% CI, 81.8 to 90.7) against the B.1.1.7 variant and 72.1% (95% CI, 66.4 to 76.8) against the B.1.351 variant. **Conclusions** > The BNT162b2 vaccine was effective against infection and disease in the population of Qatar, despite the B.1.1.7 and B.1.351 variants being predominant within the country > Vaccine effectiveness against the B.1.351 variant was approximately 20% lower than the effectiveness (>90%) reported in the clinical trial and in real-world conditions in Israel and the United States. > The reduced protection against infection with the B.1.351 variant did not seem to translate into poor protection against the most severe forms of infection (greater than 90%)

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Nature Commun. 04MAY21	**Human kidney is a target for novel severe acute respiratory syndrome coronavirus 2 infection**	Diao B., *et al*. China [gotopaper](#)	Clinics	**Methods** > Retrospective analysis of clinical parameters from 85 patients with laboratory-confirmed coronavirus disease 2019 (COVID-19); moreover, kidney histopathology from six additional COVID-19 patients with post-mortem examinations was performed. **Findings** > We find that 27% (23/85) of patients exhibited AKI. The elderly patients and cases with comorbidities (hypertension and heart failure) are more prone to develop AKI. > Haematoxylin & eosin staining shows that the kidneys from COVID-19 autopsies have moderate to severe tubular damage. > In situ hybridization assays illustrate that viral RNA accumulates in tubules. > Immunohistochemistry shows nucleocapsid and spike protein deposits in the tubules, and immunofluorescence double staining shows that both antigens are restricted to the angiotensin converting enzyme-II-positive tubules. > Immunohistochemistry shows nucleocapsid and spike protein deposits in the tubules, and immunofluorescence double staining shows that both antigens are restricted to the angiotensin converting enzyme-II-positive tubules. > SARS-CoV-2 infection triggers the expression of hypoxic damage-associated molecules, including DP2 and prostaglandin D synthase in infected tubules. Moreover, it enhances CD68+ macrophages infiltration into the tubulointerstitium, and complement C5b-9 deposition on tubules is also observed. **These results suggest that SARS-CoV-2 directly infects human kidney to mediate tubular pathogenesis and AKI.**
Clin Microbiol Infect. 03MAY2021	**Antibody response to mRNA SARS-CoV-2 vaccine among kidney transplant recipients – Prospective cohort study**	Rozen-Zvi, B., *et al.* Israel [gotopaper](#)	Vaccines	**Aim:** To assess rates of antibody response to mRNA SARS-CoV-2 vaccine among kidney transplant recipients, and to identify factors associated with reduced immunogenicity. **Methods** > Prospective cohort study including consecutive kidney transplant recipients in a single referral transplant center. > Anti-spike (anti-S) antibodies test 2-4 weeks following second vaccine dose. Primary outcome: rate of seropositivity. **Findings:** > 308 kidney transplant recipients included, only 112 (36.4%) tested positive for anti-S antibodies 2-4 weeks after receiving the second dose of BNT162b2 vaccine. > Median antibody titers: was 15.5 AU/mL > Factors associated with antibody response: (i) higher estimated glomerular filtration rate (eGFR) (odds ratio [OR] 1.025 per ml/min/1.73m2, 95% confidence interval [CI] 1.014 - 1.037, p<0.001), (ii) lower mycophenolic acid dose (OR 2.347 per 360 mg decrease, 95% CI 1.782 - 3.089, p<0.001), (iii) younger age (OR 1.032 per year decrease, 95% CI 1.015 - 1.05, p<0.001) (iv) lower calcineurin inhibitors (CNI) blood level (OR 1.987, 95% CI 1.146 - 3.443, p=0.014). > No serious adverse events to the vaccine were reported. **Conclusions:** Kidney transplant recipients demonstrated inadequate antibody response to mRNA SARS-CoV-2 vaccination. Immunosuppression level was a significant factor in this response.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 01MAY2021	**Tocilizumab 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 effects of tocilizumab in adult patients admitted to hospital with COVID-19 with both hypoxia and systemic inflammation. **Methods:** Randomised, controlled, open-label, platform trial assessing several possible treatments in patients hospitalised with COVID-19 in the UK. Participants with hypoxia (oxygen saturation <92% on air or requiring oxygen therapy) and evidence of systemic inflammation (C-reactive protein ≥75 mg/L) were eligible for random assignment in a 1:1 ratio to usual standard of care alone versus usual standard of care plus tocilizumab at an IV dose of 400 mg–800 mg (depending on weight). The primary outcome was 28-day mortality, assessed in the intention-to-treat population. **Findings:** > 4116 adults of 21 550 patients enrolled into the RECOVERY trial were included in the assessment of tocilizumab, including 3385 (82%) patients receiving systemic corticosteroids. > Overall, 621 (31%) of the 2022 patients allocated tocilizumab and 729 (35%) of the 2094 patients allocated to usual care died within 28 days (rate ratio 0·85; 95% CI 0·76–0·94; p=0·0028). > Consistent results were seen in all prespecified subgroups of patients, including those receiving systemic corticosteroids. **Patients allocated to tocilizumab were more likely to be discharged from hospital within 28 days** (57% vs 50%; rate ratio 1·22; 1·12–1·33; p<0·0001). > Among those not receiving invasive mechanical ventilation at baseline, patients allocated tocilizumab were less likely to reach the composite endpoint of invasive mechanical ventilation or death (35% vs 42%; risk ratio 0·84; 95% CI 0·77–0·92; p<0·0001). **In hospitalised COVID-19 patients with hypoxia and systemic inflammation, tocilizumab improved survival and other clinical outcomes.**
JAMA 30APR2021	**US Case Reports of Cerebral Venous Sinus Thrombosis With Thrombocytopenia After Ad26.COV2.S Vaccination, March 2 to April 21, 2021**	See I., *et al.* USA gotopaper	Vaccines	**Aim:** To describe reports of CVST with thrombocytopenia following Ad26.COV2.S vaccine receipt. **Methods** Case series of 12 US patients with CVST and thrombocytopenia following use of Ad26.COV2.S vaccine under EUA reported to the Vaccine Adverse Event Reporting System (VAERS) from March 2 to April 21, 2021 (with follow-up reported through April 21, 2021). <u>Main Outcomes and Measures:</u> Clinical course, imaging, laboratory tests, and outcomes after CVST diagnosis obtained from VAERS reports, medical record review, and discussion with clinicians. **Findings** > Patients chracteristics: (i) age: 18 to younger than 60 years (ii) all White women. (iii) seven patients had at least 1 CVST risk factor, including obesity (n = 6), hypothyroidism (n = 1), and oral contraceptive use (n = 1); none had documented prior heparin exposure. > Time from Ad26.COV2.S vaccination to symptom onset: 6 to 15 days. > 11 patients initially presented with headache; 1 patient initially presented with back pain and later developed headache. > Of the 12 patients with CVST, 7 also had intracerebral hemorrhage; 8 had non-CVST thromboses. > After diagnosis of CVST, 6 patients initially received heparin treatment. > Platelet nadir ranged from 9 ×103/μL to 127 ×103/μL. All 11 patients tested for the heparin-platelet factor 4 HIT antibody by enzyme-linked immunosorbent assay (ELISA) screening had positive results. > All patients were hospitalized (10 in an intensive care unit [ICU]). As of April 21, 2021, outcomes were death (n = 3), continued ICU care (n = 3), continued non-ICU hospitalization (n = 2), and discharged home (n = 4). **Conclusions** The initial 12 US cases of CVST with thrombocytopenia after Ad26.COV2.S vaccination represent serious events.

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Science 30APR2021	**Prior SARS-CoV-2 infection rescues B and T cell responses to variants after first vaccine dose**	Reynolds C.J., et al. UK [gotopaper](#)	Vaccines	**Aim**: to investigated if single dose vaccination, with or without prior infection, confers cross protective immunity to variants. - Analysis of T and B cell responses after first dose vaccination with the Pfizer/BioNTech mRNA vaccine BNT162b2 in healthcare workers (HCW) followed longitudinally, with or without prior Wuhan-Hu-1 SARS-CoV-2 infection. > After one dose, individuals with prior infection showed **enhanced T cell immunity**, antibody secreting memory B cell response to spike and neutralizing antibodies effective against B.1.1.7 and B.1.351. > By comparison, HCW receiving one vaccine dose without prior infection showed **reduced immunity against variants**. > B.1.1.7 and B.1.351 spike mutations resulted in increased, abrogated or unchanged T cell responses **depending on human leukocyte antigen (HLA)** polymorphisms. **Single dose vaccination with BNT162b2 in the context of prior infection with a heterologous variant substantially enhances neutralizing antibody responses against variants.**
Lancet 30APR2021	**Ethnic differences in SARS-CoV-2 infection and COVID-19-related hospitalisation, intensive care unit admission, and death in 17 million adults in England: an observational cohort study using the OpenSAFELY platform**	Mathur R., et al. UK [gotopaper](#)	Public Health / Epidemiology	**Aim**: to quantify ethnic differences in SARS-CoV-2 infection and COVID-19 outcomes during the first and second waves of the COVID-19 pandemic in England. **Methods** - Observational cohort study of adults (aged ≥18 years) who had at least 1 year of continuous registration with primary care practices in England at the start of each study period (3 waves). - Multivariable Cox regression was used to examine ethnic differences in the outcomes of interest. Models were adjusted for age, sex, deprivation, clinical factors and comorbidities, and household size, with stratification by geographical region. **Results** > 17 288 532 adults included: 10 877 978 (62·9%) White, 1 025 319 (5·9%) South Asian, 340 912 (2·0%) Black, 170 484 (1·0%) of mixed ethnicity, 320 788 (1·9%) of other ethnicity, and 4 553 051 (26·3%) of unknown ethnicity. > In wave 1, the likelihood of being tested for SARS-CoV-2 infection was slightly higher in the South Asian group (adjusted hazard ratio 1·08 [95% CI 1·07–1·09]), Black group (1·08 [1·06–1·09]), and mixed ethnicity group (1·04 [1·02–1·05]) and was decreased in the other ethnicity group (0·77 [0·76–0·78]) relative to the White group. > The risk of testing positive for SARS-CoV-2 infection was higher in the South Asian group (1·99 [1·94–2·04]), Black group (1·69 [1·62–1·77]), mixed ethnicity group (1·49 [1·39–1·59]), and other ethnicity group (1·20 [1·14–1·28]). > Compared with the White group, the four remaining high-level ethnic groups had an increased risk of COVID-19-related hospitalisation (South Asian group 1·48 [1·41–1·55], Black group 1·78 [1·67–1·90], mixed ethnicity group 1·63 [1·45–1·83], other ethnicity group 1·54 [1·41–1·69]), COVID-19-related ICU admission (2·18 [1·92–2·48], 3·12 [2·65–3·67], 2·96 [2·26–3·87], 3·18 [2·58–3·93]), and death (1·26 [1·15–1·37], 1·51 [1·31–1·71], 1·41 [1·11–1·81], 1·22 [1·00–1·48]). > In wave 2, the risks of hospitalisation, ICU admission, and death relative to the White group were increased in the South Asian group but attenuated for the Black group compared with these risks in wave 1. > Disaggregation into 16 ethnicity groups showed important heterogeneity within the five broader categories. **Some minority ethnic populations in England have excess risks of testing positive for SARS-CoV-2 and of adverse COVID-19 outcomes compared with the White population, even after accounting for differences in sociodemographic, clinical, and household characteristics.**

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Science 29APR2021	**Household COVID-19 risk and in-person schooling**	J. Lessler, et al. USA https://doi.org/10.1126/science.abh2939	Public Health / Epidemiology	**Aims:** Estimate the COVID-19 risk of infection of members of households with children attending school in person. **Methods:** > Massive online survey administered through Facebook throughout the United States (576 051 respondents with at least one child in school age); analysis adjusts for non-response and coverage bias. > COVID-19 infection assessed through: i) reporting COVID-19-like illness (CLI; fever, cough/shortness of breath), ii) loss of taste or smell, and/or iii) positive SARS-CoV-2 test result within the previous 14 days. > Questions on type of schooling (in-person or not, full-time or part-time), and on mitigation measures in place at school. **Findings:** > Living in a household with a child engaged in full-time in-person schooling is associated with a substantial increase in the odds reporting COVID-19 like illness (CLI), loss of taste or smell, or a positive SARSCoV- test result within the previous 14 days. > When the child is engaged in part-time schooling, the association is attenuated but still statistically significant. > There is a negative relationship between the number of mitigation measures implemented and the risk of COVID-19 outcomes among adult household members responding to the survey. > Daily symptom screening is associated with the greater risk reduction; mask mandates and cancelling extra-curricular activities are also associated with risk reduction. > Limits: self-reporting; confounding factors (heterogeneities of economic and racial status) **Conclusion:** The results of this massive online survey in the US provide evidence that in-person schooling poses a risk to those living in the households of children, but that this risk can be managed through commonly implemented school-based mitigation measures.
Clin Infect Dis. 29APR2021	**Development and validation of the long covid symptom and impact tools, a set of patient-reported instruments constructed from patients' lived experience**	Tran V., et al. France gotopaper	Diagnostics	**Aim**: To develop and validate patient-reported instruments, based on patients' lived experiences, for monitoring the symptoms and impact of long covid. **Design** - The long covid Symptom and Impact Tools (ST and IT) were constructed from the answers to a survey with open-ended questions to 492 patients with long COVID. - Tool validation: adult patients with suspected or confirmed COVID-19 and symptoms >3 weeks after onset. - Construct validity was assessed by examining the relations of the ST and IT scores with health related quality of life (EQ-5D-5L), function (PCFS, post-COVID functional scale), and perceived health (MYMOP2). Reliability was determined by a test-retest. "Patient acceptable symptomatic state" (PASS) was determined by the percentile method. **Results** > Validation involved 1022 participants (55% confirmed cases, 79% female, and 12.5% hospitalized for COVID-19). > The long COVID ST and IT scores were strongly correlated with the EQ-5D-5L (rs = -0.45 and rs = -0.59 respectively), the PCFS (rs = -0.39 and rs = -0.55), and the MYMOP2 (rs = -0.40 and rs = -0.59). > Reproducibility was excellent with an interclass correlation coefficient of 0.83 (95% CI 0.80-0.86) for the ST score, 0.84 (0.80-0.87) for the IT score. > 793 (77.5%) patients reported an unacceptable symptomatic state, thereby setting the PASS for the long covid IT score at 30 (28 to 33). **The long covid ST and IT tools provide the first validated and reliable instruments for monitoring the symptoms and impact of long covid.**

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Lancet HIV 29APR21	**SARS-CoV-2 seroprevalence, and IgG concentration and pseudovirus neutralising antibody titres after infection, compared by HIV status: a matched case-control observational study**	Spinelli A.M., *et al*. USA [gotopaper](#)	Public Health / Epidemiology	We aimed to compare SARS-CoV-2 IgG seroprevalence, disease severity, and neutralising antibody activity after infection among people with and without HIV receiving care in a county hospital system over a 3-month period. **Methods** > In this matched case-control observational study, remnant serum samples were collected between Aug 1 and Oct 31, 2020, from all people living with HIV who underwent routine outpatient laboratory testing in a municipal health-care system **Findings** > 1138 samples from 955 people living with HIV and 1118 samples from 1062 people without HIV were tested. > SARS-CoV-2 IgG seroprevalence was 3·7% (95% CI 2·4 to 5·0) among people with HIV compared with 7·4% (5·7 to 9·2) among people without HIV (adjusted odds ratio 0·50, 95% CI 0·30 to 0·83). > Among 31 people with HIV and 70 people without HIV who had evidence of past infection, the odds of severe COVID-19 were 5·52 (95% CI 1·01 to 64·48) times higher among people living with HIV. > Adjusting for time since PCR-confirmed infection, SARS-CoV-2 IgG concentrations were lower (percentage change −53%, 95% CI −4 to −76), pseudovirus neutralising antibody **titres were lower** (−67%, −25 to −86), and **avidity was similar** (7%, −73 to 87) among people living with HIV compared with those without HIV. **Although fewer infections were detected by SARS-CoV-2 IgG testing among people living with HIV than among those without HIV, people with HIV had more cases of severe COVID-19. Among people living with HIV with past SARS-CoV-2 infection, lower IgG concentrations and pseudovirus neutralising antibody titres might reflect a diminished serological response to infection, and the similar avidity could be driven by similar time since infection.**
Clin Infect Dis. 29APR21	**SARS-CoV-2 detection on self-collected saliva or anterior nasal specimens compared with healthcare personnel-collected nasopharyngeal specimens**	Marx G.E., *et al*. USA [gotopaper](#)	Public Health / Epidemiology	Self-collected saliva or anterior nasal specimens (ANS) for SARS-CoV-2 detection are less invasive but the sensitivity of these specimen types has not been thoroughly evaluated. **Methods** > During September–November 2020, 730 adults undergoing SARS-CoV-2 testing at community testing events and homeless shelters in Denver provided self-collected saliva and ANS specimens before NPS collection and answered a short survey about symptoms and specimen preference. > Subgroup analyses included test outcomes by symptom status and culture results **Findings** > Sensitivity for SARS-CoV-2 detection by rRT-PCR appeared higher for saliva than for ANS (85% vs. 80%) and among symptomatic participants than among those without symptoms (94% vs. 29% for saliva; 87% vs. 50% for ANS). > Among participants with culture-positive SARS-CoV-2 by any specimen type, sensitivity of saliva and ANS by rRT-PCR was 94% and 100%, respectively. > Saliva and ANS were equally preferred by participants; most would undergo NPS again despite being least preferred. **Saliva was slightly more sensitive than ANS for SARS-CoV-2 detection by rRT-PCR. Both saliva and ANS reliably detected SARS-CoV-2 among participants with symptoms. Self-collected saliva and ANS offer practical advantages, are preferred by patients, and might be most useful for testing people with COVID-19 symptoms.**

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Lancet Diabetes Endocrinol. 28APR2021	**Associations between body-mass index and COVID-19 severity in 6·9 million people in England: a prospective, community-based, cohort study**	Gao M., *et al.* UK gotopaper	Public Health / Epidemiology	**Aim:** to examine the association between obesity the risk of severe COVID-19, including interactions with demographic and behavioural characteristics, type 2 diabetes, and other health conditions. **Methods:** Prospective, community-based, cohort study, using de-identified patient-level data from the QResearch database of general practices in England, UK. Data was exctracted from patients aged 20 years and older who were registered at a practice eligible for inclusion in the QResearch database, and with available data on BMI. Outcomes, as a proxy measure of severe COVID-19, were admission to hospital, admission to an intensive care unit (ICU), and death due to COVID-19. **Findings:** >Among 6 910 695 eligible individuals (mean BMI 26·78 kg/m2 [SD 5·59]), 13 503 (0·20%) were admitted to hospital, 1601 (0·02%) to an ICU, and 5479 (0·08%) died after a positive test for SARS-CoV-2. >J-shaped associations were found between BMI and admission to hospital due to COVID-19 (adjusted hazard ratio [HR] per kg/m2 from the nadir at BMI of 23 kg/m2 of 1·05 [95% CI 1·05–1·05]) and death (1·04 [1·04–1·05]), and a linear association across the whole BMI range with ICU admission (1·10 [1·09–1·10]). >A significant interaction was found between BMI and age and ethnicity, with higher HR per kg/m2 above BMI 23 kg/m2 for younger people (20–39 years age group vs 80–100 years group) and Black people than White people (1·07 vs 1·04). >The risk of admission to hospital and ICU due to COVID-19 associated with unit increase in BMI was slightly lower in people with type 2 diabetes, hypertension, and cardiovascular disease than in those without these morbidities. **The relative risk due to increasing BMI is particularly notable in people younger than 40 years and of Black ethnicity.**

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Lancet Infect Dis. 27APR2021	**Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study**	Menni C., *et al*. UK gotopaper	Vaccines	**Aim:** to investigate the safety and effectiveness of BNT162b2 and ChAdOx1 nCoV-19 vaccines in a UK community setting. **Methods:** Prospective observational study examining proportion and probability of self-reported systemic and local side-effects ≤8 days of vaccination in individuals using the COVID Symptom Study app who received 1 or 2 doses of BNT162b2 or 1 dose of ChAdOx1 nCoV-19. Infection rates were compared in vaccinated individuals tested for SARS-CoV-2 (PCR, lateral flow tests) and in unvaccinated controls. **Findings:** **>** Between Dec 8, and March 10, 2021, 627 383 individuals reported being vaccinated with 655 590 doses: 282 103 received one dose of BNT162b2, of whom 28 207 received a second dose, and 345 280 received one dose of ChAdOx1 nCoV-19. > Systemic side-effects were reported by 13·5% of individuals after the first dose of BNT162b2, by 22·0% after the second dose of BNT162b2, and by 33·7% after the first dose of ChAdOx1 nCoV-19. > Local side-effects were reported by 71·9% of individuals after the first dose of BNT162b2, by 68·5% after the second dose of BNT162b2, and by 58·7% after the first dose of ChAdOx1 nCoV-19. > Systemic side-effects were more common (1·6 times after the first dose of ChAdOx1 nCoV-19 and 2·9 times after the first dose of BNT162b2) among individuals with previous SARS-CoV-2 infection than among those without known past infection. **> 3106 of 103 622 vaccinated individuals and 50 340 of 464 356 unvaccinated controls tested positive for SARS-CoV-2 infection.** **> Significant reductions in infection risk were seen starting at 12 days after the first dose**, reaching 60% (95% CI 49–68) for ChAdOx1 nCoV-19 and 69% (66–72) for BNT162b2 at 21–44 days and 72% (63–79) for BNT162b2 after 45–59 days.
Lancet Oncol. 27APR21	**Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study**	Monin L., *et al*. UK gotopaper	Vaccines	**Assesement of the safety and immunogenicity of the BNT162b2 (Pfizer–BioNTech) vaccine in patients with cancer (interim data)** **Methods** > Prospective observational study. > Patients with cancer and healthy controls (mostly HCW) >Participants who were vaccinated between Dec 8 and Dec 29, 2020, received two 30 µg doses of BNT162b2 administered intramuscularly 21 days apart; patients vaccinated after this date received only one 30 µg dose with a planned follow-up boost at 12 weeks. > Blood samples taken before vaccination and at 3 and 5 weeks after the first vaccination. Where possible (rRT-PCR) swab tests were done every 10 days or in cases of symptomatic COVID-19. Primary endpoints: seroconversion to SARS-CoV-2 spike (S) protein in patients with cancer following the first vaccination with the BNT162b2 vaccine, effect of vaccine boosting after 21 days on seroconversion. **Findings** > 151 patients with cancer (95 patients with solid cancer and 56 patients with haematological cancer) and 54 healthy controls. > The proportion of positive anti-S IgG titres at 21 days after a single vaccine dose across the three cohorts were 32 (94%; 95% CI 81–98) of 34 healthy controls; 21 (38%; 26–51) of 56 patients with solid cancer, and 8 (18%; 10–32) of 44 patients with haematological cancer. > 16 healthy controls, 25 patients with solid cancer, and six patients with haematological cancer received a second dose on day 21. Of the patients with available blood samples 2 weeks following a 21-day vaccine boost, 18 (95%; 95% CI 75–99) of 19 patients with solid cancer, 12 (100%; 76–100) of 12 healthy controls, and three (60%; 23–88) of five patients with haematological cancers were seropositive, compared with ten (30%; 17–47) of 33, 18 (86%; 65–95) of 21, and four (11%; 4–25) of 36, respectively, who did not receive a boost. > The vaccine was well tolerated. No vaccine-related deaths reported. **Conclusion** In patients with cancer, one dose of the BNT162b2 vaccine yields poor efficacy. Immunogenicity increased significantly in patients with solid cancer within 2 weeks of a vaccine boost at day 21 after the first dose.

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Clin Infect Dis. 27APR2021	**Vaccinated and convalescent donor-derived SARS-CoV-2-specific T cells as adoptive immunotherapy for high-risk COVID-19 patients**	Papayanni P.G., *et al*. Greece [gotopaper]	Therapeutics	**Aim:** to provide the rationale towards the development of a SARS-CoV-2-specific T-cell (CoV-2-ST) bank from convalescent donors as T-cell immunotherapy against severe COVID-19. **Methods:** SARS-CoV-2-specific T-cell immunity and expansion was tested in unexposed donors, COVID-19 infected individuals (convalescent), asymptomatic PCR-positive subjects, vaccinated individuals, non-ICU hospitalized patients and ICU patients who either recovered and were discharged (ICU recovered) or had a prolonged stay and/or died (ICU critical). CoV-2-STs were generated from all types of donors and underwent phenotypic and functional assessment. **Findings:** > A causal relationship between the expansion of endogenous CoV-2-STs and the disease outcome was shown; insufficient expansion of circulating CoV-2-STs identified hospitalized patients at high-risk for an adverse outcome. > CoV-2-STs with a similarly functional and non-alloreactive, albeit highly cytotoxic, profile against SARS-CoV-2 could be expanded from both convalescent and vaccinated donors generating clinical-scale, SARS-CoV-2-specific T-cell products with functional activity against both the unmutated virus and its B.1.1.7 variant. > Critical COVID-19 patient-originating CoV-2-STs failed to expand, recapitulating the in vivo failure of CoV-2-specific T-cell immunity to control the infection. > CoV-2-STs generated from asymptomatic PCR+ individuals presented weak responses whereas their counterparts originating from exposed to other seasonal coronaviruses subjects failed to kill the virus, thus disempowering the hypothesis of protective cross-immunity. **The authors provide evidence on risk stratification of hospitalized COVID-19 patients and the feasibility of generating powerful CoV-2-ST products from both convalescent and vaccinated donors as an "off-the shelf" T-cell immunotherapy for high-risk patients**
Clin Infect Dis. 27APR2021	**Age-dependent immune response to the Biontech/Pfizer BNT162b2 COVID-19 vaccination**	Müller L., *et al*. Germany [gotopaper]	Vaccines	Cohort study with two age groups (young vaccinees <60 years old and elderly vaccinees >80, to compare antibody responses to the first and second dose of the BNT162b2 COVID-19 vaccination. > While the majority of participants in both groups produced specific IgG antibody titers against SARS-CoV-2 spike protein, **titers were significantly lower in elderly participants**. > The **increment of antibody levels after the second immunization** was higher in elderly participants, but the absolute mean titer of this group remained lower than the <60 group. > After the second vaccination, **31.3 % of the elderly had no detectable neutralizing antibodies** in contrast to the younger group, in which only 2.2% had no detectable neutralizing antibodies. These data show differences between the antibody responses raised after the first and second BNT162b2 vaccination, in particular lower frequencies of neutralizing antibodies in the elderly group.
Lancet 23APR2021	**Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: a national prospective cohort study**	Vasileiou E., *et al*. UK [gotopaper]	Vaccines	**Aim**: prospective cohort study to investigate the association between the mass roll-out of the first doses of BNT162b2 mRNA and ChAdOx1 nCoV-19 COVID-19 vaccines and hospital admissions for COVID-19. > 1 331 993 people were vaccinated between Dec 8, 2020, and Feb 22, 2021 (mean age 65· years (SD 16·2)). > The first dose of the **BNT162b2 mRNA vaccine was associated with a vaccine effect of 91%** (95% CI 85–94) for reduced COVID-19 hospital admission at 28–34 days post-vaccination. > Vaccine effect at the same time interval for the **ChAdOx1 vaccine was 88%** (95% CI 75–94). > Results of combined vaccine effects against hospital admission due to COVID-19 were similar when restricting the analysis to **those aged 80 years and older** (83%, 95% CI 72–89 at 28–34 days post-vaccination). **Mass roll-out of the first doses of the BNT162b2 mRNA and ChAdOx1 vaccines was associated with substantial reductions in the risk of hospital admission due to COVID-19 in Scotland.**

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Clin Microbiol Infect. 26APR2021	**Clinical characteristics and factors associated with hospital admission or death in 43,103 adult outpatients with COVID-19 managed with the Covidom telesurveillance solution: a prospective cohort study**	Yordanov Y., *et al*. France gotopaper	Public Health / Epidemiology	**Aim**: to assess the clinical characteristics, outcomes and factors associated with hospital admission or death in adult outpatients with COVID-19. **Methods** > Prospective cohort of outpatients with suspected or confirmed COVID-19, registered in Covidom telesurveillance solution for home monitoring of patients with COVID-19 in the Greater Paris area, from March to August 2020. **Findings:** > Among 43,103 patients, mean age was 42.9 years (SD=14.3); 93.0% (n=40,081) of patients were < 65 years old and 61.9% (n=26,688) were women. Of these 43,103 patients, 67.5% (n=29,104) completed a medical questionnaire on comorbidities and symptoms. > The main reported comorbidities were asthma (12.8%; n=3,685), hypertension (12.3%; n=3,546) and diabetes (4.8%; n=1,385). > A small proportion of all eligible patients (4.1% [95% CI: 3.9–4.2]; 1,751/43,103) experienced clinical worsening. The rate of hospitalisation was 4.0% (95% CI: 3.8–4.2; n=1,728) and 0.1% (95% CI: 0.1–0.2; n=64) died. > Probability of worsening was reduced with anosmia/ageusia. **Clinical worsening was rare among outpatients. Male sex, older age and comorbidities such as chronic renal disease, active cancers or obesity were independently associated with clinical worsening. However, our cohort may include patients younger and healthier than the general population.**
Lancet 23APR2021	**COVID-19 vaccine coverage in health-care workers in England and effectiveness of BNT162b2 mRNA vaccine against infection (SIREN): a prospective, multicentre, cohort study**	Hall V.J., *et al*. UK gotopaper	Vaccines	SIREN prospective cohort study among staff (aged ≥18 years) working in publicly-funded hospitals in the UK. Aim was to determine factors associated with vaccine coverage for BNT162b2 mRNA and ChAdOx1 nCOV-19 and document BNT162b2 effectiveness in a cohort of health-care workers undergoing regular asymptomatic testing. **Findings:** > 23 324 participants from 104 sites were enrolled. Median age: 46·1 years (IQR 36·0–54·1), 19 692 (84%) were female; > 8203 (35%) assigned to the positive cohort, 15 121 (65%) assigned to the negative cohort. > Total follow-up time was 2 months and 1 106 905 person-days (396 318 vaccinated and 710 587 unvaccinated). > Vaccine coverage was 89% on Feb 5, 2021, 94% had BNT162b2. > Significantly lower coverage was associated with previous infection, gender, age, ethnicity, job role, Index of Multiple Deprivation score. > During follow-up, there were 977 new infections in the unvaccinated cohort, an incidence density of 14 infections per 10 000 person-days; the vaccinated cohort had 71 new infections 21 days or more after their first dose (incidence density of eight infections per 10 000 person-days) and nine infections 7 days after the second dose (incidence density four infections per 10 000 person-days). > In the unvaccinated cohort, 543 (56%) participants had typical COVID-19 symptoms and 140 (14%) were asymptomatic on or 14 days before their PCR positive test date, compared with 29 (36%) with typical COVID-19 symptoms and 15 (19%) asymptomatic in the vaccinated cohort. > A single dose of BNT162b2 vaccine showed vaccine effectiveness of 70% (95% CI 55–85) 21 days after first dose and 85% (74–96) 7 days after two doses in the study population. **Our findings show that the BNT162b2 vaccine can prevent both symptomatic and asymptomatic infection in working-age adults. This cohort was vaccinated when the dominant variant in circulation was B1.1.7 and shows effectiveness against this variant.**

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JAMA Netw Open 23APR2021	**Association of Maternal Perinatal SARS-CoV-2 Infection With Neonatal Outcomes During the COVID-19 Pandemic in Massachusetts**	Angelidou A., *et al.* USA gotopaper	Public health / Epidemiology	**Ascertain the percentage of neonates who were born to mothers with positive SARS-CoV-2 test results during birth hospitalization, clinical and sociodemographic factors associated with neonatal test positivity, and clinical and virological outcomes for newborns during hospitalization and 30 days after discharge.** **Methods** > Multicenter cohort study. Neonates were born to mothers with positive SARS-CoV-2 test results within 14 days before to 72h after delivery, and were followed up for 30 days after hospital discharge. Primary outcomes for neonates: (1) positive SARS-CoV-2 test results, (2) indicators of adverse health, and (3) clinical signs and viral testing. **Findings** > The cohort included 255 neonates (mean [SD] gestational age at birth, 37.9 [2.6] weeks; 62 [24.3%] with low birth weight or preterm delivery) with 250 mothers (mean [SD] age, 30.4 [6.3] years; 121 [48.4%] were of Hispanic ethnicity). > Of the 255 neonates who were born to mothers with SARS-CoV-2 infection, 225 (88.2%) were tested for SARS-CoV-2 and 5 (2.2%) had positive results during the birth hospitalization. >High maternal social vulnerability was associated with higher likelihood of neonatal test result positivity (adjusted odds ratio, 4.95; 95% CI, 1.53-16.01; P = .008), adjusted for maternal COVID-19 symptoms, delivery mode, and rooming-in practice. > Adverse outcomes during hospitalization were associated with preterm delivery indicated by worsening maternal COVID-19 symptoms. > Of the 151 newborns with follow-up data, 28 had nonroutine clinical visits, 7 underwent SARS-CoV-2 testing, and 1 had a positive result. **Conclusion** Newborns exposed to SARS-CoV-2 were at risk for both direct and indirect adverse health outcomes
Science 23APR2021	**Resurgence of SARS-CoV-2: detection by community viral surveillance**	Riley S., *et al.* UK gotopaper	Public Health / Epidemiology	**Aims**: To estimate prevalence of COVID-19 in England through a community-wide national representative surveillance program in England (REACT-1 study); to detect resurgence from low prevalence. **Methods:** > Repeated random population-based sampling: 2.4 Million people were invited to join the study over 4 rounds from May 2020 to beginning of September 2020; 596,000 tested swabs were obtained (overall response rate of 25%) > Estimation of prevalence in this random sample (correcting for variation in response rate), over time, fitting a model of constant exponential growth and decay, and a model with a flexible p-spline. > Geographical variation in prevalence investigated by fitting a spatio-temporal logistic model **Findings:** > More reliable estimates of prevalence than from routine surveillance, is affected by test availability and test-seeking behaviour > Detection of epidemic resurgence in the summer 2020 (between end of July and mid-August), that led to the announcement of the "rule of six" social distancing measure by the UK government > Substantial variations in age patterns over time; the second wave started in young adults; > Case data (routine surveillance) consistently underestimates infections at 5-14yo compared to random population based sampling > Higher prevalence (x2) in participants of Asian ethnicity, also higher in Black people – higher rates of hospitalization and mortality from COVID-19 for minority ethnic groups in England may therefore reflect their higher rates of infection rather than a poorer prognosis once infected. > Spatial heterogeneity in prevalence detected at sub-regional level **Conclusions:** > Demonstration of the capability of a large national community surveillance program to detect a resurgence of SARS-CoV-2 infection at low prevalence. > The prevalence in the 5-14 age group is higher in this random testing study compared to case data.

