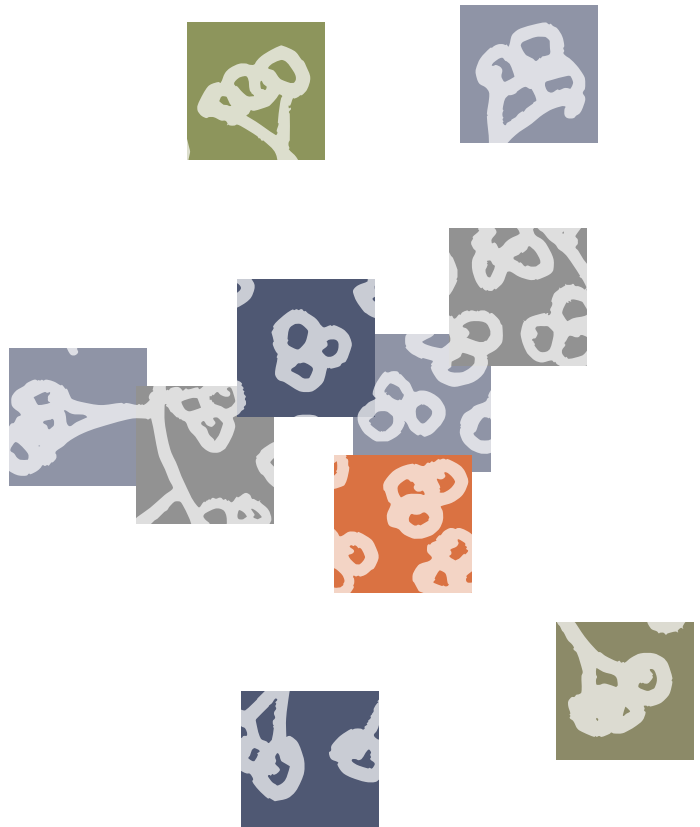


*Christian Hoffmann  
Bernd Sebastian Kamps*

# COVID REFERENCE *top10* *Daily Science vol. 2/2*



  
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# Volume 2

November 2020 – 14 March 2021

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# **COVID Reference Top 10**

*Daily Science*

Volume 2: November 2020 – 14 March 2021

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## Preface

The pandemic continues, Europe enters lockdown again. We will need this second volume.

[Christian Hoffmann](#) & [Bernd Sebastian Kamps](#)

1 November 2020

## Preface to Volume 1

Here we publish in a single PDF the [daily Top 10 scientific papers](#) we have presented ever since COVID Reference's first edition on 29 March 2020. There is no secret to our procedure: the daily scanning of the literature helps us to stay afloat in the never-ending waves of new publications about SARS-CoV-2 and COVID-19. Many papers discussed in the Top 10 will eventually make it into subsequent editions of COVID Reference.

We dedicate this book to our students. May this selection of approx. 1,000 fine articles and full-text links deepen their understanding of the new coronavirus and prepare them for the challenges ahead.

[Christian Hoffmann](#) & [Bernd Sebastian Kamps](#)

15 July 2020



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# November 2020

## 1 November

### Virology

Shang J, Han N, Chen Z, et al. **Compositional diversity and evolutionary pattern of coronavirus accessory proteins**. Briefings in Bioinformatics, October 30, 2020, bbaa262. Full-text: <https://doi.org/10.1093/bib/bbaa262>

Accessory proteins play important roles in the interaction between coronaviruses and their hosts. The authors developed a standardized genome annotation tool for coronavirus (CoroAnnoter) by combining open reading frame prediction, transcription regulatory sequence recognition and homologous alignment. This tool builds a comprehensive profile for coronavirus accessory proteins covering their composition, classification, evolutionary pattern and host interaction.

### Transmission

Wang Y, Xu G, Huang YW. **Modeling the load of SARS-CoV-2 virus in human expelled particles during coughing and speaking**. PLoS One. 2020 Oct 30;15(10):e0241539. PubMed: <https://pubmed.gov/33125421> . Full-text: <https://doi.org/10.1371/journal.pone.0241539>

The authors investigated the dependence of airborne viral load on the size distributions of the human expelled particles from coughing and speaking. Of note, differentiating “aerosols” and “droplets” using a specific size, e.g., 5  $\mu\text{m}$ , did not reflect the actual evolution of virus-containing particles over time and space, because a large number of particles above 5  $\mu\text{m}$  remained airborne after an extended period of time. Simulation showed that after ten seconds of a cough, although most evaporated particles are larger than 5  $\mu\text{m}$ , 59.5% of the original virus-containing particles were still able to remain airborne. Simulation also showed that wearing a mask can effectively reduce the spread of the viruses. The results challenge the false dichotomy of using aerosols and droplets to separate the modes of disease transmission.

## Vaccine

Kahn JP, Henry LM, Mastroianni C, et al. **Opinion: For now, it's unethical to use human challenge studies for SARS-CoV-2 vaccine development.** PNAS October 29, 2020. Full-text: <https://doi.org/10.1073/pnas.2021189117>

Important comment: see title. According to the authors, human challenge studies (HCS) to address SARS-CoV-2 face unacceptable ethics challenges, and, further, undertaking them would do a disservice to the public by undermining already strained confidence in the vaccine development process. Ultimately, the social value of these HCS (in terms of deaths averted) hinges on the premise that people at greatest risk of COVID-19-related mortality will receive a safe and efficacious vaccine sooner than they would without HCS. Read why this will be probably not the case and why HCS would do more harm than good.

## Diagnostics

Ward H, Cooke G, Atchison C, et al. **Declining prevalence of antibody positivity to SARS-CoV-2: a community study of 365 000 adults.** [Preprint] 2020. Full-text: <https://www.imperial.ac.uk/media/imperial-college/institute-of-global-health-innovation/MEDRXIV-2020-219725v1-Elliott.pdfdoi:10.1101/2020.10.26.20219725>.

Not yet peer reviewed, but important data. Results from the large, nationwide REACT (real time assessment of community transmission) antibody study which was led by Imperial College London, show that the national antibody prevalence in the UK was 6% around 12 weeks after the epidemic's April peak. Since then, the rates had fallen to 4.4% 24 weeks after the peak. These data suggest that antibodies induced by natural infection may be short lived, as is the case for other seasonal coronaviruses.

Henss L, Scholz T, von Rhein C, et al. **Analysis of humoral immune responses in SARS-CoV-2 infected patients.** J Infect Dis. 2020 Oct 31;jiaa680. Pub-Med: <https://pubmed.gov/33128369> . Full-text: <https://doi.org/10.1093/infdis/jiaa680>

Do previous coronavirus infections protect from severe courses? Lisa Henss and colleagues from Frankfurt University analyzed the humoral immune response of a cohort of 143 COVID-19 patients, using ELISA and neutralization assays. Disease severity correlated with the amount of SARS-CoV-2 specific IgG and IgA and the neutralization activity of the antibodies. Neutralizing titers of patients with mild disease were very low and higher titers

were only detected in severe cases. Of note, compared to patients with mild-moderate disease, patients with severe disease had only weakly neutralizing antibodies against coronavirus-NL63. Although the numbers of severe cases were low, it remains tempting to speculate that preexisting immunity to NL63 or other common cold coronaviruses might reduce the risk of severe disease.

## Clinical

Hoffmann C, Wolf E. **The Low Case Fatality Rate of COVID-19 in Hong Kong Could Be Deceptive.** *Clin Infect Dis.* 2020 Oct 29;ciaa1676. PubMed: <https://pubmed.gov/33119056> . Full-text: <https://doi.org/10.1093/cid/ciaa1676>

Last Monday, we published data from the 20 most affected European countries and the USA and Canada, showing that during the first wave of the pandemic, the variance of crude CFR of COVID-19 was predominantly (80-96%) determined by the proportion of older individuals who are diagnosed with SARS-CoV-2 (Hoffmann 2020).

Here we show that our model might apply to other countries. In Hong Kong, for example, a very low CFR of only 0.4% has been reported during the first weeks (Lui GC 2000). In contrast to the authors, we believe that this was mainly due to the low number of older persons among the confirmed SARS-CoV-2 cases. We also show that the overall CFR in Hong Kong has increased since then, paralleling the increasing proportion of older persons among confirmed cases. Thanks to the incredible speed of Clinical Infectious Diseases' publishing policies (contrasting many other journals), the authors from Hong Kong have been already able to respond (in some points they agree, in other points they don't). Please read the discussion (Lui GC 2000).

Why is this important? In many countries facing a low CFR during the first wave, there is a widespread feeling that this was mainly due to a good health care system such as ICU or testing capacities. We believe that this perception can be deceptive and that the picture in these countries will change immediately when more elderly people are infected.

Hoffmann C, Wolf E. **Older age groups and country-specific case fatality rates of COVID-19 in Europe, USA and Canada.** *Infection.* 2020 Oct 24;1-6. PubMed: <https://pubmed.gov/33098532> . Full-text: <https://doi.org/10.1007/s15010-020-01538-w>

Lui GC, Yip TC, Wong VW, et al. **Significantly Lower Case-fatality Ratio of Coronavirus Disease 2019 (COVID-19) than Severe Acute Respiratory Syndrome (SARS) in Hong Kong-A Territory-Wide Cohort Study.** *Clin In-*

fect Dis. 2020 Oct 1:ciaa1187. PubMed: <https://pubmed.gov/33005933>. Full-text: <https://doi.org/10.1093/cid/ciaa1187>

Lui CG, Yip TC, Hui D, et al. **Reply to Hoffmann and Wolf**. Clinical Infectious Diseases, October 29, ciaa1678, <https://doi.org/10.1093/cid/ciaa1678>.

Lim ZJ, Subramaniam A, Reddy MP, et al. **Case Fatality Rates for COVID-19 Patients Requiring Invasive Mechanical Ventilation: A Meta-analysis**. Am J Respir Crit Care Med. 2020 Oct 29. PubMed: <https://pubmed.gov/33119402> . Full-text: <https://doi.org/10.1164/rccm.202006-2405OC>

Definitive hospital outcome on 13,120 patients receiving invasive mechanical ventilation. Among studies where age-stratified CFR was available, pooled CFR estimates ranged from 47.9% (95% CI 46.4-49.4%) in younger patients (age ≤40) to 84.4% (95% CI 83.3-85.4) in older patients (age >80). CFR was also higher in early COVID-19 epicenters.

Prieto-Alhambra D, Balló E, Mora N, et al. **Filling the gaps in the characterization of the clinical management of COVID-19: 30-day hospital admission and fatality rates in a cohort of 118 150 cases diagnosed in outpatient settings in Spain**. International Journal of Epidemiology, October 29, 2020, dyaa190. Full-text: <https://doi.org/10.1093/ije/dyaa190>

Filling the missing link in the natural history of COVID-19, from first (usually milder) symptoms to hospitalization and/or death, the authors characterized a huge number of COVID-19 patients at the time at which they were diagnosed in outpatient settings and estimated 30-day hospital admission and fatality rates. In the month after diagnosis, 14.8% (14.6–15.0) were hospitalized, with a greater proportion of men and older people, peaking at age 75–84 years. Thirty-day fatality was 3.5%, higher in men, increasing with age and highest in those residing in nursing homes (24.5%).

Kim T, Roslin M, Wang JJ, et al. **Body Mass Index as a Risk Factor for Clinical Outcomes in Patients Hospitalized with COVID-19 in New York**. Obesity (Silver Spring). 2020 Oct 31. PubMed: <https://pubmed.gov/33128848> . Full-text: <https://doi.org/10.1002/oby.23076>

Risk factor obesity. In total, 10,861 COVID-19 patients admitted to the Northwell Health system hospitals during March and April, were classified according to their BMI: underweight (2%), normal (only 23%!), overweight (38%), obesity class I (22%), II (9%), and III (7%). Patients who were overweight (OR=1.27), obesity class I (OR=1.48), obesity class II (OR=1.89), and obesity class

III (OR=2.31) had increased risk of requiring invasive mechanical ventilation. Overall, underweight and obesity classes II and III were statistically associated with death (OR=1.25-1.61). However, once mechanically ventilated, all patients regardless of BMI had similar odds of death.

## Treatment

Chow JH, Khanna AK, Kethireddy S, et al. **Aspirin Use is Associated with Decreased Mechanical Ventilation, ICU Admission, and In-Hospital Mortality in Hospitalized Patients with COVID-19.** *Anesth Analg.* 2020 Oct 21. PubMed: <https://pubmed.gov/33093359> . Full-text: <https://doi.org/10.1213/ANE.0000000000005292>

Aspirin may help (a little bit). In this retrospective, observational cohort study of 412 adult patients admitted with COVID-19 to multiple US hospitals between March and July, 98 (24%) received aspirin within 24 hours of admission or 7 days prior to admission. Aspirin use had a crude association with less mechanical ventilation (36% vs. 48%,  $p=0.03$ ) and ICU admission (39% vs. 51%,  $p=0.04$ ), but no crude association with in-hospital mortality (26% vs. 23%  $p=0.51$ ). After adjusting for 8 confounding variables, aspirin use was independently associated with decreased risk of mechanical ventilation (adjusted HR 0.56, 95% CI 0.37-0.85,  $p=0.007$ ), ICU admission (adjusted HR 0.57, 95% CI 0.38-0.85,  $p=0.005$ ), and in-hospital mortality (adjusted HR 0.53, 95% CI 0.31-0.90,  $p=0.02$ ). According to the authors, a sufficiently powered randomized controlled trial is needed.

## 2 November

### Virology

Miller D, Martin MA, Harel N et al. **Full genome viral sequences inform patterns of SARS-CoV-2 spread into and within Israel.** *Nat Commun* 11, 5518 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19248-0>

This group from Israel has analyzed 212 SARS-CoV-2 sequences, in order to perform a comprehensive analysis to trace the origins and spread of the virus. Travelers returning from the US significantly contributed to viral spread in Israel. The basic reproduction number of the virus was initially around 2.5, dropping by more than two-thirds following the implementation of social distancing measures. Transmission heterogeneity in SARS-CoV-2 spread was high, with between 2-10% of infected individuals resulting in 80% of secondary infections.

Du P, Ding N, Li J, et al. **Genomic surveillance of COVID-19 cases in Beijing.** Nat Commun. 2020 Oct 30;11(1):5503. PubMed: <https://pubmed.gov/33127911>. Full-text: <https://doi.org/10.1038/s41467-020-19345-0>

To understand the genetic characteristics of SARS-CoV-2 in Beijing, the authors collected pharyngeal swabs and sputa samples from 126 patients to perform viral genome sequencing after admission and consent procedures. Here they present genomic surveillance data on 102 imported cases, which account for 17.2% of the total cases in Beijing. Genomic comparisons reveal higher genomic diversity in the imported group compared to both the Wuhan exposure and local transmission groups, indicating continuous genomic evolution during global transmission.

Borges V, Isidoro J, Cortes-Martins H. **Massive dissemination of a SARS-CoV-2 Spike Y839 variant in Portugal.** Emerg Microbes Infect 2020 Nov 2;1-58. Full-text: <https://doi.org/10.1080/22221751.2020.1844552>

Here, the authors track the geotemporal spread of a SARS-CoV-2 variant with a mutation (D839Y) in a potential host-interacting region involving the Spike fusion peptide, which is a target motif of anti-viral drugs that plays a key role in SARS-CoV-2 infectivity. The Spike Y839 variant was most likely imported from Italy in mid-late February and massively disseminated in Portugal during the early epidemic. Between March 14th and April 9th (covering the exponential epidemic phase) the relative frequency of the Spike Y839 variant increased at a rate of 12.1% every three days, being potentially associated with 24.8% of all COVID-19 cases in Portugal during this period. The data supports population/epidemiological (founder) effects contributing to the Y839 variant superspread. This variant was likely one of the first SARS-CoV-2 to be introduced in Portugal, so it might have had more opportunity to spread. Its introduction is strongly linked to an international trade fair in Milan with many Portuguese attendees. The potential existence of selective advantage is also discussed, although experimental validation is required.

## Diagnostic

Chan CW, Shahul S, Coleman C, et al. **Evaluation of the Truview Easy Check COVID-19 IgM/IgG Lateral Flow Device for Rapid Anti-SARS-CoV-2 Antibody Detection.** American Journal of Clinical Pathology, 02 November 2020, aqaa22. Full-text: <https://doi.org/10.1093/ajcp/aqaa221>



Clarence W. Chan and colleagues from Chicago evaluated the analytical and clinical performance of the Truvian Easy Check COVID-19 IgM/IgG antibody test. This test was designed to detect the nucleocapsid and S1 spike protein RBD epitopes of SARS-CoV-2. Results are available at 10 minutes after test initiation for serum and possibly fingerstick blood samples. The Easy Check device showed excellent clinical and analytical performance; the test compares well with the Roche Elecsys anti-SARS-CoV-2 antibody assay. Of 99 patient samples that were positively confirmed by PCR for SARS-CoV-2, antibodies against the virus were detected by both tests in 88 of the samples, whereas 9 of the 99 samples eluded detection by both testing modalities. All samples from 41 pre-pandemic volunteers remained negative.

## Clinical

Gandhi RT, Lynch JB, del Rio C. **Mild or Moderate Covid-19**. *N Engl J Med*, October 29, 2020; 383:1757-1766. Full-text: <https://doi.org/10.1056/NEJMcp2009249>

Brief overview for clinicians. In patients with moderate disease, dexamethasone is not efficacious (and may be harmful) and data are insufficient to recommend for or against routine use of remdesivir. Efforts center on personal protective equipment for health care workers, social distancing, and testing.

Giustino G, Croft LB, Stefanini GG, et al. **Characterization of Myocardial Injury in Patients With COVID-19**. *J Am Coll Cardiol*. 2020 Nov 3;76(18):2043-2055. PubMed: <https://pubmed.gov/33121710>. Full-text: <https://doi.org/10.1016/j.jacc.2020.08.069>

This multicenter cohort study (7 hospitals in New York City and Milan) analyzed hospitalized COVID-19 patients who had undergone transthoracic echocardiographic (TTE) and electrocardiographic evaluation during their index hospitalization. Myocardial injury was defined as any elevation in cardiac troponin at the time of clinical presentation or during the hospitalization. Overall, myocardial injury was observed in 190 patients (62.3%). Among patients with COVID-19 who underwent TTE, cardiac structural abnormalities were present in nearly two-thirds of patients with myocardial injury. Rates of in-hospital mortality were 5.2%, 18.6%, and 31.7% in patients without myocardial injury, with myocardial injury without TTE abnormalities, and with myocardial injury and TTE abnormalities.

## Collateral damage

Qu Z, Oedingen C, Bartling T, Schrem H, Krauth C. **Organ procurement and transplantation in Germany during the COVID-19 pandemic.** Lancet. 2020 Oct 31;396(10260):1395. PubMed: <https://pubmed.gov/33129390>. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32213-3](https://doi.org/10.1016/S0140-6736(20)32213-3)

No damage in this area: Compared with the previous year, the cumulative numbers of deceased organ donors and transplants showed no significant reduction in Germany. Kidney transplantation numbers were stable, while the numbers of heart, lung, and liver transplantations from deceased donors even increased from January to April, 2020, when compared with the same period of the previous year. In contrast, transplant activities in Italy and Spain were reduced by 30–50%.

Sors F, Grassi M, Agostini T, Murgia M. **The sound of silence in association football: Home advantage and referee bias decrease in matches played without spectators.** Eur J Sport Sci. 2020 Nov 1;1-21. Full-text: <https://doi.org/10.1080/17461391.2020.1845814>

We have eagerly awaited this news for decades: spectators can significantly contribute to determine the dynamics and the outcomes of professional football matches (home advantage and referee bias are two well-documented phenomena in professional sports). COVID-19 has made it possible: focusing on the first and second divisions of the top four UEFA countries, the authors analyzed 841 matches behind closed doors during the pandemic. This extremely important work revealed that observed frequencies for home victories, draws and away victories were significantly different from the expected frequencies calculated based on the last three complete seasons with spectators. The absence of a referee bias in favor of the home teams for yellow cards indicated that this factor might be particularly affected by the presence/absence of social pressure by spectators. Various parameters were considered, and the analyses revealed a reduction of home advantage and the absence of referee bias. They'll walk alone now.

## Pregnancy

Sahin D, Tanacan A, Erol SA, et al. **Updated experience of a tertiary pandemic center on 533 pregnant women with COVID-19 infection: A prospective cohort study from Turkey.** Int J Gynaecol Obstet. 2020 Nov 1. PubMed: <https://pubmed.gov/33131057>. Full-text: <https://doi.org/10.1002/ijgo.13460>

Huge prospective cohort from Turkey: Of 533 cases, 509 (95.5%) had mild disease, 7 (1.3%) were admitted to the intensive care unit (ICU), and invasive mechanical ventilation was necessary in 2 (0.4%) patients. Maternal mortality was observed in 2 (0.4%) cases. In total, 66 (12.4) had pregnancy complications (preterm delivery 4.1%). All neonates were negative for COVID-19. The rate of admission to the neonatal ICU was 9.9%. One specimen of breast milk was positive for the infection.

