COVID-19
Selection of peer-reviewed articles

Special focus on Pharmaceutical and non-Pharmaceutical interventions starting from 18-06-20

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
MOVCOV19: https://modcov19.math.cnrs.fr/veille_public/

Journal and date	Title	Authors and link	Field of expertise	Key facts
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.**

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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%.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
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.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
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.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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. |

Journal and date	Title	Authors and link	Field of expertise	Key facts
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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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.

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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 inoculums, 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.

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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.**

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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.**

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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). **Cellular 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 gotopaper	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 gotopaper	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). <u>Primary outcome</u>: 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

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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. <u>Treatments</u>: usual care plus azithromycin 500 mg daily for three days, usual care plus other interventions, or usual care alone. <u>Coprimary endpoints</u> 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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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**

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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.

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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.

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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 – including transmission-blocking vaccines – 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.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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**.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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 in the ensuing 6 months**.
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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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**.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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 × 102, 5 × 104 and 5 × 106 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 × 102 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.