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JAMA Pediatr. 22APR2021	**Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection**	Villar J., *et al*. International [gotopaper]	Public Health / Epidemiology	**Evaluation of the risks associated with COVID-19 in pregnancy on maternal and neonatal outcomes compared with not-infected, concomitant pregnant individuals.** **Methods:** Cohort study involving 43 institutions in 18 countries, 2 unmatched, consecutive, not-infected women concomitantly enrolled immediately after each infected woman was identified, at any stage of pregnancy or delivery. Women and neonates were followed up until hospital discharge. Main Outcomes: indices of (maternal and severe neonatal/perinatal) morbidity and mortality (adjusted for country, month entering study, maternal age, and history of morbidity) **Findings** > A total of 706 pregnant women with COVID-19 diagnosis and 1424 pregnant women without COVID-19 diagnosis enrolled > Broadly similar demographic characteristics (mean [SD] age, 30.2 [6.1] years). > Overweight early in pregnancy occurred in 323 women (48.6%) with COVID-19 diagnosis and 554 women (40.2%) without. > Women with COVID-19 diagnosis were at higher risk for preeclampsia/eclampsia (relative risk [RR], 1.76; 95% CI, 1.27-2.43), severe infections (RR, 3.38; 95% CI, 1.63-7.01), intensive care unit admission (RR, 5.04; 95% CI, 3.13-8.10), maternal mortality (RR, 22.3; 95% CI, 2.88-172), preterm birth (RR, 1.59; 95% CI, 1.30-1.94), medically indicated preterm birth (RR, 1.97; 95% CI, 1.56-2.51), severe neonatal morbidity index (RR, 2.66; 95% CI, 1.69-4.18), and severe perinatal morbidity and mortality index (RR, 2.14; 95% CI, 1.66-2.75). > Fever and shortness of breath for any duration was associated with increased risk of severe maternal complications (RR, 2.56; 95% CI, 1.92-3.40) and neonatal complications (RR, 4.97; 95% CI, 2.11-11.69). > Asymptomatic women with COVID-19 diagnosis remained at higher risk only for maternal morbidity (RR, 1.24; 95% CI, 1.00-1.54) and preeclampsia (RR, 1.63; 95% CI, 1.01-2.63). > Among women who tested positive (98.1% by real-time polymerase chain reaction), 54 (13%) of their neonates tested positive. > Cesarean delivery (RR, 2.15; 95% CI, 1.18-3.91) but not breastfeeding (RR, 1.10; 95% CI, 0.66-1.85) was associated with increased risk for neonatal test positivity. **Conclusions** COVID-19 in pregnancy was associated with consistent and substantial increases in severe maternal morbidity and mortality and neonatal complications, compared to healthy pregnant women.
Nature 22APR2021	**High-dimensional characterization of post-acute sequalae of COVID-19**	Al-Aly Z., *et al*. USA [gotopaper]	Clinics	**Aim:** To identify incident sequalae in 30-day survivors of COVID-19 from the national healthcare databases (US Dept. of Veterans Affairs). **Methods:** Approach to comprehensively identify the 6-months out-comes of incident diagnoses (from 379 diagnostic categories), incident medication use (from 380 medication classes), and incident laboratory abnormalities (from 62 laboratory tests) in people who survived the first 30 days of COVID-19. The cohort included 73,435 users. **Findings:** > Beyond the first 30 days of illness, people with COVID-19 exhibit higher risk of death and health resource utilization. > Increased incident use of several therapeutics including pain medications (opioids and non-opioids), antidepressants, anxiolytics, antihypertensives, and oral hypoglycemics and evidence of laboratory abnormalities in multiple organ systems. > Analysis of an array of pre-specified outcomes reveals a risk gradient that increased across severity of the acute COVID-19 infection (non-hospitalized, hospitalized, admitted to intensive care). > Beyond the acute illness, substantial burden of health loss — spanning pulmonary and several extrapulmonary organ systems — is experienced by COVID-19 survivors. **The results provide a roadmap to inform health system planning and development of multidisciplinary care strategies to reduce chronic health loss among COVID-19 survivors.**

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Cell Rep Med. 21APR2021	**Asymptomatic and symptomatic SARS-CoV-2 infections elicit polyfunctional antibodies.**	Dufloo J., *et al*. France <u>gotopaper</u>	Immunology	**Aim**: to study the extent and quality of the antiviral humoral response of symptomatic and asymptomatic Covid-19 patients. Study groups: 52 asymptomatic infected individuals, 119 mild and 21 hospitalized COVID-19 patients. > **COVID-19 patient sera activates the complement system and kills infected cells** by Antibody-Dependent Cellular Cytotoxicity (ADCC). > **Sera from asymptomatic individuals harbor polyfunctional antibodies**. They neutralize the virus, activate ADCC and trigger complement deposition. > Antibody levels and functions are **lower in asymptomatic individuals** than in symptomatic cases. Antibody functions are correlated, regardless of disease severity. > Longitudinal samplings show that **antibody functions follow similar kinetics of induction and contraction**. Overall, asymptomatic SARS-CoV-2 infection elicits polyfunctional antibodies neutralizing the virus and targeting infected cells.
PNAS 21APR2021	**Dynamic prioritization of COVID-19 vaccines when social distancing is limited for essential workers**	Buckner J.H., *et al*. USA <u>gotopaper</u>	Public Health / Epidemiology	**Aims:** To evaluate the optimal allocation of a limited vaccine supply in the United States across groups defined by age and essential worker status, which constrains opportunities for social distancing. **Methods:** > Compartmental model of transmission dynamics capturing key sources of group heterogeneity. The model contains 9 epidemiological status per group, 6 age classes, 2 groups depending on the essential worker status for age classes 20-39 and 40-59 and 4 possible locations (home, work, school, other). > Three alternative policy objectives are considered: minimizing infections, years of life lost, or deaths. > Assuming vaccines are available for 60% of the population for the first 6 months, the optimal vaccine allocation strategy, that evolves with the epidemiological state of the population, is computed. **Findings:** > The model predicts that older essential workers should be targeted first whatever the objective. > With the objective of minimizing infection, younger essential workers must be prioritized next. > With the objective of reducing mortality, older age classes must be prioritized next. > The dynamic optimal policy outperforms an untargeted approach from 17% to 44%, depending on the objective, the vaccine effectiveness and non-pharmaceutical interventions. > There are trade-offs in what can be achieved between the objectives. For example, policies that minimize infections result in substantially more deaths than a policiy that minimizes deaths. > The optimal priorization is sensitive to several factors, most notably vaccine effectiveness and supply, rate of transmission and the magnitude of initial infections. **Conclusions:** > Temporal flexibility of the allocation strategy is important to optimize public health goals. > Distinguishing between essential and non-essential workers is important for vaccine allocation.

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NEJM 21APR2021	**Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19**	Sadoff J.S., *et al*. International [gotopaper](#)	Vaccines	**Methods:** > International, randomized, double-blind, placebo-controlled, phase 3 trial. Participants randomly assigned in a 1:1 ratio to receive a single dose of Ad26.COV2.S (5×1010 viral particles) or placebo. Primary end points vaccine efficacy against moderate to severe–critical Covid-19 with an onset at least 14 days and at least 28 days **Findings:** > 19,630 SARS-CoV-2–negative participants who received Ad26.COV2.S and 19,691 who received placebo. > Ad26.COV2.S protected against moderate to severe–critical Covid-19 with onset at least 14 days after administration (116 cases in the vaccine group vs. 348 in the placebo group; efficacy, 66.9%; adjusted 95% confidence interval [CI], 59.0 to 73.4) and at least 28 days after administration (66 vs. 193 cases; efficacy, 66.1%; adjusted 95% CI, 55.0 to 74.8). > Vaccine efficacy was higher against severe–critical Covid-19 (76.7% [adjusted 95% CI, 54.6 to 89.1] for onset at ≥14 days and 85.4% [adjusted 95% CI, 54.2 to 96.9] for onset at ≥28 days). > Despite 86 of 91 cases (94.5%) in South Africa with sequenced virus having the 20H/501Y.V2 variant, vaccine efficacy was 52.0% and 64.0% against moderate to severe–critical Covid-19 with onset at least 14 days and at least 28 days after administration, respectively, and efficacy against severe–critical Covid-19 was 73.1% and 81.7%, respectively. > Reactogenicity was higher with Ad26.COV2.S than with placebo but was generally mild to moderate and transient. > The incidence of serious adverse events was balanced between the two groups. Three deaths occurred in the vaccine group (none were Covid-19–related), and 16 in the placebo group (5 were Covid-19–related). **Conclusion:** A single dose of Ad26.COV2.S protected against symptomatic Covid-19 and asymptomatic SARS-CoV-2 infection and was effective against severe–critical disease, including hospitalization and death. Safety appeared to be similar to that in other phase 3 trials of Covid-19 vaccines.
NEJM 21APR2021	**Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons**	Shimabukuro T., *et al*. USA [gotopaper](#)	Vaccination	**Methods:** Assesement of data from "v-safe after vaccination health checker" surveillance system, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting System (VAERS) to characterize the initial safety of mRNA Covid-19 vaccines in pregnant persons. Findings: > 35,691 v-safe participants 16 to 54 years of age identified as pregnant. > Injection-site pain was reported more frequently among pregnant persons than among nonpregnant women, whereas headache, myalgia, chills, and fever were reported less frequently. >Among 3958 participants enrolled in the v-safe pregnancy registry, 827 had a completed pregnancy, of which 115 (13.9%) resulted in a pregnancy loss and 712 (86.1%) resulted in a live birth (mostly among participants with vaccination in the third trimester). > Adverse neonatal outcomes included preterm birth (in 9.4%) and small size for gestational age (in 3.2%); no neonatal deaths were reported. > Although not directly comparable, calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against Covid-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the Covid-19 pandemic. > Among 221 pregnancy-related adverse events reported to the VAERS, the most frequently reported event was spontaneous abortion (46 cases). **Conclusions:** Preliminary findings did not show obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines.

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Nature Med. 19APR2021	**COVID-19 dynamics after a national immunization program in Israel**	Rossman H., *et al.* Israel [gotopaper]	Vaccines	**Real-life effect of the BNT162b2 vaccine for COVID-19** **Methods:** > Retrospective analysis of data from the Israeli Ministry of Health (28 August 2020-24 February 2021) > Temporal dynamics of the number of new COVID-19 cases and hospitalizations after the vaccination campaign, initiated on 20 December 2020. To distinguish the possible effects of the vaccination on cases and hospitalizations from other factors, including a third lockdown (8 January 2021) 3 comparision were performed: (1) individuals aged 60 years and older prioritized to receive the vaccine first versus younger age groups (2) the January lockdown versus the September lockdown (3) early-vaccinated versus late-vaccinated cities. **Findings:** > 2 months after the initiation of the vaccination campaign, with 85% of individuals older than 60 years already vaccinated with two doses (24 February 2021), there was an approximately 77% drop in cases, a 45% drop in positive test percentage, a 68% drop in hospitalizations and a 67% drop in severe hospitalizations compared to peak values > consecutive drops in younger age groups later, according to the order of vaccine prioritization, including earlier drops in some young age groups (16–21 years) prioritized over older age groups (21–35 years). > Similar pattern of a larger and faster decline of cases and hospitalizations in older individuals during the previous lockdown implemented in Israel (between 18 September 2020 and 18October 2020) were not observed. **Conclusion:** Analysis of large-scale, real-world data from Israel demonstrating real-life effectiveness of a national vaccination campaign
Cell 20APR2021	**Transmission, infectivity, and neutralization of a spike L452R SARS-CoV-2 variant**	Deng X., *et al.* USA [gotopaper]	Public Health / Epidemiology - Variants	> We identified an emerging SARS-CoV-2 variant by viral whole-genome sequencing of 2,172 nasal/nasopharyngeal swab samples from 44 counties in California, a state in the Western United States > Named B.1.427/B.1.429 to denote its 2 lineages, the variant emerged in May 2020 and increased from 0% to >50% of 42 sequenced cases from September 2020 to January 2021 > Showing 18.6-24% increased transmissibility relative to wild-type circulating strains > The variant carries 3 mutations in the spike protein, including an L452R substitution. **Findings** > 2-fold increased B.1.427/B.1.429 viral shedding in vivo and increased L452R pseudovirus infection of cell cultures and lung organoids albeit decreased relative to pseudoviruses carrying the N501Y mutation common to variants B.1.1.7, B.1.351, and P.1 > Antibody neutralization assays revealed 4.0 to 6.7-fold and 2.0-fold decreases in neutralizing titers from convalescent patients and vaccine recipients, respectively **The increased prevalence of a more transmissible variant in California exhibiting decreased antibody neutralization warrants further investigation**

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Cell 20APR2021	**Transmission, infectivity, and neutralization of a spike L452R SARS-CoV-2 variant**	Deng X., *et al.* USA [gotopaper]	Public Health / Epidemiology Variants	> We identified an emerging SARS-CoV-2 variant by viral whole-genome sequencing of 2,172 nasal/nasopharyngeal swab samples from 44 counties in California, a state in the Western United States > Named B.1.427/B.1.429 to denote its 2 lineages, the variant emerged in May 2020 and increased from 0% to >50% of 42 sequenced cases from September 2020 to January 2021 > Showing 18.6-24% increased transmissibility relative to wild-type circulating strains > The variant carries 3 mutations in the spike protein, including an L452R substitution. **Findings** > 2-fold increased B.1.427/B.1.429 viral shedding in vivo and increased L452R pseudovirus infection of cell cultures and lung organoids albeit decreased relative to pseudoviruses carrying the N501Y mutation common to variants B.1.1.7, B.1.351, and P.1 > Antibody neutralization assays revealed 4.0 to 6.7-fold and 2.0-fold decreases in neutralizing titers from convalescent patients and vaccine recipients, respectively **The increased prevalence of a more transmissible variant in California exhibiting decreased antibody neutralization warrants further investigation**
Lancet Infect Dis. 19APR2021	**Safety and immunogenicity of SARS-CoV-2 recombinant protein vaccine formulations in healthy adults: interim results of a randomised, placebo-controlled, phase 1–2, dose-ranging study**	Goepfert P.A., *et al*. International [gotopaper]	Vaccines	**Interim safety and immunogenicity results of the first-in-human study of the CoV2 preS dTM vaccine with two different adjuvant formulations.** **>** Phase 1–2, randomised, double-blind study in healthy, SARS-CoV-2-seronegative adults in ten clinical research centres in the USA. > Stratified by age (18–49 years and ≥50 years) > One dose (on day 1) or two doses (on days 1 and 22) of placebo or candidate vaccine, containing low-dose (effective dose 1·3 µg) or high-dose (2·6 µg) antigen with adjuvant AF03 (Sanofi Pasteur) or AS03 (GlaxoSmithKline) or unadjuvanted high-dose antigen (18–49yrs only). Primary endpoints: were safety (up to day 43), and immunogenicity (SARS-C0V-2 neutralising antibodies on 1, 22, and 36. **Findings** > Interim safety analyses included 439 (>99%) of 441 randomly assigned participants (299 aged 18–49 years and 140 aged ≥50 years). > Nab titres analysed in 326 (74%) of 441 participants (235 [79%] of 299 aged 18–49 years and 91 [64%] of 142 aged ≥50 years). > No vaccine-related unsolicited immediate adverse events, serious adverse events, medically attended adverse events classified as severe, or adverse events of special interest. > Solicited local and systemic reactions of any grade after two vaccine doses were reported in 81% (95% CI 61–93; 21 of 26) of participants in the low-dose plus AF03 group, 93% (84–97; 74 of 80) in the low-dose plus AS03 group, 89% (70–98; 23 of 26) in the high-dose plus AF03 group, 95% (88–99; 81 of 85) in the high-dose plus AS03 group, 29% (10–56; five of 17) in the unadjuvanted high-dose group, and 21% (8–40; six of 29) in the placebo group. > A single vaccine dose did not generate neutralising antibody titres above placebo levels in any group at days 22 or 36. >Among participants aged 18–49 years, neutralising antibody titres after two vaccine doses were 13·1 (95% CI 6·40–26·9) in the low-dose plus AF03 group, 20·5 (13·1–32·1) in the low-dose plus AS03 group, 43·2 (20·6–90·4) in the high-dose plus AF03 group, 75·1 (50·5–112·0) in the high-dose plus AS03 group, 5·00 (not calculated, NT) in the unadjuvanted high-dose group, and 5·00 (NT) in the placebo group. >Among participants aged 50 years or older, neutralising antibody titres after two vaccine doses were 8·62 (1·90–39·0) in the low-dose plus AF03 group, 12·9 (7·09–23·4) in the low-dose plus AS03 group, 12·3 (4·35–35·0) in the high-dose plus AF03 group, 52·3 (25·3–108·0) in the high-dose plus AS03 group, and 5·00 (NT) in the placebo group. **Conclusions:** Lower than expected immune responses, especially in the older age groups, and high reactogenicity after dose two probably due to higher than anticipated host-cell protein content and lower than planned antigen doses in the formulations tested, which was discovered during characterisation studies on the final bulk drug substance. Further studies will focus on optimal antigen formulation and dose.

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Lancet Infect Dis. 19APR2021	**Safety and immunogenicity of an MF59-adjuvanted spike glycoprotein-clamp vaccine for SARS-CoV-2: a randomised, double-blind, placebo-controlled, phase 1 trial**	Chappel K.J., *et al.* Australia <u>gotopaper</u>	Vaccines	Safety and immunogenicity of an MF59-adjuvanted subunit vaccine for COVID-19 based on recombinant SARS-CoV-2 spike glycoprotein stabilised in a pre-fusion conformation by a novel molecular clamp **Methods** > Phase 1, double-blind, placebo-controlled, block-randomised trial in a single clinical trial site in Brisbane, QLD, Australia. NCT04495933. > Healthy adults (aged ≥18 to ≤55 years). No history of SARS-CoV-2 infection; randomly assigned to one of five treatment groups and received two doses via intramuscular injection 28 days apart of either placebo, sclamp vaccine at 5 µg, 15 µg, or 45 µg, or one dose of sclamp vaccine at 45 µg followed by placebo. <u>Primary safety endpoints:</u> solicited local and systemic adverse events in the 7 days after each dose and unsolicited adverse events up to 12 months after dosing. <u>Primary immunogenicity endpoints:</u> were antigen-specific IgG ELISA and SARS-CoV-2 microneutralisation assays assessed at 28 days after each dose. **Findings:** > 120 volunteers randomly assigned to groups (n=24 per group). > 114 (95%) completed the study up to day 57 (mean age 32·5 years [SD 10·4], 65 [54%] male, 55 [46%] female). > Both solicited reactions and unsolicited adverse events occurred at a similar frequency in participants receiving placebo and the SARS-CoV-2 sclamp vaccine. > Solicited reactions occurred in 19 (79%) of 24 participants receiving placebo and 86 (90%) of 96 receiving the SARS-CoV-2 sclamp vaccine at any dose. Unsolicited adverse events occurred in seven (29%) of 24 participants receiving placebo and 35 (36%) of 96 participants receiving the SARS-CoV-2 sclamp vaccine at any dose. > Vaccination with SARS-CoV-2 sclamp elicited a similar antigen-specific response irrespective of dose: 4 weeks after the initial dose (day 29) with 5 µg dose ([GMT] 6400, 95% CI 3683–11 122), with 15 µg dose (7492, 4959–11 319), and the two 45 µg dose cohorts (8770, 5526–13 920 in the two-dose 45 µg cohort; 8793, 5570–13 881 in the single-dose 45 µg cohort); 4 weeks after the second dose (day 57) with two 5 µg doses (102 400, 64 857–161 676), with two 15 µg doses (74 725, 51 300–108 847), with two 45 µg doses (79 586, 55 430–114 268), only a single 45 µg dose (4795, 2858–8043). At day 57, 67 (99%) of 68 participants who received two doses of sclamp vaccine at any concentration produced a neutralising immune response, compared with six (25%) of 24 who received a single 45 µg dose and none of 22 who received placebo. Participants receiving two doses of sclamp vaccine elicited similar neutralisation titres, irrespective of dose: two 5 µg doses (GMT 228, 95% CI 146–356), two 15 µg doses (230, 170–312), and two 45 µg doses (239, 187–307)**.** **Conclusions:** > Subunit vaccine MF59-adjuvanted, molecular clamp-stabilised recombinant spike protein elicits strong immune responses with a promising safety profile. > However, the glycoprotein 41 peptide present in the clamp created HIV diagnostic assay interference, a possible barrier to widespread use highlighting the criticality of potential non-spike directed immunogenicity during vaccine development. > Studies are ongoing with alternative molecular clamp trimerisation domains to ameliorate this response.
Cell Rep Med. 18APR2021	**BNT162b2 Vaccination Effectively Prevents the Rapid Rise of SARS-CoV-2 Variant B.1.1.7 in high risk populations in Israel**	Munitz A., *et al.* Israel <u>gotopaper</u>	Vaccines - Variants	**Aim**: evaluating the impact on B.1.1.7 variant spreading of three Israeli national programs: massive RT-PCR testing, focused surveillance in nursing homes and robust prioritized vaccination with BNT162b2. Analysis of ~300,000 RT-PCR samples (Dec 6th 2020 – Feb 10th 2021). > B.1.1.7 variant is **45% (95% CI:20-60%) more transmissible** than the wild-type strain, and became the dominant in Israel within 3.5 weeks. > **Active surveillance** through focused RT-PCR testing markedly reduces the transmission of B.1.1.7 in nursing homes. > **Prioritized vaccination** programs seem capable of preventing the spread of the B.1.1.7 variant in the elderly. > **Proactive surveillance combined with prioritized vaccination are achievable, and reduce severe illness and subsequent death.**

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Blood 16APR2021	**Efficacy of the BNT162b2 mRNA COVID-19 Vaccine in Patients with Chronic Lymphocytic Leukemia**	Herishanu Y., *et al*. Israel gotopaper	Vaccines	The goal of this study was to determine the efficacy of COVID-19 vaccine (BNT162b2 mRNA) in patients with CLL. **Methods** > We evaluated humoral immune responses to BNT162b2 mRNA COVID-19 vaccine in patients with CLL and compared responses with those obtained in age-matched healthy controls. > Patients received two vaccine doses, 21 days apart, and antibody titers were measured using Elecsys® Anti-SARS-CoV-2S assay after administration of the second dose. **Findings** > In 167 total patients with CLL the antibody response rate was 39.5%. > A comparison between 52 patients with CLL and 52 sex- and aged-matched healthy controls, revealed a significantly reduced response rate among patients (52% vs 100%, respectively; adjusted odds ratio=0.010, 95% CI 0.001-0.162; p<0.001). > Response rate was highest in patients who obtained clinical remission after treatment (79.2%), followed by 55.2% in treatment-naïve and 16% in patients under treatment at the time of vaccination. > None of the patients exposed to anti-CD20 antibodies <12 months prior to vaccination responded. > In a multivariate analysis, the independent predictors of response were younger age, females, lack of currently active treatment, IgG levels ≥550 mg/dL and IgM levels ≥40mg/dL **> Antibody response to BNT162b2 mRNA COVID19 vaccine in CLL patients with is markedly impaired and affected by disease activity and treatment.** **> In patients treated with either Bruton's tyrosine kinase inhibitors or venetoclax ± anti-CD20 antibody, responses are relatively low ((16.0% and 13.6%, respectively).** **In conclusion, antibody-mediated response to BNT162b2 mRNA COVID-19 vaccine in patients with CLL is markedly impaired and affected by disease activity and treatment.**
Blood 16APR2021	**Low Neutralizing Antibody Responses Against SARS-CoV-2 in Elderly Myeloma Patients After the First BNT162b2 Vaccine Dose**	Terpos E., *et al*. Greece gotopaper	Vaccines	We report the development of neutralizing antibodies (NAbs) against SARS-CoV-2 in MM patients (above 18 years) after the first dose of the BNT162b2 vaccine. **Methods** > Included 48 MM patients (29males/19females; median age: 83years, range: 59-92years) and 104controls (57males/47females; median age: 83 years, range: 65-95 years), who were vaccinated during the same period,at the same vaccinationcenter (Greece). **Findings** > After the first doseof the vaccine, on D22, MM patients had lower NAb titers compared to controls:medianNAb inhibition titersand rangewas 20.6% (0-96.7%) for MMpatients versus 32.5% (5.2-97.3%)for controls; P<0.01. More, specifically, only12 (25.0%) MM patientsversus 57 (54.8%)controls developed NAb titers ≥30% on D22. > The respective number of MM patients and controls who developed NAb titers ≥50% (which corresponds to clinically relevantviral inhibition11) was 4 (8.3%) and 21 (20.2%), respectively. > Interestingly, only one (11.1%) out of nine patients with smoldering myeloma had NAb titers of equal or more than 30% (positivity cut-off) versus 11/39 (28.2%) patients with active MM. > This observationis of great interest as hypoglobulinemia has been associated withinferior antibody response among patients with chronic lymphocytic leukemia and COVID-19 **> Our data indicate that the first dose of BNT162b2leads to production of lower levels of NAbsagainstSARS-CoV-2 compared to non-MM controls of similar ageand genderand without malignant disease.** **> This low antibody response of elderly myeloma patients after the first BNT162b2 dosemay not be seen in younger patients.** **> Some anti-myeloma therapies have a B-cell depleting activity which in turn may impair immune response to vaccines, whereas both myeloma microenvironment and anti-myeloma treatmentsmay impair T-cell function.**

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Science 16APR2021	**SARS-CoV-2 within-host diversity and transmission**	Lythgoe K.A,. *et al*. UK [gotopaper](#)	Genomics / Phylogenomics	**Aim:** Characterize SARS-CoV-2 within-host diversity and transmission **Methods:** Deep-sequencing of 1313 clinical samples from the UK (including 16 assumed transmission pairs), transmission bottleneck inference with exact beta-binomial sampling method, phylogenetics **Key facts:** > Within-host viral diversity is relatively low during acute infection; selection seems to be mostly negative (removal of deleterious mutations) > Estimation of the bottleneck size for transmission: of 1 to 8 viruses > Narrow transmission bottleneck, so most often transmission of the majority within-host variant; but sometimes transmission of minority variant (leading to change in consensus sequence, i.e. variation at the host level), and possible transmission of mixed infection. > Identification of spike mutations present in multiple samples with known phenotypic effect (e.g. L5F, G446V, A879V) **Conclusion:** Emergence of vaccine and therapeutic escape mutations likely to be rare during early infection, but observation of immune-escape variants underlines the need for continued vigilance. Key role of open, large and rigorously controlled datasets, integrating genomic, clinical and epidemiological information.
NEJM 16APR21	**Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination**	Scully M., *et al*. UK [gotopaper](#)	Vaccination	**Methods:** > 23 patients presenting thrombosis and thrombocytopenia 6 to 24 days after receiving the first dose of the ChAdOx1 nCoV-19 vaccine (AstraZeneca). **Findings:** > Median age was 46 years (range, 21 to 77). 16 patients (70%) younger than 50 years. 14 patients (61%) female > 22 patients presented with acute thrombocytopenia and thrombosis, primarily cerebral venous thrombosis, and 1 patient presented with isolated thrombocytopenia and a hemorrhagic phenotype. > All the patients had low or normal fibrinogen levels and elevated d-dimer levels at presentation. No evidence of thrombophilia or causative precipitants was identified. > Testing for antibodies to platelet factor 4 (PF4) was positive in 22 patients (with 1 equivocal result) and negative in 1 patient. **Conclusions:** A pathogenic PF4-dependent syndrome, unrelated to the use of heparin therapy, can occur after the administration of the ChAdOx1 nCoV-19 vaccine.
Clin Infect Dis. 16APR2021	**Impact of convalescent plasma therapy on SARS CoV-2 antibody profile in COVID-19 patients**	Tang J., *et al*. USA [gotopaper](#)	Therapeutics	**Aim:** to better understand the impact of convalescent plasma (CP) on antibody response in COVID-19 patients **Methods:** longitudinal analysis of antibody profile on 115 sequential plasma samples from 16 hospitalized COVID-19 patients treated with either CP or standard of care **Findings:** >Differential antibody kinetics was observed for antibody binding, IgM/IgG/IgA distribution, and affinity maturation in 'survived' vs. 'fatal' COVID-19 patients. >Surprisingly, CP treatment did not predict survival. Strikingly, marked decline in neutralization titers was observed in the fatal patients prior to death, and convalescent plasma treatment did not reverse this trend. >Irrespective of CP treatment, higher antibody affinity to the SARS-CoV-2 prefusion spike was associated with survival outcome, while sustained elevated IgA response was associated with fatal outcome in COVID-19 patients. >**Treatment of COVID-19 patients with CPa should be carefully targeted, and effectiveness of treatment may depend on the clinical and immunological status of COVID-19 patients as well as the quality of the antibodies in the CP.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
PNAS 16APR2021	**A high-throughput microfluidic nanoimmunoassay for detecting anti–SARS-CoV-2 antibodies in serum or ultralow-volume blood samples**	Swank Z., et al. Switzerland gotopaper	Diagnostics	**Aim:** developement of a sensitive and specific microfluidic nanoimmunoassay (NIA) for the detection of anti–SARS-CoV-2 IgG antibodies in 1,024 samples in parallel. **Methods:** To eliminate the need for venipuncture, they developed a low-cost, ultralow-volume whole blood sampling methods based on two commercial devices and repurposed a blood glucose test strip. The glucose test strip permits the collection, shipment, and analysis of 0.6 µL of whole blood easily obtainable from a simple finger prick. High-throughput NIA was conducted using a PDMS microfluidic device **Findings:** >The method achieved a specificity of 100% and a sensitivity of 98% based on the analysis of 289 human serum samples (155 positive SARS-CoV-2–infected and 134 negative individuals) >A single researcher can achieve a throughput of one or two devices, or 512 to 1,024 samples per day (analyzed in duplicate) in a small research laboratory not dedicated or equipped for high-throughput molecular diagnostics. **The combination of a high-throughput, highly specific and sensitive NIA and the ability to analyze minute volumes of dried blood samples have enormous potential for SARS-CoV-2 serology, epidemiological studies, vaccine trial, and therapeutic development support.**
Lancet Respir Med. 15APR2021	**SARS-CoV-2 seropositivity and subsequent infection risk in healthy young adults: a prospective cohort study**	Letizia A.G., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim:** To investigate the risk of subsequent SARS-CoV-2 infection among young adults seropositive for a previous infection **Methods:** 3249 participants (US Marine recruits, aged 18–20 years, following a 2-week unsupervised quarantine at home) were enrolled and were assessed for baseline SARS-CoV-2 IgG seropositivity, defined as a dilution of 1:150 or more on receptor-binding domain and full-length spike protein ELISA. **Findings:** >Among 189 seropositive participants, 19 (10%) had at least one positive PCR test for SARS-CoV-2 during the 6-week follow-up (1·1 cases per person-year). > In contrast, 1079 (48%) of 2247 seronegative participants tested positive (6·2 cases per person-year) IR 0.18. >Among seropositive recruits, infection was more likely with lower baseline full-length spike protein IgG titres than in those with higher baseline full-length spike protein IgG titres (hazard ratio 0·45). >**Infected seropositive participants had viral loads that were about 10-times lower than those of infected seronegative participants.** >Among seropositive participants, baseline neutralising titres were detected in 45 (83%) of 54 uninfected and in six (32%) of 19 infected participants during the 6 weeks of observation. **Seropositive young adults had about one-fifth the risk of subsequent infection compared with seronegative individuals. Although antibodies induced by initial infection are largely protective, they do not guarantee effective SARS-CoV-2 neutralisation activity or immunity against subsequent infection**.

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Brain 15APR2021	**COVID-19 neuropathology at Columbia University Irving Medical Center/New York Presbyterian Hospital**	Thakur K.T., *et al*. USA gotopaper	Clinics	**Aim**: to present the clinical, neuropathological, and molecular findings of 41 consecutive patients with SARS-CoV-2 infections who died and underwent autopsy in a medical center **Findings:** >Hospital-associated complications were common, including 8 (20%) with deep vein thrombosis/pulmonary embolism (DVT/PE), 7 (17%) patients with acute kidney injury requiring dialysis, and 10 (24%) with positive blood cultures during admission. >Neuropathological examination of 20–30 areas from each brain revealed hypoxic/ischemic changes in all brains, both global and focal; large and small infarcts, many of which appeared hemorrhagic; and microglial activation with microglial nodules accompanied by neuronophagia, most prominently in the brainstem. > Sparse T lymphocyte accumulation was observed in either perivascular regions or in the brain parenchyma. >qRT-PCR revealed low to very low, but detectable, viral RNA levels in the majority of brains, although they were far lower than those in nasal epithelia. >RNAscope and immunocytochemistry failed to detect viral RNA or protein in brains. **Microglial activation, microglial nodules and neuronophagia, observed in the majority of brains, do not result from direct viral infection of brain parenchyma, but rather likely from systemic inflammation**
JAMA 15APR2021	**Spike Antibody Levels of Nursing Home Residents With or Without Prior COVID-19 3 Weeks After a Single BNT162b2 Vaccine Dose**	Blain, H., *et al*. France gotopaper	Vaccines	Older adults living in nursing homes are at higher risk for severe COVID-19, and the immune response to the vaccine may differ from that of younger, healthier adults. **Findings:** > 102 residents : 60 had no prior SARS-CoV-2 infection (COVID-19), 36 had a positive RT-PCR result and were seropositive for SARS-CoV-2 N-protein IgG in June 2020, and 6 had a positive RT-PCR result or were seropositive for SARS-CoV-2 N-protein IgG. > All 36 residents with prior COVID-19 were seropositive for S-protein IgG after 1 vaccine dose vs 29 of 60 residents (49.2%) without prior COVID-19. > Among residents with prior COVID-19, the median level of S-protein IgG was 40 000 AU/mL or greater vs 48.0 AU/mL in those without prior COVID-19 > One resident with a positive RT-PCR result in April 2020 tested seronegative for N-protein IgG in June 2020 and January 2021; the resident had a robust S-protein IgG level (≥40 000 AU/mL) > Five residents were found to be seropositive for N-protein IgG in June 2020 while having repeated negative RT-PCR results in April 2020. All 5 of these residents had high levels of S-protein IgG antibody > Among the 6 residents with a positive RT-PCR result or who were seropositive for N-protein IgG, the levels of S-protein IgG antibody were significantly higher than among the 60 without prior COVID-19 and were not statistically significantly different from the 36 who had a positive RT-PCR result and were seropositive for N-protein IgG **Conclusions:** This preliminary study suggests that a single dose of BNT162b2 vaccine may be sufficient to obtain a high level of S-protein IgG antibody in nursing home residents previously diagnosed with COVID-19 based on RT-PCR results

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Science Immunol. 15APR2021	**Distinct antibody and memory B cell responses in SARS-CoV-2 naïve and recovered individuals following mRNA vaccination**	Goel R.R., *et al*. USA [gotopaper]	Immunology	Study of **antibody and antigen-specific memory B cells** over time after mRNA vaccination in 33 SARS-CoV-2 naïve and 11 SARS-CoV-2 recovered subjects. > SARS-CoV-2 naïve individuals required **both vaccine doses** for optimal increases in antibodies, particularly for neutralizing titers against the B.1.351 variant. > **Memory B cells** specific for full-length spike protein and the spike receptor binding domain (RBD) were also **efficiently primed by mRNA vaccination** and detectable in all SARS-CoV-2 naive subjects after the second vaccine dose, though the memory B cell response declined slightly with age. > In SARS-CoV-2 recovered individuals, antibody and memory B cell responses were significantly boosted **after the first vaccine dose**; however, there was no increase in circulating antibodies, neutralizing titers, or antigen-specific memory B cells after the second dose. > The robust boosting after the first vaccine dose **strongly correlated with levels of pre-existing memory B cells in recovered individuals**, identifying a key role for memory B cells in mounting recall responses to SARS-CoV-2 antigens. **Robust serological and cellular priming by mRNA vaccines were demonstrated. COVID-19 recovered subjects may only require a single vaccine dose to achieve peak antibody and memory B cell responses.**
Science Immunol. 14APR2021	**SARS-CoV-2 genome-wide T cell epitope mapping reveals immunodominance and substantial CD8+ T cell activation in COVID-19 patients**	Saini S.K., *et al*. Denmark [gotopaper]	Immunology	**Aim**: to examine the full-spectrum of CD8+ T cell immunity in COVID-19, by experimentally evaluating 3141 major histocompatibility (MHC) class I-binding peptides covering the complete SARS-CoV-2 genome. **Results** > A comprehensive list of 122 immunogenic and a subset of immunodominant SARS-CoV-2 T cell epitopes was reported. > Substantial CD8+ T cell recognition was observed in COVID-19 patients, with up to 27% of all CD8+ lymphocytes interacting with SARS-CoV-2-derived epitopes. > Most immunogenic regions were derived from ORF1 and ORF3, with ORF1 containing most of the immunodominant epitopes. > CD8+ T cell recognition of lower affinity was also observed in healthy donors toward SARS-CoV-2-derived epitopes. This pre-existing T cell recognition signature was partially overlapping with the epitope landscape observed in COVID-19 patients and may drive the further expansion of T cell responses to SARS-CoV-2 infection. > The phenotype of the SARS-CoV-2-specific CD8+ T cells revealed a strong T cell activation in COVID-19 patients, while minimal T cell activation was seen in healthy individuals. > Patients with severe disease displayed significantly larger SARS-CoV-2-specific T cell populations compared to patients with mild diseases and these T cells displayed a robust activation profile. **These results further the understanding of T cell immunity to SARS-CoV-2 infection and hypothesize that strong antigen-specific T cell responses are associated with different disease outcomes.**
Clin Infect Dis. 15APR2021	**Viral sequencing reveals US healthcare personnel rarely become infected with SARS-CoV-2 through patient contac**	Braun K.M., *et al*. USA [gotopaper]	Public Health / Epidemiology	**Aim**: to infer the most likely source of infection in health personnel (HCP) by combining epidemiological data and viral sequences from healthcare and the general community. > SARS-CoV-2 infection clusters involving 95 HCP and 137 possible patient contact sequences. > The majority of HCP infections could not be linked to a patient or co-worker (55/95; 57.9%) and were genetically similar to viruses circulating concurrently in the community. > 10.5% of infections could be traced to a coworker (10/95). Strikingly, only 4.2% of HCP infections could be traced to a patient source (4/95). **This study found no evidence for healthcare-associated transmission in the majority of HCP infections evaluated. It appears that HCP most commonly becomes infected with SARS-CoV-2 via community exposure.**

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Clin Infect Dis. 14APR2021	**Sera neutralizing activities against SARS-CoV-2 and multiple variants six month after hospitalization for COVID-19**	Betton M., *et al*. France [gotopaper](#)	Immunology	**Aim**: To characterise Igs neutralising activity. Prospective study on sera of 107 hospitalised Covid-19 patients, collected at 3- and 6-months post-infection. > Levels of sero-neutralization and IgG rates against the ancestral strain **decreased significantly over time**. After 6 months, 2.8% of the patients had a negative serological status for both anti-S (spike) and anti-NP (Nucleocapsid) IgG. > All sera had a **persistent and effective neutralizing effect** against SARS-CoV-2. IgG levels correlated with sero-neutralization and this **correlation was stronger for anti-S** than for anti-NP antibodies. > The level of sero-neutralization quantified at 6 months **correlated with markers of initial severity**, notably ICU admission and the need for mechanical invasive ventilation. > Sera collected at 6 months showed **efficient neutralizing effects against D614G, B.1.1.7 and P.1 variants but a significantly weaker activity against B.1.351 variant**. These results indicate a sustained humoral response against the ancestral strain and the D614G, B.1.1.7 and P.1 variants for at least 6 months in patients previously hospitalized for COVID-19.
Science 14APR2021	**Genomics and epidemiology of the P.1 SARS-CoV-2 lineage in Manaus, Brazil**	Faria N.R., *et al*. UK [gotopaper](#)	Public Health / Epidemiology - Variants	Genome sequencing of viruses sampled in Manaus between November 2020 and January 2021 revealed the emergence and circulation of a novel SARS-CoV-2 variant of concern: Investigate the emergence of the P.1 lineage and explore epidemiological explanations for the resurgence of COVID-19 in Manaus. **Methods** > Using genomic data, structure-based mapping of mutations of interest onto the spike protein, and dynamical epidemiology modelling of genomic and mortality data (two-category dynamical model that integrates genomic and mortality data) > We sequenced SARS-CoV-2 genomes from 184 samples from patients seeking COVID-19 testing in two diagnostic laboratories in Manaus between November and December 2020, using the ARTIC V3 multiplexed amplicon scheme (24) and the MinION sequencing platformindings **Findings** > Lineage P.1, acquired 17 mutations, including a trio in the spike protein (K417T, E484K and N501Y) associated with increased binding to the human ACE2 receptor. > Molecular clock analysis shows that P.1 emergence occurred around mid-November 2020 and was preceded by a period of faster molecular evolution > We estimate that P.1 may be 1.7–2.4-fold more transmissible, and that previous (non-P.1) infection provides 54–79% of the protection against infection with P.1 that it provides against non-P.1 lineages. > The B.1.1.7 lineage exhibits similar evolutionary characteristics, which was hypothesized to have occurred in a chronically infected or immunocompromised patient > Our results further show that natural immunity waning alone is unlikely to explain the observed dynamics in Manaus, with support for P.1 possessing altered epidemiological characteristics robust to a range of values assumed for the date of the lineage's emergence and the rate of natural immunity waning **Enhanced global genomic surveillance of variants of concern, which may exhibit increased transmissibility and/or immune evasion, is critical to accelerate pandemic responsiveness. Studies to evaluate real-world vaccine efficacy in response to P.1 are urgently needed.**

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NEJM 14APR21	**Thrombotic Thrombocytopenia after Ad26.COV2.S Vaccination**	Muir K.L., *et al.* USA gotopaper	Vaccines	**Case report:** of extensive thrombosis associated with severe thrombocytopenia and disseminated intravascular coagulation that resembled autoimmune heparin-induced thrombocytopenia3 in a patient who had received the Ad26.COV2.S vaccine (Johnson & Johnson/Janssen) (Correspondace) > 48-year-old woman, PCR - for SARS CoV 2. Receiving the Ad26.COV2.S vaccine 14 days before symptom onset > Mild anemia and severe thrombocytopenia. MMarked reduction in the platelet count with occasional schistocytes, prolonged activated partial thromboplastin time, and a marked elevation in the d-dimer level, indicating a disseminated intravascular coagulation–like state. > Screening test for antibodies against platelet factor 4 (PF4)–heparin by latex-enhanced immunoassay negative. However, the result of enzyme-linked immunosorbent assay for antibodies against PF4–polyanion was strongly positive **Conclusions:** Rare occurrence of vaccine-induced immune thrombotic thrombocytopenia could be related to adenoviral vector vaccines.
Clin Infect Dis. 14APR21	**Nosocomial outbreak of COVID-19 by possible airborne transmission leading to a superspreading event**	Chi-Chung Cheng, V., *et al.* China gotopaper	Public Health / Epidemiology	Description of a nosocomial outbreaks with superspreading of COVID-19 due to a possible airborne transmission **Methods:** Epidemiological analysis, environmental samplings, and whole genome sequencing (WGS) were performed for a hospital outbreak. **FIndings:** > Superspreading event involving 12 patients and 9 healthcare workers (HCWs) occurred within 4 days in 3 of 6 cubicles at an old-fashioned general ward with no air exhaust built within the cubicles. > Environmental contamination by SARS-CoV-2 RNA was significantly higher in air grilles than high-touch clinical surfaces. > Six (66.7%) of 9 contaminated air exhaust grilles were located outside patient cubicle. > The clinical attack rate of patients was significantly higher than HCWs (15.4%, 12/78 exposed-patients vs 4.6%, 9/195 exposed-HCWs, p=0.005). > Clinical attack rate of ward-based HCWs was significantly higher than non-ward-based HCWs (8.1%, 7/68 vs 1.8%, 2/109, p=0.045). > The outbreak strains belong to SARS-CoV-2 lineage, B.1.36.27 ith the unique S-T470N mutation on WGS. **Conclusion** This nosocomial point source superspreading due to possible airborne transmission demonstrated the need for stringent SARS-CoV-2 screening at admission to healthcare facilities and better architectural design of the ventilation system to prevent such outbreaks. Portable high-efficiency particulate filters were installed in each cubicle to improve ventilation before resumption of clinical service.