## Pediatrics

Belhadjer Z, Auriau J, Méot M, et al. **Addition of Corticosteroids to Immune Globulins is Associated with Recovery of Cardiac Function in Multi-inflammatory Syndrome in Children (MIS-C)**. *Circulation*, 28 October 2020. Full-text: <https://doi.org/10.1161/CIRCULATIONAHA.120.050147>

Steroids may help in MIS-C: 18 patients admitted before 1 May received immune globulins (IVIG 2g/Kg once) as first line treatment, and the 22 patients admitted after this date received a combination of IVIG and intravenous methylprednisolone (0.8mg/kg/day during 5 days). These two populations had similar clinical, cardiac and biological characteristics at baseline. The main finding was the reduction of time to recovery of left ventricle ejection fraction (LVEF) and isovolumic relaxation time (IVRT), as well as pediatric intensive care unit (PICU) stay in the group receiving a combination of IVIG and steroids compared to the group receiving only IVIG: respectively 2.9 vs. 5.4 days, 6.4 vs. 20.6 days, and 3.4 vs. 5.3 days ( $p < 0.05$ ).

## 3 November

### Transmission

Ng OT, Marimuthu K, Koh V, et al. **SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study**. *Lancet Infect Dis* 2020, published 2 November. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30833-1](https://doi.org/10.1016/S1473-3099(20)30833-1)

Excellent retrospective cohort study by [Vernon Lee](#), Oon Tek Ng and colleagues Between Jan 23 and April 3, 2020, the authors identified 7,518 close contacts (1779 [23%] household contacts, 2231 [30%] work contacts, and 3508 [47%] social contacts) linked to 1114 PCR-confirmed index cases. The secondary clinical attack rate:

**Household contacts:** 5.9% (95% CI 4.9–7.1).

Particular risk factors:

1. Sharing a bedroom (multivariable odds ratio [OR] 5.38)
2. Being spoken to by an index case for 30 min or longer (7.86)

**Non-household contact:** Work contacts, 1.3% (0.9–1.9); social contacts, 1.3% (1.0–1.7).

Particular risk factors:

1. Exposure to more than one case (3.92)
2. Being spoken to by an index case for 30 min or longer (2.67)
3. Sharing a vehicle with an index case (3.07).

Among both household and non-household contacts, indirect contact, meal sharing, and lavatory co-usage were **not** independently associated with SARS-CoV-2 transmission.

## Immunology

Khoury DS, Wheatley AK, Ramuta MD, et al. **Measuring immunity to SARS-CoV-2 infection: comparing assays and animal models.** *Nat Rev Immunol* (2020). Full-text: <https://doi.org/10.1038/s41577-020-00471-1>

Assays to measure naturally acquired immunity and test the efficacy of immune interventions are key to the development of novel prophylactic and therapeutic interventions. Here, Miles Davenport, David Khoury and colleagues analyze a selection of existing assays for measuring antibody-mediated virus neutralization and animal models of infection with SARS-CoV-2. Their message: identify what you want to measure and match these goals to your experimental design.

Bošnjak B, Stein SC, Willenzon S, et al. **Low serum neutralizing anti-SARS-CoV-2 S antibody levels in mildly affected COVID-19 convalescent patients revealed by two different detection methods.** *Cell Mol Immunol* (2020). Full-text: <https://doi.org/10.1038/s41423-020-00573-9>

Reinhold Förster, Berislav Bošnjak and colleagues performed a surrogate virus neutralization test (sVNT) and SARS-CoV-2 S protein-pseudotyped vesicular stomatitis virus (VSV) vector-based neutralization assay (pVNT) to assess the degree to which serum antibodies from coronavirus disease 2019 (COVID-19) convalescent patients interfere with the binding of SARS-CoV-2 S to ACE2. They analyzed 40 patients with mild SARS-CoV-2 infection, 10 patients with

severe infection and 12 healthy controls. Both tests revealed neutralizing anti-SARS-CoV-2 S antibodies in the sera of approximately 90% of mildly and 100% of severely affected COVID-19 convalescent patients. Levels of neutralizing antibodies correlated with the duration and severity of clinical symptoms but not with patient age. The authors conclude that that sVNT is technically less complicated, cheaper, and much faster than pVNT, making it more suitable for the rapid screening of a large number of samples.

Meffre E, Iwasaki A. **Interferon deficiency can lead to severe COVID.** Nature 2020, published 2 November. Full-text: <https://www.nature.com/articles/d41586-020-03070-1>

In this *News & Views* articles, the authors highlight the possible key role for the signaling pathway mediated by type I interferon proteins in the development of severe COVID-19. The authors discuss the papers by Bastard et al. and Zhang et al. we presented on [September 25](#):

Bastard P, Rosen LB, Zhang Q, et al. **Auto-antibodies against type I IFNs in patients with life-threatening COVID-19.** Science 2020, published 24 September. Full-text: <https://science.sciencemag.org/content/early/2020/09/23/science.abd4585>

Zhang Q, Bastard P, Liu Z, et al: **Inborn errors of type I IFN immunity in patients with life-threatening COVID-19.** Science 2020, published 24 September. Full-text: <https://science.sciencemag.org/content/early/2020/09/23/science.abd4570>

## Clinical

Zhong P, Xu J, Yang D, et al. **COVID-19-associated gastrointestinal and liver injury: clinical features and potential mechanisms.** Sig Transduct Target Ther 5, 256 (2020). Full-text: <https://doi.org/10.1038/s41392-020-00373-7>

Besides common respiratory symptoms, some patients with COVID-19 experience gastrointestinal symptoms, such as diarrhea, nausea, vomiting, and loss of appetite. In this review, Yangbai Sun, Peijie Zhong and colleagues highlight the manifestations and potential mechanisms of gastrointestinal and hepatic injuries in COVID-19.

## (Future?) Treatment

Sokolowska M. Outsmarting SARS-CoV-2 by empowering a decoy ACE2. *Sig Transduct Target Ther* 5, 260 (2020), published 3 November. Full-text: <https://doi.org/10.1038/s41392-020-00370-w>

There are currently a few therapeutic approaches which focus on blocking SARS-CoV-2 binding to its key receptor, an angiotensin-converting enzyme 2 (ACE2), or on inhibition of virus spike cleavage. Milena Sokolowska discusses soluble recombinant human ACE2 (rhACE2) and a paper we presented on **August 4**: Chan KK, Dorosky D, Sharma P, et al. **Engineering human ACE2 to optimize binding to the spike protein of SARS coronavirus 2**. *Science* 2020, published 4 August. Full-text: <https://science.sciencemag.org/content/early/2020/08/03/science.abc0870>

Abd El-Aziz TM, Al-Sabi A, Stockand JD. **Human recombinant soluble ACE2 (hrsACE2) shows promise for treating severe COVID-19**. *Sig Transduct Target Ther* 5, 258 (2020). Full-text: <https://doi.org/10.1038/s41392-020-00374-6>

Tarek Mohamed Abd El-Aziz and colleagues discuss encouraging data from the first severe COVID-19 patient successfully treated with human recombinant soluble angiotensin-converting enzyme-2 (hrsACE2): the disappearance of the virus from the serum, the nasal cavity and lungs, and a reduction of inflammatory cytokine. (See the paper by Zoufaly et al. we presented on **September 25**: Zoufaly A, Poglitsch M, Aberle JH, et al. **Human recombinant soluble ACE2 in severe COVID-19**. *Lancet Resp Med* September 24, 2020. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30418-5](https://doi.org/10.1016/S2213-2600(20)30418-5).) Notably, the use of hrsACE2 did not impede the generation of neutralizing antibodies. The patient improved rapidly.

## Pediatrics

Martinez OM, Bridges ND, Goldmunth E, et al. **The immune roadmap for understanding multi-system inflammatory syndrome in children: opportunities and challenges**. *Nat Med* (2020). Full-text: <https://doi.org/10.1038/s41591-020-1140-9>

In June 2020, immunologists and clinicians met to identify key questions surrounding the ‘multi-system inflammatory syndrome in children’ (MIS-C). This Meeting Report describes the main findings from the workshop. Read about B cell immunity, T cell immunity, innate immunity, genetics and epigenetics.

## Spanish

If you read Spanish, read Mouzo J, Valdés I, Battista G. **Los médicos en las UCI: “Aún no es el infierno, pero sí el purgatorio”** – El País, published 31 October. Full-text: <https://elpais.com/sociedad/2020-10-30/los-medicos-en-las-uci-aun-no-es-el-infierno-pero-si-el-purgatorio.html>

Una cuarta parte de las UCI españolas están ocupadas por pacientes con covid-19. EL PAÍS entra en dos unidades, en Madrid y Barcelona, que bordean el colapso

## French

If you read French, read Jérôme B. **Covid-19 : dans le Grand Paris, les personnes âgées défavorisées sont les premières victimes.** Full-text : Le Monde 2020, published 3 November. Full-text: [https://www.lemonde.fr/planete/article/2020/11/03/dans-le-grand-paris-les-personnes-agees-defavorisees-premieres-victimes-du-covid-19\\_6058265\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/03/dans-le-grand-paris-les-personnes-agees-defavorisees-premieres-victimes-du-covid-19_6058265_3244.html)

Au printemps, en Ile-de-France, le virus a d’abord fauché les plus de 65 ans dans les communes où les revenus sont les plus bas et les logements les plus exigus, selon une étude universitaire qu’a pu se procurer « Le Monde ».

Jérôme B. **Covid-19 : « Le tissu social doit devenir notre allié, plus encore que lors de la première vague ».** Le Monde 2020, published 3 November. Full-text: [https://www.lemonde.fr/planete/article/2020/11/03/covid-19-le-tissu-social-doit-devenir-notre-allie-plus-encore-que-lors-de-la-premiere-vague\\_6058334\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/03/covid-19-le-tissu-social-doit-devenir-notre-allie-plus-encore-que-lors-de-la-premiere-vague_6058334_3244.html)

Le directeur de la santé publique de l’agence régionale de santé d’Ile-de-France, Luc Ginot, évoque la surmortalité dans les villes pauvres de la région et les moyens mis en œuvre pour y faire face.

## 4 November

### Epidemiology

O’Driscoll M, Dos Santos GR, Wang L, et al. **Age-specific mortality and immunity patterns of SARS-CoV-2.** Nature (2020). Full-text: <https://doi.org/10.1038/s41586-020-2918-0>

The age distribution of deaths in younger age groups (<65 years) is consistent across different settings. This is the result of a study by Henrik Salje, Megan

O’Driscoll and colleagues who used age-specific COVID-19 death data from 45 countries and the results of 22 seroprevalence studies to investigate the fatality patterns across multiple countries. The authors also demonstrate how outbreaks in nursing homes can drive overall population IFRs (infection-to-fatality ratio), through both increased attack rates and increased vulnerability. They estimate that around 5% of the populations had been infected by the 1st of September 2020, with much higher transmission likely to have occurred in a number of Latin American countries.

Vijayan T, Shin M, Adamson PC, et al. **Beyond the 405 and the 5: Geographic variations and factors associated with SARS-CoV-2 positivity rates in Los Angeles County.** Clin Infect Dis 2020, published 3 November. Full-text: <https://doi.org/10.1093/cid/ciaa1692>

SARS-CoV-2 infection was more frequent in communities with high proportions of Latino/a residents, those living below the federal poverty line and with high household densities. This is the conclusion of a study by Tara Vijayan et al. in Los Angeles County (LAC) after analyzing more than 800,000 SARS-CoV-2 tests. The overall positivity rate was 10.2%.

## Immunology

Zohar T, Loos C, Fischinger S, et al. **Compromised humoral functional evolution tracks with SARS-CoV-2 mortality.** Cell 2020, published 3 November. Full-text: <https://doi.org/10.1016/j.cell.2020.10.052>

Both IgA and IgM evolve rapidly across all levels of disease severity, but rapid and potent IgG class switching is linked to survival. This is the key message of a paper by Galit Alter, Tomer Zohar and colleagues who analyzed the early evolution of the humoral response in 193 hospitalized individuals with moderate to severe COVID-19. The data highlight distinct humoral trajectories associated with resolution of SARS-CoV-2 infection.

Files JK, Boppana S, Perez MD, et al. **Sustained cellular immune dysregulation in individuals recovering from SARS-CoV-2 infection.** J Clin Invest. 2020 Oct 29;140491. PubMed: <https://pubmed.gov/33119547>. Full-text: <https://doi.org/10.1172/JCI140491>

A prolonged period of immune dysregulation may follow SARS-CoV-2, both in hospitalized and non-hospitalized patients. This is the result of a study by Nathaniel Erdman, Jacob Files and colleagues who analyzed samples and data from 46 hospitalized and 29 non-hospitalized patients as well as 20 controls.



The authors also report that the dysregulation of T-cell activation and exhaustion markers in non-hospitalized individuals appears to be more pronounced in the elderly.

Stervbo U, Rahmann S, Roch T, et al. **Epitope similarity cannot explain the pre-formed T cell immunity towards structural SARS-CoV-2 proteins.** *Sci Rep* 10, 18995 (2020). Full-text: <https://doi.org/10.1038/s41598-020-75972-z>

Biobanked venous blood contains T cells reactive to SARS-CoV-2 S-protein even before the outbreak in Wuhan, suggesting that there is a preformed T cell memory towards structural proteins in individuals not exposed to SARS-CoV-2. Here, Ulrik Stervbo et al. utilize a combination of epitope prediction and similarity to common human pathogens to identify potential sources of the SARS-CoV-2 T cell memory. Their data suggests that the observed SARS-CoV-2 pre-formed immunity to structural proteins is not driven by near-identical epitopes.

Chen Y, Zuiani A, Fischinger S, and al. **Quick COVID-19 Healers Sustain Anti-SARS-CoV-2 Antibody Production.** *Cell* 2020, published 3 November. Full-text: <https://doi.org/10.1016/j.cell.2020.10.051>

After SARS-CoV-2 infection, some individuals maintain stable or increased SARS-CoV-2 IgG, displaying an immune phenotype that connects rapid symptom clearance to differential antibody durability dynamics. Those who sustain virus-specific IgG production might tend to have shorter disease courses despite similar distribution of initial anti-SARS-CoV-2 IgG levels, and their anti-S memory B cells harbor increased levels of somatic hypermutation (SHM) shortly after disease resolution. This is a result of an analysis by Duane Wesemann, Yuezhou Chen and colleagues who charted longitudinal antibody responses to SARS-CoV-2 in 76 subjects after symptomatic COVID-19 followed longitudinally to ~100 days.

Custódio TF, Das H, Sheward DJ, et al. **Selection, biophysical and structural analysis of synthetic nanobodies that effectively neutralize SARS-CoV-2.** *Nat Commun* 11, 5588 (2020). Full-text: <https://doi.org/10.1038>

Traditional antibody production is hampered by long development times and costly production. Here, Christian Löw, Tânia Custódio and colleagues report the rapid isolation and characterization of nanobodies that target the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein. Several of the 85

binders isolated by the authors had low nanomolar affinities and efficient neutralization activity.

## Severe COVID

Evans RM, Lippman SM. **Shining Light on the COVID-19 Pandemic: A Vitamin D Receptor Checkpoint in Defense of Unregulated Wound Healing.** *Cell Metab.* 2020 Sep 11;32(5):704-9. PubMed: <https://pubmed.gov/32941797>. Full-text: <https://doi.org/10.1016/j.cmet.2020.09.007>

Ronald Evans and Scott Lippman propose repurposing paricalcitol (vitamin D analog) infusion therapy to restrain the COVID-19 cytokine storm, reasoning that vitamin D deficiency and the failure to activate the vitamin D receptor can aggravate this respiratory syndrome by igniting a wounding response in stellate cells of the lung. Find out what could be the appropriate dose and the potential complications.

## Pediatrics

Hurst JH, Heston SM, Chambers HN, et al. **SARS-CoV-2 Infections Among Children in the Biospecimens from Respiratory Virus-Exposed Kids (BRAVE Kids) Study.** *Clin Infect Dis* 2020, published 3 November. Full-text: <https://doi.org/10.1093/cid/ciaa1693>

Children ages 6-13 years are frequently asymptomatic (39%) and have respiratory symptoms less often than younger children (29% vs. 48%) or adolescents (29% vs. 60%). However, Matthew Kelly, Jillian Hurst and colleagues found no differences in nasopharyngeal viral load by age or between symptomatic and asymptomatic children.

	6-13 years	14-20 years
Respiratory symptoms	29%	60%
Influenza-like symptoms	39%	61%
Gastrointestinal symptoms	9%	27%
Sensory symptoms	9%	42%
Disease duration	4 (IQR 3,8)	7 (4,12)

## Society

Editors (Int J Refug Law). **Human Mobility and Human Rights in the COVID-19 Pandemic: Principles of Protection for Migrants, Refugees, and Other Displaced Persons**. Int J Refug Law 2020, published 4 November. Full-text: <https://doi.org/10.1093/ijrl/eeaa028>

During the SARS-CoV-2 pandemic, many States have taken harsh and unprecedented measures against migrants, refugees, and other displaced persons. These have included border closures, quarantines, expulsions, and lockdowns of migrant worker communities and refugee camps. Read about

- Equal treatment and non-discrimination
- Right to health
- State obligations to combat stigma, racism and xenophobia
- Restrictions on movement between and within States
- Enforcement of immigration law, including detention
- Right to protection of life and health for persons in camps, collective shelters, and settlements
- Right to information and protection of privacy
- Gender considerations and labor rights of workers

## Spanish

If you read Spanish, read De Benito E. **La niebla en la mente que deja el virus: “Soy filóloga y se me olvidan palabras como sartén”** – El País 2020, published 4 November. Full-text: <https://elpais.com/sociedad/2020-11-03/la-niebla-en-la-mente-que-deja-el-virus-soy-filologa-y-se-me-olvidan-palabras-como-sarten.html>

Afectados por la covid sufren pérdidas de memoria o problemas de concentración meses después de erradicar la infección

## French

If you read French, read Gaudin C. **Covid-19 : « Dans les mesures sanitaires, il y a des nuances entre pays européens, mais un gouffre entre l’Asie et l’Occident »** – Le Monde 2020, published 4 November. Full-text: [https://www.lemonde.fr/idees/article/2020/11/04/covid-19-dans-les-mesures-sanitaires-il-y-a-des-nuances-entre-pays-europeens-mais-un-gouffre-entre-l-asie-et-l-occident\\_6058407\\_3232.html](https://www.lemonde.fr/idees/article/2020/11/04/covid-19-dans-les-mesures-sanitaires-il-y-a-des-nuances-entre-pays-europeens-mais-un-gouffre-entre-l-asie-et-l-occident_6058407_3232.html)

Les jeunes démocraties de Taïwan et de Corée du Sud font face à l'épidémie bien mieux que la dictature chinoise et sans attenter aux libertés. C'est d'elles que l'Occident doit s'inspirer, souligne le politiste Christophe Gaudin, maître de conférences à Séoul, dans une tribune au « Monde ».

Cabut S. **Covid-19 : le taux de mortalité des patients en réanimation lors de la première vague a baissé.** Le Monde 2020, published 3 November. Full-text : [https://www.lemonde.fr/planete/article/2020/11/03/covid-19-la-mortalite-a-baisse-en-reanimation\\_6058305\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/03/covid-19-la-mortalite-a-baisse-en-reanimation_6058305_3244.html)

Selon une étude menée au printemps sur plus de 4 200 malades, le taux de mortalité est passé de 42 % à 25 %. Ces cas graves sont surtout des hommes, souvent en surpoids. Un quart a moins de 54 ans.

Mandard S. **Covid-19 : 15 % des décès attribuables à la pollution de l'air.** Le Monde 2020, published 3 November. Full-text : [https://www.lemonde.fr/planete/article/2020/11/03/covid-19-la-mauvaise-qualite-de-l-air-facteur-de-risques-supplementaires\\_6058298\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/03/covid-19-la-mauvaise-qualite-de-l-air-facteur-de-risques-supplementaires_6058298_3244.html)

Une étude internationale évalue à 15 % la part de décès dus au nouveau coronavirus liée à l'exposition aux particules fines.

## 5 November

### Epidemiology

Pozzer A, Dominici F, Haines A, et al. **Regional and global contributions of air pollution to risk of death from COVID-19.** Cardiovasc Res 2020, published 26 October. Full-text: <https://doi.org/10.1093/cvr/cvaa288>

Air pollution might be an important cofactor increasing the risk of mortality from COVID-19. Jos Lelieveld, Andrea Pozzer and colleagues characterized global exposure to fine particulates based on satellite data and estimate that particulate air pollution contributed around 15% to COVID-19 mortality worldwide (East Asia, 27%; Europe, 19%; North America, 17%).

### Virology

Zhang Q. Chen, CZ, Swaroop M, et al. **Heparan sulfate assists SARS-CoV-2 in cell entry and can be targeted by approved drugs in vitro.** Cell Discov 6, 80 (2020). <https://doi.org/10.1038/s41421-020-00222-5>

The authors report that entry of SARS-CoV and CoV-2 requires the cell surface heparan sulfate (HS) as an assisting cofactor and that ablation of genes involved in HS biosynthesis or incubating cells with a HS mimetic inhibit Spike-mediated viral entry. After screening of approved drugs they identified various inhibitors: Mitoxantrone, Sunitinib and 7-benzylidenenaltrexone (BNTX).

Murugan NA, Kumar S, Jeyakanthan J, et al. **Searching for target-specific and multi-targeting organics for Covid-19 in the Drugbank database with a double scoring approach.** *Sci Rep* 10, 19125 (2020). <https://doi.org/10.1038/s41598-020-75762-7>

Next study on the use of computational screening approaches to identify lead drug-like compounds for Covid-19. The harvest (selection): Baloxavir marboxil, Phthalocyanine, Tadalafil, Lonafarnib, Nilotinib, Dihydroergotamine.

## Transmission

Tufekci Z. **We Need to Talk About Ventilation.** *The Atlantic* 2020, published 30 July. Full-text: <https://www.theatlantic.com/health/archive/2020/07/why-arent-we-talking-more-about-airborne-transmission/614737/>

Published more than three months ago but still instructive.

Harvey AP, Fuhrmeister ER, Cantrell M, et al. **Longitudinal monitoring of SARS-CoV-2 RNA on high-touch surfaces in a community setting.** *medRxiv* 2020, posted 1 November. Full-text: <https://doi.org/10.1101/2020.10.27.20220905>

The estimated risk of infection from touching a contaminated surface was less than 5 in 10,000 in a study by Amy Pickering, Abigail Harvey and colleagues. From April to June 2020, they repeatedly sampled 33 surfaces in public places like liquor and grocery stores, banks, gas stations, laundromats, restaurants and on metro doors and crosswalk buttons. Twenty-nine of 348 (8.3 %) surface samples were positive for SARS-CoV-2. The authors suggest that fomites might play only a minimal role in SARS-CoV-2 community transmission.

A second, not less important point: The weekly percentage of positive samples in one postal district peaked about 7 days before a spike in new SARS-CoV-2 cases. Surveillance on high-touch surfaces might therefore provide precious early warning clues.

## Immunology

Weisberg SP, Connors TJ, Zhu Y, et al. **Distinct antibody responses to SARS-CoV-2 in children and adults across the COVID-19 clinical spectrum.** Nat Immunol (2020). Full-text: <https://doi.org/10.1038/s41590-020-00826-9>

Children and adults have distinct immune responses after SARS-CoV-2 infection. Here, Donna Farber, Stuart Weisberg and colleagues present data from two adult (n=32) and two pediatric cohorts (n=47). They show that adult COVID-19 cohorts had anti-spike (S) IgG, IgM and IgA antibodies, as well as anti-nucleocapsid (N) IgG antibody, while children with and without MIS-C had reduced breadth of anti-SARS-CoV-2-specific antibodies, predominantly generating IgG antibodies specific for the S protein but not the N protein. The authors present possible explanations for these findings.

Tandon R, Mitra D, Sharma P. **Effective screening of SARS-CoV-2 neutralizing antibodies in patient serum using lentivirus particles pseudotyped with SARS-CoV-2 spike glycoprotein.** Sci Rep 10, 19076 (2020). Full-text: <https://doi.org/10.1038/s41598-020-76135-w>

Pseudotyped particles have significant importance and use in virology as tools for studying the biology of highly pathogenic viruses in a lower biosafety environment. Here, Ritesh Tandon et al. report a third generation lentiviral pseudotyping system for SARS-CoV-2 (pLV-S) and its efficacy in detecting neutralizing antibody titers in convalescent patient serum. The authors conclude that these pseudoparticles could be utilized for screening of potential vaccine candidates as they represent SARS-CoV-2 Spike glycoprotein on their surface in its native confirmation.

## Treatment

Tsai A, Diaware O, Nahass RG, et al. **Impact of tocilizumab administration on mortality in severe COVID-19.** Sci Rep 10, 19131 (2020). Full-text: <https://doi.org/10.1038/s41598-020-76187-y>

Another study that does not support the use of tocilizumab for the management of cytokine storm in patients with COVID-19. In this single-center propensity-score matched cohort study, 132 patients were included in the matched dataset (tocilizumab = 66; no tocilizumab = 66). Approximately 73% of the patients were male. Hypertension (55%), diabetes mellitus (31%), and chronic pulmonary disease (15%) were the most common co-morbidities pre-

sent. There were 18 deaths (27.3%) in the tocilizumab group and 18 deaths (27.3%) in the no tocilizumab group.

### Collateral Effects

Huh K, Jung J, Hong J, et al. **Impact of non-pharmaceutical interventions on the incidence of respiratory infections during the COVID-19 outbreak in Korea: a nationwide surveillance study.** Clin Infect Dis 2020, published 5 November. Full-text: <https://doi.org/10.1093/cid/ciaa1682>

Non-pharmaceutical interventions (NPIs) implemented to slow the spread of SARS-CoV-2 have led to the decline in the incidences of highly transmissible respiratory infections. This is the result of a study by Ji-Man Kang, Kyungmin Huh and colleagues from the Children's Hospital, Yonsei University College of Medicine, Seoul. Comparing the period February–July 2020 to the previous 4 years, the authors found that the incidences of chickenpox and mumps were significantly lower than in the prediction model (chickenpox: 36%, mumps: 63%).

### Spanish

If you read Spanish, read Limón R. **Ni ingerir vitamina D como suplemento ni tomar el sol son eficaces frente al coronavirus.** El País, published 5 November. Full-text: <https://elpais.com/ciencia/2020-11-04/ni-ingerir-vitamina-d-como-suplemento-ni-tomar-el-sol-son-eficaces-frente-al-coronavirus.html>

Un ensayo clínico identifica un compuesto que activa el sistema inmunitario y mitiga la gravedad de la covid. Attention: small numbers!

### French

If you read French, read Gozlan M. **Covid-19 : ce que l'on sait sur les enfants et adolescents et ce qu'il reste à apprendre.** Le Monde 2020, published 2 November. Full-text : <https://www.lemonde.fr/blog/realitesbiomedicales/2020/11/02/covid-19-ce-que-lon-sait-sur-les-enfants-et-adolescents-et-ce-quil-reste-a-apprendre>

Depuis le début de l'épidémie de Covid-19, les données attestent que les enfants développent rarement une forme sévère de Covid-19. En effet, les enfants infectés présentent le plus souvent des symptômes légers.

## 6 November

### Diagnostics

Zilla M, Wheeler BJ, Keetch C, et al. **Variable Performance in 6 Commercial SARS-CoV-2 Antibody Assays May Affect Convalescent Plasma and Seroprevalence Screening.** American Journal of Clinical Pathology, aqaa228. Full-text: <https://doi.org/10.1093/ajcp/aqaa228>

Megan Zilla and colleagues from Pittsburgh have compared six SARS-CoV-2 antibody assays, namely Beckman Coulter, Euroimmun (IgG, IgA), Roche, and Siemens (Centaur, Vista). Assays were assessed for specificity (n=184), sensitivity (n=154), and seroconversion in a defined cohort with clinical correlates and molecular SARS-CoV-2 results. Assay specificity was 99% or greater for all assays except the Euroimmun IgA (95%). Sensitivity at more than 21 days from symptom onset were 84%, 95%, 72%, 98%, 67%, and 96% for Beckman Coulter, Centaur, Vista, Roche, Euroimmun IgA, and Euroimmun IgG, respectively. These findings raise concerns that seroprevalence studies may vary significantly based on the serologic assay utilized, even when the assays are from reliable manufacturers with proven methodologies and have similar targets and initial specificity and sensitivity measures.

### Clinical

Santos-Ferreira D, Tomás R, Dores H. **Return-to-Play Guidelines for Athletes After COVID-19 Infection.** JAMA Cardiol. November 4, 2020. Full-text: <https://doi.org/10.1001/jamacardio.2020.5345>

What to do with athletes after recovery? The clinical implications of asymptomatic to mild COVID-19 still remain undetermined. Pulmonary and cardiac fibrosis are potentially the most relevant for athletes, which may lead to reduced lung capacity or cardiac dysfunction, malignant arrhythmias, and sudden death. Complications from the disease must be excluded prior to returning to play. According to the authors, those with suspected or confirmed COVID-19 (including mild or complicated disease) or presenting with suggestive signs or symptoms should undergo additional investigations according to presentation and disease severity. These may include blood tests, electrocardiography, echocardiography, 24-hour and/or 48-hour Holter monitoring, exercise testing, or lung function tests.



Smilowitz NR, Jethani N, Chen J, et al. **Myocardial Injury in Adults Hospitalized with COVID-19.** *Circulation* 5 Nov 2020. Full-text: <https://doi.org/10.1161/CIRCULATIONAHA.120.050434>

Nathaniel R. Smilowitz and colleagues have analyzed myocardial injury at admission and during hospitalization in a large cohort of 2163 patients with COVID-19 from a high-volume health care system in New York. Nearly a third (32%) had myocardial injury at presentation, and nearly half had injury detected during the course of their hospitalization. Regardless of when it was first detected, myocardial injury was associated with increased odds of mortality and critical illness, with higher cardiac Troponin (cTn) measurements associated with worse outcomes.

## Comorbidities

Rentsch CT, De Vito NJ, MacKenna B, et al. **Effect of pre-exposure use of hydroxychloroquine on COVID-19 mortality: a population-based cohort study in patients with rheumatoid arthritis or systemic lupus erythematosus using the OpenSAFELY platform.** *Lancet Neurology*, November 05, 2020. Full-text: [https://doi.org/10.1016/S2665-9913\(20\)30378-7](https://doi.org/10.1016/S2665-9913(20)30378-7)

This population-based cohort study using national primary care data and linked death registrations in the OpenSAFELY platform, which covers approximately 40% of the general population in England, UK. Between September 1, 2019, and March 1, 2020, of 194,637 people with rheumatoid arthritis or systemic lupus erythematosus, 30,569 (16%) received two or more prescriptions of HCQ. Between March 1 and July 13, 2020, there were 547 COVID-19 deaths, 70 among HCQ users. Estimated standardized cumulative COVID-19 mortality was 0.23% among users and 0.22% among non-users. These findings are not surprising given the mounting body of literature suggesting no clinical benefit for HCQ. However, this study is the largest to date and adds further evidence to the lack of any preventive effect.

## Treatment

Xiang Y, Nambulli S, Xiao Z, et al. **Versatile and multivalent nanobodies efficiently neutralize SARS-CoV-2.** *Science* 05 Nov 2020. Full-text: <https://doi.org/10.1126/science.abe4747>

An early inhalation of nanobodies - the future treatment?  $V_{\text{H}}\text{H}$  antibodies or nanobodies (Nbs) are minimal, monomeric antigen-binding domains derived from camelid single-chain antibodies. Unlike IgG antibodies, Nbs are small, highly soluble and stable, readily bioengineered into bi/multivalent forms,

and are amenable to low-cost, efficient microbial production. They can also be administered by inhalation, making their use against respiratory viruses very appealing. The authors discovered several Nbs with picomolar to femtomolar affinities that inhibit viral infection at sub-ng/ml concentration and determined a structure of one of the most potent in complex with RBD. Multivalent Nb constructs achieved ultra-high neutralization potency and may prevent mutational escape. While the research is still preliminary, it is hoped that Nbs might someday be the key ingredient in an antiviral drug that could be easily delivered via nasal spray.

Schoof M, Faust B, Saunders RA, et al. **An ultrapotent synthetic nanobody neutralizes SARS-CoV-2 by stabilizing inactive Spike.** Science 05 Nov 2020. Full-text: <https://doi.org/10.1126/science.abe3255>

Michael Schoof and colleagues from San Francisco focused on such an ultrapotent Nb. Nb6 binds Spike in a fully inactive conformation with its receptor binding domains (RBDs) locked into their inaccessible down-state, incapable of binding ACE2. Affinity maturation and structure-guided design of multi-valency yielded a trivalent nanobody, mNb6-tri, with femtomolar affinity for Spike and picomolar neutralization of SARS-CoV-2 infection. mNb6-tri retains function after aerosolization, lyophilization, and heat treatment, which enables aerosol-mediated delivery of this potent neutralizer directly to the airway epithelia.

Linsky TW, Vergara R, Codina N, et al. **De novo design of potent and resilient hACE2 decoys to neutralize SARS-CoV-2.** Science 05 Nov 2020. Full-text: <https://doi.org/10.1126/science.abe0075>

Another new way to combat COVID-19. Thomas W. Linsky and colleagues from Seattle and other US cities developed a computational protein design strategy that enables the rapid and accurate design of hyperstable *de novo* protein “decoys”. The decoys replicate the protein receptor interface that a virus binds to in order to infect a cell. Thus, they out-compete viral interaction with the cell. The best ACE2 decoy, CTC-445.2, did bind with low nanomolar affinity and high specificity to the RBD of the spike protein. Because the decoy replicates the spike protein target interface in hACE2, it is intrinsically resilient to viral mutational escape. A bivalent decoy, CTC-445.2d, showed 10-fold improvement in binding. CTC-445.2d potently neutralizes SARS-CoV-2 infection of cells *in vitro* and a single intranasal prophylactic dose of decoy protected Syrian hamsters from a subsequent lethal SARS-CoV-2 challenge.

## Pregnancy

Woodworth KR, Olsen EO, Neelam V, et al. **Birth and Infant Outcomes Following Laboratory-Confirmed SARS-CoV-2 Infection in Pregnancy — SET-NET, 16 Jurisdictions, March 29–October 14, 2020.** MMWR Morb Mortal Wkly Rep 2020;69:1635–1640. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6944e2>

The Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET) collects information on pregnancy and infant outcomes in 16 US jurisdictions. Among 3912 infants with known gestational age born to women with SARS-CoV-2 infection, 12,9% were preterm (< 37 weeks), higher than a national estimate of 10,2%. Among 610 (21,3%) infants with testing results, 2,6% had positive SARS-CoV-2 results, primarily those born to women with infection at delivery. Among the infants with positive test results, one half were born preterm, which might reflect higher rates of screening in the ICU.

Zambrano LD, Ellington S, Strid P, et al. **Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–October 3, 2020.** MMWR Morb Mortal Wkly Rep 2020;69:1641–1647. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6944e3>

In an analysis of approximately 400,000 women aged 15–44 years with symptomatic COVID-19, the absolute risks for severe COVID-19-associated outcomes among women were low. However, pregnant women were at significantly higher risk for severe outcomes: Compared with non-pregnant women, pregnant women more frequently were admitted to ICU (10,5 versus 3,9 per 1000 cases; aRR = 3,0; 95% CI = 2,6–3,4), received invasive ventilation (2,9 versus 1,1 per 1,000 cases; aRR = 2,9; 95% CI = 2,2–3,8) and received ECMO (0.7 versus 0.3 per 1,000 cases; aRR = 2,4; 95% CI = 1,5–4,0). Thirty-four deaths (1,5 per 1000 cases) were reported among 23,434 symptomatic pregnant women, and 447 (1,2 per 1000 cases) were reported among 386,028 nonpregnant women, reflecting a 70% increased risk for death associated with pregnancy (aRR = 1,7; 95% CI = 1,2–2,4).

## 9 November

### Epidemiology

Siegenfeld AF, Bar-Yam Y. **The impact of travel and timing in eliminating COVID-19.** Commun Phys 3, 204 (2020). Full-text: <https://doi.org/10.1038/s42005-020-00470-7>

Mathematical models show that these are not good times for travel. When a reduction in travel is coupled with other control measures, the travel reduction will not only delay the spread of the outbreak but in some cases will also be the determining factor in whether or not the outbreak is eliminated.

Kanu FA, Smith EE, Offutt-Powell T, et al. **Declines in SARS-CoV-2 Transmission, Hospitalizations, and Mortality After Implementation of Mitigation Measures— Delaware, March–June 2020.** MMWR Morb Mortal Wkly Rep. ePub: 6 November 2020. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6945>

No single mitigation strategy is likely to be effective alone: state-mandated stay-at-home orders and public mask mandates coupled with case investigations and contact tracing contributed to an 82% reduction in COVID-19 incidence, 88% reduction in hospitalizations, and 100% reduction in mortality in Delaware during late April–June.

## Virology

Zheng J, Wong LR, Li K et al. **COVID-19 treatments and pathogenesis including anosmia in K18-hACE2 mice.** Nature (2020). Full-text: <https://doi.org/10.1038/s41586-020-2943-z>

SARS-CoV-2-infected K18-hACE2 mice developed dose-dependent lung disease with features similar to severe human COVID-19, including diffuse alveolar damage, inflammatory cell infiltration, tissue injury, lung vascular damage, and death. Remarkably, K18-hACE2 mice also support SARS-CoV-2 replication in the and associated with this pathology develop anosmia, a common feature of human disease.

## Immunology

Chakraborty S, Gonzalez J, Edwards K et al. **Proinflammatory IgG Fc structures in patients with severe COVID-19.** Nat Immunol 2020, November 9. Full-text: <https://doi.org/10.1038/s41590-020-00828-7>

Another (important) piece in the puzzle: Saborni Chakraborty and colleagues from Stanford show that specific pro-inflammatory antibody forms are elevated in more patients with severe COVID-19, in contrast to those with mild symptoms and seropositive children. The unique serologic signature is characterized by IgG3 and IgG1 with F0N0 glycoform modification and includes an increased likelihood of IgG1 with afucosylated Fc glycans. This Fc modification on SARS-CoV-2 IgGs enhanced interactions with the activating Fcγ recep-

tor Fc $\gamma$ RIIIa; when incorporated into immune complexes, Fc afucosylation enhanced production of inflammatory cytokines by monocytes, including interleukin-6 and tumor necrosis factor. This may explain why some patients develop severe COVID-19.

Ng KW, Faulkner N, Cornish GH, et al. **Preexisting and de novo humoral immunity to SARS-CoV-2 in humans.** *Science* 06 Nov 2020. Full-text: <https://doi.org/10.1126/science.abe1107>

Using multiple independent assays (including flow cytometry-based assay for SARS-CoV-2-binding antibodies), the authors demonstrated the presence of pre-existing antibodies recognizing SARS-CoV-2 in at least some uninfected individuals. SARS-CoV-2 spike glycoprotein (S)-reactive antibodies were particularly prevalent in children and adolescents. They were predominantly of the IgG class and targeted the S2 subunit. By contrast, SARS-CoV-2 infection induced higher titers of SARS-CoV-2 S-reactive IgG antibodies, targeting both the S1 and S2 subunits, and concomitant IgM and IgA antibodies, lasting throughout the observation period.

Angioni R, Sánchez-Rodríguez R, Munari F, et al. **Age-severity matched cytokine profiling reveals specific signatures in Covid-19 patients.** *Cell Death Dis* 11, 957 (2020). Full-text: <https://doi.org/10.1038/s41419-020-03151-z>

Roberta Angioni and colleagues analyzed the cytokine and leukocyte profile of COVID-19 patients at hospital admission and identified distinctive immunological signatures that characterize younger or older severe patients. They found that severe patients under the age of 60 did not show major leukocyte alterations and expressed high levels of IL-1RA, IL-6, CCL2, CXCL1, CXCL9, CXCL10, and EGF. In contrast, older patients expressed high levels of CXCL8, IL-10, IL-15, IL-27, and TNF- $\alpha$ , presented a significant reduction in the total T lymphocyte number and an increased expression of T cell exhaustion markers as compared to those younger.

## Clinical

Avanzato VA, Matson MJ, Seifert SN, et al. **Case Study: Prolonged infectious SARS-CoV-2 shedding from an asymptomatic immunocompromised cancer patient.** *Cell* November 04, 2020. Full-text: <https://doi.org/10.1016/j.cell.2020.10.049>

Immunocompromised patients may shed infectious virus for longer durations than previously recognized: Victoria Avanzato and colleagues describe an interesting case of a female immunocompromised patient with chronic lymphocytic leukemia and acquired hypogammaglobulinemia. Shedding of infectious SARS-CoV-2 was observed for up to 70 days.

### Collateral damage

Jahrami H, BaHammam AS, Bragazzi NL, Saif Z, Faris M, Vitiello MV. **Sleep problems during COVID-19 pandemic by population: a systematic review and meta-analysis.** J Clin Sleep Med. 2020 Oct 27. PubMed: <https://pubmed.gov/33108269>. Full-text: <https://doi.org/10.5664/jcsm.8930>

Forty-four papers, involving a total of 54,231 participants from 13 countries, contributed to this systematic review and meta-analysis of sleep problems during COVID-19. The global pooled prevalence rate of sleep problems among all populations was 35,7%. COVID-19 patients appeared to be the most affected group, with a pooled rate of 74,8%. Healthcare workers and the general population had comparative rates of sleep problems with rates of 36,0% and 32,3%, respectively.

Dyer O. **Covid-19: Denmark to kill 17 million minks over mutation that could undermine vaccine effort.** BMJ 2020; 371:m4338. Full-text: <https://doi.org/10.1136/bmj.m4338>

Among 5102 samples of virus taken from Danish patients since June, five infection clusters affecting 214 people involved mink variant virus. One of these, known as cluster 5, seems to be a problematic variant which could be less susceptible to some antibodies and/or vaccines (unproven). This variant has been detected with four simultaneous changes in the genes for the Spike protein (for nerds: H69del/V70del, Y453F, I692V and M1229I) and has affected 11 people in North Jutland. Conclusion: 17 million minks will be culled.