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Clinical Infect Dis. 13APR2021	**Real-World Experience of Bamlanivimab for COVID-19: A Case-Control Study**	Kumar R.N., *et al*. USA [gotopaper](#)	Therapeutics	**Aim**: to describe a single center, real-world experience of the use of bamlanivimab in high-risk ambulatory patients with mild to moderate COVID-19 and its impact on hospitalization rate. **Methods:** retrospective case-control study across a single healthcare system of non-hospitalized patients, with documented positive SARS-CoV-2 testing, risk factors for severe COVID-19, and referrals for bamlanivimab via emergency use authorization. **Findings:** >The most reported and documented symptoms of COVID-19 illness at initial presentation were cough (65.8%), fever (42.3%), myalgias (37.7%), and fatigue (34.8%) >The 30-day hospitalization rate was significantly lower among patients who received bamlanivimab (7.3% v 20.0%, RR 0.37), and the number needed to treat was 8. >On logistic regression, odds of hospitalization were increased in patients not receiving bamlanivimab and with a higher number of pre-specified comorbidities (OR 4.19 CI: 1.31-2.16, p<0.001; OR 1.68, CI: 2.12-8.30, p<0.001, respectively). **Ambulatory patients with COVID-19 who received bamlanivimab had a lower 30-day hospitalization than control patients in real-world experience.**
Br J Sports Med. 13APR2021	**Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients**	Sallis R., *et al*. USA [gotopaper](#)	Public Health / Epidemiology	**Aim**: To compare hospitalisation rates, ICU admissions and mortality for 48 440 patients with COVID-19 who were consistently inactive, doing some activity or consistently meeting physical activity guidelines. > Patients with COVID-19 who were consistently inactive had a greater risk of hospitalisation (OR 2.26; 95% CI 1.81-2.83), admission to the ICU (OR 1.73; 95% CI 1.18-2.55) and death (OR 2.49; 95% CI 1.334.67) due to COVID-19 than patients who were consistently meeting physical activity guidelines. > Patients who were consistently inactive also had a greater risk of hospitalisation (OR 1.20; 95% CI 1.10-1.32), admission to the ICU (OR 1.10; 95% CI 0.93-1.29) and death (OR 1.32; 95% CI 1.09-1.60) due to COVID-19 than patients who were doing some physical activity. **Consistently meeting physical activity guidelines was strongly associated with a reduced risk for severe COVID-19 outcomes among infected adults**.
JAMA 12APR2021	**SARS-CoV-2–Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women**	Perl S.H., *et al*. Israel [gotopaper](#)	Vaccines	Aim: to investigate if maternal immunization with the Pfizer-BioNTech vaccine results in secretion of SARS-CoV-2 antibodies into breast milk. > 504 breast milk samples from 84 women (weekly sampling for 6 weeks from week 2 after one dose of vaccine). > Mean levels of **anti–SARS-CoV-2-specific IgA antibodies** in the breast milk increased rapidly and were significantly elevated at 2 weeks after the first vaccine (2.05 ratio; P < .001), when 61.8% of samples tested positive, increasing to 86.1% at week 4 (1 week after the second vaccine). Mean levels remained elevated for the duration of follow-up. At week 6, 65.7% of samples tested positive. > **Anti–SARS-CoV-2-specific IgG antibodies** increased at week 4 (20.5 U/mL; P = .004), when 91.7% of samples tested positive, increasing to 97% at weeks 5 and 6. > No mother or infant experienced any serious adverse event during the study period. Mild vaccine-related adverse effects were observed in vaccinees, and fever with upper respiratory tract symptoms were observed in 4 enfants. SARS-CoV-2 specific IgA and IgG antibodies in breast milk after vaccination were found. These showed strong neutralizing effects, suggesting infant protection.

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Lancet Public Health 12APR2021	**Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study**	Graham M.S., *et al.* UK [gotopaper](#)	Public Health / Epidemiology - Variants	Aim to investigate whether increases in the proportion of infections with this variant are associated with differences in symptoms or disease course, reinfection rates, or transmissibility. **Methods** > Data on types and duration of symptoms were obtained from longitudinal reports from users of the COVID Symptom Study app who reported a positive test for COVID-19 > We assessed the Spearman correlation between the proportion of B.1.1.7 cases and number of reinfections over time, and between the number of positive tests and reinfections. **Findings** > From Sept 28 to Dec 27, 2020, positive COVID-19 tests were reported by 36920 COVID Symptom Study app users whose region was known and who reported as healthy on app sign-up. We found no changes in reported symptoms or disease duration associated with B.1.1.7. > For the same period, possible reinfections were identified in 249 (0·7% [95% CI 0·6–0·8]) of 36509 app users who reported a positive swab test before Oct 1, 2020, but there was no evidence that the frequency of reinfections was higher for the B.1.1.7 variant than for pre-existing variants. einfection occurrences were more positively correlated with the overall regional rise in cases (Spearman correlation 0·56–0·69 for South East, London, and East of England) than with the regional increase in the proportion of infections with the B.1.1.7 variant (Spearman correlation 0·38–0·56 in the same regions), suggesting B.1.1.7 does not substantially alter the risk of reinfection. > We found a multiplicative increase in the Rt of B.1.1.7 by a factor of 1·35 (95% CI 1·02–1·69) relative to pre-existing variants. However, Rt fell below 1 during regional and national lockdowns, even in regions with high proportions of infections with the B.1.1.7 variant. **The lack of change in symptoms identified in this study indicates that existing testing and surveillance infrastructure do not need to change specifically for the B.1.1.7 variant. In addition, given that there was no apparent increase in the reinfection rate, vaccines are likely to remain effective against the B.1.1.7 variant.**
Lancet Infect Dis. 12APR2021	**Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study**	Frampton D., et al. UK [gotopaper](#)	Public Health / Epidemiology - Variants	Describe the emergence of the B.1.1.7 variant of concern (VOC), including virological characteristics and clinical severity in contemporaneous patients with and without the variant. **Methods** > In this cohort study, samples positive for SARS-CoV-2 on PCR that were collected from Nov 9, 2020, for patients acutely admitted to one of two hospitals on or before Dec 20, 2020, in London, UK > Poisson regression models to investigate the association between B.1.1.7 infection and severe disease **Findings** > Of 496 patients with samples positive for SARS-CoV-2 on PCR and who met inclusion criteria, 341 had samples that could be sequenced. 198 (58%) of 341 had B.1.1.7 infection and 143 (42%) had non-B.1.1.7 infection. > No evidence of an association between severe disease and death and lineage (B.1.1.7 vs non-B.1.1.7) in unadjusted analyses (prevalence ratio [PR] 0·97 [95% CI 0·72–1·31]), or in analyses adjusted for hospital, sex, age, comorbidities, and ethnicity (adjusted PR 1·02 [0·76–1·38]). > We detected no B.1.1.7 VOC-defining mutations in 123 chronically shedding immunocompromised patients or in 32 remdesivir-treated patients. > Viral load by proxy was higher in B.1.1.7 samples than in non-B.1.1.7 samples, as measured by cycle threshold value (mean 28·8 [SD 4·7] vs 32·0 [4·8]; p=0·0085) and genomic read depth (1280 [1004] vs 831 [682]; p=0·0011). Emerging evidence exists of increased transmissibility of B.1.1.7, and we found increased virus load by proxy for B.1.1.7 in our data. We did not identify an association of the variant with severe disease.

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Nature Commun. 09APR2021	**Seroprevalence and correlates of SARS-CoV-2 neutralizing antibodies from a population-based study in Bonn, Germany**	Aziz N.A., *et al*. Germany gotopaper	Immunology	**Aim**: to estimate the seroprevalence and temporal course of SARS-CoV-2 neutralizing antibodies. Anti-SARS-CoV-2 IgG levels were assessed by immunoassay, followed by confirmatory testing of borderline and positive test results with a recombinant spike-based immunofluorescence assay and a plaque reduction neutralization test (PRNT). Borderline or positive individuals were retested after 4-5 months. > At baseline, 4771 persons participated (April 24th - June 30th, 2020). > **Seroprevalence** was 0.97% (95% CI: 0.72–1.30) by immunoassay and 0.36% (95% CI: 0.21–0.61) when considering only those with two additional positive confirmatory tests. > Antibody response magnitude, total number of symptoms experienced, and presence of particular symptoms were **associated with the presence of neutralizing antibodies** in those with a positive immunoassay test result. > In those with a **borderline immunoassay result, the presence of neutralizing antibodies was extremely rare** and apparently transient. > About **20% of PRNT+ individuals lost their neutralizing antibodies within 5 months**. Neutralizing antibodies are detectable in only one third of those with a positive immunoassay result, and **wane relatively quickly**. > The probability of neutralizing antibody loss was inversely related to the magnitude of the IgG response. > Self-referral bias can lead to substantial overestimation of seroprevalence.
Lancet 09APR2021	**SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN)**	Hall V.J., *et al*. UK gotopaper	Public Health / Epidemiology	Investigate whether antibodies against SARS-CoV-2 were associated with a decreased risk of symptomatic and asymptomatic reinfection. **Methods** > The primary outcome was a reinfection in the positive cohort or a primary infection in the negative cohort, determined by PCR tests. > A proportional hazards frailty model using a Poisson distribution was used to estimate incidence rate ratios (IRR) to compare infection rates in the two cohorts. **Findings** > From June 18, 2020, to Dec 31, 2020, 30625 participants were enrolled into the study. 51 participants withdrew from the study, 4913 were excluded, and 25661 participants (with linked data on antibody and PCR testing) were included in the analysis. Data were extracted from all sources on Feb 5, 2021, and include data up to and including Jan 11, 2021. > 155 infections were detected in the baseline positive cohort of 8278 participants, collectively contributing 2 047 113 person-days of follow-up. This compares with 1704 new PCR positive infections in the negative cohort of 17383 participants, contributing 2971436 person-days of follow-up. > The incidence density was 7·6 reinfections per 100000 person-days in the positive cohort, compared with 57·3 primary infections per 100000 person-days in the negative cohort, between June, 2020, and January, 2021. > The adjusted IRR was 0·159 for all reinfections (95% CI 0·13–0·19) compared with PCR-confirmed primary infections. The median interval between primary infection and reinfection was more than 200 days. **A previous history of SARS-CoV-2 infection was associated with an 84% lower risk of infection, with median protective effect observed 7 months following primary infection. This time period is the minimum probable effect because seroconversions were not included. This study shows that previous infection with SARS-CoV-2 induces effective immunity to future infections in most individuals.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 09APR21	**Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination**	Schultz, N., *et al.* Norway [gotopaper]	Vaccines	**Case report:** findings in five patients who presented with venous thrombosis and thrombocytopenia 7 to 10 days after receiving the first doseof theAZ vaccine against Covid-19. **Findings:** > Health care worker, 32 to 54 years of age. > All five patients were negative for antibodies to SARS-CoV-2 nucleocapsid protein. > All five patients had high levels of antibodies to platelet factor 4–polyanion complexes; > No previous exposure to heparin. > Platelets in serum from Patients 1, 3, 4, and 5 were clearly activated in the absence of added heparin > Four of the patients had severe cerebral venous thrombosis with intracranial hemorrhage, and the outcome was fatal in three. **Conclusions:** Findings indicate a shared pathophysiological basis of the condition in these five patients and should raise awareness that a syndrome similar to autoimmune heparin-induced thrombocytopenia may occur in some persons after vaccination with AZ vaccine (Five cases in a population of more than 130,000 vaccinated persons)
NEJM 09APR21	**Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination**	Greinacher, A., *et al.* International [gotopaper]	Vaccines	**Aim** Assesement of clinical and laboratory features of 11 patients in Germany and Austria developping thrombosis or thrombocytopenia after AZ vaccination. **Methods** ELISA detection of platelet factor 4 (PF4)–heparin antibodies and a modified (PF4-enhanced) platelet-activation test to detect platelet-activating antibodies under various reaction conditions Included in this testing were samples from patients who had blood samples referred for investigation of vaccine-associated thrombotic events, with 28 testing positive on a screening PF4–heparin immunoassay. **Findings** > 11 patiens, including 9 women. Median age: 36 years (22 to 49). > Patients presented with one or more thrombotic events beginning 5 to 16 days after vaccination. 9 had cerebral venous thrombosis, 3 had splanchnic-vein thrombosis, 3 had pulmonary embolism, and 4 had other thromboses; of these patients, 6 died. 5 patients had disseminated intravascular coagulation. > One patient presented with fatal intracranial hemorrhage. > None of the patients had received heparin before symptom onset. > All 28 patients who tested positive for antibodies against PF4–heparin tested positive on the platelet-activation assay in the presence of PF4 independent of heparin. Platelet activation was inhibited by high levels of heparin, Fc receptor–blocking monoclonal antibody, and immune globulin (10 mg per milliliter). Additional studies with PF4 or PF4–heparin affinity purified antibodies in 2 patients confirmed PF4-dependent platelet activation. **Conclusions** Vaccination with ChAdOx1 nCov-19 can result in the rare development of immune thrombotic thrombocytopenia mediated by platelet-activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia.

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Lancet Respir Med. 09APR21	**Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial**	Ramakrishnan S., *et al.* UK gotopaper	Therapeutics	**Aim :** to evaluate the efficacy of the widely used inhaled glucocorticoid budesonide in individuals with early COVID-19 in the community. **Methods:** open-label, parallel-group, phase 2, randomised controlled trial (Steroids in COVID-19; STOIC) of inhaled budesonide, compared with usual care, in adults within 7 days of the onset of mild COVID-19 symptoms. -Primary endpoint : COVID-19-related urgent care visit, including emergency department assessment or hospitalisation. -Secondary outcomes : self-reported clinical recovery (symptom resolution). **Findings:** > For the per-protocol population (n=139), the primary outcome occurred in ten (14%) of 70 participants in the budesonide group and one (1%) of 69 participant in the usual care group. > For the Intention-to-treat population, the primary outcome occurred in 11 (15%) participants in the usual care group and two (3%) participants in the budesonide group. > Clinical recovery was 1 day shorter in the budesonide group compared with the usual care group (median 7 days in the budesonide group vs 8 days in the usual care group) > The mean total score change in the CCQ and FLUPro over 14 days was significantly better in the budesonide group compared with the usual care group > Budesonide was safe, with only five (7%) participants reporting self-limiting adverse events. **Early administration of inhaled budesonide reduced the likelihood of needing urgent medical care and reduced time to recovery after early COVID-19.**
JAMA 07APR21	**Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers**	Havervall S., *et al.* Sweden gotopaper	Public Health / Epidemiology	**Aim**: to investigated COVID-19–related long-term symptoms in health care professionals **Methods**: The COMMUNITY (COVID-19 Biomarker and Immunity) study investigates long-term immunity after mild COVID-195. Between April 15, 2020, and May 8, 2020, health care professionals at Danderyd Hospital, Stockholm, Sweden, were invited to participate **Findings:** >Seropositive participants who reported no or mild prior symptoms had a median age of 43 years and 83% were women >Comparing seropositive vs seronegative participants, 26% vs 9% reported at least 1 moderate to severe symptom lasting for at least 2 months (RR, 2.9) and 15% vs 3% reported at least 1 moderate to severe symptom lasting for at least 8 months (RR, 4.4). >The most common moderate to severe symptoms lasting for at least 2 months in the seropositive group were anosmia, fatigue, ageusia, and dyspnea. > Of the seropositive participants, 8% reported that their long-term symptoms moderately to markedly disrupted their work life, compared with 4% of the seronegative participants (RR, 1.8). >15% reported their long-term symptoms moderately to markedly disrupted their social life, compared with 6% of the seronegative participants (RR, 2.5). >12% reported that their long-term symptoms moderately to markedly disrupted their home life, compared with 5% of the seronegative participants (RR, 2.3) **A considerable portion of low-risk individuals with mild COVID-19 reported a diversity of long-term symptoms, and these symptoms disrupted work, social, and home life.**

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NEJM 08APR21	**Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine**	Krammer F., *et al*. USA [gotopaper](#)	Vaccines	Immune response to one dose of BNT162b2 or mRNA-1273 in persons with previous Covid-19. **Methods:** 110 PARIS study participants with or without documented preexisting SARS-CoV-2 immunity. 67 seronegative participants and 43 seropositive participants receiving received their first spike mRNA vaccine dose in 2020 **Findings:** > The majority of seronegative participants had variable and relatively low SARS-CoV-2 IgG responses within 9 to 12 days after vaccination. In contrast, participants with SARS-CoV-2 antibodies at baseline before the first vaccine injection rapidly developed uniform, high antibody titers within days after vaccination > The antibody titers of vaccinees with preexisting immunity were 10 to 45 times as high as those of vaccinees without preexisting immunity > No increase in antibody titers was observed in the Covid-19 survivors who received the second vaccine dose (3-fold in non infected participants). > No substantial difference was noted in the dynamics of antibody responses elicited by the Pfizer and Moderna vaccines after the first dose. **>** Vaccine recipients with preexisting immunity had systemic side effects at higher frequencies than those without preexisting immunity (fatigue, headache, chills, muscle pain, fever, and joint pain, in order of decreasing frequency). **Conclusion:** A single dose of mRNA vaccine elicited rapid immune responses in seropositive participants, with postvaccination antibody titers that were similar to or exceeded titers found in seronegative participants who received two vaccinations. Whether a single dose of mRNA vaccine provides effective protection in seropositive persons requires investigation.
NEJM 07APR21	**Neutralizing Response against Variants after SARS-CoV-2 Infection and One Dose of BNT162b2**	Lustig Y., *et al*. Israel [gotopaper](#)	Vaccines - Variants	**Aim**: to investigate whether one dose of the BNT162b2 vaccine would increase neutralizing activity against the B.1.1.7, B.1.351, and P.1 variants in persons previously infected with SARS-CoV-2. **Methods**: microneutralization assay with isolates of the original virus (sublineage B.1) and the B.1.1.7, B.1.351, and P.1 variants on 6 HCW previously infected with the original variant of SARS-CoV-2 and vaccinated (3 time points: 1-12 weeks after natural infection, immediately before vaccination, and 1-2 weeks after vaccination). **Findings:** > Time point 1: Samples obtained had neutralizing activity against the original virus and the B.1.1.7 and P.1 variants, with geometric mean titers (GMT) of 456, 256, and 71, respectively, but had little or no neutralizing activity against the B.1.351 variant (GMT 8). > Time point 2: GMT were 81, 40, 36, and 7 for the original virus and the B.1.1.7, P.1, and B.1.351 variants, respectively. > Time point 3: GMT were 9195, 8192, 2896, and 1625 for the original virus and the B.1.1.7, P.1, and B.1.351 variants, respectively — that is, the titers after vaccination were 114, 203, 81, and 228 times as high as the titers immediately before vaccination. **This study showed that one vaccine dose substantially increased neutralizing activity against all variants tested, highlighting the importance of vaccination even in previously infected patients.**

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NEJM 07APR2021	**Cross-Reactive Neutralizing Antibody Responses Elicited by SARS-CoV-2 501Y.V2 (B.1.351)**	Moyo-Gwete T., *et al.* South Africa [gotopaper]	Vaccines - Variants	**Aim**: Assessment of the immune response to 501Y.V2 (B.1.351) and its cross-reactivity with other variants. Samples were collected when 501Y.V2 prevalence was 90% in Cape Town. **Findings:** > 501Y.V2 elicited high-titer binding and neutralizing antibody responses. > Titers of binding antibodies to RBD and the full spike protein of the original variant were highly correlated with titers of binding antibodies to the corresponding proteins of 501Y.V2. > Plasma samples (46) had higher titers to the spike protein of 501Y.V2 than to the spike protein of the original variant (mean of 1.7 times as high), but high-level binding to the original variant remained. > 53 of 57 tested samples maintained neutralization activity against the original variant, with a geometric mean titer of 203 (95% CI, 141-292), approximately one third of the titer against the 501Y.V2 variant. When limiting the analysis to 22 sequencing-confirmed infection with 501Y.V2 with positive titers of binding antibodies, the same pattern was observed. > Testing a subset of 10 plasma samples against the 501Y.V3 (P.1) variant revealed high levels of neutralization, with some samples showing higher potency against 501Y.V3 (P.1) than against 501Y.V2, possibly due to the very different N-terminal domains. **501Y.V2 elicits robust neutralizing antibody responses against both the original variant and 501Y.V3 (P.1), indicating high levels of cross-reactivity.**
NEJM 07APR2021	**Neutralization of SARS-CoV-2 Variants B.1.429 and B.1.351**	Shen X., *et al.* USA [gotopaper]	Vaccines - Variants	**Aim**: to measure the neutralizing activity against SARS-CoV-2 variant B.1.429 (California) and B.1.351 (South Africa) of serum specimens obtained from 14 convalescent persons and from 49 recipients of mRNA-1273 (26) or protein nanoparticle vaccine NVX-CoV2373 (23). **Findings** > As compared with the D614G variant, **B.1.429** was approximately **2 to 3 times less sensitive to neutralization** by convalescent serum and by serum samples obtained from vaccinated persons > **B.1.351** was approximately **9 to 14 times less sensitive to neutralization**. > Neutralisation assays with pseudoviruses: - B.1.429 was neutralized by convalescent serum and by vaccinee serum. The geometric mean ID50 titers against B.1.429 were **3.1 times (1.4-8.8) lower** than those against D614G for convalescent serum and were **2.0 and 2.5 times (0.7-8.6) lower** than against D614G for serum from persons who had received the mRNA-1273 and NVX-CoV2373 vaccines, respectively. - The geometric mean ID50 titer against B.1.351 was **13.1 times lower** than against D614G for convalescent serum and **9.7 times and 14.5 times lower** than against D614G for serum from persons who had received the mRNA-1273 and NVX-CoV2373 vaccines, respectively. **These results suggest that vaccine-elicited neutralizing antibodies are likely to remain effective against the B.1.429 variant. The magnitude of resistance seen with the B.1.351 variant is of greater concern with respect to current vaccines.**

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NEJM 06APR21	**Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19**	Doria-Rose N., *et al*. USA [gotopaper](#)	Vaccines	The durability of protection of mRNA-1273 vaccine from Moderna currently unknown. **Findings:** > mRNA1273-elicited binding and neutralizing antibodies in 33 healthy adult participants 180 days after the second dose of 100 μg (day 209). > S protein binding antibodies had geometric mean end-point titers of 92,451 (95% [CI], 57,148 to 149,562) in participants 18 to 55 years of age, 62,424 (95% CI, 36,765 to 105,990) in those 56 to 70 years of age, and 49,373 (95% CI, 25,171 to 96,849) in those 71 years of age or older. > All the participants had detectable neutralization activity, with ID50 GMTs of 406 (95% CI, 286 to 578), 171 (95% CI, 95 to 307), and 131 (95% CI, 69 to 251) depending on age. > The estimated half-life of binding antibodies after day 43 for all the participants ranged between 52 and 109 days depending on the method use for assessment. The neutralizing antibody half-life estimates was between 68 and 202 days > Antibodies that were elicited by mRNA-1273 persisted through 6 months after the second dose, as detected by three distinct serologic assays. Ongoing studies are monitoring immune responses beyond 6 months as well as determining the effect of a booster dose to extend the duration and breadth of activity against emerging viral variants. **Conclusion:** Our data show antibody persistence and thus support the use of this vaccine in addressing the Covid-19 pandemic.
Blood 06APR2021	**Post-Discharge Thromboembolic Outcomes and Mortality of Hospitalized COVID-19 Patients: The CORE-19 Registry**	Giannis D., *et al*. USA [gotopaper](#)	Public Health / Epidemiology	Thromboembolic events including venous thromboembolism (VTE), arterial thromboembolism (ATE), and mortality from sub-clinical thrombotic events occur frequently in COVID-19 inpatients. **Methods:** Prospective registry included consecutive COVID-19 patients hospitalized within our multi hospital system from March 1st - May 31st 2020 Primary outcome = a composite of adjudicated VTE, ATE, and all-cause mortality (ACM) Principal safety outcome = major bleeding (MB) **Findings:** > Among 4,906 patients (53.7% male) mean age was 61.7 years. Comorbidities included hypertension (38.6%), diabetes (25.1%),obesity (18.9%), and cancer history (13.1%) > Post-discharge thromboprophylaxis was prescribed in 13.2%.VTE rate was 1.55%, ATE 1.71%, ACM 4.83%, and MB 1.73%. > The composite primary outcome rate was 7.13% and was significantly associated with advanced age (OR: 3.66, 95%CI: 2.84-4.71), prior VTE (OR: 2.99, 95%CI:2.00-4.47), ICU stay (OR: 2.22, 95%CI: 1.78-2.93), chronic kidney disease (CKD) (OR: 2.10, 95%CI: 1.47-3.0), peripheral arterial disease (OR: 2.04, 95%CI: 1.10-3.80), carotid occlusive disease (OR: 2.02,95%CI: 1.30-3.14), IMPROVE-DD VTE score ≥4 (OR: 1.51, 95%CI: 1.06-2.14), and coronary artery disease(OR: 1.50, 95%CI: 1.04-2.17). > Post-discharge anticoagulation was significantly associated with reducing the primary outcome (OR: 0.54, 95%CI: 0.47-0.81). **Conclusions:** **Post-discharge VTE, ATE, and ACM occur frequently following COVID-19 hospitalization. Advanced age, cardiovascular risk factors, CKD, IMPROVE–DD VTE score ≥4, and ICU stay increase risk. Post-discharge anticoagulation reduced risk by 46%.**

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Lancet Psychiatry 06APR2021	**6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records**	Taquet M., *et al*. UK gotopaper	Public Health / Epidemiology	**Aim**: to provide robust estimates of incidence rates and relative risks of neurological and psychiatric diagnoses in patients in the 6 months following a COVID-19 diagnosis. > Among 236 379 patients diagnosed with COVID-19, the estimated **incidence of a neurological or psychiatric diagnosis in the following 6 months** was 33·62% (95% CI 33·17–34·07), with 12·84% (12·36–13·33) receiving their first such diagnosis. > For patients who had been admitted to an **intensive therapy unit (ITU)**, the estimated incidence of a diagnosis was 46·42% (44·78–48·09) and for a first diagnosis was 25·79% (23·50–28·25). > The whole COVID-19 cohort had estimated incidences of 0·56% (0·50–0·63) for intracranial haemorrhage, 2·10% (1·97–2·23) for ischaemic stroke, 0·11% (0·08–0·14) for parkinsonism, 0·67% (0·59–0·75) for dementia, 17·39% (17·04–17·74) for anxiety disorder, and 1·40% (1·30–1·51) for psychotic disorder, among others. > In the group with ITU admission, estimated incidences were 2·66% (2·24–3·16) for intracranial haemorrhage, 6·92% (6·17–7·76) for ischaemic stroke, 0·26% (0·15–0·45) for parkinsonism, 1·74% (1·31–2·30) for dementia, 19·15% (17·90–20·48) for anxiety disorder, and 2·77% (2·31–3·33) for psychotic disorder. > **Most diagnostic categories were more common in patients who had COVID-19** than in those who had influenza (hazard ratio [HR] 1·44, 95% CI 1·40–1·47, for any diagnosis; 1·78, 1·68–1·89, for any first diagnosis) and those who had other respiratory tract infections (1·16, 1·14–1·17, for any diagnosis; 1·32, 1·27–1·36, for any first diagnosis). > **HRs were higher** in patients who had more severe COVID-19 (eg, those admitted to ITU compared with those who were not: 1·58, 1·50–1·67, for any diagnosis; 2·87, 2·45–3·35, for any first diagnosis). **Substantial neurological and psychiatric morbidity were observed in the 6 months after COVID-19 infection. Risks were greatest in, but not limited to, patients who had severe COVID-19.**
JAMA Netw Open 01APR2021	**Mortality and Readmission Rates Among Patients With COVID-19 After Discharge From Acute Care Setting With Supplemental Oxygen**	Banerjee J., *et al*. USA gotopaper	Clinics	**Aim**: to assess outcomes of patients with COVID-19 pneumonia discharged via the expected practice approach to home or quarantine housing with supplemental home oxygen. **Methods:** retrospective cohort study of 621 patients with COVID-19 discharged with supplemental home oxygen (at least 3 L per minute of oxygen) from emergency department and inpatient encounters at 2 large urban medical centers. Main Outcomes and Measures : All-cause mortality and all-cause 30-day return admission. **Findings:** > A total of 621 patients with COVID-19 pneumonia (404 male [65.1%] and 217 female [34.9%]) were discharged with home oxygen. > Median age of these patients was 51 years (interquartile range, 45-61 years), with 149 (24.0%) discharged from the emergency department and 472 (76%) discharged from inpatient encounters. > The all-cause mortality rate was 1.3% (95% CI, 0.6%-2.5%) and the 30-day return hospital admission rate was 8.5% (95% CI, 6.2%-10.7%) with a median follow-up time of 26 days (interquartile range, 15-55 days). > **No deaths occurred in the ambulatory setting.** **Ambulatory management of COVID-19 with home oxygen has an acceptable safety profile, and the expected practice approach may help optimize outcomes.**

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Nature Med. 01APR2021	**Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2**	Ebinger J.E., *et al.* USA gotopaper	Vaccines	**Background:** Detectable presence of anti-SARS-CoV-2 antibodies and virus-specific T cells suggest possible alternate vaccination strategies for previously infected individuals. As thus, individuals with prior infection might have naturally acquired immunity that could be sufficiently enhanced by a single dose rather than a double dose of administered vaccine **Methods:** Cohort of BNT162b2 (Pfizer–BioNTech) mRNA vaccine recipients (n= 1,090). Antibody levels were measured at three time points: before or up to 3 d after dose 1; within 7–21 d after dose 1; and within 7–21 d after dose 2 **Findings:** > For both IgG(N) (representing response to prior infection) and IgG(S-RBD) (representing response to either prior infection or vaccine), individuals with prior SARS-CoV-2 infection had higher antibody levels at all time points > IgG(S-RBD) levels were not significantly different among previously infected individuals after a single dose and infection-naive individuals who had received two doses > ACE2 binding inhibition was significantly higher among previously infected individuals than infection-naive individuals after a single vaccine dose, with no between-group difference seen after the second dose > Post-vaccine symptoms were more prominent for those with prior infection after the first dose, but symptomology was similar between groups after the second dose **Conclusions:** Individuals previously infected with SARS-CoV-2 developed vaccine-induced antibody responses after a single dose of the BNT162b2 mRNA vaccine similar to those seen after a two-dose vaccination in infection-naive individuals.
Am J Obstet Gynecol 25MAR2021	**COVID-19 vaccine response in pregnant and lactating women: a cohort study**	Gray K.J., *et al.* USA gotopaper	Vaccines	**Aim**: to evaluate the immunogenicity and reactogenicity of COVID-19 mRNA vaccination in pregnant and lactating women compared to: (1) non-pregnant controls and (2) natural COVID-19 infection in pregnancy. > 131 reproductive-age vaccine recipients (84 pregnant, 31 lactating, and 16 non-pregnant) **Findings** > Vaccine-induced **antibody titers were equivalent in pregnant and lactating compared to non-pregnant women** (median [IQR] 5.59 [4.68-5.89] pregnant, 5.74 [5.06-6.22] lactating, 5.62 [4.77-5.98] non-pregnant, p = 0.24). > All titers were significantly **higher than those induced by SARS-CoV-2 infection** during pregnancy (p < 0.0001). > Vaccine-generated antibodies were present **in all umbilical cord blood and breastmilk samples**. > Neutralizing antibody titers were lower in umbilical cord compared to maternal sera, but it was not achieve statistically significant (median [IQR] 104.7 [61.2-188.2] maternal sera, 52.3 [11.7-69.6] cord sera, p=0.05). > The second vaccine dose (boost dose) increased SARS-CoV-2-specific IgG, but not IgA, in maternal blood and breastmilk. > No differences were noted in reactogenicity across the groups. **COVID-19 mRNA vaccines generated robust humoral immunity in pregnant and lactating women, significantly greater than the response to natural infection. Immune transfer to neonates occurred via placenta and breastmilk.**

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BMJ 31MAR2021	**Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study**	Ayoubkhani D., *et al*. UK gotopaper	Public Health / Epidemiology - Long Covid	**Aim**: to quantify rates of organ specific dysfunction in a cohort of 47 780 individuals with covid-19 after discharge from hospital compared with a matched control group from the general population. > Over a mean follow-up of 140 days, **nearly a third of individuals who were discharged from hospital after acute covid-19 were readmitted (14 060 of 47 780) and more than 1 in 10 (5875) died after discharge**, with these events occurring at rates 4 and 8 times greater, respectively, than in the matched control group. > Rates of respiratory disease (P<0.001), diabetes (P<0.001), and cardiovascular disease (P<0.001) were also **significantly raised in patients with covid-19**, with 770 (95% CI 758-783), 127 (122-132), and 126 (121-131) diagnoses per 1000 person years, respectively. > **Rate ratios were greater for individuals aged <70** than for those aged ≥70, **and in ethnic minority groups** compared with the white population. Largest differences was seen for respiratory disease (10.5 (95% CI 9.7-11.4) for age < 70 years v 4.6 (4.3 to 4.8) for age ≥70, and 11.4 (9.8-13.3) for non-white v 5.2 (5.0-5.5) for white individuals). Individuals discharged from hospital after covid-19 had increased rates of multiorgan dysfunction compared with the expected risk in the general population. The increase in risk was not confined to the elderly and was not uniform across ethnicities.
Lancet 30MAR2021	**Efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine against SARS-CoV-2 variant of concern 202012/01 (B.1.1.7): an exploratory analysis of a randomised controlled trial**	Emary K.R.W., *et al*. UK gotopaper	Vaccines	**Background:** A new variant of SARS-CoV-2, B.1.1.7, emerged as the dominant cause of COVID-19 disease in the UK from November, 2020. We report a post-hoc analysis of the efficacy of the adenoviral vector vaccine, ChAdOx1 nCoV-19 (AZD1222), against this variant. **Methods:** > Volunteers (aged ≥18 years), enrolled during the phase 2/3 vaccine efficacy studies in the UK receiving randomly ChAdOx1 nCoV-19 or a meningococcal conjugate control (MenACWY) vaccine > Upper airway swabs on a weekly basis and recording of COVID-19 disease symptoms if any > Swabs were tested by nucleic acid amplification test (NAAT) for SARS-CoV-2 and positive samples were sequenced > Assessment of neutralising antibody responses against the B.1.1.7 lineage and a canonical non-B.1.1.7 lineage (Victoria). **Findings:** > 8534 participants, 6636 (78%) aged 18–55 years and 5065 (59%) female. > 520 participants developed SARS-CoV-2 infection. > 1466 NAAT positive nose and throat swabs were collected from these participants during the trial. > Of these, 401 swabs from 311 participants were successfully sequenced. > Laboratory virus neutralisation activity by vaccine-induced antibodies was lower against the B.1.1.7 variant than against the Victoria lineage (geometric mean ratio 8·9, 95% CI 7·2–11·0). > Clinical vaccine efficacy against symptomatic NAAT positive infection was 70·4% (95% CI 43·6–84·5) for B.1.1.7 and 81·5% (67·9–89·4) for non-B.1.1.7 lineages. **Conclusion:** ChAdOx1 nCoV-19 showed reduced neutralisation activity against the B.1.1.7 variant compared with a non-B.1.1.7 variant in vitro, but the vaccine showed efficacy against the B.1.1.7 variant of SARS-CoV-2.