### Severe COVID

Liu Y, Lv J, Liu J. et al. **Mucus production stimulated by IFN-AhR signaling triggers hypoxia of COVID-19.** Cell Res November 6, 2020. Full-text: <https://doi.org/10.1038/s41422-020-00435-z>

It's mucus: this great work may potentially explain the silent hypoxia that has emerged as a unique feature of COVID-19. Yuying Liu and colleagues from Beijing, China show that mucins are accumulated in the bronchoalveolar lavage fluid and are up-regulated in the lungs of severe SARS-CoV-2-infected

mice and macaques. They also found that induction of either interferon (IFN)- $\beta$  or IFN- $\gamma$  on SARS-CoV-2 infection results in activation of aryl hydrocarbon receptor (AhR) signaling through an IDO-Kyn-dependent pathway, leading to transcriptional upregulation of the expression of mucins, both the secreted and membrane-bound, in alveolar epithelial cells. Consequently, accumulated alveolar mucus affects the blood-gas barrier, thus inducing hypoxia and diminishing lung capacity, which can be reversed by blocking AhR activity.

## 10 November

### Epidemiology

Brown KA, Jones A, Daneman N, et al. **Association Between Nursing Home Crowding and COVID-19 Infection and Mortality in Ontario, Canada.** JAMA Intern Med. November 9, 2020. Full-text: <https://doi.org/10.1001/jamainternmed.2020.6466>

In this cohort study that included 78,607 residents of 618 nursing homes in Ontario, Canada, 5218 (6.6%) developed COVID-19 infection and 1452 (1.8%) died of COVID-19 infection as of May 20, 2020. The case fatality rate was 27.8% (1452/5218). Of note, COVID-19 mortality in homes with low crowding (number of occupants per room and bathroom across an entire home) was less than half (1.3%) than that of homes with high crowding (2.7%).

### Virology

Relman DA. **Opinion: To stop the next pandemic, we need to unravel the origins of COVID-19.** PNAS first published November 3, 2020. Full-text: <https://doi.org/10.1073/pnas.2021133117>

Important comment. According to David A. Relman from Stanford, “a more complete understanding of the origins of COVID-19 clearly serves the interests of every person in every country on this planet. It will limit further re-creations and diminish the likelihood of conflict; it will lead to more effective responses to this pandemic, as well as efforts to anticipate and prevent the next one. It will also advance our discussions about risky science. And it will do something else: Delineating COVID-19’s origin story will help elucidate the nature of our very precarious coexistence within the biosphere.”

## Vaccine

Callaway E. **What Pfizer's landmark COVID vaccine results mean for the pandemic.** Nature NEWS 09 November 2020. Full-text: <https://www.nature.com/articles/d41586-020-03166-8>

Yesterday, Pfizer and BioNTech announced that their mRNA-based vaccine candidate, BNT162b2, demonstrated “evidence of efficacy“, based on the first interim efficacy and safety analysis conducted on November 8, 2020 by an external, independent Data Monitoring Committee from the Phase III clinical study.

- BNT162b2 was found to be “more than 90% effective” in preventing COVID-19 in participants without evidence of prior SARS-CoV-2 infection
- Analysis evaluated 94 confirmed cases of COVID-19 in trial participants
- Study enrolled 43,538 participants, with 42% having diverse backgrounds, and no serious safety concerns have been observed
- Clinical trial to continue through to final analysis at 164 confirmed cases in order to collect further data and characterize the vaccine candidate’s performance against other study endpoints

That’s what we know. Read how scientists welcome the first compelling evidence that a vaccine can prevent COVID-19. But many questions remain about how much protection it offers, to whom and for how long.

Che Y, Liu X, Pu Y, et al. **Randomized, double-blinded and placebo-controlled phase II trial of an inactivated SARS-CoV-2 vaccine in healthy adults.** Clinical Infectious Diseases, 09 November 2020 ciaa1703. Full-text: <https://doi.org/10.1093/cid/ciaa1703>

In this randomized, double-blinded Phase II trial, 742 healthy adults received a medium (MD) or a high dose (HD) of an inactivated vaccine at an interval of either 14 days or 28 days. Neutralizing antibody (NAb) and anti-S and anti-N antibodies were detected at different times, and adverse reactions were monitored for 28 days after full immunization. The seroconversion rates of NAb in MD and HD groups were 89% and 96% at day 14 and 92% and 96% at day 28 after immunization. Of note, the vaccine was safe (still an issue with inactivated vaccines), and no severe adverse effects were reported.



## Clinical

Lavery AM, Preston LE, Ko JY, et al. **Characteristics of Hospitalized COVID-19 Patients Discharged and Experiencing Same-Hospital Readmission — United States, March–August 2020.** *MMWR Morb Mortal Wkly Rep.* ePub: 9 November 2020. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6945e2>

Who will be re-admitted? In a cohort of 106,543 patients discharged after an index COVID-19 hospitalization, 9% experienced at least one readmission to the same hospital within 2 months of discharge. Multiple readmissions occurred in 1.6% of patients. Not very surprising: risk factors for readmission included age  $\geq$  65 years, presence of certain chronic conditions (chronic obstructive pulmonary disease, heart failure, diabetes with chronic complications, chronic kidney disease, and obesity), hospitalization within the 3 months preceding the first COVID-19 hospitalization, and discharge to a skilled nursing facility or with home health care.

## Comorbidities

Taquet M, Luciano S, Geddes JR, et al. **Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62,354 COVID-19 cases in the USA.** *Lancet Psychiatry* November 09, 2020. Full-text: [https://doi.org/10.1016/S2215-0366\(20\)30462-4](https://doi.org/10.1016/S2215-0366(20)30462-4)

Survivors of COVID-19 appear to be at increased risk of psychiatric sequelae. Here, Maxime Taquet and colleagues used a global federated network that captures anonymized data from electronic health records in 54 health care organizations in the US, totaling 69.8 million patients and 62,354 patients diagnosed with COVID-19. In patients with no previous psychiatric history, a diagnosis of COVID-19 was associated with increased incidence of a first psychiatric diagnosis in the following 14 to 90 days compared with six other health events (i.e., hazard ratio [HR] 2.1 vs influenza). The HR was greatest for anxiety disorders, insomnia, and dementia. The incidence of a first diagnosis of dementia in the 14 to 90 days after COVID-19 diagnosis was 1.6% in people older than 65 years. A psychiatric diagnosis in the previous year was associated with a higher incidence of COVID-19 diagnosis (relative risk 1.65).

## Treatment

Hoang TN, Pino M, Boddapati AK. **Baricitinib treatment resolves lower airway macrophage inflammation and neutrophil recruitment in SARS-CoV-2-infected rhesus macaques.** Cell November 09, 2020.ft <https://doi.org/10.1016/j.cell.2020.11.007>

Timothy Hoang and colleagues investigated the immunologic and virologic efficacy of baricitinib (approved JAK1/2 inhibitor) in rhesus macaques. Viral shedding measured from nasal and throat swabs, bronchoalveolar lavages and tissues was NOT reduced with baricitinib and type I IFN antiviral responses and SARS-CoV-2-specific T cell responses remained similar between the two groups. However, animals treated with baricitinib showed reduced inflammation, decreased lung infiltration of inflammatory cells, reduced NETosis activity, and more limited lung pathology. Importantly, baricitinib-treated animals had a rapid and remarkably potent suppression of lung macrophage production of cytokines and chemokines responsible for inflammation and neutrophil recruitment.

Self WH, Semler MW, Leither LM. **Effect of Hydroxychloroquine on Clinical Status at 14 Days in Hospitalized Patients With COVID-19 - A Randomized Clinical Trial.** JAMA. November 9, 2020. Full-text: <https://doi.org/10.1001/jama.2020.22240>

No, there was no effect of HCQ in this RCT among 479 adults hospitalized with respiratory illness from COVID-19. Do we need more clinical studies?

Saag MS. **Misguided Use of Hydroxychloroquine for COVID-19. The Infusion of Politics Into Science.** JAMA. November 9, 2020. Full-text: <https://doi.org/10.1001/jama.2020.22389>

Nice comment on the HCQ story. According to Michael Saag, the clear, unambiguous, and compelling lesson from the hydroxychloroquine story for the medical community and the public is that science and politics do not mix.

## Pediatrics

Gale C, Quigley MA, Placzek A, et al. **Characteristics and outcomes of neonatal SARS-CoV-2 infection in the UK: a prospective national cohort study using active surveillance.** Lancet November 09, 2020. Full-text: [https://doi.org/10.1016/S2352-4642\(20\)30342-4](https://doi.org/10.1016/S2352-4642(20)30342-4)

A prospective UK population-based cohort study of 66 babies with confirmed SARS-CoV-2 infection in the first 28 days of life who received in-patient care between March and April. Of these, 28 (42%) had severe neonatal SARS-CoV-2 infection and 16 (24%) were born preterm. Only half were of white ethnic groups. Of 17 (26%) babies with confirmed infection who were born to mothers with known perinatal SARS-CoV-2 infection, only two (3%) were considered to have possible vertically acquired infection. As of July 28, 2020, 58 (88%) babies had been discharged home, seven (11%) were still in hospital, and one (2%) had died of a cause unrelated to SARS-CoV-2 infection.

## 11 November

### Epidemiology

Kurian SJ, Bhatti AUR, Alvi MA, et al. **Correlations Between COVID-19 Cases and Google Trends Data in the United States: A State-by-State Analysis.** *Mayo Clin Proc.* 2020 Nov;95(11):2370-2381. PubMed: <https://pubmed.gov/33164756>. Full-text: <https://doi.org/10.1016/j.mayocp.2020.08.022>

Google might see a nascent epidemic two weeks before the first reported cases. This is the result of a study by Mohamad Bydon, Shyam J. Kurian and colleagues from Mayo Clinic, Rochester after developing a digital surveillance model using Google Trends. The authors searched the following keywords: *COVID symptoms, coronavirus symptoms, sore throat+shortness of breath+fatigue+cough, coronavirus testing center, loss of smell, Lysol (sanitizer), antibody, face mask, coronavirus vaccine, and COVID stimulus check.* Find out which one did best. The authors suggest that this information could enable better preparation and planning for health care systems.

### Transmission

Chang S, Pierson E, Koh PW. **Mobility network models of COVID-19 explain inequities and inform reopening.** *Nature* (2020). Full-text: <https://doi.org/10.1038/s41586-020-2923-3>

A small minority of “superspreader” events account for a large majority of infections. What we have known for a long time is now being confirmed by a mobility network model which mapped the hourly movements of 98 million people from neighborhoods to points of interest (POIs) such as restaurants and religious establishments. Jure Leskovec, Serina Chang and colleagues, connected 57,000 neighborhoods to 553,000 POIs and found that restricting

maximum occupancy at each POI would be more effective than uniformly reducing mobility. Their model also correctly predicted higher infection rates among disadvantaged racial and socioeconomic groups: disadvantaged groups cannot reduce mobility as sharply as other groups and the POIs they visit are more crowded.

See also the comment by Ma KC, Lipsitch M. **Big data and simple models used to track the spread of COVID-19 in cities.** Nature 2020, published 10 November. Full-text: <https://www.nature.com/articles/d41586-020-02964-4>

See also Cyranoski D. **How to stop restaurants from driving COVID infections.** Nature 2020, published 10 November. Full-text: <https://www.nature.com/articles/d41586-020-03140-4> | US mobile data suggests restaurants, gyms and cafes can be COVID hotspots — and reveals strategies for limiting spread.

## Vaccine

Walls AC, Fiala B, Schäfer A, et al. **Elicitation of Potent Neutralizing Antibody Responses by Designed Protein Nanoparticle Vaccines for SARS-CoV-2.** Cell. 2020 Oct 31:S0092-8674(20)31450-1. PubMed: <https://pubmed.gov/33160446>. Full-text: <https://doi.org/10.1016/j.cell.2020.10.043>

Are self-assembling protein nanoparticles that display 60 SARS-CoV-2 spike receptor-binding domains (RBDs) and induce neutralizing antibody titers comparable to those produced by people after SARS-CoV-2 infection? That's what Neil King and David Veessler and colleagues from University of Washington, Seattle, US, report. The authors anticipate that manufacture of the nanoparticle vaccines might be very scalable.

McPartlin SO, Morrison J, Rohrig A, Weijer C. **Covid-19 vaccines: Should we allow human challenge studies to infect healthy volunteers with SARS-CoV-2?** BMJ. 2020 Nov 9;371:m4258. PubMed: <https://pubmed.gov/33168564>. Full-text: <https://doi.org/10.1136/bmj.m4258>

The need for COVID-19 vaccines has prompted thousands of otherwise healthy people to volunteer to be infected with the virus to test candidate vaccines. **Seán O'Neill McPartlin, Abie Rohrig, and Josh Morrison** urge us to embrace the altruism of volunteers, but **Charles Weijer** argues that it would be dangerous and unjustified.

## Treatment

D'Alessio A, Del Poggio P, Bracchi F, et al. **Low-dose ruxolitinib plus steroid in severe SARS-CoV-2 pneumonia.** *Leukemia* (2020). <https://doi.org/10.1038/s41375-020-01087-z>

Results from a small non-randomized study might suggest a benefit from ruxolitinib in patients with severe COVID-19 pneumonia not requiring mechanical ventilation at baseline. D'Alessio et al. report an analysis of 32 patients (Group A) who received ruxolitinib, a JAK 1/2 (Janus Kinase) inhibitor, and 43 patients who served as a control group (Group B). Ruxolitinib was administered orally at a dose of 5 mg twice daily for 7 days and then tapered to 5 mg daily to complete a 10-day course of treatment. All patients received methylprednisolone. Concomitant administration of hydroxychloroquine, lopinavir/ritonavir or remdesivir was not permitted during treatment with ruxolitinib. Kaplan–Meier estimates of the percentage of patients who were alive and clinically recovered at the end of follow-up were 89% for group A and 57% for group B (SE ± 6.1). As always: to be confirmed in larger trials.

## Severe COVID

Wang F, Huang S, Gao R. **Initial whole-genome sequencing and analysis of the host genetic contribution to COVID-19 severity and susceptibility.** *Cell Discov* 6, 83 (2020). Full-text: <https://doi.org/10.1038/s41421-020-00231-4>

HLA-A\*11:01, B\*51:01, and C\*14:02 alleles might predispose to severe COVID-19. This is the result of a host genetic study deeply sequencing and analyzing 332 COVID-19 patients categorized by varying levels of severity. Lei Liu, Fang Wang and colleagues conducted single-variant and gene-based association tests among five severity groups: asymptomatic, mild, moderate, severe, and critically ill patients. Find out more about genes involved in the interleukin-1 (IL-1) signaling pathway and the stability of the TMPRSS2 protein.

## Collateral Effects

Abdallah HO, Zhao C, Kaufman E, et al. **Increased Firearm Injury During the COVID-19 Pandemic: A Hidden Urban Burden.** *J Am Coll Surg.* 2020 Oct 26:S1072-7515(20)32413-3. PubMed: <https://pubmed.gov/33166665>. Full-text: <https://doi.org/10.1016/j.jamcollsurg.2020.09.028>

Lockdown causes domicile discord which in turn causes more penetrating trauma? Jose Pascual, Hatem Abdallah and colleagues tested the hypothesis that intentional injury might have increased during stay-at-home-orders (SAHO) and assessed injury patterns from 6 weeks pre- to 10 weeks post-

statewide stay-at-home order. 357 and 480 trauma patients presented pre- and post-SAHO, respectively. Pre- and post- groups demonstrated differences in sex, age, and race. Post-SAHO mechanism of injury (blunt vs. penetrating) revealed more intentional injury.

Lee PH, Marek J, Nálezka P. **Sleep pattern(s) in the US and 16 European countries during the COVID-19 outbreak using crowdsourced smartphone data.** Eur J Public Health 2020, published 10 November. Full-text: <https://doi.org/10.1093/eurpub/ckaa208>

When you sleep, your smartphone is taking notes and you may end up in a scientific publication. Here Paul Lee and colleagues utilized a large crowdsourced database ([Sleep as Android](#)) and analyzed the (your?) sleep behavior of 25,217 users with 1,352,513 sleep records between 1<sup>st</sup> January and 29<sup>th</sup> April 2020 in 16 European countries (Germany, United Kingdom, Spain, France, Italy, the Netherlands, Belgium, Hungary, Denmark, Finland, Norway, Czech, Sweden, Austria, Poland, and Switzerland) and in the US. The unsurprising result: during lockdown, people delayed their bedtime and slept longer than usual.

## 12 November

### Transmission

Letizia AG, Ramos I, Obla A, et al. **SARS-CoV-2 Transmission among Marine Recruits during Quarantine.** N Engl J Med 2020, published 11 November. Full-text: <https://doi.org/10.1056/NEJMoa2029717>

A two-week quarantine at home is not sufficient to prevent SARS-CoV-2 from entering into a closed college campus. That's one of the results of a study by Stuart Sealfon, Andrew Letizia and colleagues who investigated SARS-CoV-2 infections among US Marine Corps. Around 2% of recruits who had had negative results for SARS-CoV-2 at the beginning of a supervised quarantine tested positive within two weeks. Most recruits who tested positive were asymptomatic, and no infections were detected through daily symptom monitoring. The author's short conclusion: "Transmission clusters occur within platoons."

See also the comment by Michael NL. **SARS-CoV-2 in the U.S. Military — Lessons for Civil Society.** N Engl J Med 2020, published 11 November. Full-text: <https://doi.org/10.1056/NEJMe2032179>

Kasper MR, Geibe JR, Sears CL, et al. **An outbreak of Covid-19 on an aircraft carrier.** *N Engl J Med* 2020, published 11 November. Full-text: <https://doi.org/10.1056/NEJMoa2019375>

Do you remember March 30? SARS-CoV-2 is spreading aboard the aircraft carrier *USS Theodore Roosevelt*. The ship's commanding officer, Captain Brett Crozier, sends an email to three admirals in his chain of command, recommending that he be given permission to evacuate all non-essential sailors, to quarantine known COVID-19 cases, and sanitize the ship. "We are not at war. **Sailors do not need to die,**" writes Crozier in his four-page memo. The letter leaks to the media and generates several headlines. Three days later, 2 April, Captain Crozier is sacked.

You can now read the final report of the outbreak. A total of 1271 crew members (26.6% of the crew) tested positive for SARS-CoV-2. Among the crew members with laboratory-confirmed infection, 76.9% (978 of 1271) had no symptoms at the time that they tested positive and 55.0% had symptoms develop some time during the clinical course. Among the 1331 crew members with suspected or confirmed COVID-19, 23 (1.7%) were hospitalized, 4 (0.3%) received intensive care, and 1 died. Crew members who worked in confined spaces appeared more likely to become infected. The conclusion: transmission of SARS-CoV-2 is facilitated by close-quarters conditions and by asymptomatic and pre-symptomatic infected crew members.

Nissen K, Krambrich J, Akaberi D, et al. **Long-distance airborne dispersal of SARS-CoV-2 in COVID-19 wards.** *Sci Rep* 10, 19589 (2020). Full-text: <https://doi.org/10.1038/s41598-020-76442-2>

Detection of coronavirus RNA, including SARS-CoV-2, in hospital and other ventilation systems has been reported. Here, Erik Salaneck, Karolina Nissen and colleagues present further evidence for SARS-CoV-2's ability to disperse from patients to ward vent openings. They detected viral RNA in ventilation exhaust filters located at least 50 m from patient room vent openings. Although the authors did not isolate infectious virus, they suggest that there may be a risk for airborne dissemination and transmission, especially at much closer distances to contagious persons in confined spaces, both in and outside hospital environments.

## Immunology

Tosif S, Neeland MR, Sutton P, et al. **Immune responses to SARS-CoV-2 in three children of parents with symptomatic COVID-19.** *Nat Commun* 11, 5703 (2020), published 11 November. <https://doi.org/10.1038/s41467-020-19545-8>

Children can mount an immune response to SARS-CoV-2 without virological confirmation of infection. This is the exciting result from a study by Shidan Tosif et al. who describe clinical features, virology, longitudinal cellular, and cytokine immune profile, SARS-CoV-2-specific serology and salivary antibody responses in a family of two parents with PCR-confirmed symptomatic SARS-CoV-2 infection and their three children, who tested repeatedly SARS-CoV-2 PCR-negative. These findings raise the possibility that immunity in children can prevent the establishment of SARS-CoV-2 infection.

Thomson EC, Rosen LE, Shepherd JG, et al. **The circulating SARS-CoV-2 spike variant N439K maintains fitness while evading antibody-mediated immunity.** *bioRxiv* 2020, posted 5 November. Full-text: <https://doi.org/10.1101/2020.11.04.355842>

A widespread variant of SARS-CoV-2 which has been identified in 12 countries might have the potential to evade recently acquired immunity. That's the result of a study by David Robertson, Gyorgy Snell, Emma Thomson and colleagues who examined the N439K mutation in the receptor binding motif (RBM) of the SARS-CoV-2 spike (S) protein. The authors found that the N439K mutation resulted in immune escape from a panel of neutralizing monoclonal antibodies (including some that are currently being developed for treatment of SARS-CoV-2 infection) as well as from polyclonal sera from a sizeable fraction of persons recovered from infection. The authors conclude that their findings might have consequences for the efficacy of emerging vaccines and antibody therapeutics.