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Cell 30MAR2021	**Antibody evasion by the P.1 strain of SARS-CoV-2**	Dejnirattisai W. *et al.* UK [gotopaper](#)	Virology	Examiniation of an isolate of P.1 variant cultured from a throat swab taken from an infected patient in Manaus, Brazil in December 2020 and comparision of its interactions with serum and antibodies with those of three other viruses, an early isolate, B.1.1.7 and B.1.351. **Findings:** Assesement of the ability of immune sera induced by infection with early strains of SARS-CoV-2 , or by vaccination with the Oxford-AstraZenca or Pfizer-BioNTech vaccines to neutralize P.1. > Reduction in the neutralizing capacity of immune serum to P.1 similar to the reduction seen with B.1.1.7, but not as severeas that seen with B.1.351 > Increased affinity of P.1 137 RBD for ACE2 > investigation of the structural basis of this through crystallography. > Neutralization by a panel of potent monoclonal antibodies which block RBD/ACE2interaction: mAb 222, which contacts both K417 and N501, is resistant to the 141 501Y and 417T/N mutations found in the P.1/B1.351 strains. > dissection of the basis for this via a series of high resolution structures of RDB-Fab complexes and based on this restoreneutralization of certain antibodies by swapping the light chain. **Conslusion:** P1 can escape neutralization by a number of monoclonal antibodies including some being developed for prophylactic or therapeutic use, while other antibodies with epitopes away from the mutated RBD residues retain broad neutralization.
Nature Commun. 30MAR2021	**Peginterferon Lambda-1a for treatment of outpatients with uncomplicated COVID-19: a randomized placebo-controlled trial**	Jagannathan P., *et al.* USA [gotopaper](#)	Therapeutics	**Aim:** to determine whether a single, 180 mcg subcutaneous dose of Peginterferon Lambda-1a (Lambda) within 72 hours of diagnosis could shorten the duration of viral shedding (primary endpoint) or symptoms (secondary endpoint) **Methods:** randomized, single-blind, placebo-controlled trial in 120 outpatients with mild to moderate COVID-19, of whom 110 (91.7%) completed 28 days of follow up. Participants were recruited within 72 h of diagnosis. **Findings:** > 60 patients receiving Lambda and 60 receiving placebo, the median time to cessation of viral shedding was 7 days (hazard ratio [HR] = 0.81; 95% confidence interval [CI] 0.56 to 1.19). > Symptoms resolved in 8 and 9 days in Lambda and placebo, respectively, and symptom duration did not differ significantly between groups (HR 0.94; 95% CI 0.64 to 1.39). > Both Lambda and placebo were well-tolerated, though liver transaminase elevations were more common in the Lambda vs. placebo arm (15/60 vs 5/60; p = 0.027). **A single dose of subcutaneous Peginterferon Lambda-1a neither shortened the duration of SARS-CoV-2 viral shedding nor improved symptoms in outpatients with uncomplicated COVID-19.**
Nature Med. 29MAR2021	**Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine**	Levine-Tiefenbrun M., *et al.* Israel [gotopaper](#)	Vaccines	Analysis of a real-world dataset of positive SARS-CoV-2 test results after inoculation with the BNT162b2 messenger RNA vaccine (Dec 21, 2020 – Feb 11, 2021). > The **viral load was substantially reduced for infections occurring 12–37 days after the first dose of vaccine**, as compared to 0-11 days. > In unvaccinated patients, viral load was comparable to that observed in vaccinated patients 0-11 days after first injection, but significantly higher than that observed at 12-37 days. > The differences of RT-PCR Ct values in post-vaccination and matched unvaccinated patients represent a decrease of 2.8–4.5-fold in viral load in vaccinated individuals, according to a regression model. **These reduced viral loads hint at a potentially lower infectiousness, further contributing to vaccine effect on virus spread.**

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Nature 29MAR2021	**Escape of SARS-CoV-2 501Y.V2 from neutralization by convalescent plasma**	Cele S., *et al.* International gotopaper	Therapeutics - Variants	Live virus neutralization assay to compare neutralization of a non-VOC variant versus the 501Y.V2 variant using plasma collected from adults hospitalized with COVID-19 from two South African infection waves, with the second wave dominated by 501Y.V2 infections. **Findings:** > Sequencing demonstrated that infections in first wave plasma donors were with viruses harbouring none of the 501Y.V2-defining mutations, except for one with the E484K mutation in the receptor binding domain. > 501Y.V2 virus was effectively neutralized by plasma from second wave infections and first wave virus was effectively neutralized by first wave plasma. > In cross-neutralization, 501Y.V2 virus was poorly neutralized by first wave plasma, with a 15.1-fold drop relative to 501Y.V2 neutralization by second wave plasma across participants. > Second wave plasma cross-neutralization of first wave virus was more effective, showing only a 2.3-fold decline relative to first wave plasma neutralization of first wave virus. **Conclusion:** Effective neutralization of first wave virus by 501Y.V2 infection elicited plasma provides preliminary evidence that vaccines based on VOC sequences could retain activity against other circulating SARS-CoV-2 lineages.
Nature Commun. 29MAR2021	**A haemagglutination test for rapid detection of antibodies to SARS-CoV-2**	Townsend A., *et al.* USA gotopaper	Diagnostics	**Aim:** to describe a quantitative Haemagglutination test (HAT) for the detection of antibodies to the receptor binding domain of the SARS-CoV-2 spike protein. **Methods:** simple HA test for the detection of Abs to the receptor binding domain (RBD) of the SARS-CoV-2 spike protein. In order to link the SARS-CoV-2 RBD to red cells, they selected the single domain antibody (nanobody) IH46, specific for a conserved epitope on glycophorin A, via a short (GSG)2 linker to produce the fusion protein IH4-RBD-6H. **Findings:** > HAT functions as a viable test for the presence of antibodies to the RBD of the SARS-CoV-2 spike protein in stored serum/plasma samples, using O−ve red cells as indicators >The HAT has a sensitivity of 90% and specificity of 99% for detection of antibodies after a PCR diagnosed infection.
Clin Infect Dis. 27MAR2021	**Assessing asymptomatic, pre-symptomatic and symptomatic transmission risk of SARS-CoV-2**	Wu P., *et al.* China gotopaper	Public Health / Epidemiology	**Methods:** > Detailed information on transmission events and symptom status based on laboratory-confirmed patient data and contact tracing data from four provinces and one municipality in China > Estimated the variation in risk of transmission over time, and the severity of secondary infections, by symptomatic status of the infector. **Findings:** > 393 symptomatic index cases with 3136 close contacts and 185 asymptomatic index cases with 1078 close contacts included into the study > The secondary attack rate among close contacts of symptomatic and asymptomatic index cases were 4.1% (128/3136) and 1.1% (12/1078), respectively, corresponding to a highertransmission risk from symptomatic cases than from asymptomatic cases (OR: 3.79, 95% CI: 2.06, 6.95) > Approximately 25% (32/128) and 50% (6/12) of the infected close contacts were asymptomatic from symptomatic and asymptomatic index cases > Pre-symptomatic transmission of COVID-19 accounted for 38% of all infections occurred from exposure to symptomatic cases. > Infected contacts of asymptomatic index cases were more likely to be asymptomatic and less likely to be severe. **Asymptomatic and pre-symptomatic transmission play an important role in spreading infection, although asymptomatic cases pose a lower risk of transmission than symptomatic cases. Early case detection and effective test-and-trace measures are important to reduce transmission.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Commun. 26MAR2021	**N-protein presents early in blood, dried blood and saliva during asymptomatic and symptomatic SARS-CoV-2 infection**	Shan D., *et al.* Germany/USA gotopaper	Diagnostics	**Aim:** to describe the development of a SARS-CoV-2 antigen test using Simoa technology to quantify N-protein in serum/plasma, dried blood microsamples (DBS), and saliva. **Methods:** SARS-CoV-2 N-protein and anti-SARS-CoV-2 spike IgG were quantified directly in serum and plasma from venous collection, capillary blood acquired by finger-stick DBS devices (DBS), and saliva **Findings:** > Compared to molecular testing, >90% PPA of SARS-CoV-2-positive patients and >98% negative percent agreement (NPA) were observed in all matrices within 7 days of positive PCR test, both for asymptomatic and symptomatic patients. > N-protein load decreases as anti-SARS-CoV-2 spike-IgG increases, and N-protein levels correlate with RT-PCR Ct-values in saliva, and between matched saliva and capillary blood samples. > N-protein levels in saliva are higher but more variable than levels in capillary blood. **The Simoa N-protein antigen test represents a robust SARS-CoV-2 detection tool, effectively detecting SARS-CoV-2 infection via antigen levels in blood or saliva, using non-invasive, swab-independent collection methods, with potential at home/point of care sampling.**
Nature Med. 26MAR2021	**Sensitivity of infectious SARS-CoV-2 B.1.1.7 and B.1.351 variants to neutralizing antibodies**	Planas D., *et al.* France gotopaper	Virology	Study on B.1.1.7 (UK) and B.1.351 (South Africa) variants. **Methods** > Examined sensitivity of the two variants to SARS-CoV-2 antibodies present in sera and nasal swabs from individuals infected with previously circulating strains or who were recently vaccinated, in comparison with a D614G reference virus > New rapid neutralization assay, based on reporter cells that become positive for GFP after overnight infection **Results** > Sera from 58 convalescent individuals collected up to 9 months after symptoms, similarly neutralized B.1.1.7 and D614G. In contrast, after 9 months, convalescent sera had a mean 6-fold reduction in neutralizing titers, and 40% of samples lacked any activity against B.1.351. > Sera from 19 individuals vaccinated twice with Pfizer Cominarty, up to 6 weeks after vaccination, were similarly potent against B.1.1.7 but less efficacious against B.1.351, when compared to D614G > Neutralizing titers increased after the second vaccine dose, but were 14-fold lower against B.1.351. Sera from convalescent or vaccinated individuals similarly bound the three spike proteins in a flow cytometry-based serological assay. **Neutralizing antibodies were rarely detected in nasal swabs from vaccinees. Faster-spreading SARS-CoV-2 variants acquired a partial resistance to neutralizing antibodies generated by natural infection or vaccination, most frequently detected in individuals with low antibody levels. Our results indicate that B1.351, but not B.1.1.7, may increase the risk of infection in immunized individuals.**
Nature 25MAR2021	**Assessing transmissibility of SARS-CoV-2 lineage B.1.1.7 in England**	Volz E., *et al.* UK gotopaper	Virology	Whole genome SARS-CoV-2 sequence data from community-based diagnostic testing shows rapid expansion of the B.1.1.7 lineage in Autumn 2020, suggesting a selective advantage. > Changes in VOC frequency inferred from genetic data correspond closely to changes inferred by S-gene target failures (SGTF) in community-based diagnostic PCR testing. > Analysis of trends in SGTF and non-SGTF case numbers in local areas across England shows that the **VOC has higher transmissibility than non-VOC lineages**, even if the VOC has a different latent period or generation time. > The SGTF data indicate a **transient shift in the age composition of reported cases**, with a larger share of under 20 year olds among reported VOC than non-VOC cases. > Time-varying reproduction numbers for the VOC and cocirculating lineages were estimated using SGTF and genomic data. The best supported models did not indicate a substantial difference in VOC transmissibility among different age groups. > **There is a consensus among all analyses that the VOC has a substantial transmission advantage with a 50% to 100% higher reproduction number**.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Infect Dis. 25MAR2021	**Performance and operational feasibility of antigen and antibody rapid diagnostic tests for COVID-19 in symptomatic and asymptomatic patients in Cameroon: a clinical, prospective, diagnostic accuracy study**	Boum Y., *et al.* Cameroon [gotopaper](#)	Diagnostics	**Aim:** to assess the performance of four antibody-based rapid diagnostic tests and one antigen-based rapid diagnostic test for detecting SARS-CoV-2 infection in the community in Cameroon. **Methods:** prospective, diagnostic accuracy study with 1195 individuals aged at least 21 years who were either symptomatic and suspected of having COVID-19 or asymptomatic and presented for screening. Peripheral blood for SARS-CoV-2 antibodies were tested using the Innovita, Wondfo, SD Biosensor, and Runkun tests , and nasopharyngeal swabs for SARS-CoV-2 antigen using the SD Biosensor test. Antigen rapid diagnostic tests were compared with Abbott PCR testing, and antibody rapid diagnostic tests were compared with Biomerieux immunoassays. Two diagnostic algorithms that incorporated rapid diagnostic tests for symptomatic and asymptomatic patients using simulation modelling were tested. **Findings:** > 347 patients (29%) tested SARS-CoV-2 PCR-positive, 223 (19%) rapid diagnostic test antigen-positive, and 478 (40%) rapid diagnostic test antibody-positive. > Antigen-based rapid diagnostic test sensitivity was 80·0% in the first 7 days after symptom onset, but Antibody-based rapid diagnostic tests had only 26·8% sensitivity. > Antibodyb rapid diagnostic test sensitivity increased to 76·4% 14 days after symptom onset. > Among asymptomatic participants, the sensitivity of antigen-based and antibody-based rapid diagnostic tests were 37·0% and 50·7%, respectively. > **An antigen-based retrospective algorithm applied to symptomatic patients showed 94·0% sensitivity and 91·0% specificity in the first 7 days after symptom onset.** > For asymptomatic participants, the algorithm showed a sensitivity of 34% and a specificity of 92·0%. **Rapid diagnostic tests had good overall sensitivity for diagnosing SARS-CoV-2 infection. Rapid diagnostic tests could be incorporated into efficient testing algorithms as an alternative to PCR to decrease diagnostic delays and onward viral transmission.**
JAMA Netw Open 24MAR2021	**Comparison of Time to Clinical Improvement With vs Without Remdesivir Treatment in Hospitalized Patients With COVID-19**	Garibaldi B.T., *et al.* USA [gotopaper](#)	Therapeutics	**Aim**: to examine whether remdesivir administered with or without corticosteroids for treatment of COVID-19 is associated with more rapid clinical improvement in a racially/ethnically diverse population. <u>Exposures</u>: No Remdesvir, Remdesivir treatment with or without corticosteroid administration. <u>Primary outcome</u>: rate of clinical improvement (hospital discharge or decrease of 2 points on the World Health Organization severity score) <u>Secondary outcome</u>: mortality at 28 days; Clinical improvement and time to death associated with combined remdesivir and corticosteroid treatment. > Of 2483 consecutive admissions, 342 individuals received remdesivir, 184 of whom also received corticosteroids. Remdesivir patients were matched with admitted patients who did not receive Remdesivir. > For these 342 patients: median age was 60 years (46-69), 55.3% were men, 80.7% self-identified as non-White race/ethnicity. > Remdesivir recipients had a **shorter time to clinical improvement** than matched controls without remdesivir treatment (median, 5.0 days [4.0-8.0] vs 7.0 days [4.0-10.0]; adjusted hazard ratio (HR), 1.47 [95% CI, 1.22-1.79]). > Remdesivir recipients had a **28-day mortality rate of 7.7% compared with 14.0%** among matched controls, but this difference was **not statistically significant in the time-to-death analysis** (adjusted HR, 0.70; 95% CI, 0.38-1.28). > The addition of **corticosteroids to remdesivir was not associated with a reduced hazard of death** at 28 days (adjusted HR, 1.94; 95% CI, 0.67-5.57). In this study of adults hospitalized with COVID-19, receipt of remdesivir was associated with faster clinical improvement. Remdesivir plus corticosteroid administration did not reduce the time to death compared with remdesivir administered alone.

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Lancet 23MAR2021	**Dynamics of SARS-CoV-2 neutralising antibody responses and duration of immunity: a longitudinal study**	Wan N.C., *et al.* Singapore gotopaper	Immunology	**Aim:** to investigate the peak levels and dynamics of neutralising antibody waning and IgG avidity maturation over time, and correlate this with clinical parameters, cytokines, and T-cell responses. **Methods:** longitudinal study of patients who had recovered from COVID-19 up to day 180 post-symptom onset by monitoring changes in neutralising antibody levels using a previously validated surrogate virus neutralisation test. **Findings:** >Five distinctive patterns of neutralising antibody dynamics were identified as follows: - Negative : individuals who did not, at our intervals of sampling, develop neutralising antibodies at the 30% inhibition level (19 [12%] of 164 patient). - Rapid waning : individuals who had varying levels of neutralising antibodies from around 20 days after symptom onset, but seroreverted in less than 180 days (44 [27%] of 164 patients). - Slow waning : Individuals who remained neutralising antibody-positive at 180 days post-symptom onset (52 [29%] of 164 patients). - Persistent: although with varying peak neutralising antibody levels, these individuals had minimal neutralising antibody decay (52 [32%] of 164 patients). - Delayed response, a small group that showed an unexpected increase of neutralising antibodies during late convalescence (at 90 or 180 days after symptom onset; three [2%] of 164 patients). >Persistence of neutralising antibodies was associated with disease severity and sustained level of pro-inflammatory cytokines, chemokines, and growth factors. By contrast, T-cell responses were similar among the different neutralising antibody dynamics groups. **Neutralising antibody response dynamics in patients who have recovered from COVID-19 vary greatly, and prediction of immune longevity can only be accurately determined at the individual level.**
JAMA Netw Open 22MAR2021	**Association of Age With SARS-CoV-2 Antibody Response**	Yang H.S., *et al.* USA gotopaper	Immunology	**Aim:** To investigate the association of age with the quantity and quality of SARS-CoV-2 antibody responses. **Methods:** Cross-sectional study evaluating 31 426 SARS-CoV-2 antibody tests from pediatric and adult patients. Data were collected from a New York City hospital from April 9 to August 31, 2020. **Findings:** > Among 31 426 antibody test results, the seroprevalence in the pediatric (197 [16.5%; 95% CI, 14.4%-18.7%]) and adult (5630 [18.6%; 95% CI, 18.2%-19.1%]) patient populations was similar. >The SARS-CoV-2 IgG level showed a negative correlation with age in the pediatric population (r = −0.45, P < .001) and a moderate but positive correlation with age in adults (r = 0.24, P < .001). >Patients aged 19 to 30 years exhibited the lowest IgG levels (eg, aged 25-30 years vs 1-10 years: 99 [44-180] relative fluorescence units [RFU] vs 443 [188-851] RFU). >Children exhibited higher median (IQR) IgG levels, TAb levels, and SNAb activity compared with adolescents (eg, IgG levels: 473 RFU vs 191 RFU; P < .001) and young adults (eg, IgG levels: 473 RFU vs 85 RFU; P < .001). > Children had higher antibody binding avidity compared with young adults, but the difference was not significant. **This study suggests that SARS-CoV-2 viral specific antibody response profiles are distinct in different age groups.** Age-targeted strategies for disease screening and management as well as vaccine development may be warranted.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Commun. 22MAR2021	**SARS-CoV-2 infection induces sustained humoral immune responses in convalescent patients following symptomatic COVID-19**	Wu J., *et al.* China [gotopaper]	Immunology	**Aim**: to quantify immunoglobulin M (IgM) and G (IgG) antibodies recognizing the SARS-CoV-2 receptor-binding domain (RBD) of the spike (S) or the nucleocapsid (N) protein, and neutralizing antibodies during a period of 6 months from disease onset in 349 symptomatic COVID-19 patients. > The positivity rate and magnitude of IgM-S and IgG-N responses increase rapidly. > High levels of **IgM-S/N and IgG-S/N at 2-3 weeks after disease onset are associated with virus control** and **IgG-S titers correlate closely with the capacity to neutralize SARS-CoV-2**. > Although specific IgM-S/N become undetectable 12 weeks after disease onset in most patients, IgG-S/N titers have an intermediate contraction phase, but **stabilize at relatively high levels over the 6 month observation period**. > At late time points, the positivity rates for binding and **neutralizing SARS-CoV-2-specific antibodies are still >70%**. These data indicate sustained humoral immunity in recovered patients who had symptomatic COVID-19, suggesting prolonged immunity.
Cell 20MAR2021	**SARS-CoV-2 variants B.1.351 and P.1 escape from neutralizing antibodies**	Hoffmann M., *et al.* Germany [gotopaper]	Viral variants	**Aim**: to test sensitivity of SARS-CoV-2 variants B.1.1.7 (UK), B.1.351 (South Africa) and P.1 (Brazil) to cell entry inhibitors and antibodies, by using pseudoparticles. > B.1.1.7, B.1.351 and P.1 do not show augmented host cell entry. > Entry of all variants into human cells is **susceptible to blockade by the entry inhibitors soluble ACE2, Camostat, EK-1 and EK-1-C4**. > Entry of the B.1.351 and P.1 variant is partially (Casirivimab) or fully (Bamlanivimab) resistant to antibodies used for COVID-19 treatment. > Entry of these variants was less efficiently inhibited by plasma from convalescent COVID-19 patients and sera from BNT162b2 vaccinated individuals. **These results suggest that SARS-CoV-2 may escape neutralizing antibody responses**.
Lancet 20MAR2021	**Seroprevalence and humoral immune durability of anti-SARS-CoV-2 antibodies in Wuhan, China: a longitudinal, population-level, cross-sectional study**	He Z., *et al.* China [gotopaper]	Immunology	Seroprevalence and kinetics of anti-SARS-CoV-2 antibodies at population level in Wuhan to inform the development of vaccination strategies. **Methods** Longitudinal cross-sectional study, population-stratified, cluster random sampling method (100 communities from the 13 districts of Wuhan). Householdssystematically selected. A venous blood sample taken for immunological testing (pan-immunoglobulins, IgM, IgA, and IgG antibodies against SARS-CoV-2 nucleocapsid protein and neutralising antibodies). **Findings** > 9542 individuals from 3556 families had sampled for analyses. > 532 participants were positive for pan-immunoglobulins against SARS-CoV-2 (baseline seroprevalence of 6·92%) > 437 of 532 (82.1%) participants who were positive for pan-immunoglobulins were asymptomatic. > 69 (13·0%) of 532 individuals were positive for IgM antibodies, 84 (15·8%) were positive for IgA antibodies, 532 (100%) were positive for IgG antibodies, and 212 (39·8%) were positive for neutralising antibodies at baseline. > On the basis of data from 335 individuals who attended all three follow-up visits and who were positive for pan-immunoglobulins, neutralising antibody levels did not significantly decrease over the study period > Neutralising antibody titres were lower in asymptomatic individuals than in confirmed cases and symptomatic individuals. > Although titres of IgG decreased over time, the proportion of individuals who had IgG antibodies did not decrease substantially **Conclusion** 6·92% of a cross-sectional sample of the population of Wuhan developed antibodies against SARS-CoV-2, with 39·8% of this population seroconverting to have neutralising antibodies.

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Nature Commun. 19MAR2021	**Favipiravir antiviral efficacy against SARS-CoV-2 in a hamster model**	Driouich J.S., *et al.* France gotopaper	Therapeutics	Assesement of antiviral efficacy of favipiravir (Syrian hamster model) **Findings:** > In vitro efficacy of favipiravir - Vero E6 cells : Infectious titer reductions (fold change in comparison with untreated cells) ≥ 2 with 125 µM of favipiravir and between 11 and 342 with 500 µM. - Caco-2 cells (no CPE with SARS-CoV-2 BavPat1 strain) infectious titer reductions around 5 with 125 µM of favipiravir and between 144 and 7721 with 500 µM. > In vivo efficacy of favipiravir - intranasally infection of Syrian hamsters with differnet inocolums, receiving favipiravir at the day of infection up to 2 dpi. Doses of favipiravir: 18.75, 37.5, and 75 mg/day. Effect of favipiravir in reducing infectious titers is dose dependent, in particular when low virus inocula were used to infect animal. Significant differences in virus replication in clarified lung homogenates between tretated and untreated animals - Antiviral effect of favipiravir correlates with incorporation of a large number of mutations into viral genomes and decrease of viral infectivity. - Antiviral efficacy is achieved with plasma drug exposure comparable with those previously found during human clinical trials (the highest dose of favipiravir tested is associated with signs of toxicity in animals) Pharmacokinetic and tolerance studies are required to determine whether similar effects can be safely achieved in humans. **Conslusion:** High doses of favipiravir are associated with antiviral activity against SARS-CoV-2 infection in a hamster model. The better antiviral efficacy was observed using a preventive strategy, suggesting that favipiravir could be more appropriate for a prophylactic use.
Nature Commun. 19MAR2021	**Exposure to SARS-CoV-2 generates T-cell memory in the absence of a detectable viral infection**	Wang Z., *et al.* China gotopaper	Immunology	**Aim**: to test SARS-CoV-2-specific T-cell immunity in virus-exposed individuals. COVID-19 patients: NAT+, hospitalised and recovered, samples taken 48–86 days after disease onset; Asymptomatic patients: NAT+, with no signs of symptoms Close contacts: NAT-, no SARS-CoV-2 specific antibodies, in contact with patients between 5 days before disease onset and hospitalisation. > Virus-specific CD4+ and CD8+ T-cell memory was observed in **recovered COVID-19 patients** (in 94.44% and 88.33% of patients, respectively) **and close contacts** (in 57.97% and 14.49%, respectively). > The size and quality of the memory T-cell pool of COVID-19 patients are larger and better than those of close contacts. > However, the proliferation capacity, size and quality of T-cell responses in close contacts are readily distinguishable from healthy donors, suggesting **close contacts are able to gain T-cell immunity against SARS-CoV-2 despite lacking a detectable infection**. > Asymptomatic and symptomatic COVID-19 patients contain **similar levels and qualities of SARS-CoV-2-specific T-cells**. > CD4+ T memory and CD8+ T memory may have contracted to a stable plateau 48-86 days after symptom onset. > Virus-specific memory **CD4+ T cell pool correlated with the titers of IgG against the S RBD region and the N protein**, whereas no apparent correlation between CD8+ T cells and IgG titers was observed. This study demonstrates the versatility and potential of memory T cells from COVID-19 patients and close contacts, which may be important for host protection.

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA Netw Open 19MAR2021	**Association of Vitamin D Levels, Race/Ethnicity, and Clinical Characteristics With COVID-19 Test Results**	Meltzer DO., *et al.* USA [gotopaper]	Public Health / Epidemiology	**Aim:** To examine whether COVID-19 test results are associated with differences in vitamin D levels of 30 ng/mL or greater, including for White individuals and for Black individuals. **Methods:** Single-center retrospective cohort study of 4638 individuals with a measured vitamin D level in the year before undergoing COVID-19 testing. The study was conducted at an academic medical center in Chicago, Illinois. Participants included individuals with data on vitamin D level within 365 days before COVID-19 testing. >Main outcome : positive result for COVID-19 in PCR testing. **Findings:** >Lower vitamin D levels were more common in Black individuals (<20 ng/mL: 829 of 2288 Black individuals [36%]) than White individuals (<20 ng/mL: 315 of 1999 White individuals [16%]). > The risk of having positive results in Black individuals was 2.64-fold greater with a vitamin D level of 30 to 39.9 ng/mL than a level of 40 ng/mL or greater and decreased by 5% per 1-ng/mL increase in level among individuals with a level of 30 ng/mL or greater. **There were no statistically significant associations of vitamin D levels with COVID-19 positivity rates in White individuals.** > Randomized clinical trials to determine whether increasing vitamin D levels to greater than 30 to 40 ng/mL affect COVID-19 risk are warranted, especially in Black individuals.
BMJ 18MAR2021	**Association between living with children and outcomes from covid-19: OpenSAFELY cohort study of 12 million adults in England**	Forbes H., *et al.* UK [gotopaper]	Public Health / Epidemiology	To investigate whether risk of infection with SARS-CoV-2 and outcomes of covid-19 differed between adults living with and without children during the first two waves of the UK pandemic > Population based cohort study: two cohorts of adults (≥18 yrs) registered at a general practice (1 Feb - 1 Sept 2020) > Adjusted hazard ratios (HR) for SARS-CoV-2 infection, covid-19 related admission to hospital or intensive care, or death from covid-19, by presence of children in the household. **Findings** > Among 9 334 392 adults aged ≤65 yrs, during **wave 1**, living with children **was not associated** with materially increased risks of recorded SARS-CoV-2 infection, covid-19 related hospital or intensive care admission, or death from covid-19. > **In wave 2**, among adults aged ≤65 yrs, living with children **of any age was associated with an increased risk of recorded SARS-CoV-2 infection** (HR 1.06 (95% CI 1.05 to 1.08) for living with children aged 0-11 years; 1.22 (1.20 to 1.24) for living with children aged 12-18 years) and covid-19 related hospital admission (1.18 (1.06 to 1.31) for living with children aged 0-11; 1.26 (1.12 to 1.40) for living with children aged 12-18). Living with children aged 0-11: > was associated with reduced risk of death from both covid-19 and non-covid-19 causes in both waves; living with children of any age was also associated with lower risk of dying from non-covid-19 causes. > For adults ≤65 yrs during wave 2, was associated with an increased absolute risk of having SARS-CoV-2 infection recorded of 40-60 per 10 000 people, from 810 to between 850 and 870, and an increase in hospital admissions of 1-5 per 10 000 people, from 160 to between 161 and 165. Living with children aged 12-18 years was associated with an increase of 160-190 per 10 000 in the number of SARS-CoV-2 infections and an increase of 2-6 per 10 000 in the number of hospital admissions. **In contrast to wave 1, evidence existed of increased risk of reported SARS-CoV-2 infection and covid-19 outcomes among adults living with children during wave 2. However, this did not translate into a materially increased risk of covid-19 mortality, and absolute increases in risk were small.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 17MAR2021	**Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study**	Hansen CH., *et al.* Denmark gotopaper	Public Health / Epidemiology	Using national PCR-test data from 2020 (4 million individuals (69% of the population) underwent 10·6 million tests), we estimated protection towards repeated infection with SARS-CoV-2. **Methods** > Analysis of infection rates during the second surge of the COVID-19 epidemic (Sept 1 - Dec 31, 2020), by comparing infection rates between individuals with positive and negative PCR tests during the first surge (March - May, 2020) > Alternative cohort analysis, comparing infection rates throughout the year between those with and without a previous confirmed infection at least 3 months earlier, irrespective of date. **Findings** > During the first surge (before June, 2020), 533381 people were tested, of whom 11727 (2·20%) were PCR positive, and 525339 were eligible for follow-up in the second surge, of whom 11068 (2·11%) had tested positive during the first surge. > Among eligible PCR-positive individuals from the first surge of the epidemic, **72 (0·65% [95% CI 0·51–0·82]) tested positive again** during the second surge compared with 16819 (3·27% [3·22–3·32]) of 514271 who tested negative during the first surge > Protection against repeat infection was 80·5% (95% CI 75·4–84·5). > In the alternative cohort analysis, among those **aged ≥65**, observed protection against repeated infection **was 47·1% (95% CI 24·7–62·8).** > No difference in estimated protection against repeated infection by sex (male 78·4% [72·1–83·2] vs female 79·1% [73·9–83·3])or evidence of waning protection over time (3–6 months of follow-up 79·3% [74·4–83·3] vs≥7 months of follow-up 77·7% [70·9–82·9]). **These findings could inform decisions on groups to vaccinate and advocate for vaccination of previously infected individuals,as natural protection, especially among older people, cannot be relied on.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 17MAR2021	**Four-Month Clinical Status of a Cohort of Patients After Hospitalization for COVID-19**	COMEBAC Study Group France gotopaper	Public Health / Epidemiology - Long Covid	**Aim**: to describe the consequences at 4 months in patients hospitalized for COVID-19. **Findings** > 478 were evaluated by telephone (mean age, 61 years [SD, 16 years]; 201 men, 277 women). > 244 patients (51%) declared at least 1 symptom that did not exist before COVID-19: fatigue in 31%, cognitive symptoms in 21%, and new-onset dyspnea in 16%. There was further evaluation in 177 patients (37%), including 97 of 142 former ICU patients. > The median 20-item Multidimensional Fatigue Inventory score (n = 130) was 4.5 (interquartile range IR, 3.0-5.0) for reduced motivation and 3.7 (IR, 3.0-4.5) for mental fatigue (possible range, 1 [best] to 5 [worst]). > The median 36-Item Short-Form Health Survey score (n = 145) was 25 (IR, 25.0-75.0) for the subscale "role limited owing to physical problems" (possible range, 0 [best] to 100 [worst]). > Computed tomographic lung-scan abnormalities were found in 108 of 171 patients (63%), mainly subtle ground-glass opacities. Fibrotic lesions were observed in 33 of 171 patients (19%), involving less than 25% of parenchyma in all but 1 patient. Fibrotic lesions were observed in 19 of 49 survivors (39%) with acute respiratory distress syndrome. > Among 94 former ICU patients, anxiety, depression, and posttraumatic symptoms were observed in 23%, 18%, and 7%, respectively. > The left ventricular ejection fraction was less than 50% in 8 of 83 ICU patients (10%). New-onset chronic kidney disease was observed in 2 ICU patients. > Serology was positive in 172 of 177 outpatients (97%). **Four months after hospitalization for COVID-19, a cohort of patients frequently reported symptoms not previously present, and lung-scan abnormalities were common among those who were tested**.
Nature 16MAR2021	**Clofazimine broadly inhibits coronaviruses including SARS-CoV-2**	Yuan S., *et al.* China gotopaper	Therapeutics	Clofazimine is an anti-leprosy drug with a favourable safety profile ***In vitro* & *in vivo* studies** > We show that clofazimine possesses pan-coronaviral inhibitory activity, and can antagonize SARS-CoV-2 and MERS-CoV replication in multiple in vitro systems. > The FDA-approved molecule was found to inhibit viral spike-mediated cell fusion and viral helicase activity. > In a hamster model of SARS-CoV-2 pathogenesis, prophylactic or therapeutic administration of clofazimine significantly reduced viral load in the lung and faecal viral shedding, and also mitigated inflammation associated with viral infection > Combinatorial application of clofazimine and remdesivir exhibited antiviral synergy in vitro and in vivo, and restricted upper respiratory tract viral shedding. **Since clofazimine is orally bioavailable and has a comparatively low manufacturing cost, it is an attractive clinical candidate for outpatient treatment and remdesivir-based combinatorial therapy for hospitalized COVID-19 patients, particularly in developing countries. Taken together, our data provide evidence that clofazimine may have a role in the control of the current pandemic SARS-CoV-2, and, possibly most importantly, emerging CoVs of the future.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 16MAR2021	**Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant**	Madhi S.A., *et al*. International [gotopaper]	Vaccines - Variants	Efficacy of ChAdOx1 against emerging SARS-CoV-2 variants of concern, including the B.1.351 (501Y.V2) variant first identified in South Africa. **Methods:** > Multicenter, double-blind, randomized, controlled trial in HIV- in South Africa. > Participants age: 18 to 65 years of age > Two doses of vaccine containing 5×10exp10 viral particles or placebo (0.9% sodium chloride solution) 21 to 35 days apart. > Serum samples obtained from 25 participants after the second dose were tested by pseudovirus and live-virus neutralization assays against the original D614G virus and the B.1.351 variant. Primary end points: safety and efficacy of the vaccine against laboratory-confirmed symptomatic coronavirus 2019 illness (Covid-19) more than 14 days after the second dose. **Findings:** > 2026 HIV-negative adults enroled (median age, 30 years); > 1010 and 1011 participants received at least one dose of placebo or vaccine, respectively. > Both the pseudovirus and the live-virus neutralization assays showed greater resistance to the B.1.351 variant in serum samples obtained from vaccine recipients than in samples from placebo recipients. > In the primary end-point analysis, mild-to-moderate Covid-19 developed in 23 of 717 placebo recipients (3.2%) and in 19 of 750 vaccine recipients (2.5%), for an efficacy of 21.9% (95% confidence interval [CI], −49.9 to 59.8). > Among the 42 participants with Covid-19, 39 cases (92.9%) were caused by the B.1.351 variant; vaccine efficacy against this variant, analyzed as a secondary end point, was 10.4% (95% CI, −76.8 to 54.8). > The incidence of serious adverse events was balanced between the vaccine and placebo groups. **Conclusion:** A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate Covid-19 due to the B.1.351 variant.
Cell Rep. 16MAR2021	**Virological and immunological features of SARS-CoV-2-infected children who develop neutralizing antibodies**	Cotugno N., *et al*. Italy [gotopaper]	Immunology	**Aim:** to define the humoral and cellular responses in SARS-CoV-2-infected children. **Methods:** Analysis of anti-SARS-CoV-2 antibodies and their neutralizing activity (PRNT) in 66 COVID-19-infected children at 7 (±2) days after symptom onset. Analysis of Ag-specific T and B cells defined as CD4+CD40L+ and SARS-CoV-2 Spike (S1+S2)-positive switched B cells. **Findings:** >Individuals with specific humoral responses presented faster virus clearance and lower viral load associated with a reduced in vitro infectivity. >The frequencies of SARS-CoV-2-specific CD4+CD40L+ T cells and Spike-specific B cells were associated with the anti-SARS-CoV-2 antibodies and the magnitude of neutralizing activity. >The plasma proteome confirmed the association between cellular and humoral SARS-CoV-2 immunity, and PRNT+ patients show higher viral signal transduction molecules (SLAMF1, CD244, CLEC4G). **C**ellular and humoral anti-SARS-CoV-2 responses in children, which may drive future vaccination trial end points and quarantine measures policies.

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Clin Infect Dis. 15MAR2021	**Reinfection Rates among Patients who Previously Tested Positive for COVID-19: a Retrospective Cohort Study**	Sheehan M.M., *et al.* USA [gotopaper](#)	Public Health / Epidemiology	**Methods** > Retrospective cohort study of one multi-hospital health system included 150,325 patients tested for COVID-19 infection via PCR from March 12, 2020 to August 30, 2020 > Testing performed up to February 24, 2021 in these patients was included for analysis > Main outcome = reinfection (defined as infection ≥ 90 days after initial testing) **Findings** > Protection offered from prior infection was 81.8% (95% confidence interval 76.6 to 85.8), and against symptomatic infection was 84.5% (95% confidence interval 77.9 to 89.1) > Prior infection in patients with COVID-19 was highly protective against reinfection and symptomatic disease. > This protection increased over time, suggesting that viral shedding or ongoing immune response may persist beyond 90 days and may not represent true reinfection. > As vaccine supply is limited, patients with known history of COVID-19 could delay early vaccination to allow for the most vulnerable to access the vaccine and slow transmission. **Patients with confirmed history of infection with SARS-CoV-2 are less likely to be retested or reinfected more than 90 days after their initial infection than those with initial negative tests. Protectiveness of prior infection against subsequent infection is high.**
Nature 15MAR2021	**Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7**	Davies N.G., *et al.* UK [gotopaper](#)	Variants	**Aim**: to determine if variant B.1.1.7 leads to changes in disease severity by analysing a dataset linking 2,245,263 positive SARS-CoV-2 community tests and 17,452 COVID-19 deaths in England (1 Sept 2020 - 14 Feb 2021). > For 1,146,534 (51%) of these tests, the presence or absence of B.1.1.7 can be identified because of mutations in this lineage preventing PCR amplification of the spike gene target (S gene target failure, SGTF). > Based on 4,945 deaths with known SGTF status, we estimate that the hazard of death associated with SGTF is **55% (95% CI 39–72%) higher** after adjustment for age, sex, ethnicity, deprivation, care home residence, local authority of residence and test date. > These data correspond to the **absolute risk of death for a 55–69-year-old male increasing from 0.6% to 0.9%** (95% CI 0.8–1.0%) within 28 days after a positive test in the community. > Correcting for misclassification of SGTF and missingness in SGTF status, we estimate a **61% (42–82%) higher hazard of death associated with B.1.1.7**. This analysis suggests that B.1.1.7 is not only more transmissible than preexisting SARS-CoV-2 variants, but **may also cause more severe illness.**
Nature Commun. 12MAR2021	**Evaluating the impact of curfews and other measures on SARS-CoV-2 transmission in French Guiana**	Andronico A., *et al.* French Guiana [gotopaper](#)	Public Health / Epidemiology	> Report and evaluate the control strategy implemented during a large SARS-CoV-2 epidemic in June–July 2020 in French Guiana that relied on curfews, targeted lockdowns, and other measures. > To describe how mathematical modelling was used during this crisis to support policy making and planning. **Methods** > Deterministic mathematical model to describe the transmission of SARS-CoV-2 and subsequent disease progression (applying age-specific probabilities to the demographic structure and expected contact patterns in French Guiana, ...) **Findings** > The combination of these interventions coincided with a reduction in the basic reproduction number of SARS-CoV-2 from 1.7 to 1.1, which was sufficient to avoid hospital saturation > We estimate that thanks to the young demographics, the risk of hospitalisation following infection was 0.3 times that of metropolitan France and that about 20% of the population was infected by July > Our model projections are consistent with a recent seroprevalence study. The study show-cases how mathematical modelling can be used to support healthcare planning in a context of high uncertainty.

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Clin Infect Dis. 12MAR2021	**Household SARS-CoV-2 transmission and children: a network prospective study**	Soriano-Arandes A., Spain <u>gotopaper</u>	Public Health / Epidemiology	**Aim**: describe the epidemiological and clinical characteristics of children with COVID-19 in Catalonia (Spain) and investigate the dynamics of household transmission. Prospective, observational, multicenter study performed during summer and school periods (1 July-31 October, 2020) on COVID-19 patients <16 years. > The study included 1040 COVID-19 patients <16 years. 47.2% were asymptomatic, 10.8% had comorbidities, and 2.6% required hospitalization. No deaths were reported. > Viral transmission was common among household members (62.3%). > More than 70% (756/1040) of pediatric cases were secondary to an adult, whereas 7.7% (80/1040) were index cases. > The Secondary Attack Rate (SAR) was significantly lower in households with COVID-19 pediatric index cases during the school period relative to summer (p=0.02), and when compared to adults (p=0.006). > No individual or environmental risk factors associated with the SAR were identified. **Children are unlikely to cause household COVID-19 clusters or be major drivers of the pandemic even if attending school.**
Nature 11MAR2021	**Sensitivity of SARS-CoV-2 B.1.1.7 to mRNA vaccine-elicited antibodies**	Collier A.C. *et al.* International <u>gotopaper</u>	Vaccines - Variants	Assessement of immune responses following vaccination with mRNA-based vaccine BNT162b2. **Methods** 37 participants (mdian age 62 years; 35% female) meausrement of neutralising antibody responses following first and second immunisations using pseudoviruses expressing the wild-type Spike protein or the 8 amino acid mutations found in the B.1.1.7 spike protein. **Findings** > The GMT against wild type (WT) following the second dose of vaccine is substantially higher than after the first dose (318 vs 77). Correlation between total Spike IgG titres and serum neutralisation titres > Broad range of T celle resposnes (IFN-Gamma). No corrleation with serum netralization titers > Vaccine sera exhibited a broad range of neutralising titres against the wild-type pseudoviruses that were modestly reduced against B.1.1.7 variant. Reduction also evident in sera from some convalescent patients. > Decreased B.1.1.7 neutralisation also observed with monoclonal antibodies targeting the N-terminal domain (9 out of 10), the RBM (5 out of 31), but not in RBD neutralising mAbs binding outside the RBM. > Introduction of the E484K mutation in a B.1.1.7 background to reflect a newly emergent Variant of Concern (VOC 202102/02) led to a more substantial loss of neutralising activity by vaccine-elicited antibodies and mAbs (19 out of 31) over that conferred by the B.1.1.7 mutations alone. **Conclusion:** >Pseudovirus bearing S protein with the full set of mutations present in the B.1.1.7 variant result in small reduction in neutralisation by sera from BNT162B2 vaccinees (more marked following the first dose than the second dose). This could be related to increased breadth/ potency/concentration of antibodies following the boost dose. >E484K emergence on a B.1.1.7 background represents a threat to the vaccine BNT162b

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JAMA 11MAR2021	**Immunogenicity of the Ad26.COV2.S Vaccine for COVID-19**	Stepherson K., *et al.* International [gotopaper](#)	Vaccines	Evaluation of the immunogenicity of the Ad26.COV2.S vaccine (Janssen/Johnson & Johnson) in humans, including the kinetics, magnitude, and phenotype of SARS-CoV-2 spike-specific humoral and cellular immune responses. **Methods:** > Randomized, double-blind, placebo-controlled phase 1 clinical trial of Ad26.COV2.S (NCT04436276). **>** Twenty-five participants; interim analysis at day 71. A single clinical site in Boston > 1 or 2 intramuscular injections with 5×10^{10} viral particles or 1×10^{11} viral particles of Ad26.COV2.S vaccine or placebo (day 1 and day 57 . Main Outcomes and Measure: Humoral immune responses included binding and neutralizing antibody responses at multiple time points following immunization. Cellular immune responses included immunospot-based and intracellular cytokine staining assays to measure T-cell responses. Findings: > Binding and neutralizing antibodies emerged rapidly by day 8 after initial immunization in 90% and 25% of vaccine recipients, respectively. > By day 57, binding and neutralizing antibodies were detected in 100% of vaccine recipients after a single immunization. > On day 71, the geometric mean titers of spike-specific binding antibodies were 2432 to 5729 and the geometric mean titers of neutralizing antibodies were 242 to 449 in the vaccinated groups. > A variety of antibody subclasses, Fc receptor binding properties, and antiviral functions were induced. CD4+ and CD8+ T-cell responses were induced. **Conclusion:** Ad26.COV2.S induces rapid binding and neutralization antibody responses as well as cellular immune responses.
PNAS 09MAR2021	**A safe and highly efficacious measles virus-based vaccine expressing SARS-CoV-2 stabilized prefusion spike**	Lu M., *et al.* USA [gotopaper](#)	Vaccines	Evaluation of a SARACoV 2 Measles virus (rMeV) vaccine efficacy in cotton rat, IFNAR−/−mice, IFNAR−/−-hCD46 mice, and golden Syrian hamsters Recombinant attenuated vaccine candidates expressing various forms of the SARS-CoV-2 spike (S) protein and its receptor binding domain (RBD). **Findings** > rMeV expressing stabilized prefusion S protein (rMeV-preS) was more potent in inducing SARS-CoV-2–specific neutralizing antibodies than rMeV expressing full-length S protein (rMeV-S), >rMeVs expressing different lengths of RBD (rMeV-RBD) were the least potent. > Animals immunized with rMeV-preS produced higher levels of neutralizing antibody than found in convalescent sera from COVID-19 patients and a strong Th1-biased T cell response. > rMeV-preS also provided complete protection of hamsters from challenge with SARS-CoV-2, preventing replication in lungs and nasal turbinates, body weight loss, cytokine storm, and lung pathology. **Conlusion** rMeV-preS is a safe and highly efficacious vaccine candidate, supporting its further development as a SARS-CoV-2 vaccine.

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BMJ 10MAR2021	**Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study**	Challen R., *et al.* UK gotopaper	Public Health / Epidemiology	To establish whether there is any change in mortality from infection with a new variant of SARS-CoV-2, designated a variant of concern (VOC-202012/1) in December 2020, compared with circulating SARS-CoV-2 variants. **Methods** > Matched cohort study (participants were matched on age, sex, ethnicity, index of multiple deprivation, lower tier local authority region, and sample date of positive specimens, and differed only by detectability of the spike protein gene using the TaqPath ass) > Community based (pillar 2) covid-19 testing centres in the UK using the TaqPath assay (a proxy measure of VOC-202012/1 infection) > 54 906 matched pairs of participants who tested positive for SARS-CoV-2 in pillar 2 between 1 October 2020 and 29 January 2021, followed-up until 12 February 2021 > Main outcome measure: Death within 28 days of the first positive SARS-CoV-2 test result. **Findings** > The mortality hazard ratio associated with infection with VOC-202012/1 compared with infection with previously circulating variants was **1.64** (95% confidence interval 1.32 to 2.04), corresponding to **64% increased risk of death**, in patients who tested positive for covid-19 in the community. > In this comparatively low risk group, this represents an increase in deaths from 2.5 to 4.1 per 1000 detected cases. **Increased risk of mortality is increased by infection with VOC-202012/01 is highly probable. If this finding applies to other populations, infection with VOC-202012/1 could cause substantial additional mortality compared with previously circulating variants. Healthcare capacity planning and national and international control policies are all impacted by this finding, which supports further coordinated and stringent measures to reduce deaths.**
Nature Med. 10MAR2021	**Attributes and predictors of long COVID**	Sudre C.H., *et al.* UK gotopaper	Clinics - Long Covid	Analysis of prevalence, risk factors and early predictors of long COVID. > 4,182 incident cases of COVID-19 in which individuals self-reported their symptoms prospectively in the COVID Symptom Study app. > **558 (13.3%)** participants reported symptoms lasting ≥28 days, **189 (4.5%)** for ≥8 weeks and **95 (2.3%)** for ≥12 weeks > Long COVID was characterized by symptoms of **fatigue, headache, dyspnea and anosmia** and was more likely with **increasing age and body mass index and female sex** > Experiencing **more than five symptoms during the first week of illness was associated with long COVID** (odds ratio = 3.53 (2.76–4.50)). > A simple model to distinguish between short COVID and long COVID at 7 days is presented, which could be used to identify individuals at risk of long COVID.
Nature 09MAR2021	**Emergence of a SARS-CoV-2 variant of concern with mutations in spike glycoprotein**	Tegally H., *et al.* South Africa gotopaper	Virology	B.1.351 lineage (VOC 501Y.V2): > Shows **marked hypermutation**: 6 non-synonymous mutations in the spike protein by to 15/10/20, then 3 more by 30/11/20, plus deletion of 3 amino acids > Mutations N501Y, E484K and K417N are at key residues of the RBD – the two latters are key for neutralizing antibody binding > E484 and N501 pattern of nucleotide variation suggest **evolution under positive selection** > B.1.351 most likely **evolved by mutation on circulating intermediate mutants** > B.1.351 likely emerged in Nelson Madela Bay in early August and became dominant in Easter Cape, Western Cape and KwaZulu-Natal Provinces within weeks > **It has a selective advantage, from increased transmissibility and/or immune escape**

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Lancet Infect Dis. 08MAR2021	**Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: interim results from a double-blind, randomised, multicentre, phase 2 trial, and 3-month follow-up of a double-blind, randomised phase 1 trial**	Ella R., *et al.* India [gotopaper](#)	Vaccines	BBV152 is a whole-virion inactivated SARS-CoV-2 vaccine (3 μg or 6 μg) formulated with a toll-like receptor 7/8 agonist molecule (IMDG) adsorbed to alum (Algel). **Methods** > Double-blind, randomised, multicentre, phase 2 clinical trial NCT04471519 to evaluate the immunogenicity and safety of BBV152 in healthy adults and adolescents (aged 12–65 years) at nine hospitals in India. > Phase 1 trial data allowed to chose phase II formulations of BBV152: 3 μg and 6 μg with Algel-IMDG administered on day 0 and day 28 > Participants with positive SARS-CoV-2 nucleic acid and serology tests were excluded. Primary outcome: SARS-CoV-2 wild-type neutralising antibody titres and seroconversion rates at 4 weeks after the second dose Secondary outcome: Cell-mediated responses (T-helper-1 profiling at 2 weeks after the second dose) Safety assessed in all participants who received at least one dose of the vaccine **Findings** > 380 participants enrolled and randomly assigned to the 3 μg with Algel-IMDG group (n=190) or 6 μg with Algel-IMDG group (n=190). > GMTs; PRNT50 at day 56 were significantly higher in the 6 μg with Algel-IMDG group (197·0 [95% CI 155·6–249·4]) than the 3 μg with Algel-IMDG group (100·9 [74·1–137·4]; p=0·0041). > Seroconversion based on PRNT50 at day 56 was reported in 171 (92·9% [95% CI 88·2–96·2] of 184 participants in the 3 μg with Algel-IMDG group and 174 (98·3% [95·1–99·6]) of 177 participants in the 6 μg with Algel-IMDG group. > GMTs (MNT50) at day 56 were 92·5 (95% CI 77·7–110·2) in the 3 μg with Algel-IMDG group and 160·1 (135·8–188·8) in the 6 μg with Algel-IMDG group. > Seroconversion based on MNT50 at day 56 was reported in 162 (88·0% [95% CI 82·4–92·3]) of 184 participants in the 3 μg with Algel-IMDG group and 171 (96·6% [92·8–98·8]) of 177 participants in the 6 μg with Algel-IMDG group. > The 3 μg with Algel-IMDG and 6 μg with Algel-IMDG formulations elicited T-cell responses that were biased to a Th1 phenotype at day 42. > No significant difference in the proportion of participants who had a solicited local or systemic adverse reaction in the 3 μg with Algel-IMDG group (38 [20·0%; 95% CI 14·7–26·5] of 190) and the 6 μg with Algel-IMDG group (40 [21·1%; 15·5–27·5] of 190) was observed on days 0–7 and days 28–35; no serious adverse events were reported in the study. **Conclusion** BBV152 induced high neutralising antibody responses that remained elevated in all participants at 3 months after the second vaccination. The 6 μg with Algel-IMDG formulation has been selected for the phase 3 efficacy trial.
PNAS 08MAR2021	**Higher airborne pollen concentrations correlated with increased SARS-CoV-2 infection rates, as evidenced from 31 countries across the globe**	Damialis A., *et al.* Germany [gotopaper](#)	Public Health / Epidemiology	> Coexposure to airborne pollen enhances susceptibility to respiratory viral infections, regardless of the allergy status. > We hypothesized this could be also true for SARS-CoV-2 infections. **Methods** > Test for relationships between SARS-CoV-2 infection rates and pollen concentrations, along with humidity, temperature, population density, and lockdown effects > Our unique dataset derives from 130 sites in 31 countries and across five continents (8,019 data points) **Findings** > Pollen, some-times in synergy with humidity and temperature, explained, on average, 44% of the infection rate variability > Lockdown halved infection rates under similar pollen concentrations > As we cannot completely avoid pollen exposure, **we suggest wide dissemination of pollen–virus coexposure information to encourage high-risk individuals to wear particle filter masks during high springtime pollen concentrations**

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Nature 08MAR2021	**Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7**	Wang P., et al. USA [gotopaper]	Virology	**Background:** Autorized therapeutic or preventive interventions against COVID are directed toward the initial SARS-CoV-2 that emerged in 2019. The recent emergence of new SARS-CoV-2 variants B.1.1.7 in the UK11 and B.1.351 in South Africa is of concern because of their purported ease of transmission and extensive mutations in the spike protein. **Findings**: Monoclonal antibodies: neutralizing activity of 12 RBD mAbs against authentic B.1.1.7 and B.1.351 viruses, as compared to the original SARS-CoV-2 strain (WT), in Vero E6 cells > neutralization of B.1.1.7: only the activities of 910-3022 and S3095 are significantly impaired. > neutralization of B.1.351: the activities of 910-30, 2-1520, LY-CoV555 (bamlanivimab)1,23, C12124, and REGN10933 (casirivimab) are completely or markedly abolished. 2-720,27, REGN10987 (imdevimab), C13524, and S309 " retain their activities against B.1.351 Convalescent plasmafrom 20 patients more than one month after documented SARS-CoV-2 infection in the Spring of 2020 > Most (16 of 20) plasma samples lost >2.5-fold neutralizing activity against B.1.351, while maintaining activity against B.1.1.7. Only plasma from 4 patients retain neutralizing activities similar to those against the WT Vaccinee Sera obtained from 12 participants of a Phase 1 clinical trial of Moderna SARS-Co-2 mRNA-1273 Vaccine conducted at the NIH. > Each vaccinee serum sample was assayed for neutralization against B.1.1.7, B.1.351, and WT viruses. No loss of neutralizing activity against B.1.1.7, whereas every sample lost activity against B.1.351.
Blood Advances 08MAR2021	**Heterogeneous NLRP3 inflammasome signature in circulating myeloid cells as a biomarker of COVID-19 severity**	Courjon J., *et al.* France [gotopaper]	Immunology	The NLRP3 inflammasome can play a crucial role during innate immunity activation, but NLRP3 response during SARS-CoV-2 infection in patients is unknown. **Aim**: Prospectively monitoring of caspase-1 activation levels in peripheral myeloid cells from healthy donors and patients with mild to critical COVID-19. > The caspase-1 activation potential in response to NLRP3 inflammasome stimulation was opposed between nonclassical monocytes and CD66b+CD16dim granulocytes in severe and critical COVID-19 patients. > CD66b+CD16dim granulocytes had decreased nigericin-triggered caspase-1 activation potential associated with an increased percentage of NLRP3 inflammasome impaired immature neutrophils and a loss of eosinophils in the blood. > In patients who recovered from COVID-19, nigericin-triggered caspase-1 activation potential in CD66b+CD16dim cells was restored and the proportion of immature neutrophils was similar to control. **NLRP3 inflammasome activation potential differs among myeloid cells. It could be used as a biomarker of COVID-19 patient evolution.**

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Nature Med. 04MAR2021	**Resistance of SARS-CoV-2 variants to neutralization by monoclonal and serum-derived polyclonal antibodies**	Chen R.E., *et al.* USA gotopaper	Virology	**Background:** Impact on antibody neutralization of a panel of authentic SARS-CoV-2 variants including a B.1.1.7 isolate, chimeric strains with South African or Brazilian spike genes and isogenic recombinant viral variants with designed mutations or deletions at positions 69-70, 417, 484, 501, 614 and/or 681 of the spike protein, using using monoclonal antibodies (mAbs), animal immune sera, human convalescent sera and human sera from recipients of the BNT162b2 mRNA vaccine **Findings:** > in vitro experiments using a B.1.1.7 isolate and engineered variants in the backbone of the WA1/2020 strain establish that mutations in the spike can impact the potency of antibody neutralization > Some neutralizing mAbs targeting the base of the RBD or NTD showed **reduced activity against the B.1.1.7 isolate**, whereas others targeting the RBM or NTD **failed to inhibit infection of Wash SA-B.1.351, Wash BR-B.1.1.248 or variants containing the E484K mutation** > **E484K** substitution as a vulnerability for multiple neutralizing mAbs > Several other highly neutralizing mAbs (such as COV2-2196, COV2-2381, COV2-3025 and S2E12) showed intact or only mildly diminished inhibitory activity against the suite of variant viruses we tested, possibly because they bind the RBM at sites other than the E484K residue > **Cocktails of mAbs binding different epitopes** of the spike protein overcame virus resistance to individual mAbs > Studies with human sera from convalescent patients and recipients of the BNT162b2 mRNA vaccine and animal sera after immunization with a vaccine encoding a similar spike gene, demonstrate a **lower potency of neutralization against E484K and N501Y-containing viruses** > Convalescent and vaccine-induced immune sera **neutralized infection of the chimeric SARS-CoV-2 strains encoding the Brazilian spike (B.1.1.248)** better than the South African spike (B.1.351) even though both viruses encoded E484 and N501 mutations **Conclusion:** Adjustments to some therapeutic antibody cocktails or existing spike sequences in vaccines might be necessary, corroborating in vivo studies are needed.
JAMA 04MAR2021	**Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19A Randomized Clinical Trial**	Lopez-Medina E., *et al*. Colombia/USA gotopaper	Therapeutics	**Aim**: To determine whether ivermectin is an efficacious treatment for mild COVID-19. Double-blind, randomized trial conducted at a single site in Cali, Colombia, on adult patients with mild disease and symptoms for 7 days or fewer (enrolment July 15-November 30, followed up through December 21, 2020) Patients were randomized to receive ivermectin, 300 μg/kg of body weight per day for 5 days (n = 200) or placebo (n = 200). Primary outcome: time to resolution of symptoms within a 21-day follow-up period. **Results** > 398 patients randomized in primary analysis population (median age, 37yo; 58% women) > Median time to resolution of symptoms was 10 days (IQR, 9-13) in the ivermectin group compared with 12 days (IQR, 9-13) in the placebo group (hazard ratio, 1.07 [95% CI, 0.87 to 1.32]; P = .53 by log-rank test). > By day 21, 82% in the ivermectin group and 79% in the placebo group had resolved symptoms. > The most common solicited adverse event was headache in 104 patients (52%) given ivermectin and 111 (56%) who received placebo. > The most common serious adverse event was multiorgan failure, occurring in 4 patients (2 in each group). **Conclusion** Among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms

Journal and date	Title	Authors and link	Field of expertise	Key facts
Blood 03MAR2021	**The SARS-CoV-2 receptor-binding domain preferentially recognizes blood group A**	Wu S.C., *et al.* USA gotopaper	Virology	> The RBD of SARS-CoV-2 shares sequence similarity with an ancient lectin family known to bind blood group antigens > Examined SARS-CoV-2 RBD binding with RBCs isolated from blood group A, B, or O individuals **Methods** > SARS-CoV receptor-binding domain (RBD) was cloned and purified > SARS-COV-2 RBD was incubated with HEK293T cells, HEK293 T cells expressing angiotensin-converting enzyme 2(ACE2), or red blood cells(RBCs), followed by detection with anti-His antibody (Anti-His-Tag mAb-Alexa Fluor 647) and flowcytometric analysis > Anti-A antibody was similarly used to detect the A antigen on blood group A RBCs **Findings** > **SARS-CoV-2 RBD binds the blood groupA expressed on respiratory epithelial cells, directly linking bloodgroup A and SARS-CoV-2** However,because these results do not definitively demonstrate that blood group A directly contributes to SARS-CoV-2 infection, future studies are needed, including an examination of the overall affinity and residueswithin the RBD responsible for blood group A interactions. Whatever the possible contribution of ABO(H)antigens to infection and possible disease progression, **the ability ofthe SARS-CoV-2 to directly interact with the blood group A antigen uniquely expressed on respiratory epithelial cells provides clear evidence of a direct association between SARS-CoV-2 and theABO(H) genetic locus.**
Lancet Respir Med. 04MAR2021	**Sarilumab in patients admitted to hospital with severe or critical COVID-19: a randomised, double-blind, placebo-controlled, phase 3 trial**	Lescure FX., *et al.* International gotopaper	Therapeutics	**Aim**: to assess safety and efficacy of sarilumab, an interleukin-6 receptor inhibitor, in patients with severe (requiring supplemental oxygen by nasal cannula or face mask) or critical (requiring greater supplemental oxygen, mechanical ventilation, or extracorporeal support) COVID-19. 60-day, randomised, double-blind, placebo-controlled, multinational phase 3 trial. Patients were randomly assigned (2:2:1 with permuted blocks of five) to receive intravenous sarilumab 400 mg, sarilumab 200 mg, or placebo. Primary endpoint: time to clinical improvement of two or more points (seven point scale ranging from 1 [death] to 7 [discharged from hospital]) in the modified intention-to-treat population. Secondary endpoint: proportion of patients alive at day 29. **Findings** > 420 patients were randomly assigned and 416 received placebo (n=84 [20%]), sarilumab 200 mg (n=159 [38%]), or sarilumab 400 mg (n=173 [42%]). > At day 29, no significant differences were seen in median time to an improvement of two or more points between placebo (12·0 days [95% CI 9·0 to 15·0]) and sarilumab 200 mg (10·0 days [9·0 to 12·0]; hazard ratio [HR] 1·03 [95% CI 0·75 to 1·40]; log-rank p=0·96) or sarilumab 400 mg (10·0 days [9·0 to 13·0]; HR 1·14 [95% CI 0·84 to 1·54]; log-rank p=0·34), or in proportions of patients alive (77 [92%] of 84 patients in the placebo group; 143 [90%] of 159 patients in the sarilumab 200 mg group; difference −1·7 [−9·3 to 5·8]; p=0·63 vs placebo; and 159 [92%] of 173 patients in the sarilumab 400 mg group; difference 0·2 [−6·9 to 7·4]; p=0·85 vs placebo). > At day 29, there were non-significant survival differences between sarilumab 400 mg (88%) and placebo (79%; difference +8·9% [95% CI −7·7 to 25·5]; p=0·25) for patients who had critical disease. > No unexpected safety signals were seen. > The rates of treatment-emergent adverse events were 65% (55 of 84) in the placebo group, 65% (103 of 159) in the sarilumab 200 mg group, and 70% (121 of 173) in the sarilumab 400 mg group, and of those leading to death 11% (nine of 84) were in the placebo group, 11% (17 of 159) were in the sarilumab 200 mg group, and 10% (18 of 173) were in the sarilumab 400 mg group. **This trial did not show efficacy of sarilumab in patients admitted to hospital with COVID-19 and receiving supplemental oxygen.**

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Lancet 04MAR2021	**Azithromycin for community treatment of suspected COVID-19 in people at increased risk of an adverse clinical course in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial**	PRINCIPLE Trial Collaborative Group UK gotopaper	Therapeutics	**Aim:** to assess the effectiveness of azithromycin to treat suspected COVID-19 among people in the community who had an increased risk of complications. Open-label, multi-arm, adaptive platform randomised trial, we randomly assigned people aged 65 years and older, or 50 years and older with at least one comorbidity, who had been unwell for 14 days or less with suspected COVID-19. Treatments: usual care plus azithromycin 500 mg daily for three days, usual care plus other interventions, or usual care alone. Coprimary endpoints within 28 days from randomisation: time to first self-reported recovery, and hospital admission or death related to COVID-19 **Findings** > 2120 participants were included in the Bayesian primary analysis, 500 participants in the azithromycin plus usual care group, 823 in the usual care alone group, and 797 in other intervention groups. > 402/500 (80%) participants in the azithromycin plus usual care group and 631/823 (77%) in the usual care alone group reported feeling recovered within 28 days. > We found little evidence of a meaningful benefit in the azithromycin plus usual care group in time to first reported recovery versus usual care alone (hazard ratio 1·08, 95% Bayesian credibility interval [BCI] 0·95 to 1·23), equating to an estimated benefit in median time to first recovery of 0·94 days (95% BCI −0·56 to 2·43). > The probability that there was a clinically meaningful benefit of at least 1·5 days in time to recovery was 0·23. 16/500 (3%) participants in the azithromycin plus usual care group and 28/823 (3%) participants in the usual care alone group were hospitalised (absolute benefit in percentage 0·3%, 95% BCI −1·7 to 2·2). > No deaths in either study group. Safety outcomes were similar in both groups. **These findings do not justify the routine use of azithromycin for reducing time to recovery or risk of hospitalisation for people with suspected COVID-19 in the community.**
Antimicrob Agents Chemother 01MAR2021	**Human Safety, Tolerability, and Pharmacokinetics of Molnupiravir, a Novel Broad-Spectrum Oral Antiviral Agent with Activity Against SARS-CoV-2**	Painter W. P., *et al.* USA gotopaper	Therapeutics	> Molnupiravir,EIDD-2801/MK-4482, prodrug of the active antiviral ribonucleoside analog 14ß-d-N4-hydroxycytidine (NHC; EIDD-1931) > Single and multiple doses of molnupiravir were evaluated in this first-in-human, **phase 1, randomized, double-blind, placebo-controlled study in healthy volunteers,** which included evaluation of the effect of food on pharmacokinetics. **Findings** > EIDD-1931 appeared rapidly in plasma, with a median time of maximum observed concentration of 1.00 to 1.75 hours, and declined with a geometric half-life of approximately 1 hour, with a slower elimination phase apparent following multiple doses or higher single doses (7.1 hours at 24the highest dose tested). Mean maximum observed concentration and area under the concentration versus time curve increased in a dose-proportional manner, and there was no accumulation following multiple doses. When administered in a fed state, there was a decrease in the rate of absorption, but no decrease in overall exposure > Molnupiravir was well tolerated. Fewer than half of subjects reported an adverse event, the incidence of adverse events was higher following administration of placebo, and 93.3% of adverse events were mild. One discontinued early due to rash. There were no serious adverse events and there were no clinically significant findings in clinical laboratory, vital signs, or electrocardiography. > Plasma exposures exceeded expected efficacious doses based on scaling from animal models; therefore, dose escalations were discontinued before a maximum tolerated dose was reached.

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Science 03MAR2021	**Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England**	Davies N.G., *et al.* UK [gotopaper]	Virology	**SARS-CoV-2 variant VOC 202012/01 (lineage B.1.1.7)** emerged in southeast England in November 2020 and is rapidly spreading toward fixation. > This variant has an estimated **43–90%** (range of 95% CI 38–130%) **higher reproduction number** than pre-existing variants. Its relative growth rate has declined slightly over time but it remains among the highest of any lineage as a function of lineage age > **No increased or decreased severity of the disease** associated to VOC 202012/01 was identified by the increased tranmissibility model > A fitted two-strain dynamic transmission model shows that VOC 202012/01 will lead to large resurgences of COVID-19 cases > VOC 202012/01 has spread globally and exhibits a similar transmission increase in **Denmark (55%)**, **Switzerland (74%)**, and the **United States (59%)**. Without stringent control measures, COVID-19 hospitalisations and deaths across England in 2021 will exceed those in 2020.
Nature Med. 02MAR2021	**SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma**	Wibmer C.K., *et al.* South Africa [gotopaper]	Therapeutics - variants	**Findings** > Lineage B.1.35 1 is defined by nine changes in the spike protein relative to the Wuhan-1 D614G spike. These changes include N501Y, which confers **enhanced affinity for ACE2** and clusters of substitutions in two immunodominant regions of spike, **suggesting escape from neutralization**. > Class 1 antibodies are most frequently elicited in SARS-CoV-2 infection and include an antibody response to an epitope only accessible in the RBD 'up' conformation. Class 2 antibodies use more diverse VH-genes and bind to RBD 'up' and RBD 'down' conformations of spike. > An analysis of 3 class 1 antibodies showed **reduced binding capacities and netralisation to 501Y.V2 pseudovirus**. 3 class 2 antibodies failed to bind 501Y.V2 RBD and were unable to neutralize the 501Y.V2 pseudovirus as well. > This pseudovirus also exhibits substantial to complete **escape from neutralization, but not binding, by convalescent plasma** **Conclusion:** The prospect of reinfection with antigenically distinct variants and foreshadows reduced efficacy of spike-based vaccines.
JAMA 01MAR2021	**Binding and Neutralization Antibody Titers After a Single Vaccine Dose in Health Care Workers Previously Infected With SARS-CoV-2**	Saadat S., *et al.* USA [gotopaper]	Therapeutics	**Background:** > Persons who have had COVID-19 are thought to have protective immunity and memory responses for at least 6 months. However, neither recall responses nor ideal vaccine dosing regimens have been studied in those previously infected with SARS-CoV-2. **Methods:** > HCW cohort. stratified into 3 groups: SARS-CoV-2 IgG-antibody negative (Ab-negative); IgG-positive asymptomatic COVID-19 (asymptomatic); and IgG-positive with history of symptomatic COVID-19 (symptomatic) > Participants were vaccinated with Pfizer-BioNTech or Moderna **Findings:** > 59 volunteers enrolled: 17 in the Ab-negative, 16 in the asymptomatic, and 26 in the symptomatic group > At 0, 7, and 14 days, median reciprocal half-maximal binding titers were higher in each of the asymptomatic (208, 29 364, and 34 033) and symptomatic (302, 32 301, and 35 460) groups compared with the Ab-negative group (<50, <50, and 924) ($P < .001$ for each). > At 0 and 14 days, median reciprocal ID99 virus neutralization titers of each of the asymptomatic (80 and 40 960) and symptomatic (320 and 40 960) groups were higher than the Ab-negative group (<20 and 80) ($P < .001$ for each) **Conclusions:** Health care workers with previous COVID-19 infection (laboratory-confirmed serology testing) had higher antibody titer responses to a single dose of mRNA vaccine than those not previously infected.

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Nature Commun. 26FEB2021	**Association between antecedent statin use and decreased mortality in hospitalized patients with COVID-19**	Gupta A., *et al*. USA gotopaper	Therapeutics	**Background:** > Statins are known to have anti-inflammatory and antithrombotic properties but their benefit has not been assessed in COVID-19. **Methods:** > Retrospective analysis of patients admitted with COVID-19 from February 1st through May 12th, 2020 with study period ending on June 11th, 2020. > Antecedent of statin use > Multivariable logistic regression model to predict the propensity of receiving statins, adjusting for baseline sociodemographic and clinical characteristics, and outpatient medications. > The primary endpoint includes in-hospital mortality within 30 days. **Findings:** > 2626 patients enroled, of whom 951 (36.2%) were antecedent statin users. > Among 1296 patients (648 statin users, 648 non-statin users) identified with 1:1 propensity-score matching, statin use is **significantly associated with lower odds of the primary endpoint** in the propensity-matched cohort (OR 0.47, 95% CI 0.36–0.62, *p* < 0.001). **Conclusion:** Antecedent statin use in patients hospitalized with COVID-19 is associated with lower inpatient mortality.
Nature 26FEB2021	**SARS-CoV-2 spike D614G change enhances replication and transmission**	Zhou B., *et al*. International gotopaper	Virology	**Aim**: to understand if the S-614G has represents a fitness advantage that improves replication and/or transmission in humans. The S-614G variant: > has **enhanced binding** to human host cell surface receptor ACE2 > has **increased replication** in primary human bronchial and nasal airway epithelial cultures and in a human ACE2 knock-in mouse model > has markedly **increased replication and transmissibility** in hamster and ferret models of SARS-CoV-2 infection. The S-614G substitution results in subtle increases in binding and replication in vitro, and it provides a real competitive advantage in vivo, particularly during the transmission bottle neck.
Clin Infect Dis. 24FEB2021	**Persistence of antibodies to SARS-CoV-2 in relation to symptoms in a nationwide prospective study**	den Hartog G., *et al.* Netherlands gotopaper	Immunology	Study change in Immunoglobulin (Ig) isotype seropositivity and IgG binding strength of SARS-CoV-2-specific serum antibodies up to 7 months following onset of symptoms in a nationwide sample **Methods** > prospective representative serological study were included based on IgG seroconversion to the Spike S1 protein of SARS-CoV-2 (N=353) with up to three consecutive serum samples per seroconverted participant (N=738) **Findings** > While SARS-CoV-2-specific IgM and IgA antibodies declined rapidly after the first month post onset of disease, specific IgG was still present in 92% (95% confidence interval, CI, 89-95) of the participants after 7 months. > The estimated 2-fold decrease of IgG antibodies was 158 days (95% CI 136-189). > Concentrations sustained better in persons reporting significant symptoms compared to asymptomatic persons or those with mild upper respiratory complaints only. > Similarly, avidity of IgG antibodies for symptomatic persons showed a steeper increase over time compared with persons with mild or no symptoms (p=0.022). **IgG antibodies sustain in 92% of the participants after 7 months post onset of symptoms whereas IgM and IgA antibodies wane. Concentrations are higher in symptomatic persons and avidity increases with time.** **SARS-CoV-2-specific IgG antibodies persist and show increasing avidity over time, indicative of underlying immune maturation. These data support development of immune memory against SARS-CoV-2 providing insight into protection of the general unvaccinated part of the population.**

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JAMA 24FEB2021	**Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19**	Feldstein F.R., *et al*. UK [gotopaper](#)	Clinics	**Aim:** To compare clinical characteristics and outcomes of children and adolescents with multisystem inflammatory syndrome in children (MIS-C) vs those with severe COVID-19 **Methods:** Case series of 1116 patients aged younger than 21 years hospitalized between March 15 and October 31, 2020, at 66 US hospitals in 31 states. **Findings:** >Of 1116 patients (median age, 9.7 years; 45% female), 539 (48%) were diagnosed with MIS-C and 577 (52%) with COVID-19. >Compared with patients with COVID-19, patients with MIS-C were more likely to be 6 to 12 years old (40.8% vs 19.4%; absolute risk difference [RD], 21.4%; adjusted risk ratios [aRR], 1.51vs 0-5 years) and non-Hispanic Black (32.3% vs 21.5%; RD, 10.8%; aRR, 1.43 vs White). >Patients with MIS-C had higher neutrophil to lymphocyte ratio (median, 6.4 vs 2.7), higher C-reactive protein level (median, 152 mg/L vs 33 mg/L), and lower platelet count (<150 ×103 cells/µL [212/523 {41%} vs 84/486 {17%}]). >A total of 398 patients (73.8%) with MIS-C and 253 (43.8%) with COVID-19 were admitted to the intensive care unit, and 10 (1.9%) with MIS-C and 8 (1.4%) with COVID-19 died during hospitalization. >Among patients with MIS-C with reduced left ventricular systolic function (34.2%) and coronary artery aneurysm (13.4%), an estimated 91.0% and 79.1%, respectively, normalized within 30 days.
JAMA Intern Med. 24FEB2021	**Association of SARS-CoV-2 Seropositive Antibody Test With Risk of Future Infection**	Harvey R.A., *et al*. UK [gotopaper](#)	Diagnostics	**Aim:** to evaluate evidence of SARS-CoV-2 infection based on diagnostic nucleic acid amplification test (NAAT) among patients with positive vs negative test results for antibodies in an observational descriptive cohort study of clinical laboratory and linked claims data. **Methods:** The study created cohorts from a deidentified data set composed of commercial laboratory tests, medical and pharmacy claims, electronic health records, and hospital chargemaster data. The cohort included 3 257 478 unique patients. **Findings:** From 3 257 478 unique patients with an index antibody test; 56% were female with a median (SD) age of 48 (20) years. Of these, 2 876 773 (88.3%) had a negative index antibody result, and 378 606 (11.6%) had a positive index antibody result. >Patients with a negative antibody test result were older than those with a positive result (mean age 48 vs 44 years). >Of index-positive patients, 18.4% converted to seronegative over the follow-up period. >During the follow-up periods, the ratio of positive NAAT results among individuals who had a positive antibody test at index vs those with a negative antibody test at index was 2.85 at 0 to 30 days, 0.67 at 31 to 60 days, 0.29 at 61 to 90 days, and 0.10 at more than 90 days. **Patients with positive antibody test results were initially more likely to have positive NAAT results, consistent with prolonged RNA shedding, but became markedly less likely to have positive NAAT results over time, suggesting that seropositivity is associated with protection from infection.**

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NEJM 24FEB2021	**BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting**	Dagan N., *et al.* Israel gotopaper	Vaccines	Evaluation of the effectiveness of the BNT162b2 mRNA vaccine based on data from Israel's largest health care organization.
				