## Vaccine

Strassle C, Jardas E, Ochoa J, et al. **Covid-19 Vaccine Trials and Incarcerated People — The Ethics of Inclusion.** *N Engl J Med* 2020; 383:1897-1899; published 12 November. Full-text: <https://doi.org/10.1056/NEJMp2025955>

The most severe COVID-19 outbreaks in the US are no longer occurring in nursing homes or meat packing plants, but in correctional facilities. Find an audio interview (19:26) with Holly Taylor on the ethical issues involved in conducting COVID-19 vaccine research in correctional facilities (19:26).



Teerawattananon Y, Dabak SV. **COVID vaccination logistics: five steps to take now.** Nature 2020, published 9 November. Full-text: <https://www.nature.com/articles/d41586-020-03134-2>

The authors point out that creating a safe and effective vaccine is just Act 1 of the 2021 Vaccine Play. Developing a comprehensive and strategic plan for vaccine roll-out is Act 2.

## Severe COVID

Ledford H. **Why do COVID death rates seem to be falling?** Nature 2020, published 11 November. Full-text: <https://www.nature.com/articles/d41586-020-03132-4>

Hard-won experience, changing demographics and reduced strain on hospitals are all possibilities – but no one knows how long this change will last. By Heidi Ledford.

## Education

Hashimoto DA, Axtell AL, Auchincloss HG. **Percutaneous Tracheostomy.** N N Engl J Med 2020; 383:e112, published 12 November. Text and video: <https://doi.org/10.1056/NEJMvcm2014884>

A tracheostomy is a surgically created airway that is kept open with a breathing tube, or tracheostomy tube. It can take place in the operating room or at the patient's bedside. Find out more about indications and contraindications; procedural modifications in patients with COVID-19; equipment and preparation; patient and provider positioning; identification of anatomical landmarks; and, finally, procedure, aftercare and complications.

## Spanish

If you read Spanish, read Criado MA. **Mujer, joven y enferma seis meses después de curarse: así son los afectados por la covid de larga duración.** El País 2020, published 11 November. Full-text: <https://elpais.com/ciencia/2020-11-11/mujer-joven-y-enferma-seis-meses-despues-de-curarse-asi-son-los-afectados-por-la-covid-de-larga-duracion.html>

Una encuesta a 2000 contagiados en España muestra la persistencia del coronavirus y sus secuelas.

Carbajosa A. **De hijos de inmigrantes turcos en Alemania a creadores de una posible vacuna contra la covid.** El País 2020, published 11 November. Full-text: <https://elpais.com/sociedad/2020-11-10/de-hijos-de-inmigrantes-turcos-en-alemania-a-creadores-de-una-posible-vacuna-contra-la-covid.html>

Los fundadores de BioNTech, la empresa alemana que trabaja en una inmunización contra la COVID, son un matrimonio de expertos en cáncer.

## French

Schittly R, Rof G, Wenger S. « **On ne veut pas d'applaudissements, on veut que les gens respectent les consignes** » : la grande fatigue des soignants face à la deuxième vague du Covid-19. Le Monde 2020, published 12 November. Full-text:

[https://www.lemonde.fr/planete/article/2020/11/12/deuxieme-vague-du-covid-19-la-grande-fatigue-des-soignants\\_6059415\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/12/deuxieme-vague-du-covid-19-la-grande-fatigue-des-soignants_6059415_3244.html)

Peu reposés depuis le printemps, en manques de moyens et de reconnaissance, les soignants témoignent de leur lassitude et de leurs craintes face au nouveau pic épidémique.

Moreau A, Longueville E, Maufay D, Da Fonseca M. **Covid-19 : quels sont les lieux les plus à risque pour attraper le Covid-19 ?** Le Monde 2020, published 11 November. Video (8 minutes) :

[https://www.lemonde.fr/planete/video/2020/11/11/covid-19-transports-repas-plein-air-quels-sont-les-lieux-les-plus-a-risque-de-contamination\\_6059357\\_3244.html](https://www.lemonde.fr/planete/video/2020/11/11/covid-19-transports-repas-plein-air-quels-sont-les-lieux-les-plus-a-risque-de-contamination_6059357_3244.html)

Quels sont les lieux les plus à risque pour attraper le Covid-19 ? Pour le savoir, de nombreux chercheurs mènent des études afin d'identifier les contextes les plus propices à la propagation du coronavirus. Parmi elles, une étude, publiée en septembre 2020 dans le revue *JAMA Internal Medicine*...

## 13 November

### Epidemiology

Uyoga S, Adetifa IMO, Karanja HK, et al. **Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Kenyan blood donors.** Science 2020, published 11 November. Full-text: <https://doi.org/10.1126/science.abe1916>

In April–June 2020, the crude prevalence of anti–SARS-CoV-2 IgG among blood donors in Kenya was 5,6% (174/3098). It was highest in urban counties, Mombasa (8,0%), Nairobi (7,3%) and Kisumu (5,5%). Of note, Kenya reported only 341 deaths by the end of that period. The authors conclude that the sharp contrast between the reported COVID-19 cases and deaths suggests that the disease might be attenuated in Africa.

Waterfield T, Watson C, Moore R, et al. **Seroprevalence of SARS-CoV-2 antibodies in children: a prospective multicentre cohort study.** Arch Dis Child. 2020 Nov 10;archdischild-2020-320558. PubMed: <https://pubmed.gov/33172887>. Full-text: <https://doi.org/10.1136/archdischild-2020-320558>

Fatigue, gastrointestinal symptoms and changes in sense of smell or taste were the symptoms most strongly associated with SARS-CoV-1 antibody positivity in children. Thomas Waterfield et al. report 68/992 (6,9%) children aged 2–15 years with positive SARS-CoV-2 antibody tests. Of these, 34/68 (50%) reported no symptoms prior to testing. Four independent variables were identified as significantly associated with SARS-CoV-2 seropositivity: known infected household contact OR=10,9; fatigue OR=16,8; gastrointestinal symptoms OR=6,6; and changes in sense of smell or taste OR=10,0.

Slot E, Hogema BM, Reusken CBEM, et al. **Low SARS-CoV-2 seroprevalence in blood donors in the early COVID-19 epidemic in the Netherlands.** Nat Commun 11, 5744 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19481-7>

One month into the outbreak and more than 2 weeks after social distancing and lockdown interventions were implemented, the proportion of SARS-CoV-2 antibody-positive individuals in the Dutch population tested was 2,7%. Hans Zaaijer, Ed Slot and colleagues also demonstrate that the hardest-hit areas had a seroprevalence of up to 9,5%; the seroprevalence was sex-independent throughout age groups (18–72 years); and antibodies were significantly more often present in young people aged 18–30 years.

## Transmission

The pre-print paper we presented on [October 25](#) has been published in Science: Hou YJ, Chiba S, Halfmann P, et al. **SARS-CoV-2 D614G variant exhibits efficient replication ex vivo and transmission in vivo.** Science 2020, published 12 November. Full-text: <https://doi.org/10.1126/science.abe8499>

This paper is a milestone work: Ralph Baric and colleagues (among the leading labs in the world) provide the possible explanation for the exploding numbers of SARS-CoV-2 infections. Engineering SARS-CoV-2 variants harboring the D614G substitution (the most prevalent SARS-CoV-2 strain circulating globally), they show that the D614G variant replicates more efficiently in primary human proximal airway epithelial cells and is more fit than wildtype virus in competition studies. Infection of human ACE2 transgenic mice and Syrian hamsters with the wildtype or D614G viruses produced similar titers in respiratory tissue and pulmonary disease. However, the D614G variant exhibited significantly faster droplet transmission between hamsters than the WT virus, early after infection. No more doubts that the SARS-CoV2 D614G substitution enhances infectivity, replication fitness, and early transmission.

Liu J, Li Y, Liu L, et al. **Infection of human sweat glands by SARS-CoV-2.** Cell Discov 6, 84 (2020). Full-text: <https://doi.org/10.1038/s41421-020-00229-y>

Manli Wang, Jia Liu and colleagues from Wuhan Institute of Virology describe skin autopsy samples from five patients with COVID-19. Immunofluorescence and immunohistochemical analyses detected SARS-CoV-2 spike proteins in three of the five patients. In these cases, the virus resided primarily in the sweat glands and sweat ducts with apparently higher amounts in the former than in the latter; in contrast, the virus was rarely detected in the epidermis or sebaceous glands. The authors conclude that “it is important to further assess the potential risk of viral transmission via perspiration and skin contact.” *Editor’s note: This paper will not change my standard protection measures.*

## Clinical

Meppiel E, Peiffer-Smadja N, Maury A, et al. **Neurological manifestations associated with COVID-19: a multicentric registry.** Clin Microbiol Infect 2020, published 12 November. Full-text: <https://doi.org/10.1016/j.cmi.2020.11.005>

Clinical spectrum and outcomes of neurological manifestations associated with SARS-CoV-2 infection may be broad and heterogeneous, suggesting different underlying pathogenic processes. This is the conclusion of a French multicenter study describing 222 patients. The most common neurological diseases were COVID-19 associated encephalopathy (30,2%), acute ischemic cerebrovascular syndrome (25,7%), encephalitis (9,5%), and Guillain-Barré Syndrome (6,8%). Neurologic manifestations appeared after the first COVID-19 symptoms with a median (IQR) delay of 6 (3-8) days in COVID-19 associated

encephalopathy, 7 (5-10) days in encephalitis, 12 (7-18) days in acute ischemic cerebrovascular syndrome and 18 (15-28) days in Guillain-Barré Syndrome.

## Treatment

Lenze EJ, Mattar C, Zorumski CF, et al. **Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients With Symptomatic COVID-19A Randomized Clinical Trial.** JAMA 2020, published 12 November. Full-text: <https://doi.org/10.1001/jama.2020.22760>

Fluvoxamine (a potent agonist of the sigma-1 receptor ( $\sigma_1R$ )), is an antidepressant which functions pharmacologically as a selective serotonin reuptake inhibitor. In this small randomized trial that included 152 adult outpatients with COVID-19 and symptom onset within 7 days, Eric Lenze et al. found that clinical deterioration occurred in 0 patients treated with fluvoxamine vs 6 (8.3%) patients treated with placebo over 15 days. The authors acknowledge the limitations of their study: a small number of endpoint events, which makes the findings fragile; 20% of study participants stopped responding to surveys during the 15-day trial; the follow-up duration was short and did not measure the effect of fluvoxamine on persistent symptoms or late deterioration. The potential advantages of fluvoxamine for outpatient treatment of COVID-19 would include its safety, widespread availability, low cost, and oral administration. Note that fluvoxamine can cause drug-drug interactions, particularly via inhibition of cytochromes P450 1A2 and 2C19. Eagerly awaiting data from larger trials. See also the comment by Seymour CW, Bauchner H, Golub RM. **COVID-19 Infection—Preventing Clinical Deterioration.** JAMA 2020, published 12 November. Full-text: <https://doi.org/10.1001/jama.2020.21720>

Monk PD, Marsden R, Tear VJ, et al. **Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial.** Lancet Respir Med 2020, published 12 November. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30511-7](https://doi.org/10.1016/S2213-2600(20)30511-7)

SNG001 is a formulation of recombinant interferon beta for inhaled delivery by nebuliser that is in development for the treatment of virus-induced lower respiratory tract illnesses. In this pilot trial, Tom Wilkinson, Phillip Monk and colleagues show that patients randomly assigned to SNG001 (n = 48) had greater odds of improvement versus placebo on the WHO Ordinal Scale for Clinical Improvement (OSCI) and more rapid recovery to a point where pa-

tients were no longer limited in their activity, with a greater proportion of patients recovering during the 28-day study period. Note that there was no significant difference between treatment groups in the odds of hospital discharge by day 28 – so await results from larger trials before drawing any conclusions.

See also the comment by Peiffer-Smadja N, Yazdanpanah Y. **Nebulised interferon beta-1a for patients with COVID-19**. Lancet Respir Med 2020, published 12 November. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30523-3](https://doi.org/10.1016/S2213-2600(20)30523-3)

## Education

Rubin EJ, Baden LR, Morrissey S. **An Update from Operation Warp Speed**. Audio interview (28:20). N Engl J Med 2020; 383: e127. Access: <https://doi.org/10.1056/NEJMe2033111>

The editors discuss the pace of discovery in the US response to COVID-19.

## Spanish

If you read Spanish, read Domínguez N. **La vacuna de la gripe puede potenciar la inmunidad contra el coronavirus**. El País 2020, published 13 November. Full-text: <https://elpais.com/ciencia/2020-11-12/la-vacuna-de-la-gripe-puede-potenciar-la-inmunidad-contra-el-coronavirus.html>

Varios estudios observan que la inmunización refuerza las defensas contra el SARS-CoV-2 y disminuye la mortalidad por COVID.

## French

If you read French, read Rosier F. **Comment les données mobiles peuvent aider à connaître les sources de contamination par le Covid-19**. Le Monde 2020, published 13 November. Full-text : [https://www.lemonde.fr/planete/article/2020/11/13/covid-19-les-donnees-mobiles-renseignent-sur-les-sources-de-contamination\\_6059582\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/13/covid-19-les-donnees-mobiles-renseignent-sur-les-sources-de-contamination_6059582_3244.html)

L'étude des communications de 98 millions d'Américains suggère qu'un petit nombre de lieux publics favorise la majorité des infections.

## 14 November

### Epidemiology

Malani A, Shah D, Kang G, et al. **Seroprevalence of SARS-CoV-2 in slums versus non-slums in Mumbai, India.** *Lancet Global Health* 2020, published 13 November. Full-text: [https://doi.org/10.1016/S2214-109X\(20\)30467-8](https://doi.org/10.1016/S2214-109X(20)30467-8)

This is the final article of a pre-print study we presented on [August 4](#): Kolthur-Seetharam U, Shah D, Shastri J, Juneja S, Kang G, Malani A, Mohanan M, Lobo GN, Velhal G, Gomare M. **SARS-CoV2 Serological Survey in Mumbai by NITI-BMC-TIFR.** Tata Institute of Fundamental Research (TIFR) 2020, published 29 June. Full-text: <https://www.tifr.res.in/TSN/article/Mumbai-Serosurvey%20Technical%20report-NITI.pdf>

“We usually prefer peer-reviewed studies and seldom present pre-published papers. We are even less readily inclined to present a PDF with just the technical details of an unpublished study. Today we make an exception. In a cross-sectional survey in Mumbai, India, [Ullas Kolthur-Seetharam](#) and colleagues estimated the prevalence of SARS-CoV-2 infection in three Mumbai areas (called ‘wards’) in July 2020. The authors found, on average, a prevalence of around 57% in the slum areas of Chembur, Matunga and Dahisar, and 16% in neighboring non-slums. If these data are confirmed, some Mumbai areas would soon reach herd immunity and could return to a pre-COVID way of life.”

See also a short comment in *The Economist*. Anonymous. **A minority of people with covid-19 account for the bulk of transmission.** *The Economist* 2020, published 7 November. Full-text: <https://www.economist.com/graphic-detail/2020/11/07/a-minority-of-people-with-covid-19-account-for-the-bulk-of-transmission>

### Prevention

Buchan AG, Yang L, Atkinson KD. **Predicting airborne coronavirus inactivation by far-UVC in populated rooms using a high-fidelity coupled radiation-CFD model.** *Sci Rep* 10, 19659 (2020). Full-text: <https://doi.org/10.1038/s41598-020-76597-y>

To mitigate transmission of aerosolised SARS-CoV-2 coronavirus, we are all following one or more of three key principles: minimize time of exposure to virus (by limiting interactions), maximize distance from sources of virus (social distancing), and/or shield yourself from the virus (wear PPE). Here, the

authors propose using narrow bandwidth, short wavelength UVC (207–222 nm) to mitigate further SARS-CoV-2 transmission. Their model shows that disinfection rates are increased by a further 50–85% when using far UVC within currently recommended exposure levels compared to the room’s ventilation alone. [Unlike typical UVC, which has been used to kill microorganisms but is carcinogenic and cataractogenic, recent evidence has shown that far UVC is safe to use around humans.]

## Immunology

Schulien I, Kemming J, Oberhardt V, et al. **Characterization of pre-existing and induced SARS-CoV-2-specific CD8<sup>+</sup> T cells.** Nat Med (2020). Full-text: <https://doi.org/10.1038/s41591-020-01143-2>

Are differences in pre-existing and induced SARS-CoV-2-specific CD8<sup>+</sup> T cell responses linked to different courses of infection? We don’t know yet. In particular, little is known about the abundance, phenotype, functional capacity and fate of pre-existing and induced SARS-CoV-2-specific CD8<sup>+</sup> T cell responses during the natural course of SARS-CoV-2 infection. In this study, Robert Thimme, Maike Hofmann, Christoph Neumann-Haefelin and colleagues established experimental tools for high-resolution *ex vivo* analyses of SARS-CoV-2-specific CD8<sup>+</sup> T cells. Find out what they discovered about heterogeneous and functionally competent cross-reactive and induced memory CD8<sup>+</sup> T cell responses in cross-sectionally analyzed individuals with mild SARS-CoV-2 disease.

## Clinical

Choi B, Choudhary MC, Regan J, et al. **Persistence and Evolution of SARS-CoV-2 in an Immunocompromised Host.** N Engl J Med 2020, published 11 November. Full-text: <https://doi.org/10.1056/NEJMc2031364>

Under special circumstances, for example in an immunocompromised state, SARS-CoV-2 has the potential for persistent infection and accelerated viral evolution. This is the result of a case report by Manuela Cernadas, Jonathan Li, Bina Choi and colleagues who describe the clinical course of a 45-year-old man with long-standing antiphospholipid syndrome, an autoimmune disorder. Before his death five months after the initial COVID-19 diagnosis, SARS-CoV-2 infection subsided and came back twice.



Wong CKH, Wong JY, Tang EHM, et al. **Clinical presentations, laboratory and radiological findings, and treatments for 11,028 COVID-19 patients: a systematic review and meta-analysis.** *Sci Rep* 10, 19765 (2020). Full-text: <https://doi.org/10.1038/s41598-020-74988-9>

Meta-analysis of 76 studies published from January-March 2020 on clinical presentation, laboratory findings and treatments of COVID-19 patients, accounting for a total of 11,028 COVID-19 patients. The most common comorbidities were hypertension (18%), followed by cardiovascular disease (12%) and diabetes (10%). The most frequently identified symptoms were fever (72%) and cough (56%). Notably, 62% and 20% of in-patients received oxygen therapy and non-invasive mechanical ventilation, respectively. In this review, radiological findings of SARS-CoV-2 pneumonia were non-specific.

### Severe COVID

Zietz M, Zucker J, Tatonetti NP. **Associations between blood type and COVID-19 infection, intubation, and death.** *Nat Commun* 11, 5761 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19623-x>

This next study is about the association between ABO and Rh blood types and infection, intubation, and death. Here, the authors used observational healthcare data on 14,112 individuals tested for SARS-CoV-2 with known blood type in the New York Presbyterian hospital system. Risk of intubation was decreased among A and increased among AB and B types, compared with type O, while risk of death was increased for type AB and decreased for types A and B. Rh-negative blood type might have a protective effect for all three outcomes.

Gude F, Riveiro V, Rodríguez-Núñez N, et al. **Development and validation of a clinical score to estimate progression to severe or critical state in COVID-19 pneumonia hospitalized patients.** *Sci Rep* 10, 19794 (2020). Full-text: <https://doi.org/10.1038/s41598-020-75651-z>

Five predictors determined within 24 h of hospital admission may identify patients at risk for COVID-19 disease progression: diabetes, higher age, a low lymphocyte count, decreasing SaO<sub>2</sub>, and any pH alteration. This is the outcome of a study by Lucía Ferreiro, Francisco Gude and colleagues who analyzed 229 patients who were admitted for pneumonia. The prediction model showed a good clinical performance, including discrimination (AUC 0.87 CI 0.81, 0.92) and calibration (Brier score = 0.11). In total, 0%, 12%, and 50% of

patients with severity risk scores  $\leq$  5%, 6–25%, and  $>$  25% exhibited disease progression, respectively.

## Comorbidities

Lim S, Bae JH, Kwon HS, et al. **COVID-19 and diabetes mellitus: from pathophysiology to clinical management.** Nat Rev Endocrinol (2020). Full-text: <https://doi.org/10.1038/s41574-020-00435-4>

Patients with diabetes mellitus are at increased risk of severe COVID-19. The authors discuss potential pathogenetic links between COVID-19 and diabetes mellitus; tight control of glucose levels; explain that insulin and dipeptidyl peptidase 4 inhibitors can be used safely in patients with diabetes mellitus and COVID-19; and caution that metformin and sodium-glucose co-transporter 2 inhibitors might need to be withdrawn in patients at high risk of severe disease.

## Spanish

If you read Spanish, read Andrino B, Grasso D, Llaneras K. **Consulta la incidencia del virus en 2.500 municipios: 40 capitales de provincia siguen en riesgo extremo.** El País 2020, published 14 November. Full-text: <https://elpais.com/sociedad/2020-11-14/consulta-la-incidencia-del-virus-en-2500-municipios-40-capitales-de-provincia-siguen-en-riesgo-extremo.html>

El 70% de la población española vive en localidades que superan los 250 casos por 100.000 habitantes. El virus ha crecido en las últimas dos semanas en 1.400 de ellas.

## French

If you read French, read Piketty T. « **La planète est traversée par de multiples fractures inégalitaires, que la pandémie va encore aggraver** » – Le Monde 2020, published 14 November. Full-text : [https://www.lemonde.fr/idees/article/2020/11/14/thomas-piketty-la-planete-est-traversee-par-de-multiples-fractures-inegalitaires-que-la-pandemie-va-encore-aggraver\\_6059700\\_3232.html](https://www.lemonde.fr/idees/article/2020/11/14/thomas-piketty-la-planete-est-traversee-par-de-multiples-fractures-inegalitaires-que-la-pandemie-va-encore-aggraver_6059700_3232.html)

De nouveaux indicateurs permettent une compréhension à la fois plus fine et plus exhaustive des inégalités au niveau mondial, détaille l'économiste Thomas Piketty dans sa chronique.

Audureau W. **Vaccins, Bill Gates, hydroxychloroquine... Nos réponses à 36 questions très partagées sur la crise du Covid-19.** Le Monde 2020, published 13 November. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2020/11/13/pourquoi-pour-qui-nos-reponses-a-36-questions-tres-partagees-sur-la-crise-du-covid\\_6059644\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2020/11/13/pourquoi-pour-qui-nos-reponses-a-36-questions-tres-partagees-sur-la-crise-du-covid_6059644_4355770.html)

Pourquoi les médecins perçoivent plus d'argent avec un cas de Covid-19 ? Pourquoi les métros sont-ils ouverts ? « Le Monde » répond à un long et populaire message viral sur Facebook.

Collectif. **Journal de crise des blouses blanches : « J'ai l'impression d'être embourbé dans une guerre de tranchée »** – Le Monde 2020, published 14 November. Full-text : [https://www.lemonde.fr/journal-blouses-blanches/article/2020/11/14/journal-de-crise-des-blouses-blanches-j-ai-l-impression-d-etre-embourbe-dans-une-guerre-de-tranchee\\_6059764\\_6033712.html](https://www.lemonde.fr/journal-blouses-blanches/article/2020/11/14/journal-de-crise-des-blouses-blanches-j-ai-l-impression-d-etre-embourbe-dans-une-guerre-de-tranchee_6059764_6033712.html)

Comme pendant la première vague épidémique au printemps, « Le Monde » donne à nouveau la parole à des personnels soignants en première ligne contre le Covid-19. Ils racontent « leur » crise sanitaire.

## 15 November

### Epidemiology

Brotons P, Launes C, Buetas E, et al. **Susceptibility to Sars-COV-2 Infection Among Children And Adults: A Seroprevalence Study of Family Households in the Barcelona Metropolitan Region, Spain.** Clinical Infectious Diseases, November 12, 2020. Full-text: <https://doi.org/10.1093/cid/ciaa1721>

Children have similar probability as adults to become infected by SARS-CoV-2 in quarantined family households. Pedro Brotons and colleagues from Barcelona performed a large cross-sectional seroprevalence study, enrolling 381 family households including 381 first-reported PCR-positive adult cases and 1084 contacts (672 children, 412 adults). SARS-CoV-2 infection seroprevalence rates were 18% (118/672) in children and 19% (77/335) in adult contacts. Nearly all positive pediatric contacts were asymptomatic or had mild symptoms.

Ebrahim SH, Ahmed Y, Algahtani SA, et al. **The Hajj pilgrimage during the COVID-19 pandemic in 2020: event hosting without the mass gathering.** Journal of Travel Medicine November 13, 2020. Full-text: <https://academic.oup.com/jtm/advance-article/doi/10.1093/jtm/taaa194/5979518>

Examples of religious congregations that resulted in seeding or surging of domestic and international COVID-19 outbreaks include events in Daegu, South Korea; Qom, Iran; Albany, Georgia; Arkansas + Maine, USA; and Mulhouse, France. Read how the science-driven steering of the 2020 Hajj with vastly reduced pilgrim numbers allowing for full compliance of the mitigation strategies avoided the cancellation of the event.

## Immunology

Shomuradova AS, Vagida MS, Sheetilov SA. **SARS-CoV-2 epitopes are recognized by a public and diverse repertoire of human T cell receptors.** Immunity November 13, 2020. Full-text: <https://doi.org/10.1016/j.immuni.2020.11.004>

Cellular and humoral immune response to SARS-CoV-2 were analyzed in 34 donors from Moscow who had recently recovered from COVID-19, as well as in two small control cohorts of healthy donors sampled before or during the pandemic. Some of the 14 healthy donors examined during the pandemic exhibited increased numbers of SARS-CoV-2-specific T cells, but no humoral response. It therefore seems possible that some people are protected by a pre-existing cross-reactive T cell response induced by other coronaviruses or had developed an asymptomatic infection that was cleared without the help of the humoral response. But can we believe this? The numbers were low and there is no doubt that his hypothesis needs to be validated in a larger cohort of donors.

## Diagnostics

Liotti FM, Menchinelli G, Marchetti S, et al. **Assessment of SARS-CoV-2 RNA Test Results Among Patients Who Recovered From COVID-19 With Prior Negative Results.** JAMA Intern Med, November 12, 2020. Full-text: <https://doi.org/10.1001/jamainternmed.2020.7570>

Many patients who recovered from COVID-19 may still be positive (albeit at lower levels) for SARS-CoV-2 RNA, but only a minority of the patients may carry replicating SARS-CoV-2 in the respiratory tract. Flora Marzia Liotti and colleagues from Rome, Italy analyzed nasal/oropharyngeal swab samples of

176 recovered patients with no fever and with 2 negative RT-PCR results for SARS-CoV-2 RNA 24 hours apart. In total, 32 of 176 samples (18%) tested positive for total SARS-CoV-2 RNA. All had low viral loads and only one of the 32 samples (3.1%) had replicative SARS-CoV-2 RNA.

## Clinical

Liao X, Wang Y, He Z, et al. **Three-month pulmonary function and radiological outcomes in COVID-19 survivors: a longitudinal patient cohort study.** *Open Forum Infectious Diseases*, 14 November 2020. Full-text: <https://doi.org/10.1093/ofid/ofaa540>

More on “Long COVID-19”. In this study, 172 survivors (33 with severe COVID-19) underwent high resolution CT of the thorax and pulmonary function tests at three months after hospital discharge. An abnormal pulmonary function was found in 11 (6%), and abnormal small airway function (FEF<sub>25-75%</sub>) in 12 (7%) patients. Obstructive and restrictive ventilation impairment was observed in six (3.5%) patients each. Lung function parameters did not differ between non-severe and severe cases. Of 142 CT scans, 122 (86%) showed residual CT abnormalities and 52 (37%) showed chronic and fibrotic changes.

## Comorbidities

Luo X, Liao Q, Shen Y, et al. **Vitamin D Deficiency Is Inversely Associated with COVID-19 Incidence and Disease Severity in Chinese People.** *The Journal of Nutrition* 13 November 2020. Full-text: <https://doi.org/10.1093/jn/nxaa332>

Vitamin D might have beneficial potential due to its immunomodulatory and anti-inflammatory properties. But is a deficiency associated with disease severity? Perhaps. In this cross-sectional study, 335 COVID-19 patients admitted to the Wuhan Tongji Hospital were retrospectively analyzed. A vitamin D deficiency (< 30 nmol/L) was significantly associated with COVID-19 severity (OR 2.7). Prospective studies have to confirm these results.

## Collateral damage

Monnet DL, Harbarth S. **Will coronavirus disease (COVID-19) have an impact on antimicrobial resistance?** *Euro Surveill.* 2020;25(45):pii=2001886. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.45.2001886>.

Good question. We don't know yet. After summarizing various determinants that may result in either an increase or, inversely, a decrease in antimicrobial

resistance (AMR), the authors found them to be balanced. The truth is that the impact of the COVID-19 pandemic on AMR will only become clear in the coming months and years as data gradually become available. Changes in AMR will most likely vary depending on the setting—e.g., ICUs vs other hospital units, hospital vs community settings—and possibly between countries.

Chan PS, Girotra S, Tang Y. **Outcomes for Out-of-Hospital Cardiac Arrest in the United States During the Coronavirus Disease 2019 Pandemic.** *JAMA Cardiology* November 14, 2020, Full-text: <https://doi.org/10.1001/jamacardio.2020.6210>

What is the association between the SARS-CoV-2 pandemic and out-of-hospital cardiac arrest (OHCA) outcomes in the US? This large registry study of 19,303 cases in 2019 and 2020 showed that the return of spontaneous circulation (ROSC) for OHCA was 18% lower overall than before the pandemic. Although the decrease was more prominent in counties most affected by the COVID-19 pandemic, lower rates of sustained ROSC and higher rates of termination of resuscitation were also observed in counties with low COVID-19 mortality rates. Delays in seeking medical care during the lockdown may not entirely explain the findings. The authors speculate that the interim recommendations for emergency medical service during this pandemic (for protecting frontline health care workers from unnecessary exposure) may also have decreased the likelihood of a successful resuscitation.

## Treatment

Hueso T, Pouderoux C, Péré H, et al. **Convalescent plasma therapy for B-cell-depleted patients with protracted COVID-19.** *Blood* 136 (20): 2290–2295. Full-text: <https://doi.org/10.1182/blood.2020008423>

The secondary humoral deficiency induced by anti-CD20 monoclonal antibodies such as rituximab may prevent the elicitation of a specific SARS-CoV-2 antibody response. Thomas Hueso and colleagues from France report on 17 consecutive patients with profound B cell lymphopenia and prolonged COVID-19 symptoms, negative SARS-CoV-2 serology, and positive RNAemia who were treated with four units of convalescent plasma. Within 48 hours of transfusion, all but 1 patient experienced an improvement of clinical symptoms. The inflammatory syndrome abated within a week. Of note, SARS-CoV-2 RNAemia decreased to below the sensitivity threshold in all 9 evaluated patients. This small series indicates that convalescent plasma could be promising at least in patients unable to mount a specific humoral response.

Mehew J, Johnson R, Roberts D, et al. **Convalescent plasma for COVID-19: male gender, older age and hospitalisation associated with high neutralising antibody levels, England, 22 April to 12 May 2020.** Euro Surveill. 2020;25(45):pii=2001754. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.45.2001754>

How to select donors of convalescent plasma (CP)? The answer: take older males with blood group AB and with severe disease – and don't wait too long. In this study from the UK, 275/330 donors had detectable neutralizing antibodies against SARS-CoV-2. For these 275 donors, median levels of neutralizing antibodies were higher in men compared with women, in those hospitalized compared with non-hospitalized, in those with blood group AB compared with other groups. Neutralizing antibody levels decreased as the time between SARS-CoV-2 diagnosis and donation increased. According to the authors, their data will be of value in the timely recruitment of CP donors most likely to have high levels of neutralizing antibodies for ongoing studies investigating its effectiveness.

## French

Wieder T. **Vaccin anti-Covid : la « success story » du couple fondateur du laboratoire allemand BioNTech** – Le Monde 2020, published 15 November. Full-text : [https://www.lemonde.fr/planete/article/2020/11/15/vaccin-anti-covid-la-success-story-du-couple-fondateur-du-laboratoire-allemand-biontech\\_6059786\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/15/vaccin-anti-covid-la-success-story-du-couple-fondateur-du-laboratoire-allemand-biontech_6059786_3244.html)

Ugur Sahin et Ozlem Türeci, aujourd'hui classés parmi les 100 personnes les plus riches d'Allemagne, sont des enfants d'immigrés turcs.

Hecketsweiler C. **Covid-19 : dans le service de réanimation de Bichat, « si le respirateur me lâche, je n'existe plus »** – Le Monde 2020, published 14 November. Full-text : [https://www.lemonde.fr/planete/article/2020/11/14/covid-19-dans-le-service-de-reanimation-de-bichat-si-le-respirateur-me-lache-je-n-existe-plus\\_6059752\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/14/covid-19-dans-le-service-de-reanimation-de-bichat-si-le-respirateur-me-lache-je-n-existe-plus_6059752_3244.html)

Le nombre de patients atteints par le Covid-19 a considérablement augmenté en quinze jours dans ce centre hospitalier parisien où les personnels font face à la détresse des malades et, parfois, à la défiance des familles.

Aeberhardt C. **Covid-19 : « On ne vaccinera sans doute pas la population française dans son ensemble »** – Full-text : [https://www.lemonde.fr/planete/article/2020/11/14/covid-19-on-ne-vaccinera-sans-doute-pas-la-population-francaise-dans-son-ensemble\\_6059736\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/14/covid-19-on-ne-vaccinera-sans-doute-pas-la-population-francaise-dans-son-ensemble_6059736_3244.html)

La vaccinologue Marie-Paule Kieny estime que les premiers vaccins pourraient être proposés en France début 2021. Selon elle, même si le virus ne pourra être éradiqué, la situation sanitaire devrait être meilleure d'ici quelques mois.

## 16 November

### Immunology

Zhang J, Wu Q, Liu Z, et al. **Spike-specific circulating T follicular helper cell and cross-neutralizing antibody responses in COVID-19-convalescent individuals.** Nat Microbiol (2020). Full-text: <https://doi.org/10.1038/s41564-020-00824-5>

T follicular help (TFH) cells, a subset of T cells, have been identified as professional B helper T cells in past decades and are required for T-dependent antibody production. Convalescent individuals who experienced severe COVID-19 showed higher neutralizing antibody titers, a faster increase in lymphocyte counts and a higher frequency of CXCR3+ TFH cells compared with COVID-19-convalescent individuals who experienced non-severe disease. Circulating TFH cells were spike specific and functional, and the frequencies of CXCR3+ TFH cells were positively associated with neutralizing antibody titers in COVID-19-convalescent individuals.

Dayarathna S, Jeewandara C, Gomes L, et al. **Similarities and differences between the ‘cytokine storms’ in acute dengue and COVID-19.** Sci Rep 10, 19839 (2020). Full-text: <https://doi.org/10.1038/s41598-020-76836-2>

Severe COVID-19 and dengue hemorrhagic fever (DHF) are two diseases that can associate with an altered immune response to the infecting virus. In both infections, a cytokine storm is thought to play a role in disease pathogenesis. Shashika Dayarathna and colleagues from Sri Lanka found similarities between the cytokines that are elevated in early illness in those who progress to severe illness but also many differences. Those who developed severe pneumonia in COVID-19 had high levels of many inflammatory cytokines and chemokines but low IFN- $\gamma$  levels. Patients who proceeded to develop DHF also



had high cytokine and chemokine levels, but most strikingly very high IL-10 levels. Low IFN- $\gamma$  response to SARS-CoV-2 and high levels of immunosuppressive cytokines such as IL-10 in both COVID-19 and dengue during early illness is likely to result in an altered antiviral response.

## Vaccine

Halstead SB, Katzelnick L. **COVID-19 Vaccines: Should We Fear ADE?** J Infect Dis. 2020 Nov 13;222(12):1946-1950. PubMed: <https://pubmed.gov/32785649>. Full-text: <https://doi.org/10.1093/infdis/jiaa518>

Scott B. Halstead and Leah Katzelnick say no. Antibody-dependent enhanced (ADE) breakthrough infections are unlikely because coronavirus diseases in humans lack the clinical, epidemiological, biological, or pathological attributes of ADE disease exemplified by dengue viruses (DENV). In contrast to DENV, SARS and MERS CoVs predominantly infect respiratory epithelium, not macrophages.

## Diagnostics

Escribano P, Álvarez-Uría A, Alonso R, et al. **Detection of SARS-CoV-2 antibodies is insufficient for the diagnosis of active or cured COVID-19.** Sci Rep 10, 19893 2020. Full-text: <https://doi.org/10.1038/s41598-020-76914-5>

Using Abbott's SARS-CoV-2 IgG assay and the Panbio™ COVID-19 IgG/IgM device, the authors found that serum IgG detection alone is insufficient for the diagnosis of active or cured COVID-19, with sensitivity values that range between 60 and 75%, respectively. Detection of IgM adds limited value to the performance of serological strategies.

Wang H, Hogan CA, Miller JA, et al. **Performance of nucleic acid amplification tests for detection of severe acute respiratory syndrome coronavirus 2 in prospectively pooled specimens.** Emerg Infect Dis. 2012 Jan. Full-text: <https://doi.org/10.3201/eid2701.203379>

Pooled nucleic acid amplification tests (NATs) could increase availability of testing at a decreased cost. However, it is not that trivial, and the effect of dilution on analytical sensitivity through sample pooling has not been well characterized. Hannah Wang and colleagues from Stanford tested 1648 prospectively pooled specimens by using 3 different NATs. Positive percent agreement (PPA) of pooled versus individual testing ranged from 71,7% to 82,6% for pools of 8 and from 82,9% to 100,0% for pools of 4. PPA was depend-

ent on the proportion of tests with positive results, cycle threshold distribution, and assay limit of detection. False negative results occurred exclusively in pools containing samples with low estimated viral load ( $Ct > 34$ ).

Manabe YC, Sharfstein JS, Armstrong K. **The Need for More and Better Testing for COVID-19**. JAMA November 13, 2020. Full-text: <https://doi.org/10.1001/jama.2020.21694>

In their viewpoint, Yukari C. Manabe, Joshua S. Sharfstein and Katrina Armstrong argue that it is more accurate to consider testing less of a prevention strategy than a mitigation strategy. Testing in the absence of other proven prevention strategies is unable to prevent outbreaks. Even as tests become faster with higher sensitivity and specificity, social distancing, mask wearing, and avoidance of large indoor and outdoor gatherings must remain central to any public health strategy. Even the perfect test cannot do it alone.

## Clinical

Chopra C, Flanders Sa, O'Malley M, et al. **Sixty-Day Outcomes Among Patients Hospitalized With COVID-19**. Annals Int Med 11 November 2020. Full-text: <https://doi.org/10.7326/M20-5661>

The toll of COVID-19 extends well beyond hospitalization. In this cohort study of 1648 patients with COVID-19 admitted to 38 hospitals in Michigan, 398 (24%) died during hospitalization and 1250 (76%) survived. Of these, 975 (78%) went home whereas 158 (13%) were discharged to a skilled nursing or rehabilitation facility. By 60 days after discharge, an additional 84 patients (7% of hospital survivors and 10% of ICU-treated hospital survivors) had died. Within 60 days of discharge, 189 patients (15% of hospital survivors) were re-hospitalized. Of patients alive 60 days after discharge, 488 (41.8%) completed a telephone survey. For most patients who survived, ongoing morbidity, including the inability to return to normal activities, physical and emotional symptoms, and financial loss, was common.

Griffith GJ, Morris TT, Tudball MJ, et al. **Collider bias undermines our understanding of COVID-19 disease risk and severity**. Nat Commun 11, 5749 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19478-2>

Numerous observational studies have attempted to identify risk factors for infection with SARS-CoV-2 and COVID-19 disease outcomes. Studies have used datasets sampled from patients admitted to hospital, people tested for active infection, or people who volunteered to participate. Here, Gareth J. Griffith

and colleagues from Bristol highlight the challenge of interpreting observational evidence from such non-representative samples. Read how the collider bias (a variable that is influenced by two other variables, for example when a risk factor and an outcome both affect the likelihood of being sampled) can have a dramatic impact on the results and what approaches are available to explore and mitigate this problem.

## Treatment

Schwaiger J, Karbiener M, Aberham C, Farcet MR, Kreil TR. **No SARS-CoV-2 Neutralization by Intravenous Immunoglobulins Produced From Plasma Collected Before the 2020 Pandemic.** *J Infect Dis.* 2020 Nov 13;222(12):1960-1964. PubMed: <https://pubmed.gov/32941626>. Full-text: <https://doi.org/10.1093/infdis/jiaa593>

Julia Schwaiger and colleagues from Baxter AG tested 54 intravenous immunoglobulin preparations, produced from plasma collected in Europe and the US. Although highly potent neutralization of a seasonal coronavirus HCoV-229E was seen, there was no cross-neutralization of the new SARS-CoV-2.

## Pediatrics

Stonoga ETS, Lanzoni LA, Rebutini PZ, Oliveira ALP, Chiste JA, Fugaça CA, et al. **Intrauterine transmission of SARS-CoV-2.** *Emerg Infect Dis.* 2021 February. Full-text: <https://doi.org/10.3201/eid2702.203824>

A case of fetal death associated with intrauterine transmission of SARS-CoV-2 in a 42 yr old woman at 27 weeks' gestation. Placenta and fetal tissue showed chronic histiocytic intervillitis, maternal and fetal vascular malperfusion, microglial hyperplasia, and lymphocytic infiltrates. Placenta and umbilical cord blood tested positive for the virus by PCR, confirming transplacental transmission.