				Findings
				> Each study group (vaccinated and control) included 596,618 persons.
				> Estimated vaccine effectiveness for the study outcomes at days 14-20 after the first dose and at ≥7 days after the second dose was as follows:
				  - for documented infection, 46% (95% confidence interval [CI], 40 to 51) and 92% (95% CI, 88 to 95);
				  - for symptomatic Covid-19, 57% (95% CI, 50 to 63) and 94% (95% CI, 87 to 98);
				  - for hospitalization, 74% (95% CI, 56 to 86) and 87% (95% CI, 55 to 100);
				  - for severe disease, 62% (95% CI, 39 to 80) and 92% (95% CI, 75 to 100).
				> Estimated effectiveness in preventing death from Covid-19 was 72% (95% CI, 19 to 100) for days 14-20 after the first dose.
				> Estimated effectiveness in specific subpopulations assessed for documented infection and symptomatic Covid-19 was consistent across age groups, with potentially slightly lower effectiveness in persons with multiple coexisting conditions.
				
				BNT162b2 mRNA vaccine is effective for a wide range of Covid-19–related outcomes, a finding consistent with that of the randomized trial.

Clin Infect Dis. 24FEB2021	**Persistence of antibodies to SARS-CoV-2 in relation to symptoms in a nationwide prospective study**	den Hartog G., *et al*. Netherlands gotopaper	Public Health / Epidemiology	**Aim:** to study changes in Immunoglobulin (Ig) isotype seropositivity and IgG binding strength of SARS-CoV-2-specific serum antibodies up to 7 months following onset of symptoms in a nationwide sample. **Methods:** prospective representative serological study in the Netherlands were included based on IgG seroconversion to the Spike S1 protein of SARS-CoV-2 (N=353), with up to three consecutive serum samples per seroconverted participant (N=738). IgM, IgA and IgG antibody concentrations to S1, and increase in IgG were determined. **Findings:** > While SARS-CoV-2-specific IgM and IgA Abs declined rapidly after the first month post onset of disease, specific IgG was still present in 92% of the participants after 7 months. >The estimated 2-fold decrease of IgG antibodies was 158 days. >Concentrations sustained better in persons reporting significant symptoms compared to asymptomatic persons or those with mild upper respiratory complaints only. >**SARS-CoV-2-specific IgG antibodies persist and show increasing avidity over time, indicative of underlying immune maturation.**
Cell 23FEB2021	**Extremely potent human monoclonal antibodies from COVID-19 convalescent patients**	Andreano E., *et al.* Italy gotopaper	Therapeutics	> **453 neutralizing antibodies** were identified by single cell sorting 4,277 SARS-CoV-2 spike protein specific memory B cells from 14 COVID-19 survivors. > The most potent neutralizing antibodies recognized the s**pike protein receptor binding domain**, followed in potency by antibodies recognizing the **S1 domain**, the s**pike protein trimer** and the **S2 subunit**. > Only 1.4% of the antibodies neutralized the authentic virus with a **potency of 1-10 ng/mL**. > The most potent monoclonal antibody, engineered to reduce the risk of antibody dependent enhancement and prolong half-life, **neutralized the authentic wild type virus and emerging variants containing D614G, E484K and N501Y** substitutions. > Prophylactic and therapeutic efficacy in the hamster model was observed at **0.25 and 4 mg/kg** respectively in absence of Fc-functions.

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Cell 23FEB2021	**No higher infectivity but immune escape of SARS-CoV-2 501Y.V2 variants**	Li Q., *et al.* China [gotopaper]	Variants	> Experiments with 18 pseudotyped viruses showed that the **501Y.V2 variants do not confer increased infectivity** in multiple cell types **except for murine ACE2-overexpressing cells**, where a substantial increase in infectivity was observed. > The susceptibility of the 501Y.V2 variants to 12 of 17 neutralizing monoclonal antibodies **was substantially diminished**. > Neutralization ability of the sera from convalescent patients and immunized mice was also **reduced for these variants**. > The neutralization resistance was mainly caused by **E484K and N501Y mutations** in the receptor-binding domain of Spike. > The enhanced infectivity in murine ACE2-overexpressing cells suggests the **possibility of spillover of the 501Y.V2 variants to mice**. > The neutralization resistance detected for the 501Y.V2 variants suggests the **potential for compromised efficacy** of monoclonal antibodies and vaccines.
Cell 23FEB2021	**Evidence of escape of SARS-CoV-2 variant B.1.351 from natural and vaccine induced sera**	Zhou D., *et al.* UK [gotopaper]	Variants	**Aim:** to describe a structure-function analysis of B.1.351 using a large cohort of convalescent and vaccinee serum samples. **Methods:** Neutralization of a B.1.351 viral isolate and compare it to 127 neutralization of Victoria, an early Wuhan related isolate. Neutralization assays were performed on a large panel of monoclonal Abs convalescent sera from early in the pandemic, sera from patients suffering from B.1.1.7 and finally from 130 recipients of the Oxford-AstraZenca and Pfizer-BioNTech vaccines. **Findings:** >The receptor binding domain mutations provide tighter ACE2 binding and widespread escape from monoclonal Ab neutralization largely driven by E484K although K417N and N501Y act together against some important antibody classes. >In a number of cases it would appear that convalescent and some vaccine serum offers limited protection against this variant. >Neutralization of B.1.351 by sera from naturally infected or vaccinated individuals is significantly reduced, leading in some cases to a complete inability to neutralize B.1.351 virus.
Lancet Infect Dis. 23FEB2021	**Identification and validation of clinical phenotypes with prognostic implications in patients admitted to hospital with COVID-19: a multicentre cohort study**	Gutiérrez-Gutiérrez B., *et al.* Spain [gotopaper]	Clinics	**Aim:** to determine whether clinical phenotypes of patients with COVID-19 can be derived from clinical data, to assess the reproducibility of these phenotypes and correlation with prognosis, and to derive and validate a simplified probabilistic model for phenotype assignment. **Methods:** data from two cohorts: the COVID-19@Spain cohort, a retrospective cohort including 4035 consecutive adult patients admitted to 127 hospitals in Spain, and the COVID-19@HULP cohort, including 2226 consecutive adult patients admitted to a teaching hospital in Madrid. The authors developed a simplified probabilistic model for phenotype assignment, including 16 variables. **Findings:** >Three distinct phenotypes were derived in the derivation cohort: A: Younger patients with, less frequently male, had mild viral symptoms, and had normal inflammatory parameters (516 [19%] patients). B: patients with obesity, lymphocytopenia, and moderately elevated inflammatory parameters (1955 [73%]). C : older patients with more comorbidities and even higher inflammatory parameters than phenotype B (116 [8%]). >30-day mortality rates were 2·5% for A patients, 30·5% for B patients and 60·7% for C patients. >The predicted phenotypes in the internal validation cohort and external validation cohort showed similar mortality rates to the assigned phenotypes (internal validation cohort: 5·3% for phen A, 31·3% for phen B, and 59·5% for phen C; external validation cohort: 3·7% for phen A, 23·7% for phen B, and 51·4% for phenotype C).

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Lancet 19FEB2021	**Single-dose administration and the influence of the timing of the booster dose on immunogenicity and efficacy of ChAdOx1 nCoV-19 (AZD1222) vaccine: a pooled analysis of four randomised trials**	Voysey M., *et al*. UK [gotopaper]	Vaccines	- Prespecified pooled analysis of trials of **ChAdOx1 nCoV-19** (Single blinded: one phase 1/2, UK; one phase 2/3, UK; one phase 3, Brazil. Double-blinded: one phase 1/2 , South Africa) - Exploratory analyses of the impact on immunogenicity and efficacy of extending the interval between priming and booster doses. - Immunogenicity and protection afforded by the first dose, before a booster dose has been offered. **FINDINGS** > 24 422 participants across the four studies (Apr 23-Dec 6, 2020), 17 178 included in the primary analysis (8597 receiving ChAdOx1 nCoV-19, 8581 receiving control vaccine). **332 NAAT-positive infections** met the primary endpoint of symptomatic infection >14 days after the second dose. > Overall **vaccine efficacy >14 days after the second dose was 66·7%** (95% CI 57·4–74·0), with 84/8597 (1·0%) cases in the ChAdOx1 nCoV-19 group and 248/8581 (2·9%) in the control group. > There were **no hospital admissions for COVID-19 in the ChAdOx1 nCoV-19 group** after the initial 21-day exclusion period, and 15 in the control group. > 108/12 282 (0·9%) participants in the ChAdOx1 nCoV-19 group and 127/11 962 (1·1%) in the control group had **serious adverse events**. There were 7 deaths considered unrelated to vaccination (2 in the ChAdOx1 nCov-19 group and 5 in the control group), including one COVID-19-related death in one participant in the control group. > Exploratory analyses showed that **vaccine efficacy after a single standard dose from day 22 to day 90 after vaccination was 76·0%** (59·3–85·9). Modelling analysis indicated that protection did not wane during this initial 3-month period. > Antibody levels were maintained during this period with **minimal waning by day 90** (geometric mean ratio [GMR] 0·66 [95% CI 0·59–0·74]). > In the participants who received two standard doses, after the second dose, **efficacy was higher in those with a longer prime-boost interval** (**vaccine efficacy 81·3%** [95% CI 60·3–91·2] at ≥12 weeks) than in those with a short interval (vaccine efficacy 55·1% [33·0–69·9] at <6 weeks). > Immunogenicity: **binding antibody responses >2-fold higher after an interval of ≥12 or more weeks** compared with an interval of <6 weeks in those who were aged 18–55 years (GMR 2·32 [2·01–2·68]). The results of this primary analysis of two doses of ChAdOx1 nCoV-19 were **consistent with those seen in the interim analysis** of the trials and confirm that the vaccine is efficacious, with results varying by dose interval. **A 3-month dose interval might have advantages over a programme with a short dose interval**.

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Lancet 18FEB2021	**Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients**	Amit S., *et al*. Israel gotopaper	Vaccines	**Aim:** to examine early reductions in SARS-CoV-2 infection and COVID-19 rates in vaccinated HCWs. **Methods:** retrospective cohort of 9109 vaccine-eligible HCWs, comparing vaccinated versus unvaccinated. **Findings:** > there were 170 SARS-CoV-2 infections among HCWs in the period between Dec 19, 2020, and Jan 24, 2021, of which 99 (58%) HCWs reported symptoms. Of the 170 HCWs who became infected, 89 (52%) were unvaccinated, 78 (46%) tested positive after the first dose, and 3 (2%) tested positive after the second dose. >Among the 125 infections that could be traced, 87 (70%) were community acquired and there were no nosocomial clusters. >Compared with a SARS-CoV-2 infection rate of 7·4 per 10 000 person-days in unvaccinated HCWs, infection rates were 5·5 per 10 000 person-days and 3·0 per 10 000 person-days on days 1–14 and 15-28 after the first dose of the vaccine, respectively. >Adjusted rate reductions of SARS-CoV-2 infections were 30% (95% CI 2–50) and 75% (72–84) for days 1–14 and days 15–28 after the first dose, respectively >**Data show substantial early reductions in SARS-CoV-2 infection and symptomatic COVID-19 rates following first vaccine dose administration.**
Clin Infect Dis. 18FEB2021	**Clinical and Laboratory Findings in Patients with Potential SARS-CoV-2 Reinfection, May–July 2020**	Lee JT., *et al*. USA gotopaper	Clinics	**Aim:** to investigate patients with potential SARS-CoV-2 reinfection in the United States during May–July 2020 **Methods:** Cases reported were screened for laboratory and clinical findings of potential reinfection followed by requests for medical records and laboratory specimens. **Findings:** > Among 73 potential reinfection patients with available records, **30 patients had recurrent COVID-19 symptoms** explained by alternative diagnoses with concurrent SARS-CoV-2 positive RT-PCR. >24 patients remained asymptomatic after recovery but had **recurrent or persistent RT-PCR.** >19 patients had recurrent COVID-19 symptoms with concurrent SARS-CoV-2 positive RT-PCR but no alternative diagnoses. These 19 patients had symptom recurrence a median of **57 days after initial symptom onset.** >Six of these patients had paired specimens available for further testing, but none had laboratory findings confirming reinfections. >No confirmation of SARS-CoV-2 reinfection **within 90 days** of the initial infection based on the clinical and laboratory characteristics of cases in this investigation.
Cell 18FEB2021	**Reduced neutralization of SARS-CoV-2 B.1.1.7 variant by convalescent and vaccine sera**	Supasa P., *et al*. UK gotopaper	Variants	Analysis of the ability of B.1.1.7 to evade antibody responses elicited by natural SARS-CoV-2 infection or vaccination, by mapping the impact of N501Y by structure/function analysis of a large panel of well-characterised monoclonal antibodies. > B.1.1.7 is harder to neutralize than parental virus, compromising neutralization by some members of a major class of public antibodies through light chain contacts with residue 501. > Original strain convalescent and vaccine sera show **reduced B.1.1.7 neutralization** > **N501Y enhances RBD: ACE2 binding affinity 7-fold** > **N501Y compromises neutralisation** by many antibodies with public V-region IGHV3-53 > **Widespread escape** from monoclonal antibodies or antibody responses generated by natural infection or vaccination was not observed.

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Nature Commun. 18FEB2021	**Interleukin-3 is a predictive marker for severity and outcome during SARS-CoV-2 infections**	Bénard A., *et al*. Germany gotopaper	Clinics	**Aim:** To identify IL-3 as an independent prognostic marker for the outcome during SARS-CoV-2 infections **Methods:** prospective multicentric study. In total, 105 (32 non-severe; 32 severe; 41 recovered) patients positive for SARS-CoV-2 PCR from oral swabs, oral fluid, or BALF were enrolled. Blood samples were collected at the onset of symptoms (≤24 h), and 1, 2, 3, 4, 5, 6, or 7 days later; or after recovery from SARS-CoV-2 infection (time of recovery = 16 days ± 2 days). - A mouse model of pulmonary HSV-1 infection was used to characterize theIL-3 mechanism **Findings:** >Patients with severe COVID-19 exhibit reduced circulating plasmacytoid dendritic cells (pDCs) and low plasma IFNα and IFNλ levels when compared to non-severe COVID-19 patients. >In a mouse model of pulmonary HSV-1 infection, treatment with recombinant IL-3 reduces viral load and mortality. Mechanistically, IL-3 increases innate antiviral immunity by promoting the recruitment of circulating pDCs into the airways by stimulating CXCL12 secretion from pulmonary CD123+ epithelial cells. **>Low plasma IL-3 levels are associated with increased severity, viral load, and mortality during SARS-CoV-2 infections.** **IL-3 might be a predictive disease marker for SARS-CoV-2 infections and recombinant IL-3, or CD123 receptor agonists, may therefore have the potential as novel therapeutic agents in SARS-CoV-2 infected patients.**
NEJM 17FEB2021	**Neutralizing Activity of BNT162b2-Elicited Serum — Preliminary Report**	Liu Y., *et al*. USA gotopaper	Vaccines - variants	Pseudoviruses of D614G substitution, B.1.351-RBD+D614G (K417N, E484K, N501Y mutations and D614G substitution), and B.1.351-spike (all the mutation of the S gene found in B.1.351) were tested against sera from BNT162b2-vaccinated individuals. > All the 20 serum samples neutralized USA-WA1/2020 (pseudovirus wild-type) and all mutant viruses **at titers of 1:40 or greater**. > As compared with neutralization of USA-WA1/2020, neutralization of Δ242-244+D614G virus was similar and **neutralization of the B.1.351-spike virus was weaker by approximately two thirds**. > Results suggest that virus with mutant residues in the receptor-binding site (K417N, E484K, and N501Y) is more poorly neutralized than virus with Δ242-244, located in the N-terminal domain of the spike protein. It is unclear what effect a reduction in neutralization would have on BNT162b2-elicited protection from Covid-19 caused by the B.1.351 lineage.
NEJM 17FEB2021	**Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine — Preliminary Report**	Wu K., *et al*. USA gotopaper	Vaccines - variants	Pseudoviruses bearing the Wuhan-Hu-1 strain, the D614G substitution, the B.1.1.7 and B.1.351 variants and others were tested against sera from mRNA-1273-vaccinated individuals. > Both the full panel of mutations in S and a subset of mutations affecting the receptor-binding domain (RBD) region of the B.1.1.7 variant had n**o significant effect on neutralization**. > A **decrease in titers of neutralizing antibodies against the B.1.351 variant** and a subset of its mutations affecting the RBD was observed. > In serum samples obtained 1 week after the participants received the second dose of vaccine, we detected **reductions by a factor of 2.7 in titers of neutralizing antibodies** against the partial panel of mutations and **by a factor of 6.4** against the full panel of mutations. > Levels of neutralization against the other tested variants that were similar to those against the Wuhan-Hu-1 (D614) isolate. Protection against the B.1.351 variant conferred by the mRNA-1273 vaccine remains to be determined.

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NEJM 18FEB2021	**Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults**	Libster R., *et al.* Argentina gotopaper	Therapeutics	Randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against SARS-CoV-2 in older adult patients within 72 hours after the onset of mild Covid-19 symptoms. Primary end point: severe respiratory disease, defined as a respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both. *The trial was stopped early at 76% of its projected sample size because cases of Covid-19 in the trial region decreased considerably*. **Findings** > A total of 160 patients underwent randomization > In the intention-to-treat population, **severe respiratory disease** developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo (relative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; P=0.03), with a relative risk reduction of 48%. > A modified intention-to-treat analysis that excluded 6 patients who had a primary end-point event before infusion of convalescent plasma or placebo **showed a larger effect size** (relative risk, 0.40; 95% CI, 0.20 to 0.81). > **No solicited adverse events** were observed. **Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19**.
NEJM 18FEB2021	**A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia**	Simonovich V.A., *et al.* Argentina gotopaper	Therapeutics	**Aim**: to gather further evidence of whether convalescent plasma improves clinical outcomes. Randomized trial on hospitalized adult patients with severe Covid-19 pneumonia in a 2:1 ratio to receive convalescent plasma or placebo. Primary outcome: the patient's clinical status 30 days after the intervention, as measured on a six-point ordinal scale ranging from total recovery to death. **Findings** > A total of 228 patients were assigned to receive convalescent plasma and 105 to receive placebo. Median time from the onset of symptoms to enrollment in the trial was 8 days, hypoxemia was the most frequent severity criterion for enrollment. > The infused convalescent plasma had a **median titer of 1:3200 of total SARS-CoV-2 antibodies** (interquartile range, 1:800 to 1:3200). No patients were lost to follow-up. > At day 30 day, **no significant difference** was noted between the convalescent plasma group and the placebo group in the distribution of clinical outcomes according to the ordinal scale (odds ratio, 0.83; 95% confidence interval [CI], 0.52 to 1.35; P=0.46). > Overall mortality was **10.96% in the convalescent plasma group** and **11.43% in the placebo group**, for a risk difference of −0.46 percentage points (95% CI, −7.8 to 6.8). > Total SARS-CoV-2 antibody titers tended to be **higher in the convalescent plasma group** at day 2 after the intervention. > Adverse events and serious adverse events were similar in the two groups. **No significant differences were observed in clinical status or overall mortality between patients treated with convalescent plasma and those who received placebo.**

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Nature Commun. 16FEB2021	**Modelling safe protocols for reopening schools during the COVID-19 pandemic in France**	Di Domenico L., *et al.* France [gotopaper](#)	Public Health / Epidemiology	**Aim**: to explored scenarios of partial, progressive, or full school reopening, through a stochastic age-structured transmission model. > Under a scenario with stable epidemic activity if schools were closed, reopening pre-schools and primary schools would lead to **up to 76% [67, 84]% occupation of ICU beds** if no other school level reopened, or if middle and high schools reopened later. > Immediately reopening all school levels may **overwhelm the ICU system**. Priority should be given to pre- and primary schools allowing younger children to resume learning and development. Full attendance in middle and high schools is not recommended for stable or increasing epidemic activity. > Large-scale **test and trace** is required for epidemic control.
Lancet Respir Med. 15FEB2021	**Patient factors and temporal trends associated with COVID-19 in-hospital mortality in England: an observational study using administrative data**	Annakan N., *et al.* UK [gotopaper](#)	Public Health / Epidemiology	Comprehensive account of all hospitalised patients with COVID-19 in England during the early phase of the pandemic and to identify the factors that influenced mortality as the pandemic evolved > Retrospective exploratory analysis using the Hospital Episode Statistics administrative dataset (between March 1 and May 31, 2020) > Multilevel logistic regression was used to model the **relationship between death and** several covariates: **age, sex, deprivation** (Index of Multiple Deprivation), **ethnicity**, **frailty** (Hospital Frailty Risk Score), presence of **comorbidities** (Charlson Comorbidity Index items), and **date of discharge** (whether alive or deceased) **Findings:** > 91 541 adult patients with COVID-19 were discharged during the study period, among which 28 200 (30·8%) in-hospital deaths occurred > Significant predictors of in-hospital death included **older age**, **male sex** (1·457 [1·408–1·509]), **greater deprivation** (1·002 [1·001–1·003]), **Asian** (1·211 [1·128–1·299]) or **mixed ethnicity** (1·317 [1·080–1·605]; vs White ethnicity), and most of the **assessed comorbidities, including moderate or severe liver disease** (5·433 [4·618–6·392]). > Later date of discharge was associated with a lower odds of death (0·977 [0·976–0·978]); adjusted **in-hospital mortality improved significantly in a broadly linear fashion, from 52·2% in the first week of March to 16·8% in the last week of May => might reflect the impact of changes in hospital strategy and clinical processes** **Conclusion:** > **The reasons for the observed <u>improvements in mortality</u> should be thoroughly investigated to inform the response to future outbreaks.** > **The higher mortality rate reported for certain <u>ethnic minority groups</u> in community-based studies compared with our hospital-based analysis might partly reflect differential infection rates in those at greatest risk, propensity to become severely ill once infected, and health-seeking behaviours.**
Pediatrics 12FEB2021	**Factors Associated With Severe SARS-CoV-2 Infection**	Ouldali N., *et al.* France [gotopaper](#)	Clincs	**Aim**: to analyze the clinical spectrum of hospitalized pediatric SARS-CoV-2 infection and predictors of severe disease evolution. <u>Main outcome</u>: proportion of children with severe disease, defined by hemodynamic or ventilatory (invasive or not) support requirement. > 397 hospitalized children with SARS-CoV-2 infection, with several clinical patterns (paucisymptomatic children, admitted for surveillance, lower respiratory tract infection or multisystem inflammatory syndrome). > Children <90 days old accounted for **37% of cases** (145 of 397), but only 4 (3%) had severe disease. > Excluding children with multisystem inflammatory syndrome in children (n = 29) and hospitalized for a diagnosis not related to SARS-CoV-2 (n = 62), 23 of 306 **(11%) children had severe disease**, including 6 deaths. > **Factors independently associated** with severity were age ≥10 years (odds ratio [OR] = 3.4), hypoxemia (OR = 8.9), C-reactive protein level ≥80 mg/L (OR = 6.6). Young age was not an independent factor associated with severe SARS-CoV-2 infection, and children <90 days old were at the lowest risk of severe disease evolution.

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Nature Med. 12FEB2021	**Humoral signatures of protective and pathological SARS-CoV-2 infection in children**	Bartsch Y.C., *et al.* USA [gotopaper]	Immunology	**Aim**: identifying immune mechanisms that result in disparate clinical phenotypes in children (largely asymptomatic disease, with rare reports of multisystem inflammatory syndrome in children (MIS-C)). > Using systems serology, in 25 children with acute mild COVID-19 we observed a **functional phagocyte and complement-activating IgG response** to SARS-CoV-2, similar to the acute responses generated in adults with mild disease. Conversely, IgA and neutrophil responses were significantly expanded in adults with severe disease. > Weeks after the resolution of SARS-CoV-2 infection, **children who develop MIS-C maintained highly inflammatory monocyte-activating SARS-CoV-2 IgG antibodies**, distinguishable from acute disease in children but with antibody levels similar to those in convalescent adults. These data provide insights into the potential mechanisms of IgG and IgA that might underlie differential disease severity in children infected with SARS-CoV-2
Cell 12FEB2021	**Human neutralizing antibodies against SARS-CoV-2 require intact Fc effector functions for optimal therapeutic protection**	Winkler ES., *et al.* USA [gotopaper]	Immunology	**Aim:** to define correlates of protection of neutralizing human monoclonal antibodies (mAbs) in SARS-CoV-2-infected animals. **Methods:** A K18-hACE2 transgenic mouse model of SARS-CoV-2 pathogenesis and a Fc region genetic variant form of IgG (LALA-73 PG) of a potent RBD-binding neutralizing mAb that cannot engage FcγRs or complement were used to define the role of Fc effector functions in antibody protection. **Findigs:** >Fc effector functions are dispensable when neutralizing mAbs are administered as prophylaxis, but are required for optimal protection when given as post-exposure therapy. >When administered after SARS-CoV-2 infection, intact but not LALA-PG mAbs reduce viral burden and lung disease. Fc engagement by Abs decreases immune cell activation and levels of inflammatory cytokines >Neutralizing mAbs require monocytes and CD8+ T cells for maximal clinical and virological benefit. In hamsters, Fc effector functions of a neutralizing mAb are required to prevent weight loss, control viral infection, and limit inflammation. >**Fc effector functions of neutralizing antibodies are necessary for optimal therapeutic outcome after SARS-CoV-2 infection**
BMJ 11FEB2021	**Early initiation of prophylactic anticoagulation for prevention of coronavirus disease 2019 mortality in patients admitted to hospital in the United States: cohort study**	Rentsch CT., *et al.* UK/USA [gotopaper]	Therapeutics	**Aim:** To evaluate whether early initiation of prophylactic anticoagulation compared with no anticoagulation was associated with decreased risk of death among COVID-19 patients admitted to hospital in USA **Methods:** Observational cohort study including 4297 patients admitted to hospital from 1 March to 31 July 2020 >Main outcome : 30 day mortality > Secondary outcomes: inpatient mortality, initiating therapeutic anticoagulation (a proxy for clinical deterioration, including thromboembolic events), and bleeding that required transfusion. **Findigs:** **>** From 4297 patients**, 3627 (84.4%) received prophylactic anticoagulation within 24 hours of admission. More than 99% (n=3600) of treated patients received subcutaneous heparin or enoxaparin >622 deaths occurred within 30 days of hospital admission, 513 among those who received prophylactic anticoagulation. >The cumulative incidence of mortality at 30 days was 14.3% among those who received prophylactic anticoagulation and 18.7% among those who did not. >Compared with patients who did not receive prophylactic anticoagulation, those who did had a 27% decreased risk for 30 day mortality (hazard ratio 0.73). >**Receipt of prophylactic anticoagulation was not associated with increased risk of bleeding that required transfusion.** **Early initiation of prophylactic anticoagulation compared with no anticoagulation among COVID-19 patients admitted to hospital was associated with a decreased risk of 30 day mortality**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Euro Surveill. 11FEB2021	**Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021**	Jabal KA., *et al.* Israel gotopaper	Vaccine	**Description of one dose immunogenicity of BNT162b2 vaccine in various age and ethnic groups** **Background:** > As at 25 January 2021, Israel had vaccinated 29.2% of its population with a single dose of vaccine (almost exclusively BNT162b2 mRNA from Pfizer/BioNTech) > Ziv Medical Center (ZMC), located in Safed, Israel, is a 350-bed hospital, staffed by a multi-ethnic workforce of ca 1,500 persons including Jews, Arabs and Druze among others. ZMC has offered the BNT162b2 mRNA-based vaccine to all its staff, including administrative and support staff , with no specific exclusion for pregnant women. As at 21 January 2021, one-dose uptake was ca 90%. **Findings:** > 519 participanst to the study (19-77 years of age). IgGs levels measured at 21d > 475 (92%) had detectable anti-SARS-CoV-2 IgG. Among these, GMC was 68.6 AU/mL (95% CI: 64–73.6). No differneces between ethnicity or sexe. Titres decreasing with age. > 39 non respondant: median age older than responsant (57 vs 45) and more likely to be Jewish (31/38 non-responders of known ethnicity, 82% vs 291/459 responders of known ethnicity; 63%) >IgGs level postvaccination were higher among those with previous evidence of infection (at least one order of magnitude regarldess the titeer before vaccination) (GMC 573 vs 61.5) **Conclusion:** age and ethnicity (but not sex) may be associated with the likelihood of non-response (findings based on 39 observations).
PNAS 09FEB2021	**Exhaled aerosol increases with COVID-19 infection, age, and obesity**	Edwards D., *et al.* USA gotopaper	Public Health / Epidemiology	> **Respiratory droplet generation and exhalation inhuman and nonhuman primate subjects** with and without COVID-19 infection to explore whether SARS-CoV-2 infection, and other changes in physiological state, translate into observable evolution of numbers and sizes of exhaled respiratory droplets in healthy and diseased subject **Method** > Observational cohort study of the exhaled breath particles of 194 healthy human subjects > Experimental infection study of 8 nonhuman primates infected, by aerosol, with SARS-CoV-2 **Findings** > Exhaled aerosol particles **vary between subjects by three orders of magnitude,with exhaled respiratory droplet number increasing with degree of COVID-19 infection and elevated BMI-years** > 18% of human subjects (35) accounted for 80% of the exhaled bioaerosol of the group (194), reflecting a superspreader distribution of bioaerosol analogous to a classical 20:80 superspreader of infection distribution > The capacity of airway lining mucus to resist breakup on breathing varies significantly between individuals with a trend to increasing with the advance of COVID-19 in-fection and body mass index multiplied by age (i.e., BMI-years) **Conclusion** > Our studies of exhaled aerosol suggest that a critical factor in these and other transmission events is the propensity of certain individuals to **exhale large numbers of small respiratory droplets.** > **Understanding the source and variance of respiratory droplet generation, and controlling it via the stabilization of airway lining mucus surfaces, may lead to effective approaches to reducing COVID-19 infection and transmission** > **These findings suggest that quantitative assessment and control of exhaled aerosol may be critical to slowing the airborne spread of COVID-19 in the absence of an effective and widely disseminated vaccine**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 10FEB2021	**mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants**	Wang Z., *et al*. USA gotopaper	Vaccines	**Antibody and memory B cell responses in volunteers who received either the Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines** **Findings:** 20 volunteer cohort > Eight weeks after the second vaccine injection volunteers showed high levels of IgM, and IgG anti-S and anti-RBD >Plasma neutralizing activity, and the relative numbers of RBD-specific memory B cells were equivalent to individuals who recovered from natural infection > Vaccine-elicited monoclonal antibodies potently neutralize SARS-CoV-2, targeting a number of different RBD epitopes in common with mAbs isolated from infected donors > However, neutralization by 14 of the 17 most potent mAbs tested was reduced or abolished by either K417N, or E484K, or N501Y mutations. >Activity against SARS-CoV-2 variants encoding E484K or N501Y or the K417N:E484K:N501Y combination was reduced by a small but significant margin. > The same mutations were selected when recombinant vesicular stomatitis virus (rVSV)/SARS-CoV-2 S was cultured in the presence of the vaccine elicited mAbs. **Conclusion:** This results suggest that the monoclonal antibodies in clinical use should be tested against newly arising variants, and that mRNA vaccines may need to be updated periodically to avoid potential loss of clinical efficacy.
Nature 09FEB2021	**Lasting antibody and T cell responses to SARS-CoV-2 in COVID-19 patients three months after infection**	Jiang X.L., *et al*. China gotopaper	Immunology	**Aim** : Longitudinal assessment of 25 SARS-CoV-2-infected patients up to 3–4 months post-infection and analysis of the specific antibody and memory T cell responses over time. **Findings :** >All patients seroconvert for IgG against N, S, or RBD, as well as IgM against RBD, and produce neutralising antibodies (NAb) by 14 days post symptoms onset (PSO) with the peak levels attained by 15–30 days PSO. >Anti-SARS-CoV-2 IgG and NAb remain detectable and relatively stable 3–4 months PSO, whereas IgM antibody rapidly decay. >**65% of patients have detectable SARS-CoV-2-specific CD4+ or CD8+ T cell responses 3–4 months PSO T cell responses maintain in most recovered patients for at least 3–4 months after infection** Assessment of the duration and resiliency of the SARS-CoV-2 antibody and T cell responses in a large cohort study would be desirable for validation of the results.
Nature 08FEB2021	**Rapid decline of neutralizing antibodies against SARS-CoV-2 among infected healthcare workers**	Marot S., *et al*. France gotopaper	Immunology	**Persistence of neutralizing antibodies (NAbs) among SARS-CoV-2-infected healthcare workers (HCW).** Follow up of 26 HCW with mild COVID-19 three weeks (D21), two months (M2) and three months (M3) after the onset of symptoms. **Findings:** > All the HCW had anti-receptor binding domain (RBD) IgA at D21, decreasing to 38.5% at M3 ($p < 0.0001$). > Concomitantly a significant decrease in NAb titers was observed between D21 and M2 ($p = 0.03$) and between D21 and M3 ($p < 0.0001$). > SARS-CoV-2 can elicit a NAb response correlated with anti-RBD antibody levels, however neutralizing activity declines, and may even be lost, in association with a decrease in systemic IgA antibody levels, from two months after disease onset. **Conclusions** This short-lasting humoral protection supports strong recommendations to maintain infection prevention and control measures in HCW, and suggests that periodic boosts of SARS-CoV-2 vaccination may be required.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Child Adolesc Health 08FEB2021	**SARS-CoV-2 transmission among children and staff in daycare centres during a nationwide lockdown in France: a cross-sectional, multicentre, seroprevalence study**	Lachassinne E., *et al.* France [gotopaper]	Public Health / Epidemiology	**Aim**: to estimate the seroprevalence of antibodies against SARS-CoV-2 in daycare centres that remained open for key workers' children during a nationwide lockdown in France (March 15 – May 09, 2020). > 327 children enrolled (mean age 1·9 years yrs), 197 daycare centre staff (40 yrs), and 164 adults in the comparator group (42 yrs). > Positive serological tests were observed for 14 children (**raw seroprevalence 4·3%**) and 14 daycare centre staff (**7·7%**). After accounting for imperfect sensitivity and specificity of the assay, we estimated that **3·7%** of the children and **6·8%** of daycare centre staff had SARS-CoV-2 infection. > The comparator group fared **similarly to the daycare centre staff**; 9 participants had a positive serological test (raw seroprevalence 5·5%), leading to a seroprevalence of 5·0% after adjusting. > An exploratory analysis suggested that **seropositive children were more likely than seronegative children to have been exposed to an adult household member with laboratory-confirmed COVID-19** (6/14 [43%] vs 19/307 [6%], relative risk 7.1). The proportion of young children in this sample with SARS-CoV-2 infection was low. **Intrafamily transmission seemed more plausible than transmission within daycare centres**.
Nature Med. 08FEB2021	**Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K and N501Y variants by BNT162b2 vaccine-elicited sera**	Xie X., *et al.* USA [gotopaper]	Immunology	> Examine the effect of several key spike mutations from the UK and SA strains on BNT162b2 vaccine-elicited neutralization. **Methods** > Engineered three SARS-CoV-2 containing key spike mutations from the newly emerged United Kingdom (UK) and South African (SA) variants - Mutant N501Y virus contains the N501Y mutation that is shared by both the UK and SA variants - Mutant Δ69/70 + N501Y +D614G virus contains two additional changes present in the UK variants: amino acid 69 and 70 deletion (Δ69/70) and D614G substitution (D614G mutation is dominant in circulating strains around the world) - Mutant E484K + N501Y +D614G virus addition-ally contains the E484K substitution, which is also located in the viral RBD > Neutralization assays with the same 20 sera samples **Findings** > All sera showed equivalent neutralization titers between the WT and mutant viruses, with differences of four-fold or less > Notably, 10 out of the 20 sera had neutralization titers against mutant Δ69/70 + N501Y + D614G virus that were twice their titers against the WT virus, whereas 6 out of the 20 sera had neutralization titers against mutant E484K + N501Y + D614G virus that were half their titers against the WT virus > The ratios of the neutralization GMTs of the sera against the N501Y, Δ69/70 + N501Y + D614G and E484K + N501Y + D614G viruses to their GMTs against the USA-WA1/2020 virus were 1.46, 1.41 and 0.81, respectively. > **Neutralization geometric mean titers (GMTs) of 20 BTN162b2 vaccine-elicited human sera against the three mutant viruses were 0.81- to 1.46-fold of the GMTs against parental virus, indicating small effects of these mutations on neutralization by sera elicited by two BNT162b2 doses** > **Clinical data are needed for firm conclusions about vaccine effectiveness against variant viruses.**