## 17 November

### Epidemiology

Mahale P, Rothfuss C, Bly S, et al. **Multiple COVID-19 Outbreaks Linked to a Wedding Reception in Rural Maine — August 7–September 14, 2020.** *MMWR Morb Mortal Wkly Rep* 2020;69:1686–1690. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6945a5>

Do you have a niece who, despite all the warnings, is unwaveringly sticking to her plans to get married in January? Who says that only 50 guests (ok, 55) will come and that temperature checks for all guests will be conducted at the facility entrance? That there will be enough space, with 10 tables, with 4–6 guests seated around each table? That signs posted at the entrance will instruct visitors to wear masks? Then give her this paper to read. A wedding reception in a small rural town in Maine was the likely source of COVID-19 outbreaks in the local community, a long-term care facility, and a correctional facility. Outcome: 177 cases, seven hospitalizations, and seven deaths. Read here why people should avoid large gatherings, practice physical distancing, wear masks, stay home when ill, and self-quarantine after exposure to a person with confirmed SARS-CoV-2 infection.

(If your niece doesn't want to read a scientific paper, provide her with "15 Benefits of A Summer Wedding": <https://www.nichemarket.co.za/blog/extravaganza/benefits-summer-wedding>. Benefit No. 16 is found probably below, in the vaccine section.)

Ali H, Kondapally K, Pordell P, et al. **COVID-19 Outbreak in an Amish Community — Ohio, May 2020**. MMWR Morb Mortal Wkly Rep 2020;69:1671–1674. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6945a2>

How social gatherings likely contributed to rapid transmission of SARS-CoV-2 in an Amish community. In May, after a cluster of seven COVID-19 cases was identified, 23/30 (77%) additional residents tested by RT-PCR received positive test results. Rapid and sustained transmission of SARS-CoV-2 was associated with multiple social gatherings. Although Amish communities might be experiencing challenges with preventing and mitigating SARS-CoV-2 transmission, the authors conclude that leveraging Amish cultural beliefs of communal responsibility could help limit the spread of SARS-CoV-2.

Wang EA, Western B, Berwick DM. **COVID-19, Decarceration, and the Role of Clinicians, Health Systems, and Payers. A Report From the National Academy of Sciences, Engineering, and Medicine**. JAMA November 16, 2020. Full-text: <https://doi.org/10.1001/jama.2020.22109>

By August 2020, 90 of the largest 100 cluster outbreaks in the United States had occurred in prisons and jails. Reducing the incarcerated population ("decarceration") is an important and urgent strategy for mitigating viral transmission in prisons and jails. In their courageous viewpoint, Emily Wang and colleagues argue that decarceration in the service of both public health

and safer communities will require sustained engagement from clinicians, health systems, and Medicaid authorities.

## Immunology

Knierman MD, Lannan MB, Spindler LJ, et al. **The Human Leukocyte Antigen Class II Immunopeptidome of SARS-CoV-2 Spike Glycoprotein.** Cell Rep November 13, 2020. Full-text: <https://doi.org/10.1016/j.celrep.2020.108454>

Using mass spectrometry, Michael D Knierman and colleagues from Lilly performed a precise and comprehensive immunopeptidomic investigation with SARS-CoV-2 spike glycoprotein. They identified 526 unique sequences from SARS-CoV-2 spike glycoprotein extracellular domain in a complex with HLA class II molecules on antigen presenting cells from a panel of healthy donors. The identified sequences spanned the entire spike protein and several sequences were isolated from a majority of the donors sampled, indicating promiscuous binding. This is good news, as both the depth and breadth of the HLA-II peptides indicate that mutational drift is not expected to dramatically alter the ability of an infected individual to mount a new B cell response.

## Vaccine

Callaway E. **COVID vaccine excitement builds as Moderna reports third positive result.** Nature NEWS November 16, 2020. Full-text: <https://doi.org/10.1038/d41586-020-03248-7>

Moderna's vaccine comprises RNA instructions for cells to produce a modified form of the coronavirus spike protein, the immune system's key target against coronaviruses. Of note, the vaccine remains stable in conventional refrigerators for a month and ordinary freezers for six months. Ewen Callaway summarizes preliminary data showing that the immunization is 94% effective and seems to prevent severe infections.

## Diagnostics

Gniffke EP, Harrington WE, Dambrauskas N, et al. **Plasma From Recovered COVID-19 Patients Inhibits Spike Protein Binding to ACE2 in a Microsphere-Based Inhibition Assay.** J Infect Dis. 2020 Nov 13;222(12):1965-1973. PubMed: <https://pubmed.gov/32798222> . Full-text: <https://doi.org/10.1093/infdis/jiaa508>

A new microsphere-based flow cytometry assay that quantifies the ability of plasma to inhibit the binding of spike protein to ACE2. Plasma from 22 pa-

tients who had recovered from mild COVID-19 and expressed anti-spike protein trimer immunoglobulin G (IgG) inhibited ACE2-spike protein binding to a greater degree than controls. The degree of inhibition was correlated with anti-spike protein IgG levels, neutralizing titers in a pseudotyped lentiviral assay, and the presence of fever during illness. This inhibition assay may be broadly useful to quantify the functional antibody response of patients recovered from COVID-19 or vaccine recipients in a cell-free assay system.

## Clinical

Coate KC, Cha , Shrestha S. **SARS-CoV-2 Cell Entry Factors ACE2 and TMPRSS2 are Expressed in the Microvasculature and Ducts of Human Pancreas but are Not Enriched in  $\beta$  Cells** *Metabolism* November 13, 2020. Full-text: <https://doi.org/10.1016/j.cmet.2020.11.006>

Isolated reports of new-onset diabetes in COVID-19 cases have led to the hypothesis that SARS-CoV-2 is directly cytotoxic to pancreatic islet  $\beta$  cells. Katie Coate and colleagues show here that it's not that easy. In pancreatic sections, ACE2 and TMPRSS2 protein (the main cell entry factors) were not detected in  $\beta$  cells from donors with and without diabetes. Instead, ACE2 protein was expressed in islet and exocrine tissue microvasculature and in a subset of pancreatic ducts, whereas TMPRSS2 protein was restricted to ductal cells. Contrasting with previous reports, this careful investigation suggests that the interaction of diabetes and SARS-CoV-2 is mediated by systemic inflammation and/or metabolic changes in other organs such as liver, muscle or adipose tissue (and not by a direct infection of  $\beta$  cells in the pancreas).

Shi Z, de Vries HJ, Vlaar AP, et al. **Diaphragm Pathology in Critically Ill Patients With COVID-19 and Postmortem Findings From 3 Medical Centers.** *JAMA Intern Med* November 16, 2020. Full-text: <https://doi.org/10.1001/jamainternmed.2020.6278>

This study focused on the diaphragm, the main muscle of respiration. Consecutive diaphragm muscle specimens from 26 deceased COVID-19 patients were compared with autopsy diaphragm specimens of 8 patients who had been critically ill without COVID-19. There was an increased expression of genes involved in fibrosis and histological evidence for the development of fibrosis in the diaphragm. Of note, this myopathic phenotype was distinctly different from that of control ICU patients, with comparable duration of mechanical ventilation and ICU length of stay. It is hypothesized that severe myopathy may lead to diaphragm weakness and might contribute to ventilator weaning failure, persistent dyspnea, and fatigue in COVID-19 survivors.

Miller DG, Piesron L, Doernberg S. **The Role of Medical Students During the COVID-19 Pandemic.** *Annals Int Med* 2020, November 17. Full-text: <https://doi.org/10.7326/L20-1195>

Interesting discussion about in-person medical student involvement during the COVID-19 pandemic. Some authors argue for it, others against it. Both sides have good arguments.

## Collateral Damage

Leske S, Kølves K, Cromton D, et al. **Real-time suicide mortality data from police reports in Queensland, Australia, during the COVID-19 pandemic: an interrupted time-series analysis.** *Lancet Psychiatry*, November 16, 2020. Full-text: [https://doi.org/10.1016/S2215-0366\(20\)30435-1](https://doi.org/10.1016/S2215-0366(20)30435-1)

Do suicide rates increase during infectious disease outbreaks? Probably not (at least in Australia). In this study, analyzing suspected suicide rates in 2020 relative to 2015–19 to assess any early effects of the COVID-19 pandemic in Queensland, no evidence of a change in suspected suicide rates was seen.

## 18 November

### Epidemiology

Denny TN, Andrews L, Bonsignori M, et al. **Implementation of a Pooled Surveillance Testing Program for Asymptomatic SARS-CoV-2 Infections on a College Campus — Duke University, Durham, North Carolina, August 2–October 11, 2020.** *MMWR Morb Mortal Wkly Rep.* ePub: 17 November 2020. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6946e1>

Test them all? In fall 2020, Duke University's COVID-19 prevention strategy included risk reduction behaviors, but also frequent testing using pooled SARS-CoV-2 PCR testing, and contact tracing. Of 10,265 students who received testing 68,913 times, 84 had positive results. Of these, 51% were asymptomatic, and some had high viral loads. This plan allowed campus to remain open for 10 weeks of classes without substantial outbreaks among residential or off-campus populations. Importantly, no evidence from contact tracing linked transmission with in-person classes. Pooled testing permitted a nearly 80% savings in use of reagents and laboratory resources compared with testing each individual specimen.

## Immunology

Samuel RM, Majd H, Richter MN, et al. **Androgen Signaling Regulates SARS-CoV-2 Receptor Levels and Is Associated with Severe COVID-19 Symptoms in Men.** Cell Stem Rep November 17, 2020. Full-text: <https://doi.org/10.1016/j.stem.2020.11.009>

Finasteride for COVID-19? Ryan M. Samuel and colleagues from San Francisco identified a link between male sex hormone signaling and regulation of the SARS-CoV-2 receptor ACE2 and co-receptor TMPRSS2, possibly explaining the higher complication rates in men. Target analysis of hit compounds revealed androgen signaling as a key modulator of ACE2 levels. Of note, treatment with anti-androgenic drugs such as finasteride reduced ACE2 expression and protected hESC-derived lung organoids against SARS-CoV-2 infection. Finally, clinical data on COVID-19 patients demonstrated that prostate diseases, which are linked to elevated androgen, are significant risk factors and genetic variants that increase androgen levels are associated with higher disease severity.

Li A, Ling Y, Song Z, et al. **Early plasma IL-37 responses accompanied with low inflammatory cytokines correlate with benign clinical outcomes during SARS-CoV-2 infection.** J Infect Dis. 2020 Nov 17:jiaa713. PubMed: <https://pubmed.gov/33197260>. Full-text: <https://doi.org/10.1093/infdis/jiaa713>

Ang Li and colleagues from Shanghai examined early responses of IL-37, a powerful anti-inflammatory cytokine, in 254 SARS-CoV-2-infected patients prior to any clinical intervention and determined its correlation with clinical prognosis. Higher early IL-37 responses correlated with earlier viral RNA negative conversion, chest CT image improvement and cough relief, consequently resulting in earlier hospital discharge. Further assays showed that higher IL-37 was associated with lower IL-6 and IL-8 and higher IFN- $\alpha$ , and facilitated biochemical homeostasis. Low IL-37 responses predicted severe clinical prognosis in combination with IL-8 and CRP. Moreover, IL-37 administration was able to attenuate lung inflammation and alleviate respiratory tissue damage in hACE2-transgenic mice infected with SARS-CoV-2.



Woldemeskel BA, Kwaa AK, Garliss CC, Laeyendecker O, Ray SC, Blankson JN. **Healthy donor T cell responses to common cold coronaviruses and SARS-CoV-2.** J Clin Invest. 2020 Nov 16;143120. PubMed: <https://pubmed.gov/32966269>. Full-text: <https://doi.org/10.1172/JCI143120>

Bezawit A. Woldemeskel and colleagues from Baltimore used the ELISPOT assay to characterize the T cell responses against peptide pools derived from the spike protein of 3 common cold coronaviruses and SARS-CoV-2 in 21 healthy donors seronegative for SARS-CoV-2. An *in vitro* expansion culture assay was also used to analyze memory T cell responses. Responses to the spike protein of the 3 common cold coronaviruses were found in many of the donors. T cell responses to SARS-CoV-2 spike and nucleocapsid proteins were present in only 1 participant and were potentially the result of cross-recognition by T cells specific for the common cold coronaviruses.

## Vaccine

Zhang Y, Zeng G, Pan H. **Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial.** Lancet November 17, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30843-4](https://doi.org/10.1016/S1473-3099(20)30843-4)

Phase I/II study of an inactivated vaccine candidate against COVID-19. In total, 743 participants at the Suining County of Jiangsu province, China, received at least one dose (n = 143 for Phase 1 and n = 600 for Phase 2; safety population). At day 28 after the days 0 and 28 vaccination schedule, seroconversion of neutralising antibodies was seen for 109 (92%) of 118 participants in the 3 µg group which is the suggested dose for efficacy assessment in future Phase III trials. Adverse events such as mild injection-site pain, occurred in 81 (17%) of 480 vaccine recipients.

Bar-Zeev N, Kochhar S. **Expecting the unexpected with COVID-19 vaccines.** Lancet November 17, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30870-7](https://doi.org/10.1016/S1473-3099(20)30870-7)

According to this detailed comment, like all Phase II trials, the results must be interpreted with caution until Phase III results are published. Neutralising titers were substantially lower than those seen in 117 convalescent patients who previously had COVID-19 tested in the same laboratory. A demonstration

of longevity of response and of empiric protection from this vaccine candidate will be important.

## Clinical

Bois MC, Boire NA, Layman AJ, et al. **COVID-19-associated Non-Occlusive Fibrin Microthrombi in the Heart**. *Circulation*. 2020 Nov 16. PubMed: <https://pubmed.gov/33197204>. Full-text: <https://doi.org/10.1161/CIRCULATIONAHA.120.050754>

What are the underlying mechanisms of cardiac complications? This small, but detailed histopathologic, immunohistochemical, ultrastructural and molecular cardiac series of 15 COVID-19 cases showed no definitive evidence of direct myocardial infection. COVID-19 cases frequently had cardiac fibrin microthrombi (12/16), without universal acute ischemic injury. Moreover, myocarditis was present in 33.3% of active and cleared COVID-19 patients, but is usually limited in extent. Histologic features of resolved infection are variable. Cardiac amyloidosis may be an additional risk factor for severe disease.

Vaira LA, Hopkins C, Sandison A, et al. **Olfactory epithelium histopathological findings in long-term coronavirus disease 2019 related anosmia**. *J Laryngol Otol*. 2020 Nov 16:1-13. PubMed: <https://pubmed.gov/33190655>. Full-text: <https://doi.org/10.1017/S0022215120002455>

Interesting case report of a patient who presented with anosmia persisting for more than three months after infection. MRI did not reveal any pathological findings: the olfactory bulb and clefts were of normal volume, without signal anomalies. However, the biopsy demonstrated significant disruption of the olfactory epithelium. This shifts the focus away from invasion of the olfactory bulb and encourages further studies of treatments targeted at the surface epithelium.

Alvarez-Garcia J, Lee S, Gupta A, et al. **Prognostic Impact of Prior Heart Failure in Patients Hospitalized With COVID-19**. *J Am Coll Cardiol*. 2020 Nov 17;76(20):2334-2348. PubMed: <https://pubmed.gov/33129663>. Full-text: <https://doi.org/10.1016/j.jacc.2020.09.549>

Retrospective analysis of 6439 patients admitted for COVID-19 at 5 hospitals in New York City between February 27 and June 26, 2020. Compared with patients without heart failure (HF), those with previous HF experienced longer

length of stay (8 days vs. 6 days;  $p < 0.001$ ), increased risk of mechanical ventilation (22.8% vs. 11.9%), and mortality (40.0% vs. 24.9%). Outcomes among patients with HF were similar, regardless of LVEF or renin-angiotensin-aldosterone inhibitor use.

### Collateral damage

De Luca G, Verdoia M, Cercek M, et al. **Impact of COVID-19 Pandemic on Mechanical Reperfusion for Patients With STEMI.** *J Am Coll Cardiol.* 2020 Nov 17;76(20):2321-2330. PubMed: <https://pubmed.gov/33183506>. Full-text: <https://doi.org/10.1016/j.jacc.2020.09.546>

A total of 6609 patients underwent primary percutaneous coronary intervention (PPCI) in 77 centers, located in 18 countries. In 2020, during the pandemic, there was a significant reduction in PPCI as compared with 2019 (incidence rate ratio: 0.81; 95% confidence interval: 0.78 to 0.84). Furthermore, the pandemic was associated with a significant increase in “door-to-balloon” and total ischemia times, which may have contributed to higher mortality during the pandemic.

### Comorbidities

Shah GL, DeWolf S, Lee YJ, et al. **Favorable outcomes of COVID-19 in recipients of hematopoietic cell transplantation.** *J Clin Invest.* 2020 Nov 16:141777. PubMed: <https://pubmed.gov/32897885>. Full-text: <https://doi.org/10.1172/JCI141777>

Gunjan L. Shah from Memorial Sloan Kettering Cancer Center and colleagues retrospectively investigated 77 patients with SARS-CoV-2 who were recipients of cellular therapy (Allo, 35; Auto, 37; CAR T, 5; median time from cellular therapy, 782 days). Overall survival at 30 days was 78%. Mortality was largely driven by patients with active malignancy, especially relapsed leukemia, in whom the goals of care were affected both by COVID-19 severity and the decision to forgo anti-cancer treatment during an active infection. Immune profiling revealed reductions and rapid recovery in lymphocyte populations across lymphocyte subsets. Many patients were able to recover from COVID-19 infection and mount an antibody response with similar overall survival to the general hospitalized population.

## 19 November

### Epidemiology

Xing Y, Wong GWK, Ni W, Hu X, Xing Q. **Rapid Response to an Outbreak in Qingdao, China.** N Engl J Med 2020, published 18 November. Full-text: <https://doi.org/10.1056/NEJMc2032361>

Three COVID-19 cases in [Qingdao](#) in October: a taxi driver who was admitted to Qingdao Central Hospital for a transient ischemic attack on October 10; his wife who had been working part-time as a nursing assistant at Qingdao Chest Hospital; and a man with pulmonary tuberculosis who was treated at the same hospital. These were the first cases after a 2-month period without local SARS-CoV-2 transmission in China. What would you have done during the next 7 days? The Chinese authorities tested 10.9 million people and identified another 9 cases related to the initial cluster. The outbreak was controlled without a lockdown.

### Prevention

Bundgaard H, Bundgaard JS, Raaschou-Pedersen DET, et al. **Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers : A Randomized Controlled Trial.** Ann Intern Med. 2020 Nov 18. PubMed: <https://pubmed.gov/33205991>. Full-text: <https://doi.org/10.7326/M20-6817>

Ammunition for your friends who deny the usefulness of wearing face masks? This Danish study finds that wearing surgical masks doesn't really reduce the SARS-CoV-2 infection rate among wearers. Don't read the article without reading the comment by Laine C, Goodman SN, Guallar E. **The Role of Masks in Mitigating the SARS-CoV-2 Pandemic: Another Piece of the Puzzle.** Ann Intern Med. 2020 Nov 18. PubMed: <https://pubmed.gov/33205993>. Full-text: <https://doi.org/10.7326/M20-7448> and the editorial by Frieden TR, Cash-Goldwasser S. **Of Masks and Methods.** Ann Intern Med. 2020 Nov 18. PubMed: <https://pubmed.gov/33205992>. Full-text: <https://doi.org/10.7326/M20-7499>. And maybe we should ask researchers from South-East Asia to repeat the study.

Continue wearing face masks!

## Immunology

Dan JM, Mateus J, Kato Y, et al. **Immunological memory to SARS-CoV-2 assessed for greater than six months after infection.** bioRxiv 2020, posted 16 November. Full-text: <https://doi.org/10.1101/2020.11.15.383323>

As we approach the end of Year 1 of the SARS-CoV-2 pandemic, we realize that although millions of people were infected during spring 2020, there is now, 8 months later, no sizeable epidemic of *re*-infections. This observation suggests that SARS-CoV-2 infection might confer a solid immunity. Now, Shane Crotty, Alessandro Sette, Daniela Weiskopf, Jennifer Dan and colleagues analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 185 COVID-19 cases, including 41 cases at > 6 months post-infection. The result: Spike IgG was relatively stable over 6+ months. Spike-specific memory B cells were more abundant at 6 months than at 1 month. SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a half-life of 3-5 months. These findings might suggest that after SARS-CoV-2 infection (or after vaccination), the vast majority of people could be protected against severe COVID-19 for years.

Read also the NYTimes article by Mandavilli A. **Immunity to the Coronavirus May Last Years, New Data Hint.** The New York Times 2020, published 17 November. Full-text: <https://www.nytimes.com/2020/11/17/health/coronavirus-immunity.html>

## Vaccine

Ramasamy MN, Minassian AM, Ewer KJ, et al. **Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial.** Lancet 2020, published 18 November. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32466-1](https://doi.org/10.1016/S0140-6736(20)32466-1)

Phase II results of a single-blind, randomized, controlled trial that describe the safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine in a wide range of participants, including adults aged 70 years and older. The results are encouraging: ChAdOx1 nCoV-19 appears to be better tolerated in older adults than in younger adults and has similar immunogenicity across all age groups after a boost dose.