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Eur J Epidemiol. 06FEB2021	**Evidence of early circulation of SARS-CoV-2 in France: findings from the population-based "CONSTANCES" cohort**	Carrat F., *et al.* France gotopaper	Public Health / Epidemiology	Analysis of serological status for SARS-CoV-2 antibodies on serum samples routinely collected in 9144 adults from a French general population-based cohort (CONSTANCES). > 353 participants with a positive anti-SARS-CoV-2 IgG test were identified, among whom **13 were sampled between November 2019 and January 2020**. > Evidence was confirmed by neutralizing antibodies testing. > Investigations in 11 of these participants revealed experience of **symptoms possibly related to a SARS-CoV-2 infection** or situations at risk of potential SARS-CoV-2 exposure. These results suggest **early circulation of SARS-CoV-2 in Europe**.
Nature 05FEB2021	**SARS-CoV-2 evolution during treatment of chronic infection**	Kemp S.A., *et al.* UK gotopaper	Virology	**Aim**: to report chronic SARS-CoV-2 with reduced sensitivity to neutralising antibodies in an immune suppressed individual treated with convalescent plasma (whole genome ultradeep sequences over 23 time points spanning 101 days). > **Little change** was observed in the overall viral population structure following two courses of remdesivir over the first 57 days. > Following convalescent plasma therapy, **large, dynamic virus population shifts** were observed, with the emergence of a dominant viral strain bearing D796H in S2 and ΔH69/ΔV70 in the S1 N-terminal domain NTD of the Spike protein. > As passively transferred serum antibodies diminished, viruses with the escape genotype **diminished** in frequency, **before returning** during a final, unsuccessful course of convalescent plasma. > In vitro, the Spike escape double mutant bearing ΔH69/ΔV70 and D796H conferred modestly **decreased sensitivity to convalescent plasma**, whilst **maintaining infectivity** similar to wild type. D796H appeared to be the main contributor to decreased susceptibility but incurred an infectivity defect. The ΔH69/ΔV70 single mutant had two-fold higher infectivity compared to wild type, possibly compensating for the reduced infectivity of D796H. These data reveal **strong selection on SARS-CoV-2 during convalescent plasma therapy** associated with emergence of viral variants with evidence of reduced susceptibility to neutralising antibodies.
Nature 05FEB2021	**Efficacy and tolerability of bevacizumab in patients with severe Covid-19**	Pang J., *et al.* China gotopaper	Therapeutics	**Aim:** to evaluate the efficacy of the anti-vascular endothelial growth factor (VEGF) drug bevacizumab for treatment of Covid-19 patients. Single-arm trial (NCT04275414) including 26 patients with severe Covid-19 followed up for 28 days, from 2-centers (China and Italy). Patients received a single dose of bevacizumab **Findings:** >PaO2/FiO2 values markedly increased at days 1 and 7 after bevacizumab administration compared to the baseline values. >24 of 26 patients (92%) showed improvement and 2 patients (8%) showed no change in oxygen-support within 28-day follow-up, 17 (65%) patients are discharged, and none show worsen oxygen-support status nor die >Significant reduction of lesion areas/ratios are shown in chest computed tomography (CT) or X-ray within 7 days. >Of 14 patients with fever, body temperature normalizes within 72 h in 13 (93%) patients. >**Relative to comparable controls, bevacizumab shows clinical efficacy by improving oxygenation and shortening oxygen-support duration**. Bevacizumab plus standard care is highly beneficial for patients with severe Covid-19.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet Respir Med. 05FEB2021	**Peginterferon lambda for the treatment of outpatients with COVID-19: a phase 2, placebo-controlled randomised trial**	Feld J.J., *et al*. Canada [gotopaper](#)	Therapeutics	**Aim** – Test therapeutic effects of **Peginterferon lambda (PGL)**, a type III interferon. Double-blind, placebo-controlled trial, on 60 outpatients with laboratory-confirmed COVID-19 receiving PGL (single subcutaneous injection, 180 µg) or placebo within 7 days of syptoms onset or first positive swab. Primary endpoint: proportion of patients who were negative for SARS-CoV-2 RNA on day 7 after the injection. > The **decline in SARS-CoV-2 RNA was greater** in patients treated with PGL than placebo from day 3 onwards, with a difference of 2·42 log copies per mL at day 7 (p=0·0041). > By day 7, 24 (80%) participants in the PGL group had an **undetectable viral load**, compared with 19 (63%) in the placebo group (p=0·15). > After controlling for baseline viral load, patients in the PGL group were more likely to have **undetectable virus by day 7** than were those in the placebo group (odds ratio [OR] 4·12). > Of those with baseline viral load above 106 copies per mL, 15/19 (79%) in the PGL group had undetectable virus on day 7, compared with 6/16 (38%) in the placebo group (OR 6·25). > PGL was **well tolerated**, and adverse events were similar between groups (mild and transient aminotransferase, concentration increases more frequently observed in the PGL group). **Peginterferon lambda accelerated viral decline in outpatients with COVID-19, increasing the proportion of patients with viral clearance by day 7**, particularly in those with high baseline viral load.
Lancet Public Health 05FEB2021	**COVID-19 vaccine hesitancy in a representative working-age population in France: a survey experiment based on vaccine characteristics**	Schwarzinger M., *et al*. France [gotopaper](#)	Public Health / Epidemiology	Aim: to assess the effects of vaccine characteristics, information on herd immunity, and general practitioner recommendation on vaccine hesitancy in a representative working-age population in France. Online survey in July 2020, adults aged 18–64 years residing in France, with no history of SARS-CoV-2 infection. Responses were analysed with a two-part model to disentangle outright vaccine refusal from vaccine hesitancy. **Findings:** Survey responses were collected from 1942 working-age adults, of whom 560 (28·8%) opted for no vaccination (outright vaccine refusal) and 1382 (71·2%) did not. >Outright vaccine refusal and vaccine hesitancy were both significantly associated with female gender, age, lower educational level, poor compliance with recommended vaccinations in the past, and no report of specified chronic conditions. >Outright vaccine refusal was associated with a lower perceived severity of COVID-19. >Vaccine hesitancy was lower when herd immunity benefits were communicated and in working versus non-working individuals, and those with experience of COVID-19 (Symptoms or close contact). >For a mass vaccination campaign involving mass vaccination centres and communication of herd immunity benefits, the model predicted outright vaccine refusal in 29·4% of the French working-age population. >Predicted hesitancy was highest for vaccines manufactured in China (vaccine acceptance 27·4%), and lowest for a vaccine manufactured in the EU (vaccine acceptance 61·3%).

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Lancet 05FEB2021	**Factors associated with the spatial heterogeneity of the first wave of COVID-19 in France: a nationwide geo-epidemiological study**	Gaudart J., *et al*. France gotopaper	Public Health / Epidemiology	> better understand the factors associated with the heterogeneity of in-hospital COVID-19 morbidity and mortality across France **Methods** > Geo-epidemiological analysis was based on data publicly available for the 96 administrative departments of metropolitan France between March 19 and May 11, 2020, Assessment : > Multidimensional variables (spatiotemporal spread of the epidemic , national lockdown, demographic population structure, baseline intensive care capacities, ...) > in-hospital COVID-19 incidence, mortality, and case fatality rates **Findings** > clear spatial heterogeneity of in-hospital COVID-19 incidence and mortality rates, following the spread of the epidemic > Delay between the first COVID-19-associated death and the onset of the national lockdown was positively associated with in-hospital incidence, mortality, and case fatality rates > Mortality and case fatality rates were higher in departments with older populations (adjusted standardised ratio for populations with a high proportion older than aged >85 years 2·17 [95% CI 1·20–3·90] for mortality and 1·43 [1·08–1·88] for case fatality rate) > Mortality rate was also associated with incidence rate (1·0004, 1·0002–1·001), but mortality and case fatality rates did **not appear to be associated with baseline intensive care capacities** > **No association between climate** and in-hospital COVID-19 incidence, or between economic indicators and in-hospital COVID-19 incidence or mortality rates **This ecological study highlights the impact of the epidemic spread, national lockdown, and reactive adaptation of intensive care capacities on the spatial distribution of COVID-19 morbidity and mortality**
Lancet Infect Dis. 03FEB2021	**Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial**	Wu Z., *et al*. China gotopaper	Vaccines	> Randomised, double-blind, placebo-controlled, phase 1/2 clinical trial of CoronaVac in healthy adults aged 60 years and older (NCT04383574). > Vaccine or placebo by IM injection (in two doses, days 0 and 28). > Phase 1: dose-escalation study. 72 participants (24 per intervention group and 24 in the placebo group; mean age 65·8 years [SD 4·8]) - Block 1: 3 µg inactivated virus in 0·5 mL of aluminium hydroxide - Block 2 (6 µg per injection). > Phase 2: 1·5 µg, 3 µg, or 6 µg per dose, or placebo. 350 participants were enrolled in phase 2 (100 in each intervention group and 50 in the placebo group; mean age 66·6 years [SD 4·7] in 349 participants) **Primary safety endpoint** : adverse reactions within 28 days after each injection in all participants who received at least one dose. **Primary immunogenicity endpoint** was seroconversion rate at 28 days after the second injection (NCT04383574). **Findings:** > Safety: any adverse reaction within 28 days after injection occurred in 20 (20%) of 100 participants in the 1·5 µg group, 25 (20%) of 125 in the 3 µg group, 27 (22%) of 123 in the 6 µg group, and 15 (21%) of 73 in the placebo group. > All adverse reactions were mild or moderate in severity and injection site pain (39 [9%] of 421 participants) was the most frequently reported event. >Eight serious adverse events, considered unrelated to vaccination, have been reported by seven (2%) participants. > In phase 1, seroconversion after the second dose was observed in 24 of 24 participants (100·0% [95% CI 85·8–100·0]) in the 3 µg group and 22 of 23 (95·7% [78·1–99·9]) in the 6 µg group. >In phase 2, seroconversion was seen in 88 of 97 participants in the 1·5 µg group (90·7% [83·1–95·7]), 96 of 98 in the 3 µg group (98·0% [92·8–99·8]), and 97 of 98 (99·0% [94·5–100·0]) in the 6 µg group. **Conslusion:** CoronaVac is safe and well tolerated in older adults. Neutralising antibody titres by the 3 µg dose were similar to those of the 6 µg dose, and higher than those of the 1·5 µg dose.

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PNAS 03FEB2021	**Modeling SARS-CoV-2 viral kinetics and association with mortality in hospitalized patients from the French COVID cohort**	Néant N., *et al.* France [gotopaper]	Public Health / Epidemiology	**Aim**: to characterize SARS-CoV-2 viral kinetics in hospitalized patients and its association with mortality in 655 hospitalized patients from the prospective French COVID cohort. > The model predicted a median peak viral load that coincided with symptom onset. > Patients with age ≥65y had a smaller loss rate of infected cells, leading to a **delayed median time to viral clearance occurring 16d after symptom onset** as compared to 13 d in younger patients. > In multivariate analysis, the risk factors associated with mortality were age ≥65y, male gender, and presence of chronic pulmonary disease (hazard ratio [HR] > 2.0). Using a joint model, **viral dynamics after hospital admission** was an independent predictor of mortality (HR = 1.31, P < 10−3). > **Simulation of effectiveness of pharmacological interventions**: a treatment able to reduce viral production by 90% upon hospital admission would shorten the time to viral clearance by 2.0 and 2.9d in patients of age <65 y and ≥65y, respectively. Assuming a similar association between viral dynamics and mortality in patients of age ≥65y with risk factors, this could translate into a reduction of mortality from 19 to 14%. **Viral dynamics is associated with mortality in hospitalized patients.**
The Lancet 02FEB2021	**Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia**	Logunov D.Y., *et al.* Russia [gotopaper]	Vaccines	**Background** > Sputnik V: heterologous recombinant adenovirus (rAd)-based vaccine. > Good safety profile and strong humoral and cellular immune responses (pahse 1/2 clinical trials. ***Preliminary results on the efficacy and safety of this vaccine from the interim analysis of this phase 3 trial. (NCT04530396).*** **Methods** > Randomised, double-blind, placebo-controlled, phase 3 trial (25 hospitals and polyclinics in Moscow, Russia). > Participants aged at least 18 years, with negative SARS-CoV-2 PCR and IgG and IgM tests, no infectious diseases in the 14 days before enrolment, and no other vaccinations in the 30 days before enrolment. > Randomly assigned (3:1) to receive vaccine or placebo (0·5 mL/dose) IM; prime-boost regimen at 21-day interval > First dose (rAd26) and the second dose (rAd5), both vectors carrying the gene for the full-length SARS-CoV-2 glycoprotein S. Primary outcome: proportion of participants with PCR-confirmed COVID-19 from day 21 after receiving the first dose. SAE: assessed in all participants who had received at least one dose at the time of database lock **Findings** > 21 977 adults randomly assigned to the vaccine group (n=16 501) or the placebo group (n=5476). > 19 866 received two doses of vaccine or placebo and were included in the primary outcome analysis. > From 21 days after the first dose of vaccine (the day of dose 2): - 16 (0·1%) of 14 964 participants in the vaccine group and 62 (1·3%) of 4902 in the placebo group were confirmed to have COVID-19: ***vaccine efficacy was 91·6% (95% CI 85·6–95·2)***. > Most reported AEwere grade 1 (7485 [94·0%] of 7966 total events). > SAE: 45 (0·3%) of 16 427 participants in the vaccine group and 23 (0·4%) of 5435 participants in the placebo group. None were considered associated with vaccination, with confirmation from the independent data monitoring committee. > Four deaths were reported during the study (three [<0·1%] of 16 427 participants in the vaccine group and one [<0·1%] of 5435 participants in the placebo group), none of which were considered related to the vaccine. **Conclusion:** This interim analysis of the phase 3 trial of Gam-COVID-Vac showed 91·6% efficacy against COVID-19 and was well tolerated in a large cohort.

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Science 02FEB2021	**Age groups that sustain resurging COVID-19 epidemics in the United States**	Monod M., *et al.* UK [gotopaper](#)	Public Health / Epidemiology	> Understanding the age demographics driving transmission and how these affect the loosening of interventions is crucial **Methods** > Analyze aggregated, age-specific mobility trends from more than **10 million individuals in the US** and link these mechanistically to age-specific COVID-19 mortality data **Findings** > Estimation: as of October 2020, individuals **aged 20-49 are the only age groups sustaining resurgent SARS-CoV-2 transmission** with reproduction numbers well above one, and that at least **65 of 100 COVID-19 infections originate from individuals aged 20-49 in the US** Targeting interventions – <u>including transmission-blocking vaccines</u> – to adults **aged 20-49 is an important consideration in halting resurgent epidemics and preventing COVID-19-attributable deaths.**
Cell 02FEB2021	**Maturation and persistence of the anti-SARS-CoV-2 memory B cell response**	Sokal A., *et al.* France [gotopaper](#)	Immunology	Analysis of the longevity and functionality of the anti-SARS-CoV-2 memory B cell response **Methods** > longitudinal deep profiling of the anti-SARS-CoV-2 memory B cell response in two parallel cohorts of patients with severe and mild COVID-19 (39 total patients) > They combined single cell transcriptomics, single cell culture and IgH VDJ sequencing to track and characterize the cellular and molecular phenotype and clonal evolution of spike-specific MBCs clones from early time points after SARS-CoV-2 infection up to 6 months after the initial symptoms **Findings** > Distinct SARS-CoV-2 spike-specific activated B cell clones fueled an **early antibody-secreting cell burst as well as a durable synchronous germinal center response** > While highly mutated memory B cells, including pre-existing cross-reactive seasonal Betacoronavirus-specific clones, were recruited early in the response, neutralizing SARS-CoV-2 RBD-specific clones accumulated with time and largely contributed to the late remarkably stable memory B-cell pool. => **Seasonal coronavirus-specific memory B cells contribute an early anti-SARS-Cov2 response** => **Spike-specific memory B cells with a resting phenotype increase up to 6 months** > Highlighting germinal center maturation, these **cells displayed clear accumulation of somatic mutations in their variable region genes over time** > Longitudinal study reveals a **temporal switch to RBD-specific neutralizing memory B cells** These findings demonstrate that an antigen-driven activation persisted and matured **up to 6 months after SARS-CoV-2 infection and may provide long-term protection.**

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Lancet 02FEB2021	**Azithromycin 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 safety and efficacy of azithromycin (500 mg once per day by mouth or intravenously for 10 days or until discharge) in patients admitted to hospital with COVID-19. Primary outcome: 28-day all-cause mortality **Results** > Between April 7 and Nov 27, 2020, 7763 were included in the assessment of azithromycin. Mean age was 65·3 years, approx. a third were women. 2582 patients were randomly allocated to receive azithromycin and 5181 to usual care alone. > Overall, 561 (**22%**) patients allocated to azithromycin and 1162 (**22%**) patients allocated to usual care died within 28 days (rate ratio 0·97). > No significant difference was seen in duration of **hospital stay** (median 10 days vs 11 days) or the proportion of patients **discharged from hospital** alive within 28 days (rate ratio 1·04). > Among those not on invasive mechanical ventilation at baseline, no significant difference was seen in the proportion meeting the composite endpoint of **invasive mechanical ventilation or death** (risk ratio 0·95). In patients admitted to hospital with COVID-19, **azithromycin did not improve survival or other prespecified clinical outcomes**.
Lancet Infect Dis. 02FEB2021	**Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study**	Marks M., *et al*. Spain/UK gotopaper	Public Health / Epidemiology	**Aim**: to analyse data from linked index cases of COVID-19 and their contacts to explore factors associated with transmission of SARS-CoV-2. > We identified 314 patients with COVID-19, with 282 (90%) having at least one contact (753 contacts in total), resulting in 282 clusters. > 90 (32%) of 282 clusters had at least one transmission event. The secondary attack rate was 17% (125/753 contacts), with a variation from 12% when the index case had a viral load lower than 1×10^6 copies per mL to 24% when the index case had a viral load of 1×10^{10} copies per mL or higher (adjusted odds ratio per log10 increase in viral load 1·3). > Increased risk of transmission was also associated with **household contact** (3·0) and **age of the contact** (per year: 1·02, 1·01–1·04). > 449 contacts had a positive PCR result at baseline. 28 (6%) of 449 contacts had symptoms at the first visit. > Of 421 contacts who were asymptomatic at the first visit, 181 (43%) developed symptomatic COVID-19, with a variation from approx. **38%** in contacts with an initial viral load lower than 1×10^7 copies per mL to >**66%** for those with an initial viral load of 1×10^{10} copies per mL or higher (hazard ratio per log10 increase in viral load 1·12). > **Time to onset of symptomatic disease decreased** from a median of 7 days (IQR 5–10) for individuals with an initial viral load lower than 1×10^7 copies per mL to 6 days (4–8) for those with an initial viral load between 1×10^7 and 1×10^9 copies per mL, and 5 days (3–8) for those with an initial viral load higher than 1×10^9 copies per mL. **The viral load of index cases was a leading driver of SARS-CoV-2 transmission. The risk of symptomatic COVID-19 was strongly associated with the viral load of contacts at baseline and shortened the incubation time of COVID-19 in a dose-dependent manner.**

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Nature 01FEB2021	**Immunogenic BNT162b vaccines protect rhesus macaques from SARS-CoV-2**	Vogel A.B., *et al*. Germany gotopaper	Immunology / Preclinical model	> Preclinical development of two BNT162b vaccine candidates: lipid-nanoparticle (LNP) formulated nucleoside-modified mRNA encoding SARS-CoV-2 **spike glycoprotein**-derived immunogens > **BNT162b1** encodes a soluble, secreted, trimerised **receptor-binding domain** (RBD-foldon) > **BNT162b2** encodes the full-length transmembrane **spike glycoprotein,** locked in its prefusion conformation (PS2) > flexibly tethered RBDs of the RBD-foldon bind ACE2 with high avidity > Approximately 20% of the P 2S trimers are in the two-RBD 'down,' one-RBD 'up' state **Findings** > In mice, one intramuscular dose of either candidate elicits a dose-dependent antibody response with high virus-entry inhibition titres and strong TH1 CD4+ and IFNγ+ CD8+ T-cell responses > **Prime/boost vaccination of rhesus macaques with BNT162b candidates elicits SARS-CoV-2 neutralising geometric mean titres 8.2 to 18.2 times that of a SARS-CoV-2 convalescent human serum panel** > Vaccine candidates protect macaques from SARS-CoV-2 challenge, **with BNT162b2 protecting the lower respiratory** tract from the presence of viral RNA and **with no evidence of disease enhancement**
Blood 01FEB2021	**Dynamic angiopoietin-2 assessment predicts survival and chronic course in hospitalized patients with COVID-19**	Villa E., *et al.* Italy gotopaper	Clinics	**Aim**: to examine the association between dynamic angiopoietin-2 assessment and COVID-19 short- and long-term clinical course. > Hospitalized patients with laboratory-confirmed COVID-19 from 2 Italian tertiary referral centres (derivation cohort, n = 187 patients; validation cohort, n = 62 patients). > Three-day angiopoietin-2 increase of at least twofold from baseline was significantly associated **with in-hospital mortality** by multivariate analysis (hazard ratio [HR], 6.69) with Area under the receiver operating characteristic curve (AUROC) = 0.845. > Ten-day angiopoietin-2 of at least twofold from baseline was instead significantly associated **with nonresolving pulmonary condition** by multivariate analysis (HR, 5.33) with AUROC = 0.969. > Patients with persistent elevation of 10-day angiopoietin-2 levels showed severe reticular interstitial thickening and fibrous changes on follow-up computed tomography scans. Angiopoietin-2 and Tie2 were diffusely colocalized in small-vessel endothelia and alveolar new vessels and macrophages. **Angiopoietin-2 course is strongly associated with COVID-19 in-hospital mortality and nonresolving pulmonary condition**, and may be an early and useful predictor of COVID-19 clinical course.
Clin Infect Dis 30JAN21	**Absence of vaccine-enhanced disease with unexpected positive protection against SARS-CoV-2 by inactivated vaccine given within three days of virus challenge in Syrian hamster model**	Li C., *et al.* China gotopaper	Vaccines (viral mutants)	**Description of disease phenotypes of SARS-CoV-2 exposure occurring around the time of vaccine administration** - Disease phenotypes of a one-dose regimen given 3 days prior (D-3), 1 (D1) or 2 (D2) days after, or on the day (D0) of virus challenge in golden Syrian hamster - Monitoring of serial clinical severity, tissue histopathology, virus burden, and antibody response of the vaccinated hamsters. **Findings:** > One-dose vaccinated hamsters had significantly lower clinical disease severity score, body weight loss, lung histology score, nucleocapsid protein expression in lung, infectious virus titres in the lung and nasal turbinate, inflammatory changes in intestines and a higher serum neutralizing antibody or IgG titre against the spike receptor-binding domain or nucleocapsid protein when compared to unvaccinated controls. > Improvements particularly noticeable in D-3, but also in D0, D1 and even D2 vaccinated hamsters to varying degrees. > No increased eosinophilic infiltration was found in the nasal turbinate, lung, and intestine after virus challenge. > Significantly higher serum titre of fluorescent foci microneutralization inhibition antibody was detected in D1 and D2 vaccinated hamsters at day 4 post-challenge compared to controls despite undetectable neutralizing antibody titre. **Vaccination just before or soon after exposure to SARS-CoV-2 does not worsen disease phenotypes and may even ameliorate infection**.

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Science 29JAN2021	**Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine–elicited human seras**	Muik M., *et al.* Germany/USA gotopaper	Vaccines (viral mutants)	**Background:** > The new SARS-CoV-2 lineage called B.1.1.7 emerged in the UK is reported to spread more efficiently and faster than other strains. > This variant contains 10 amino acid changes in the spike protein: ΔH69/V70, ΔY144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H. > N501Y mutation is located in the receptor binding site. The spike with this mutation binds more tightly to its cellular receptor ACE-2 *Is this virus strain recognized by neutralizing antibodies induced after vaccination?* **Methods:** > VSV SARS-CoV-2-S pseudoviruses bearing the Wuhan reference strain or the B.1.1.7 lineage spike protein tested with sera of 40 participants given the BNT162b2 vaccine from Pfizer (phase I/II, DE) > The 50% neutralization geometric mean titer (GMT) of sera against the SARS-CoV-2 lineage B.1.1.7 spike-pseudotyped VSV for the younger adult group and the full analysis set were **slightly,** statistically significantly reduced compared to the GMTs against the Wuhan reference spike-pseudotyped VSV. > GMTs were not significantly different for the older adult group (0.78 [0.68;0.89] for the younger and 0.83 [0.65;1.1] for the older adults (0.80 [0.71;0.89] CI 95%). **Conslusions:** > Based on experience from antibody correlates of disease protection for influenza virus vaccines, a 20% reduced titer does not indicate a biologically significant change in neutralization activity > The largely preserved neutralization of pseudoviruses bearing the B.1.1.7 spike by BNT162b2-immune sera makes it unlikely that the UK variant virus will escape BNT162b2-mediated protection.
JAMA Pediatr. 29JAN2021	**Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios**	Flannery D.D., *et al.* USA gotopaper	Public Health / Epidemiology	> Understanding the dynamics of maternal antibody (Ab) responses to SARS-CoV-2 infection during pregnancy and transplacental Ab transfer > Assessing association between maternal and neonatal SARS-CoV-2–specific Ab concentrations **Methods** > Maternal and cord blood sera were available for Ab measurement for 1471 mother/newborn dyads (09Apr-08Aug 2020) > IgG and IgM to the receptor-binding domain of the SARS-CoV-2 spike protein were measured by enzyme-linked immunosorbent assay > Ab concentrations and transplacental transfer ratios were analyzed in combination with demographic and clinical data **Findings** > SARS-CoV-2 IgG Ab were transferred across the placenta in 72 of 83 pregnant women who were seropositive > Cord blood IgG concentrations were directly associated with maternal Ab concentrations > IgM antibodies were not detected in any cord blood sera > Transfer ratios **were associated with time elapsed from maternal infection to delivery** and **not associated with severity of maternal infection** **Efficient transplacental transfer of SARS-CoV-2 IgG Ab supports potential maternal Ab neonate protection from SARS-CoV-2 infection**
Cell 28JAN2021	**Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity**	Thomson E.C., *et al.* UK/USA gotopaper	Virology	> The immunodominant SARS-CoV-2 spike (S) receptor binding motif (RBM) is a **highly variable region of S**, and provide epidemiological, clinical, and molecular characterization of a prevalent, sentinel RBM mutation, N439K. > N439K S protein has **enhanced binding affinity** to the hACE2 receptor, and N439K viruses have **similar in vitro replication fitness** and cause infections with **similar clinical outcomes** to wild-type. > The N439K mutation confers **resistance against several neutralizing monoclonal antibodies**, including one authorized for emergency use by the FDA, and **reduces the activity of some polyclonal sera** from persons recovered from infection. Immune evasion mutations that maintain virulence and fitness such as N439K can emerge within SARS-CoV-2 S, highlighting the need for ongoing molecular surveillance.

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Nature Commun. 27JAN2021	**Integrating deep learning CT-scan model, biological and clinical variables to predict severity of COVID-19 patients**	Lassau N., *et al.* France [gotopaper]	Diagnostics	Identifying predictors of disease severity is a priority > Collect 58 clinical and biological variables, and chest CT scan data, from 1003 coronavirus-infected patients from two French hospitals. > Train a deep learning model based on **CT scans to predict severity** > **Construct the multimodal AI-severity score that includes 5 clinical and biological variables (age, sex, oxy-genation, urea, platelet) in addition to the deep learning model** **Findings** Neural network analysis of CT-scans brings unique prognosis information, although it is correlated with other markers of severity (oxygenation, LDH, and CRP) explaining the measurable but limited 0.03 increase of AUC obtained when adding CT-scan information to clinical variables. When comparing AI-severity with 11 existing severity scores, we find significantly improved prognosis performance; AI-severity can therefore rapidly become a reference scoring approach.
JAMA Netw Open 27JAN2021	**Respiratory and Psychophysical Sequelae Among Patients With COVID-19 Four Months After Hospital Discharge**	Bellan M., *et al* Italy [gotopaper]	Public Health / Epidemiology - Long Covid	**Aim**: Evaluate the prevalence of lung function anomalies, exercise function impairment, and psychological sequelae among patients hospitalized for COVID-19, 4 months after discharge **Methods** > Prospective cohort study at an academic hospital > Patients ≥18 years old (or their caregivers) hospitalized with SARS-CoV-2 infection (March 1-June 29, 2020) > Confirmed via RT-PCR testing, bronchial swab, serological testing, or suggestive computed tomography results To describe proportion of patients with: > Diffusing lung capacity for carbon monoxide (DLCO) <80% of expected value > Severe lung function impairment (DLCO <60% expected value) > Posttraumatic stress symptoms (measured using the Impact of Event Scale–Revised total score) > Functional impairment (assessed using the Short Physical Performance Battery [SPPB] score and 2-minute walking test); > Identification of factors associated with DLCO reduction and psychologicalor functional sequelae **Findings** > 238/767 patients (31.0%) (median age, 61 [50-71] years; 142 [59.7%] men; median comorbidities, 2 [1-3]) had sequelae. > 219 patients were able to complete both pulmonary function tests and DLCO measurement. DLCO was reduced to <80% of the estimated value in 113 patients (51.6%) and <60% in 34 patients (15.5%) > The SPPB score was suggested limited mobility (score <11) in 53 patients (22.3%). Patients with normal SPPB scores underwent a 2-minute walk test, which was outside reference ranges of expected performance for age and sex in 75 patients (40.5%) → 128 patients (53.8%) had functional impairment. Posttraumatic stress symptoms were reported in a total of 41 patients (17.2%) **4 months after discharge,respiratory, physical, and psychological sequelae were common among patients who had been hospitalized for COVID-19.**
Cell 26JAN2021	**Two-component spike nanoparticle vaccine protects macaques from SARS-CoV-2 infection**	Brouwer P.J.M., *et al.* The Netherlands [gotopaper]	Vaccines	> **Two-component protein nanoparticles display multiple copies of the SARS-CoV-2 Spike protein** potentially protecting from infection Immunization studies : > **Vaccination induces potent neutralizing antibody responses in mice, rabbits and cynomolgus macaques** > **Spike protein nanoparticles enhance cognate B cell activation in vitro** > **Vaccination protects macaques against a high-dose SARS-CoV-2 challenge, resulting in strongly reduced viral infection and replication in upper and lower airways.** These nanoparticles are a promising vaccine candidate.

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Nature 25JAN2021	**Global absence and targeting of protective immune states in severe COVID-19**	Combes A.J., *et al.* USA [gotopaper]	Immunology	**Aim:** Understand immune biology amongst COVID-19 patients, holistic understanding of the severe/mild distinction in COVID-19 pathology. **Methods**: whole-blood preserving single-cell analysis to integrate contributions from all major cell types including neutrophils, monocytes, platelets, lymphocytes and the contents of serum. **Findings:** > Patients with mild COVID-19 disease display a coordinated pattern of interferon-stimulated gene (ISG) expression across every cell population and these cells are systemically absent in patients with severe disease > Severe COVID-19 patients paradoxically produce very high anti-SARS-CoV-2 antibody titers and have lower viral load as compared to mild disease eve two weeks beyond symptom onset. > Examination of the serum from severe patients demonstrates that they uniquely produce Abs that functionally block the production of the mild disease-associated ISG-expressing cells, by engaging conserved signaling circuits that dampen cellular responses to interferons Global targeting of ISG archetypes might be addressable with drugs such as rituximab to reduce B cell responses, perhaps in the presence of convalescent serum, through introduction of IVIG to compete with serum antibodies for FcR engagement, or with rapid development of antibodies that clinically block FCyRIIb.
Science 25JAN2021	**Prospective mapping of viral mutations that escape antibodies used to treat COVID-19**	Starr T.N., *et al.* USA [gotopaper]	Immunology	**Aim:** mapping how all mutations to SARS-CoV-2's receptor-binding domain (RBD) affect binding by the antibodies in the REGN-COV2 cocktail and the antibody LY-CoV016. **Methods**: To validate the antigenic effects of key mutations, neutralization assays using spike-pseudotyped lentiviral particles were made. **Findings:** > Regarding REGN-COV2 antibodies: **a** mutation at site 486 escaped neutralization only by REGN10933, whereas mutations at sites 439 and 444 escaped neutralization only by REGN10987 > One mutation (E406W) strongly escapes the cocktail of both antibodies > E406W is not accessible by a single-nucleotide change, which may explain why it was not identified by the Regeneron cocktail > Mutations at RBD residues that contact antibody do not always mediate escape, and several prominent escape mutations occur at residues not in contact with antibody. > T**he maps reveal that mutations escaping the individual antibodies are already present in circulating SARS-CoV-2 strains.**
Science 25JAN21	**Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A**	White K.M., *et al.* International [gotopaper]	Therapeutics	Previous authror's work on SARS-CoV-2 highlighted 332 host proteins that are likely to play a role in the viral life cycle of SARS-CoV-2. Drugs modulating these host proteins were tested and those that targeted the eukaryotic translation machinery (eIF4H interacts with SARS-CoV-2 Nsp9) demonstrated particularly potent antiviral activities. In this study, **the eEF1A inhibitor plitidepsin was tested**. Plitidepsin has been clinically developed for the treatment of multiple myeloma with a well-established safety profile and pharmacokinetics. **Findings:** > Antiviral activity (IC90 = 0.88 nM) 27.5-fold more potent than remdesivir against SARS-CoV-2 in vitro, limiting toxicity > The dynamics between the antiviral effects of plitidepsin and remdesivir when used together in vitro suggests that plitidepsin has an additive effect with remdesivir > The antiviral activity of plitidepsin against SARS-CoV-2 is mediated through inhibition of the known target eEF1A. > in vivo studies in mouse models of SARS-CoV-2 infection showed a reduction of viral replication in the lungs by two orders of magnitude when using Pltidepsin in prophylactic treatment. **Conclusions:** This study establishes plitidepsin as a host-targeted anti-SARS-CoV-2 agent with in vivo efficacy. *Phase II/III study to come*

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Int J Infect Dis 24JAN2021	**Is there a need to widely prescribe antibiotics in patients hospitalized for COVID-19?**	Moretto F., *et al.* France [gotopaper](#)	Clinics	Comparison of the characteristics and outcomes between patients **with and without antibiotics** using propensity score matching. > Among the 222 patients included, 174 (78%) were on antibiotics. > Univariate analysis: patients with antibiotics were significantly **older, frailer and with a more severe presentation** at admission. > An **unfavorable outcome** was more frequent in patients with antibiotic therapy (HR = 2.94). > In multivariate analysis and on propensity score, antibiotic therapy was **not significantly associated with outcome** (HR = 1.612). Antibiotics were frequently prescribed in our study and associated with a more severe presentation at admission. However, receiving antibiotics was not associated with outcome.
Lancet Resp Med. 22JAN2021	**Effect of anakinra versus usual care in adults in hospital with COVID-19 and mild-to-moderate pneumonia (CORIMUNO-ANA-1): a randomised controlled trial**	The CORIMUNO-19 Collaborative group France [gotopaper](#)	Therapeutics	**Aim**: to determine whether anakinra, a recombinant human IL-1 receptor antagonist, could improve outcomes in patients in hospital with mild-to-moderate COVID-19 pneumonia. - Usual care + anakinra (200 mg twice a day on days 1–3, 100 mg twice on day 4, 100 mg once on day 5) vs usual care only. <u>Two coprimary outcomes</u>: proportion of patients who had died or needed non-invasive or mechanical ventilation by day 4 (ie, a score of >5 on the WHO-CPS) and survival without need for mechanical or non-invasive ventilation (including high-flow oxygen) at day 14. **Results** > 116 patients recuited: 59 in the anakinra group, and 57 in the usual care group (2 withdrew). Median age was 66 years, 70% were men. > In the anakinra group, 21/59 (36%) patients had a WHO-CPS score >5 at day 4 versus 21/55 (38%) in the usual care group (median posterior absolute risk difference [ARD] −2·5%), with a posterior probability of ARD of less than 0 (ie, anakinra better than usual care) of 61·2%. > At day 14, 28 (47%) patients in the anakinra group and 28 (51%) in the usual care group needed ventilation or died, with a posterior probability of any efficacy of anakinra (hazard ratio [HR] <1) of 54·5% (median posterior HR 0·97). > At day 90, 16 (27%) patients in the anakinra group and 15 (27%) in the usual care group had died. Serious adverse events occurred in 27 (46%) patients in the anakinra group and 21 (38%) in the usual care group (p=0·45). **Anakinra did not improve outcomes in patients with mild-to-moderate COVID-19 pneumonia.**
JAMA 21JAN2021	**Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19**	Gottlieb R.L., *et al.* USA [gotopaper](#)	Therapeutics	**Aim**: to determine the effect of **bamlanivimab monotherapy and combination therapy with bamlanivimab and etesevimab on SARS-CoV-2 viral load** in mild to moderate COVID-19 (BLAZE-1 study). - Bamlanivimab: a single infusion of 700 mg (n = 101), 2800 mg (n = 107), or 7000 mg (n = 101) - Combination treatment: 2800 mg of bamlanivimab and 2800 mg of etesevimab [n = 112] - Placebo (n = 156). <u>Primary end point</u>: change in SARS-CoV-2 log viral load at D11 (±4dys). > Among the 577 randomized (mean age, 44.7 years; 54.6% women), 533 (92.4%) completed the efficacy evaluation period (day 29). > Change in log viral load from baseline at D11 was −3.72 for 700 mg, −4.08 for 2800 mg, −3.49 for 7000 mg, −4.37 for combination treat, and −3.80 for placebo. Compared with placebo, differences in the change in log viral load at D11 were **0.09 for 700 mg, −0.27 for 2800 mg, 0.31 for 7000 mg, and −0.57 for combination treatment**. > Among the secondary outcome measures, differences between each treatment group vs the placebo group were statistically significant for 10 of 84 end points. The proportion of patients with **COVID-19–related hospitalizations or ED visits** was 5.8% (9 events) for placebo, 1.0% (1 event) for 700 mg, 1.9% (2 events) for 2800 mg, 2.0% (2 events) for 7000 mg, and 0.9% (1 event) for combination treatment. > **Immediate hypersensitivity** reactions were reported in 9 patients (6 bamlanivimab, 2 combination treatment, and 1 placebo). > **No deaths** occurred during the study treatment. In nonhospitalized patients with mild to moderate COVID-19, **bamlanivimab and etesevimab treatment, compared with placebo, was associated with a reduction** in SARS-CoV-2 viral load at day 11.

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Lancet Infect Dis 21JAN21	**Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial**	Ella R., *et al.* India [gotopaper]	Vaccines	**Background** BBV152: whole-virion inactivated SARS-CoV-2 vaccine formulated with a toll-like receptor 7/8 agonist molecule adsorbed to alum (Algel-IMDG) or alum (Algel). **Methods** > Double-blind, multicentre, randomised, controlled phase 1 trial to assess the safety and immunogenicity of BBV152 at 11 hospitals across India. (NCT04471519). > Healthy adults aged 18–55 years Individuals with positive SARS-CoV-2 nucleic acid and/or serology tests excluded. > Participants randomly assigned to receive either one of three vaccine formulations: - 3 µg with Algel-IMDG / 6 µg with Algel-IMDG / 6 µg with Algel / Algel only > Two IM doses at d0 et d14 > Primary outcomes: solicited local and systemic reactogenicity events at 2 h and 7 days after vaccination > Secondary outcome: seroconversion > Cell-mediated responses were evaluated by intracellular staining and ELISpot. **Findings** > 375 participants enrolled: 100 each were randomly assigned to the three vaccine groups, and 75 were randomly assigned to the control group (Algel only). > Solicited local and systemic adverse reactions after 2 doses: 17 (17%; 95% CI 10·5–26·1) participants in the 3 µg with Algel-IMDG group, 21 (21%; 13·8–30·5) in the 6 µg with Algel-IMDG group, 14 (14%; 8·1–22·7) in the 6 µg with Algel group, and ten (10%; 6·9–23·6) in the Algel-only group. > Most common solicited adverse events: injection site pain (17 [5%] of 375 participants), headache (13 [3%]), fatigue (11 [3%]), fever (nine [2%]), and nausea or vomiting (seven [2%]). All solicited adverse events were mild or moderate, and more frequent after the first dose. > One SAE(viral pneumonitis) reported in the 6 µg with Algel group, unrelated to the vaccine. >Seroconversion rates (%) of 87·9, 91·9, and 82·8 in the 3 µg with Algel-IMDG, 6 µg with Algel-IMDG, and 6 µg with Algel groups, respectively. >CD4+ and CD8+ T-cell responses were detected in a subset of 16 participants from both Algel-IMDG groups. **BBV152 led to tolerable safety outcomes and enhanced immune responses. Both Algel-IMDG formulations were selected for phase 2 immunogenicity trials**.
Science Immunol. 21JAN2021	**Severely ill COVID-19 patients display impaired exhaustion features in SARS-CoV-2-reactive CD8+ T cells**	Kusnadi A., *et al.* USA [gotopaper]	Immunology	**Aim:** Understand anti-viral immune responses. Report from data generated by single-cell RNA sequencing of virus-reactive CD8+ T cells from COVID-19 patients with different clinical severity. **Methods:** single-cell transcriptomes of >80,000 virus-reactive CD8+ T cells, obtained using a modified Antigen-Reactive T cell Enrichment (ARTE) assay, from 39 COVID-19 patients and 10 healthy subjects. >Recent reports from COVID-19 patients have suggested the presence of exhaustion-related markers in global CD8+ T cell populations. COVID-19 patients were segregated into two groups based on whether the dominant CD8+ T cell response to SARS-CoV-2 was "exhausted" or not. **Findings:** > SARS-CoV-2-reactive cells in the exhausted subset were increased in frequency and displayed lesser cytotoxicity and inflammatory features in COVID-19 patients with mild compared to severe illness. > SARS-CoV-2-reactive cells in the dominant non-exhausted subset from patients with severe disease showed enrichment of transcripts linked to co-stimulation, pro-survival NF-κB signaling, and anti-apoptotic pathways, **suggesting the generation of robust CD8+ T cell memory responses in patients with severe COVID-19 illness** > Overall, the single-cell analysis revealed **substantial diversity in the nature of CD8+ T cells responding to SARS-CoV-2.**

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Lancet Public Health 20JAN2021	**Quarantine and testing strategies in contact tracing for SARS-CoV-2: a modelling study**	Quilty B.J., *et al.* UK [gotopaper](#)	Public Health / Epidemiology	**Aim**: to assess the merit of testing contacts to avert onward transmission and to replace or reduce the length of quarantine for uninfected contacts. > Assuming moderate levels of adherence to quarantine and self-isolation, self-isolation on symptom onset alone can prevent **37%** of onward transmission potential from secondary cases. > 14 days of post-exposure quarantine reduces transmission by **59%**. > Quarantine with release after a negative PCR test 7 days after exposure might avert a **similar proportion** (**54%**; risk ratio [RR] 0·94), as would quarantine with a negative lateral flow antigen test 7 days after exposure (**50%**; RR 0·88) or daily testing without quarantine for 5 days after tracing (**50%**; RR 0·88) if all tests are returned negative. **Testing might allow for a substantial reduction in the length of, or replacement of, quarantine** with a small excess in transmission risk. Decreasing test and trace delays and increasing adherence will further increase the effectiveness of these strategies.
BMJ 20JAN21	**Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial**	V.C. Veiga, *et al.* Brazil [gotopaper](#)	Therapeutics	Does tocilizumab improves clinical outcomes for patients with severe or COVID-19?. **Methods:** > Randomised, open label trial (NCT04403685) > Nine hospitals in Brazil, 8 May to 17 July 2020. > Adults with confirmed Covid-19 who were receiving supplemental oxygen or mechanical ventilation and had abnormal levels of at least two serum biomarkers (C reactive protein, D dimer, lactate dehydrogenase, or ferritin). > Interventions Tocilizumab (single intravenous infusion of 8 mg/kg) plus standard care (n=65) versus standard care alone (n=64). > Main outcome: clinical status measured at 15 days, analysed as a composite of death or mechanical ventilation (assumption of odds proportionality was not met). *> The data monitoring committee recommended stopping the trial early, after 129 patients had been enrolled, because of an increased number of deaths at 15 days in the tocilizumab group.* **Findings:** > 129 patients enrolled (mean age 57 years; 68% men) and all completed follow-up. > All patients in the tocilizumab group and two in the standard care group received tocilizumab. > 18 of 65 (28%) patients in the tocilizumab group and 13 of 64 (20%) in the standard care group were receiving mechanical ventilation or died at day 15 (odds ratio 1.54). > Death at 15 days occurred in 11 (17%) patients in the tocilizumab group compared with 2 (3%) in the standard care group (odds ratio 6.42). > Adverse events were reported in 29 of 67 (43%) patients who received tocilizumab and 21 of 62 (34%) who did not receive tocilizumab. In patients with severe or critical Covid-19, **tocilizumab plus standard care was not superior to standard care alone in improving clinical outcomes at 15 days, and it might increase mortality**.

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Lancet Microbe 19JAN2021	**Insight into the practical performance of RT-PCR testing for SARS-CoV-2 using serological data: a cohort study**	Zhang Z., *et al*. China gotopaper	Diagnostics	**Aim:** Assess the practical performance of RT-PCR-based surveillance protocols and determine the extent of undetected SARS-CoV-2 infection in Shenzhen, China. **Methods:** cohort study in Shenzhen, China. All RT-PCR-(-) close contacts (defined as those who lived in the same residence as, or shared a meal, travelled, or socially interacted with, an index case within 2 days before symptom onset) of all RT-PCR- (+) cases of SARS-CoV-2 detected since January, 2020. **Findings:** >Serological samples from 2345 of 4422 RT-PCR (-) close contacts of cases of RT-PCR-confirmed SARS-CoV-2. >40 of 880 RT-PCR (-) close contacts were positive on total antibody ELISA. >The seropositivity rate with total Ab ELISA among RT-PCR (-) close contacts, adjusted for assay performance, was 4·1%, which was significantly higher than among individuals residing in neighbourhoods with no reported cases >RT-PCR (+) individuals were 8·0 times more likely to report symptoms than those who were RT-PCR (-) but seropositive. >RT-PCR did not detect 48 of 134 infected close contacts, and false-negative rates appeared to be associated with stage of infection. **Even rigorous RT-PCR testing protocols might miss a substantial proportion of SARS-CoV-2 infections**, perhaps in part due to difficulties in determining the timing of testing in asymptomatic individuals for optimal sensitivity.
Ann Intern Med. 19JAN2021	**Characteristics, Outcomes, and Trends of Patients With COVID-19–Related Critical Illness at a Learning Health System in the United States**	Anesi G.L., *et al*. USA gotopaper	Public Health / Epidemiology	**Aim**: to describe the epidemiology, trends outcomes and care delivery of COVID-19–related critical illness. Single–health system, multihospital retrospective cohort study. <u>Primary outcome</u>: all-cause 28-day in-hospital mortality. <u>Secondary outcomes</u>: all-cause death at any time, receipt of mechanical ventilation (MV), readmissions. > Among 468 patients with COVID-19–related critical illness, 319 (68.2%) were treated with **MV** and 121 (25.9%) with **vasopressors**. > **All-cause 28-day in-hospital mortality rate** was 29.9%, median **ICU stay** was 8 days (IQR, 3-17), median **hospital stay** was 13 days (IQR, 7-25), and all-cause **30-day readmission rate** (among nonhospice survivors) was 10.8%. > **Mortality decreased over time**, from 43.5% (CI, 31.3-53.8) to 19.2% (CI, 11.6- 26.7) between the first and last 15-day periods in the core adjusted model, whereas patient acuity and other factors did not change. Among patients with COVID-19–related critical illness admitted to ICUs, **mortality seemed to decrease over time despite stable patient characteristics**.
Nature 18JAN2021	**Evolution of antibody immunity to SARS-CoV-2**	Gaebler C., *et al*. USA gotopaper	Immunology	**Aim:** Assess the humoral memory response in a cohort of 87 individuals assessed at 1.3 and 6.2 months after infection. **Findings:** > IgM, and IgG anti-SARS-CoV-2 spike protein receptor binding domain (RBD) antibody titres decrease significantly with IgA being less affected. > The number of RBD-specific memory B cells is unchanged. Memory B cells display clonal turnover after 6.2 months, and the antibodies they express have greater somatic hypermutation, increased potency and resistance to RBD mutations. >Analysis of intestinal biopsies obtained from asymptomatic individuals, revealed persistence of SARS-CoV-2 nucleic acids and immunoreactivity in the small bowel (7/14 volunteers). >T**he memory B cell response to SARS-CoV-2 evolves between 1.3 and 6.2 months after infection in a manner that is consistent with antigen persistence.** Individuals who are infected with SARS-CoV-2 could mount a rapid and effective response to the virus upon re-exposure.

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JAMA Int Med. 15JAN2021	**Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2A Systematic Review and Meta-analysis**	Butler-Laporte G., *et al.* Canada [gotopaper](#)	Diagnostics	**Aim**: to assess the diagnostic accuracy of saliva nucleic acid amplification testing (NAAT) for COVID-19. Systematic review and meta-analysis. > 385 references, 16 unique studies (5922 unique patients). Significant variability in patient selection, study design, setting and stage of illness at which patients were enrolled. > In the primary analysis, the **saliva NAAT** pooled sensitivity was 83.2% (95% credible interval [CrI], 74.7%-91.4%) and the pooled specificity was 99.2% (95% CrI, 98.2%-99.8%). > The **nasopharyngeal swab** NAAT had a sensitivity of 84.8% (95% CrI, 76.8%-92.4%) and a specificity of 98.9% (95% CrI, 97.4%-99.8%). > Results were similar in secondary analyses (on peer-reviewed studies, and on ambulatory settings). **Saliva NAAT diagnostic accuracy is similar to that of nasopharyngeal swab NAAT**, especially in the ambulatory setting, supporting larger-scale research on the use of saliva NAAT as an alternative.
NEJM 13JAN2021	**Interim Results of a Phase 1–2a Trial of Ad26.COV2.S Covid-19 Vaccine**	Sadoff J., *et al*. USA [gotopaper](#)	Vaccines	**Ad26.COV2.S candidate vaccine (Janssen Vaccines and Prevention)**: recombinant, replication-incompetent adenovirus serotype 26 (Ad26) vector encoding a full-length and stabilized SARS-CoV-2 spike protein. Methods: > Multicenter, placebo-controlled, phase 1–2a trial, randomised > Healthy adults: between the ages of **18 and 55 years (cohort 1)** and those **65 years of age or older (cohort 3)** (=> 805 participants) > Cohorte 1& 3 : receive the Ad26.COV2.S vaccine at a dose of 5×10¹⁰viral particles (low dose) or 1×10¹¹ viral particles (high dose) per milliliter or placebo in a single-dose or two-dose schedule > **Cohorte 2: Longer-term data comparing a single-dose** regimen with a **two-dose** regimen are being collected Findings related to safety & reactogenicity After first vaccine dose in cohorts 1 & 3 and after second dose in cohort 1: > Most frequent solicited adverse events (AE) were fatigue, headache, myalgia, and injection-site pain & most frequent systemic AE = fever > Systemic adverse events were less common in cohort 3 than in cohort 1 and in those who received the low vaccine dose than in those who received the high dose. > Reactogenicity was lower after the second dose. Findings related to immunogenicity profiles > Neutralizing-antibody titers against wild-type virus were **detected in 90% or more of all partici-pants on day 29 after the first vaccine dose , and reached 100% by day 57 with a further increase in titers in cohort 1a.** > Titers **remained stable until at least day 71**. A second dose provided an increase in the titer by a factor of 2.6 to 2.9 (GMT, 827 to 1266). Spike-binding antibody responses were similar to neutralizing-antibody responses. > On day 14, CD4+ T-cell responses were detected in 76 to 83% of the par-ticipants in cohort 1 and in 60 to 67% of those in cohort 3, with a clear skewing toward type 1 helper T cells. CD8+ T-cell responses were robust overall but lower in cohort 3. **The safety and immunogenicity profiles of Ad26.COV2.S support further develop-ment of this vaccine candidate.**

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NEJM 13JAN2021	**Convalescent Plasma Antibody Levels and the Risk of Death from Covid-19**	Joyner M.J., *et al.* USA [gotopaper](#)	Therapeutics	**Aim**: to assess whether convalescent plasma with high antibody levels rather than low antibody levels is associated with a lower risk of death. Primary outcome: death within 30 days after plasma transfusion. > Of the 3082 patients included in the analysis, death within 30 days after plasma transfusion occurred in 115 of 515 patients **(22.3%) in the high-titer group**, 549 of 2006 patients **(27.4%) in the medium-titer group**, and 166 of 561 patients **(29.6%) in the low-titer group**. > Association of anti–SARS-CoV-2 antibody levels with risk of death from Covid-19 was moderated by mechanical ventilation status -->A **lower risk of death** within 30 days in the high-titer group than in the low-titer group was observed among patients **who had not received mechanical ventilation** before transfusion (relative risk, 0.66), and **no effect on the risk of death** was observed among patients **who had received mechanical ventilation** (relative risk, 1.02). In patients hospitalized with Covid-19 who were **not receiving mechanical ventilation, transfusion of plasma with higher anti–SARS-CoV-2 IgG antibody levels was associated with a lower risk of death** than transfusion of plasma with lower antibody levels.
Science 12JAN2021	**Mosaic nanoparticles elicit cross-reactive immune responses to zoonotic coronaviruses in mice**	Cohen A.A., *et al.* USA [gotopaper](#)	Immunology	Construction of **homotypic nanoparticles displaying the RBD of SARS-CoV-2 or co-displaying SARS-CoV-2 RBD along with RBDs from animal betacoronaviruses** (mosaic nanoparticles; 4-8 distinct RBDs). > Mice immunized with RBD-nanoparticles, but not soluble antigen, elicited **cross-reactive binding and neutralization responses**. > **Mosaic-RBD-nanoparticles** elicited antibodies with superior cross-reactive recognition of heterologous RBDs compared to sera from immunizations with homotypic SARS-CoV-2–RBD-nanoparticles or COVID-19 convalescent human plasmas. > Sera from mosaic-RBD–immunized mice neutralized heterologous pseudotyped coronaviruses equivalently or better after priming than sera from homotypic SARS-CoV-2–RBD-nanoparticle immunizations -- > **no immunogenicity loss** against particular RBDs resulting from co-display. A single immunization with mosaic-RBD-nanoparticles provides a potential strategy to simultaneously protect against SARS-CoV-2 and emerging zoonotic coronaviruses.
Nature Commun. 11JAN2021	**Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19)**	van Kampen J.J.A., *et al.* Netherlands [gotopaper](#)	Public Health / Epidemiology	**Aim:** assess the duration and key determinants of infectious SARS-CoV-2 shedding in patients with severe and critical COVID-19 **Methods:** Analysis of viral loads, neutralizing antibody titers (nAb), detection of the subgenomic RNAs from 129 hospitalized individuals diagnosed with COVID-19 by RT-PCR **Findings:** >Infectious virus shedding was detected by virus cultures in 23/129 patients (17.8%) hospitalized with COVID-19 >The median duration of shedding infectious virus is **8 days** post onset of symptoms and **drops below 5% after 15.2 days post onset of symptoms**. >The probability of isolating infectious virus was less than 5% when the nAb titer was 1:80 or higher >A serum nAb titre of at least 1:20 (OR of 0.01) is independently associated with non-infectious SARS-CoV-2. >Quantitative viral RNA load assays and serological assays could be used in test-based strategies to discontinue or de-escalate infection prevention and control precautions. >Detection of viral subgenomic RNA correlated poorly with shedding of infectious virus

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The Lancet 08JAN2021	**6-month consequences of COVID-19 in patients discharged from hospital: a cohort study**	Huang C.H., *et al.* China [gotopaper]	Public Health / Epidemiology - Long COVID	**Aim**: to describe the long-term health consequences of patients with COVID-19 who have been discharged from hospital and investigate the associated risk factors. > 1733 discharged patients with COVID-19 enrolled: median age of 57 years and 52% were men. The median follow-up time after symptom onset was 186·0 days. > **Fatigue or muscle weakness** (63%, 1038/1655) and **sleep difficulties** (26%, 437/1655) were the most common symptoms. **Anxiety or depression** was reported among 23% (367/1617) of patients. > The proportions of median **6-min walking distance** less than the lower limit of the normal range were 24% for those at severity scale 3, 22% for severity scale 4, and 29% for severity scale 5–6. > The corresponding proportions of patients with **diffusion impairment** were 22% for severity scale 3, 29% for scale 4, and 56% for scale 5–6, and median CT scores were 3·0 for severity scale 3, 4·0 for scale 4, and 5·0 for scale 5–6. > A**fter multivariable adjustment**, patients showed an odds ratio (OR) 1·61 for scale 4 versus scale 3 and 4·60 for scale 5–6 versus scale 3 for diffusion impairment; OR 0·88 for scale 4 versus scale 3 and OR 1·77 for scale 5–6 versus scale 3 for anxiety or depression, and OR 0·74 for scale 4 versus scale 3 and 2·69 for scale 5–6 versus scale 3 for fatigue or muscle weakness. > Of 94 patients with **blood antibodies** tested at follow-up, the seropositivity (96·2% vs 58·5%) and median titres (19·0 vs 10·0) of the neutralising antibodies were significantly lower compared with at the acute phase. > 107 of 822 participants without acute kidney injury and with estimated glomerular filtration rate (eGFR) 90 mL/min per 1·73 m2 or more at acute phase had **eGFR** less than 90 mL/min per 1·73 m2 at follow-up. **At 6 months after acute infection, COVID-19 survivors were mainly troubled with fatigue or muscle weakness, sleep difficulties, and anxiety or depression. Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations**.
JAMA Netw. Open 07JAN2021	**SARS-CoV-2 Transmission From People Without COVID-19 Symptoms**	Johansson M.A., *et al.* USA [gotopaper]	Public Health/Epidemiology	**Aim**: to assess the proportion of SARS-CoV-2 transmissions in the community that likely occur from persons without symptoms. Baseline assumptions for the model: incubation period at 5 days, infectious period of 10 days, peak infectiousness occurred at the median of symptom onset, 30% of individuals with infection never develop symptoms and are 75% as infectious as those who do develop symptoms. This implies that persons with infection who never develop symptoms may account for approximately 24% of all transmission. > In this base case, **59% of all transmission came from asymptomatic transmission**, comprising **35%** from presymptomatic individuals and **24%** from individuals who never develop symptoms. > Under a broad range of values for each assumption, **at least 50% of new infections** was estimated to have originated from exposure to individuals with infection but without symptoms. In this decision analytical model, transmission from asymptomatic individuals was **estimated to account for more than half of all transmissions**. Measures such as wearing masks, hand hygiene, social distancing, and strategic testing of people who are not ill will be foundational to slowing the spread of COVID-19.

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Clin Infect Dis. 07JAN2021	**Association Between Chronic Use of Immunosuppresive Drugs and Clinical Outcomes From Coronavirus Disease 2019 (COVID-19) Hospitalization: A Retrospective Cohort Study in a Large US Health System**	Anderson K.M., *et al.* USA [gotopaper]	Public Health / Epidemiology	**Does chronic use of immunosuppressive drugs worsens or improves the severity of COVID-19?** > Retrospective cohort study, adults with acute inpatient hospital admission (March -August 2020) > confirmed or suspected COVID-19 > chronic immunosuppression was defined as prescriptions for immunosuppressive drugs current at the time of admission. > Outcomes: **mechanical ventilation, in-hospital mortality, and length of stay.** **Findings:** > 2121 patients admitted with laboratory-confirmed (1967; 93%) or suspected (154; 7%) COVID-19 > median age of 55 years (40–67). > of these, 108 (5%) were classified as immunosuppressed before COVID-19, primarily with prednisone (>7.5 mg/day), tacrolimus, or mycophenolate mofetil. > Among the entire cohort, 311 (15%) received mechanical ventilation > The median (interquartile range) length of stay was 5.2 (2.5–10.6) days > 1927 (91%) survived to discharge > no significant differences in the risk of mechanical ventilation, in-hospital mortality or length of stay among individuals with immunosuppression and counterparts. Chronic use of immunosuppressive drugs **was neither associated with worse nor better clinical outcomes** among adults hospitalized with COVID-19 in this setting.
JAMA Otolaryngol Head Neck Surg. 07JAN2021	**Diagnostic Value of Patient-Reported and Clinically Tested Olfactory Dysfunction in a Population Screened for COVID-19**	Villerabel C., *et al.* France [gotopaper]	Diagnostics	**Have olfactory and gustatory dysfunction a diagnostic value for COVID-19? Evaluation of a semiobjective olfactory test developed to assess patient-reported chemosensory dysfunction prior to testing for the presence SARS-CoV-2** > Diagnostic study conducted in a COVID-19 screening center in France (March-April, 2020) > Paricipants: health care workers or outpatients with symptoms or with close contact with an index case. **>** Participants interviewed to ascertain their symptoms and then Clinical Olfactory Dysfunction Assessment (CODA) (ad hoc test developed for a simple and fast evaluation of olfactory function). Assessment followed a standardized procedure in which participants identified and rated the intensity of 3 scents (lavender, lemongrass, and mint) to achieve a summed score ranging from 0 to 6. The COVID-19 status was assessed using RT PCR. **Findings:** > 809 participants, female to male sex ratio: 2.8. Mean age: 41.8 years (18-94). > Asymptomatic or mild disease patients; 58 (7.2%) tested positive for SARS-CoV-2. > Chemosensory dysfunction was reported by 20 of 58 participants (34.5%) with confirmed COVID-19 vs 29 of 751 participants (3.9%) who tested negative for COVID-19 > Olfactory dysfunction, either self-reported or clinically ascertained (CODA score ≤3), yielded similar sensitivity and specificity for COVID-19 diagnosis. > Concordance was high between reported and clinically tested olfactory dysfunction, with a Gwet AC1 of 0.95 (95% CI, 0.93-0.97). > Of 19 participants, 15 (78.9%) with both reported olfactory dysfunction and a CODA score of 3 or lower were confirmed to have COVID-19. > The CODA score also revealed 5 of 19 participants (26.3%) with confirmed COVID-19 who had previously unperceived olfactory dysfunction. **Olfactory dysfunction was suggestive of COVID-19, particularly when clinical testing confirmed anamnesis. However, normal olfaction was most common among patients with COVID-19.**

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NEJM 07JAN2021	Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers	Lumley S.F., *et al.* UK [gotopaper](#)	Immunology	> Study relationship between the presence of antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the risk of subsequent reinfection > Incidence of SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR) in **seropositive and seronegative** HCW attending testing of **asymptomatic and symptomatic** staff at Oxford University Hospitals > Baseline antibody status was determined by anti-spike (primary analysis) and anti-nucleocapsid IgG assays > Followed for up to 31 weeks > 12,541 health care workers participated having anti-spike IgG measured **Findings** > A total of 223 anti-spike–seronegative health care workers had a positive PCR test (1.09 per 10,000 days at risk), 100 during screening while they were asymptomatic and 123 while symptomatic, whereas 2 anti-spike–seropositive health care workers had a positive PCR test (0.13 per 10,000 days at risk), and both workers were asymptomatic when tested (adjusted incidence rate ratio, 0.11; 95% confidence interval, 0.03 to 0.44; P = 0.002) > The presence of **anti-spike or anti-nucleocapsid IgG antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection <u>in the ensuing 6 months</u>**.
NEJM 06JAN21	Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults	Libster R., *et al.* Argentina/USA [gotopaper](#)	Therapeutics	**Convalescent plasma administration at early COVID19 patients** > Randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against SARS-CoV-2 in older adult patients within 72 hours after the onset of mild Covid-19 symptoms. > 160 patients randomized **Primary end point:** severe respiratory disease (respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both) *Trial stopped early at 76% of projected sample size because a decrease in Covid-19.* **Findings:** > Severe respiratory disease developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo (relative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; P=0.03), with a relative risk reduction of 48%. > No solicited adverse events were observed. **Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19.**
Nature 06JAN2021	A longitudinal study of SARS-CoV-2-infected patients reveals a high correlation between neutralizing antibodies and COVID-19 severity	Legros V., *et al.* France [gotopaper](#)	Immunology	Cohort study of 140 SARS-CoV-2 qPCR-confirmed infections, including patients with mild symptoms and more severe forms (intensive care included). The neutralizing antibody (nAb) responses were assessed using either live SARS-CoV-2 particles or retroviruses pseudotyped with the SARS-CoV-2 S viral surface protein (Spike). **Findings:** >ICU patients displayed high nAb activity compared to other groups with milder disease symptoms. nAb titers correlated strongly with disease severity and with anti-spike IgG levels. >The anti-S IgG response can be used as a marker of neutralizing activity in individuals. > Serum from individuals diagnosed with OC43, 229E, NL63, and HKU1 coronavirus infections but not infected with SARS-CoV-2 failed to cross-neutralize SARS-CoV-2 suggesting the **absence of cross-neutralization between SARS-CoV-2 and endemic coronaviruses.** >**The D614G mutation did not affect the nAb activity** of the serum samples from our cohort indicating that this highly prevalent mutation is not associated with SARS-CoV-2 resistance to neutralization.

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Science 06JAN2021	Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection	Dan J.M., *et al.* USA gotopaper	Immunology	> Understanding immune memory to SARS-CoV-2 and for assessing the likely future course of the COVID-19 pandemic. > 2254 samples from 188 COVID-19 cases, including **43 samples at ≥ 6 months post-infection** **Findings** **>** IgG to the Spike protein was relatively stable over 6+ months > Spike-specific memory B cells were more abundant at 6 months than at 1 month post symptom onset > SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a half-life of 3-5 months **Each component of SARS-CoV-2 immune memory exhibited distinct kinetics**
Clin Infect Dis. 06JAN2021	The duration, dynamics and determinants of SARS-CoV-2 antibody responses in individual healthcare workers	Lumley S.F., *et al*. USA gotopaper	Immunology	> SARS-CoV-2 IgG antibody measurements used to estimate the proportion of a population exposed or infected and may be informative about the risk of future infection > 6 months of data from a longitudinal seroprevalence study of 3276 UK healthcare workers with measurements of SARS-CoV-2 anti-nucleocapsid and anti-spike IgG > Interval censored survival analysis was used to investigate the duration of detectable responses > Bayesian mixed linear models were used to investigate anti-nucleocapsid waning **Findings** > SARS-CoV-2 anti-nucleocapsid antibodies **wane within months** (Anti-nucleocapsid IgG levels rose to a peak at 24 (95% credibility interval, CrI 19-31) days post first PCR-positive test, before beginning to fall), **and faster in younger adults and those without symptoms.** > Higher maximum observed anti-nucleocapsid titres were associated with longer estimated antibody half-lives > Anti-spike IgG remains stably detected. > Ongoing longitudinal studies are required to track the long-term duration of antibody levels and their association with immunity to SARS-CoV-2 reinfection
JAMA Netw. 05JAN2021	Estimation of US SARS-CoV-2 Infections, Symptomatic Infections, Hospitalizations, and Deaths Using Seroprevalence Surveys	Angulo F.J., *et al.* USA gotopaper	Public Health / Epidemiology	Cross-sectional study of respondents of all ages, data from 4 regional and 1 nationwide Centers for Disease Control and Prevention (CDC) seroprevalence surveys between April and August 2020 were used to estimate infection and symptomatic underreporting multipliers. Main Outcomes: SARS-CoV-2 infections, symptomatic infections, hospitalizations, and deaths. **Findings:** >An estimation of 46 910 006 SARS-CoV-2 infections, 28 122 752 symptomatic infections, 956 174 hospitalizations, and 304 915 deaths occurred in the US through Nov 15, 2020. >14.3% of the US population was infected with SARS-CoV-2 and 8.6% had a symptomatic infection, with an infection hospitalization ratio of 2.0% and symptomatic fatality ratio of 1.1% through Nov 15, 2020. The US population remains a long way from herd immunity. **The number of estimated COVID-19 deaths is also remarkably more than the reported deaths** in the US through Nov 15, 2020, **supporting the conclusion that approximately 35% of COVID-19 deaths are not reported.** Limitations: Estimate the COVID-19 disease burden in the US using underreporting multipliers derived from the 10 specific states may not be nationally representative.

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BMJ Thorax 05JAN2021	Current smoking and COVID-19 risk: results from a population symptom app in over 2.4 million people	Hopkinson N.S., *et al.* UK [gotopaper]	Public Health / Epidemiology	**Main study outcome: development of 'classic' symptoms of COVID-19 during the pandemic defined as fever, new persistent cough and breathlessness and their association with current smoking.** > UK users of the Zoe COVID-19 Symptom Study app provided baseline data including demographics, anthropometrics, smoking status and medical conditions, and were asked to log their condition daily. > Participants who reported that they did not feel physically normal were then asked by the app to complete a series of questions, including 14 potential COVID-19 symptoms and about hospital attendance. > The number of concurrent COVID-19 symptoms was used as a proxy for severity and the pattern of association between symptoms was also compared between smokers and non-smokers. **Findings:** Data on 2 401 982 participants, mean (SD) age 43.6 (15.1) years, 63.3% female, overall smoking prevalence 11.0%. > 834 437 (35%) participants reported being unwell and entered one or more symptoms. >Current smokers were more likely to report symptoms suggesting a diagnosis of COVID-19; classic symptoms adjusted OR (95% CI) 1.14 (1.10 to 1.18); >5 symptoms 1.29 (1.26 to 1.31); >10 symptoms 1.50 (1.42 to 1.58). > The pattern of association between reported symptoms did not vary between smokers and non-smokers. **Data are consistent with people who smoke being at an increased risk of developing symptomatic COVID-19.**
JAMA Netw. 04JAN2021	Risk Factors Associated With All-Cause 30-Day Mortality in Nursing Home Residents With COVID-19	Panagiotou O.A., *et al.* USA [gotopaper]	Public Health / Epidemiology	Cohort study conducted at 351 US nursing homes among 5256 nursing home residents with COVID-19–related symptoms who had SARS-CoV-2 infection confirmed by PCR testing between March 16 and September 15, 2020. Main Outcome: Death due to any cause within 30 days of the 1st positive SARS-CoV-2 test result. **Findings:** >Compared with residents aged 75 to 79 years, the odds of death were 1.46 times higher for residents aged 80 to 84 years, 1.59 times higher for residents aged 85 to 89 years, and 2.14 times higher for residents aged 90 years or older. >Women had lower risk for 30-day mortality than men (odds ratio 0.69). >Comorbidities associated with 30-day mortality: diabetes (OR, 1.21) and chronic kidney disease (OR, 1.33). >Fever (OR, 1.66), shortness of breath (OR, 2.52), tachycardia (OR, 1.31), and hypoxia (OR, 2.05). >Compared with intact cognitively residants: the odds of death among residents with moderate cognitive impairment (CI) were 2.09 times higher, and 2.79 times higher for residents with severe CI. >Compared with residents with no or limited impairment in physical function (IPF), the odds of death among residents with moderate IPF were 1.49 times higher, and 1.64 times higher among residents with severe IPF. Once infected, **those with baseline functional limitations, cognitive impairment, and disease severity are at heightened risk for mortality**.

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Science 04JAN2021	Neutralizing antibody titres in SARS-CoV-2 infections	Lau E.H.Y., *et al.* USA [gotopaper](#)	Immunology	**Characterization of neutralizing antibody persistence in Infected patients.** Testing of 293 sera from an observational cohort of 195 reverse transcription polymerase chain reaction (RT-PCR) confirmed SARS-CoV-2 infections collected from 0 to 209 days after onset of symptoms. **Findings:** > Of 115 sera collected ≥61 days after onset of illness tested using plaque reduction neutralization (PRNT) assays, 99.1% remained seropositive for both 90% (PRNT90) and 50% (PRNT50) neutralization endpoints. > PRNT50 titres dropping to the detection limit of a titre of 1:10 for severe, mild and asymptomatic patients takes at least 372, 416 and 133 days > At day 90 after onset of symptoms (or initial RT-PCR detection in asymptomatic infections), it took 69, 87 and 31 days for PRNT50 antibody titres to decrease by half (T1/2) in severe, mild and asymptomatic infections, respectively. > Patients with severe disease had higher peak PRNT90 and PRNT50 antibody titres than patients with mild or asymptomatic infections. > Age did not appear to compromise antibody responses, even after accounting for severity. **SARS-CoV-2 infection elicits robust neutralizing antibody titres in most individuals.**
Nature Commun. 04JAN2021	Dose-dependent response to infection with SARS-CoV-2 in the ferret model and evidence of protective immunity	Ryan K.A., *et al.* UK [gotopaper](#)	Immunology / Preclinical model	> Understand if ferrets are a suitable species for a model of human SARS-CoV-2 infection > Dose titration study of SARS-CoV-2 in the ferret model > Animals are challenged intranasally with a range of titres of SARS-CoV-2 (5×10^2, 5×10^4 and 5×10^6 pfu) in 1 ml volume **Findings** > After a high (5×10^6 pfu) and medium (5×10^4 pfu) dose of virus is delivered, **intranasally**, viral RNA shedding in the **upper respiratory tract** (URT) is observed in 6/6 animals > Only 1/6 ferrets show similar signs after low dose (5×10^2 pfu) challenge > Ferrets re-challenged, after virus shedding ceased, are fully protected from acute lung pathology > The endpoints of URT viral RNA replication & distinct lung pathology are observed most consistently in the high dose group > This ferret model of SARS-CoV-2 infection presents a mild clinical disease
Clin Infect Dis. 03JAN2021	Distinct disease severity between children and older adults with COVID-19: Impacts of ACE2 expression, distribution, and lung progenitor cells	Zhang Z., *et al.* China [gotopaper](#)	Epidemiology	> Examine the expression pattern of angiotensin-converting enzyme 2 (ACE2), the cell-entry receptor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the role of lung progenitor cells in children and older patients. > cohort of 299 patients with COVID-19 > Expression and distribution of ACE2 and lung progenitor cells examinations: combination of public single-cell RNA-seq datasets, lung biopsies, and ex vivo infection of lung tissues with SARS-CoV-2 pseudovirus in children and older adults **Findings** > Compared to children, **ACE2 positive cells are generally decreased in older adults** and **mainly presented in the lower pulmonary tract** (alveolar region) and rarely in airway regions in the older adults ($p < 0.01$). > The lung progenitor cells are also decreased. These risk factors may impact disease severity and recovery from pneumonia caused by SARS-Cov-2 infection in older patients.