See also the comment by Andrew MK, McElhaney JE. **Age and frailty in COVID-19 vaccine development.** Lancet 2020, published 18 November. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32481-8](https://doi.org/10.1016/S0140-6736(20)32481-8)

Knipe DM, Levy O, Fitzgerald KA, Mühberger E. **Ensuring vaccine safety.** Science 2020, published 17 November. Full-text: <https://doi.org/10.1126/science.abf0357>

Vaccines are among the most successful medical and public health measures ever implemented and prevent ~6 million deaths globally per year. Efficient SARS-CoV-2 vaccines might prevent a similar number of deaths over the coming years. However, caution the authors, the urgent need for COVID-19 vaccines must be balanced with the imperative of ensuring safety and public confidence in vaccines by following the established clinical safety testing protocols throughout vaccine development, including both pre- and post-deployment.

Wadman M. **Fever, aches from Pfizer, Moderna jabs aren't dangerous but may be intense for some.** Science 2020, published 18 November. Full-text: <https://www.sciencemag.org/news/2020/11/fever-aches-pfizer-moderna-jabs-aren-t-dangerous-may-be-intense-some>

Both the BioNTech/Pfizer and the Moderna/NIH mRNA vaccine reached 95% efficacy in clinical trials of tens of thousands of people. The trials revealed no serious safety concerns. We will learn to accept fever and aches as signs that the vaccine works. Even bone and muscle aches and an almost unbearable 38.9°C fever that lasts 12 hours...

## Clinical

Dhawan R, Gopalan D, Howard L, et al. **Beyond the clot: perfusion imaging of the pulmonary vasculature after COVID-19.** Lancet Respiratory Medicine 2020, published 17 October. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30407-0](https://doi.org/10.1016/S2213-2600(20)30407-0)

The long-term outcomes in survivors of COVID-19 are unknown at present. As pulmonary thrombosis and thromboembolism occur during clinical SARS-CoV-2 infection, the authors propose a proactive follow-up strategy to evaluate residual clot burden, small vessel injury, and potential hemodynamic sequelae that might affect quality of life for a long time.

## Education

Rubin EJ, Baden LR, Morrissey S. **Covid-19 in Europe and New Information on Vaccines.** Audio interview (26:44). N Engl J Med 2020; 383: e134. Access: <https://doi.org/10.1056/NEJMe2033666>

The editors discuss both recent vaccine trial results and the state of the pandemic in Europe.

## Spanish

If you read Spanish, read Sámano J. **España abochorna a Alemania**. El País 2020, published 17 November. Full-text: <https://elpais.com/deportes/2020-11-17/espana-abochorna-a-alemania.html>

La nueva generación de la Roja lo borda con una goleada de época a la selección de Löw y jugará la fase final de la Liga de las Naciones.

Ansede M. **El mayor estudio hasta la fecha sugiere que las defensas contra el coronavirus pueden durar años**. El País 2020, published 19 November. Full-text: <https://elpais.com/ciencia/2020-11-18/el-mayor-estudio-hasta-la-fecha-sugiere-que-las-defensas-contra-el-coronavirus-pueden-durar-anos.html>

Un análisis exhaustivo de 185 personas que han superado la covid muestra una respuesta inmune potente y duradera.

Domínguez N. **Las incógnitas sobre la primera vacuna “eficaz” contra el coronavirus**. El País 2020, published 19 November. Full-text: <https://elpais.com/ciencia/2020-11-14/las-incognitas-sobre-la-primera-vacuna-eficaz-contra-el-coronavirus.html>

El anuncio de una inyección efectiva en un 90% realizado por Pfizer esta semana deja más preguntas que respuestas.

## French

If you read French, read Simonnet G. « **L'être humain n'accepte plus d'être malade** » | Le Monde 2020, published 19 November. Full-text: [https://www.lemonde.fr/idees/article/2020/11/19/guy-simonnet-l-etre-humain-n-accepte-plus-d-etre-malade\\_6060282\\_3232.html](https://www.lemonde.fr/idees/article/2020/11/19/guy-simonnet-l-etre-humain-n-accepte-plus-d-etre-malade_6060282_3232.html)

Rappelant que « le vivant est avant tout incertitude », le neurobiologiste Guy Simonnet souligne qu'une « tolérance zéro maladie » ne peut qu'être la source d'une nouvelle vulnérabilité.

Caramel L. « **Peu de malades ont développé des formes graves du Covid-19 en Afrique** » – Le Monde 2020, published 19 November. Full-text : [https://www.lemonde.fr/afrique/article/2020/11/18/peu-de-malades-ont-developpe-des-formes-graves-du-covid-en-afrique\\_6060239\\_3212.html](https://www.lemonde.fr/afrique/article/2020/11/18/peu-de-malades-ont-developpe-des-formes-graves-du-covid-en-afrique_6060239_3212.html)

Laurence Caramel, journaliste au « Monde Afrique », a répondu à vos questions sur les raisons de l'« exception africaine » face à la pandémie mondiale.

Audureau W. **Covid-19 : pourquoi bars et restaurants sont considérés comme étant à risque F** – Le Monde 2020, published 18 November. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2020/11/18/pourquoi-bars-et-restaurants-sont-consideres-comme-etant-a-risques\\_6060234\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2020/11/18/pourquoi-bars-et-restaurants-sont-consideres-comme-etant-a-risques_6060234_4355770.html)

S'il est globalement très difficile de remonter le fil, plusieurs études de cas ont démontré le risque de ces lieux, malgré les démentis des restaurateurs.

## 20 November

### Epidemiology

Van Dorp L, Tan CCS, Datt Lam S, et al. **Recurrent mutations in SARS-CoV-2 genomes isolated from mink point to rapid host-adaptation.** bioRxiv 2020, posted 16 November. Full-text: <https://doi.org/10.1101/2020.11.16.384743>

If you introduce SARS-CoV-2 in mink farms, it spreads and mutates rapidly. This is the result of a study which looked into 239 viral genomes isolated from farmed animals in the Netherlands and Denmark. The authors identified 23 recurrent mutations including three mutations in the Receptor Binding Domain of the SARS-CoV-2 spike protein that independently emerged at least four times but are only rarely observed in human lineages. Reassuringly, the authors state that the low prevalence of mink-adapted mutations in strains circulating in humans to date (November 2020) suggests that they are not expected to increase transmission of SARS-CoV-2 in humans.

### Virology

Klein S, Cortese M, Winter SL, et al. **SARS-CoV-2 structure and replication characterized by in situ cryo-electron tomography.** Nat Commun 11, 5885 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19619-7>

How is the unusually large SARS-CoV-2 genome incorporated into the virion? Find the answer in this paper by Petr Chlanda, Ralf Bartenschläger, Steffen



Klein and colleagues. The authors characterized the viral replication compartment and report critical insights into the budding mechanism of SARS-CoV-2.

## Transmission

Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J, Ho A. **SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis.** *Lancet Microbe* 2020, published 19 November. Full-text: [https://doi.org/10.1016/S2666-5247\(20\)30172-5](https://doi.org/10.1016/S2666-5247(20)30172-5)

After this meta-analysis of 79 studies (5340 individuals) on SARS-CoV-2, the authors report that **no study detected live virus beyond day 9 of illness**, despite persistently high viral loads. Although SARS-CoV-2 RNA shedding in respiratory and stool samples can be prolonged, duration of viable virus is relatively short-lived. Please communicate this finding to state authorities (for example, in Italy) which require negative RT-PCR tests before allowing citizens who recovered from SARS-CoV-2 infection to go back to normal life.

Heidt A. **COVID-19 Diagnostics: How Do Saliva Tests Compare to Swabs?** *The Scientist* 2020, published 9 October. Full-text: <https://www.the-scientist.com/news-opinion/covid-19-diagnostics-how-do-saliva-tests-compare-to-swabs--68035>

A lay press article going in the same direction. From hospitals and college campuses to remote villages in French Guiana, scientists pit the two approaches against one other.

## Immunology

Yu X, Cragg MS. **Engineered antibodies to combat viral threats.** *Nature* 2020, published 18 November. Full-text: <https://www.nature.com/articles/d41586-020-03196-2>

A *Nature News and Views* article by Xiaojie Yu and Mark Cragg. As the COVID-19 pandemic rages globally, interest in antiviral treatments has never been higher. Antibodies are key defense components and engineering them to better exploit their natural functions might boost therapeutic options.

## Vaccine

Editorial. **COVID-19 vaccines: no time for complacency.** Lancet 2020, published 21 November. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32472-7](https://doi.org/10.1016/S0140-6736(20)32472-7)

“‘Yes. Yes. Yes.’ That was the response of John Bell, Regius Professor of Medicine at the University of Oxford, when asked whether we could be confident that life will be returning to normal by spring.” Of course, we will not return to normal life within 6 months. Let’s lean back and be satisfied that in less than a year, we have characterized a novel illness, sequenced a new viral genome, developed diagnostics, produced treatment protocols, and established the efficacy of drugs and vaccines in randomized controlled trials. There is no hurry. If we can achieve some kind of pre-COVID-19 ‘normalcy’ by 2022, it would be a feat remembered by generations.

## Diagnostics

Karp DG, Danh K, Espinoza NF, et al. **A serological assay to detect SARS-CoV-2 antibodies in at-home collected finger-prick dried blood spots.** Sci Rep 10, 20188 (2020). Full-text: <https://doi.org/10.1038/s41598-020-76913-6>

The authors report a self-collection kit for at-home finger-prick dried blood spot collection. The results suggest 100% sensitivity and specificity. If proven successful at a large scale, such methods could facilitate the conduct of unbiased serosurveys in hard-to-reach populations.

## Clinical

Meduri A, Oliverio GW, Mancuso G, et al. **Ocular surface manifestation of COVID-19 and tear film analysis.** Sci Rep 10, 20178 (2020). <https://doi.org/10.1038/s41598-020-77194-9>

No SARS-CoV-2 in tears – that’s the result of a study in 29 hospitalized patients. Ocular symptoms, reported in a third of the patients, included eye burning, foreign body sensation and three reported tearing. Seven patients presented conjunctival hyperemia and/or chemosis, and eleven patients presented blepharitis signs such as lid margin hyperemia and/or telangiectasia, crusted eyelashes, and alterations of the meibomian orifices.

## Severe COVID

Jain A, Chaurasia R, Sengar NS, et al. **Analysis of vitamin D level among asymptomatic and critically ill COVID-19 patients and its correlation with inflammatory markers.** Sci Rep 10, 20191 (2020). <https://doi.org/10.1038/s41598-020-77093-z>

A higher fatality rate in vitamin D deficient patients (21% vs 3.1%)? Vitamin D levels markedly low in patients with severe COVID-19? These are the conclusions of a study including asymptomatic 91 COVID-19 patients (Group A) and 63 severely ill patients requiring ICU admission (Group B). The prevalence of vitamin D deficiency was 32.96% and 96.82% respectively in Group A and Group B.

Gu SX, Tyagi T, Jain K, et al. **Thrombocytopeny and endotheliopathy: crucial contributors to COVID-19 thromboinflammation.** Nat Rev Cardiol (2020). <https://doi.org/10.1038/s41569-020-00469-1>

The authors summarize evidence pointing to both platelet and endothelial dysfunction as essential components of COVID-19 pathology and highlight the distinct contributions of coagulopathy, thrombocytopeny and endotheliopathy to the pathogenesis of COVID-19. Discover potential therapeutic strategies in the management of patients with COVID-19.

## Spanish

If you read Spanish, please read Camhaji E, Barragán A, Cullerell JM, Breña CM, Galindo J. **100.000 muertos en México – Radiografía de un país.** El País 2020, published 20 November. Full-text: <https://elpais.com/mexico/2020-11-20/100000-muertos-en-mexico-radiografia-de-un-pais-roto.html>

México rompe la barrera psicológica de un millón de casos confirmados y 100.000 fallecimientos por coronavirus con hartazgo, desgaste y más dudas que certezas sobre el fin de la pandemia.

González B. **¿Por qué los colegios no se han convertido en un foco de contagios de covid?** – El País 2020, published 19 November. Full-text: <https://elpais.com/buenavida/salud/2020-11-18/por-que-los-colegios-no-se-han-convertido-en-un-foco-de-contagios-de-covid.html>

Los expertos analizan distintas teorías que explican que las clases en cuarentena sean solo en torno al 1.5% del total.

## 21 November

### Epidemiology

Firestone MJ, Wienkes H, Garfin J, et al. **COVID-19 Outbreak Associated with a 10-Day Motorcycle Rally in a Neighboring State – Minnesota, August–September 2020**. MMWR Morb Mortal Wkly Rep. ePub: 20 November 2020. DOI: <http://dx.doi.org/10.15585/mmwr.mm6947e1>

August 2020? Too soon for news about SARS-CoV-2 to have spread through western South Dakota, USA. Unaware of the pandemic, approximately 460,000 persons attended a motorcycle rally with numerous indoor and outdoor events over a 10-day period. The results: 51 confirmed primary event-associated cases, 21 secondary cases, and five tertiary cases. An additional nine likely rally-associated secondary or tertiary cases occurred. Four patients were hospitalized, and one died.

Cao S, Gan Y, Wang C, et al. **Post-lockdown SARS-CoV-2 nucleic acid screening in nearly ten million residents of Wuhan, China**. Nat Commun 11, 5917 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19802-w>

Which government wouldn't like to have correct estimates of the prevalence of SARS-CoV-2 infection following the release of lockdown restrictions? Here is what happened in Wuhan between May 14 and June 1, 2020, where authorities ordered a city-wide SARS-CoV-2 screening program. All city residents aged six years or older were eligible and 9,899,828 (92,9%) participated. No new symptomatic cases and 300 asymptomatic cases (detection rate 0,303/10,000) were identified. There were no positive tests amongst 1174 close contacts of asymptomatic cases.

Al-Mandhari AS, Brennan RJ, Abubakar A, Hajjeh R. **Tackling COVID-19 in the Eastern Mediterranean Region**. Lancet 2020, published 19 November. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32349-7](https://doi.org/10.1016/S0140-6736(20)32349-7)

Most countries in the Eastern Mediterranean region saw fairly slow transmission of SARS-CoV-2 during the early months of the pandemic but in May, as social measures, such as restrictions and partial or full lockdowns, were relaxed during the holy month of Ramadan, disease transmission accelerated.

## Immunology

Bourdon M, Manet C, Montagutelli X. **Host genetic susceptibility to viral infections: the role of type I interferon induction.** *Genes Immun* (2020). <https://doi.org/10.1038/s41435-020-00116-2>

The innate immune response is the major front line of defense against viral infections. It involves hundreds of genes with antiviral properties whose expression is induced by type I interferons (IFNs) and are therefore called interferon-stimulated genes (ISGs). The authors review the role of the molecular partners of the type I IFNs induction pathway and their implication in the control of viral infections and of their complications. Be prepared: not all mechanisms are yet fully understood.

Meyerholz DK, Perlman S. **Does common cold coronavirus infection protect against severe SARS-CoV-2 disease?** *J Clin Invest* 2020, published 20 November. Full-text: <https://doi.org/10.1172/JCI144807>

Read this comment by David Meyerholz and Stanley Perlman on a paper we presented on 9 October [Sagar M, Reifler K, Rossi M, et al. **Recent endemic coronavirus infection is associated with less severe COVID-19.** *J Clin Invest.* 2020 Sep 30;143380. PubMed: <https://pubmed.gov/32997649>. Full-text: <https://doi.org/10.1172/JCI143380>] where Joseph Mizgerd, Manish Sagar and colleagues showed that individuals with a previously detected eCoV infection had less severe COVID-19 illness.

## Diagnostics

Qian J, Boswell SA, Chidley C, et al. **An enhanced isothermal amplification assay for viral detection.** *Nat Commun* 11, 5920 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19258-y>

Michael Springer, Jason Qian and colleagues from Harvard Medical School report the development of a molecular diagnostic test for SARS-CoV-2 based on an enhanced recombinase polymerase amplification (eRPA) reaction. eRPA has a detection limit on patient samples down to 5 viral copies, requires minimal instrumentation, and is highly scalable and inexpensive. The protocol reported here was developed and optimized in less than 3 weeks, with an additional 4 weeks for sample preparation optimization, and patient sample acquisition. Good news for future pandemics.

Arizti-Sanz J, Freije CA, Stanton AC, et al. **Streamlined inactivation, amplification, and Cas13-based detection of SARS-CoV-2.** *Nat Commun* 11, 5921 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19097-x>

Cameron Myhrvold, Jon Arizti-Sanz and colleagues from Princeton University describe SHINE (Streamlined Highlighting of Infections to Navigate Epidemics), an extraction-free, rapid, and sensitive detection tool for SARS-CoV-2 RNA. The results can be visualized with an in-tube fluorescent readout – reducing contamination risk as amplification reaction tubes remain sealed – and interpreted by a companion smartphone application. Validation on 50 nasopharyngeal patient samples showed 90% sensitivity and 100% specificity with a sample-to-answer time of 50 min.

## Clinical

Datta SD, Talwar A, Lee JT. **A Proposed Framework and Timeline of the Spectrum of Disease Due to SARS-CoV-2 Infection: Illness Beyond Acute Infection and Public Health Implications.** *JAMA*. Published online November 18, 2020. Full-text: <https://doi.org/10.1001/jama.2020.22717>

Morbidity from SARS-CoV-2 goes beyond acute infection. Amish Talwar, Deblina Datta and James Lee from the CDC propose a framework of three distinct illness periods associated with SARS-CoV-2 infection: 1) acute infection; 2) a rare post-acute hyperinflammatory illness after roughly two weeks; and 3) a stage of late inflammatory and virological sequelae. These illness periods also capture distinct phases of host-viral interaction.

## Severe COVID

Al-Salameh A, Lanoix JP, Bennis Y, et al. **The association between body mass index class and coronavirus disease 2019 outcomes.** *Int J Obes* (2020). Full-text: <https://doi.org/10.1038/s41366-020-00721-1>

Being overweight (and not only obesity) is associated with ICU admission, but is not associated with death. This is the result of a retrospective study from Amiens University Hospital, France. In total, 433 consecutive patients were included, and BMI data were available for 329: 20 were underweight (6,1%), 95 had a normal weight (28,9%), 90 were overweight (27,4%), and 124 were obese (37,7%). The ORs for ICU admission were similar for overweight (3.16) and obesity (3.05).

## 22 November

### Epidemiology

Thompson CN, Baumgartner J, Pichardo C, et al. **COVID-19 Outbreak — New York City, February 29–June 1, 2020**. MMWR 2020;69:1725–1729. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6946a2>

During March–May 2020, approximately 203,000 laboratory-confirmed COVID-19 cases were reported to the NYC Department of Health and Mental Hygiene (DOHMH). The crude fatality rate (CFR) among confirmed cases was 9.2% overall and 32.1% among hospitalized patients. Incidence, hospitalization rates, and mortality were highest among Black/African American and Hispanic/Latino persons, as well as those who were living in neighborhoods with high poverty, aged  $\geq 75$  years, and with underlying medical conditions. Of note, the overall CFR of 9.2% is an overestimate because of underascertainment of cases, given the restrictive testing guidance and limited availability of tests during the first 2 months of the epidemic.

### Virology

Volz E, Hill V, McCrone JT, et al. **Evaluating the effects of SARS-CoV-2 Spike mutation D614G on transmissibility and pathogenicity**. Cell November 18, 2020. Full-text: <https://doi.org/10.1016/j.cell.2020.11.020>

Investigating the hypothesis for positive selection of Spike D614G in more than 25,000 whole genome SARS-CoV-2 sequences from the UK, not all approaches showed a conclusive signal of positive selection. However, population genetic analysis indicated that 614G increased in frequency relative to 614D in a manner consistent with a selective advantage. 614G was also associated with higher viral load and younger age of patients.

### Transmission

Van Dyke ME, Rogers TM, Pevzner E, et al. **Trends in County-Level COVID-19 Incidence in Counties With and Without a Mask Mandate — Kansas, June 1–August 23, 2020**. MMWR Morb Mortal Wkly Rep. ePub: 20 November 2020. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6947e2>

Masks work! The governor of Kansas issued an executive order requiring wearing masks in public spaces, effective July 3, 2020, which was subject to county authority to opt out. After July 3, COVID-19 incidence decreased in 24 counties with mask mandates but continued to increase in 81 counties without mask mandates. By August 17–23, 2020, the 7-day rolling average COVID-

19 incidence had decreased by 6% to 16 cases per 100.000 among mandated counties and increased by 100% to 12 per 100.000 among non-mandated counties.

## Vaccine

Lewis JR. **What Is Driving the Decline in People's Willingness to Take the COVID-19 Vaccine in the United States?** JAMA Health Forum. 2020; 1(11):e201393. Full-text: <https://doi.org/10.1001/jamahealthforum.2020.1393>

People in the US are ready to move on from the COVID-19 pandemic, but when it comes to a vaccine, many have a wait-and-see attitude. Jarrett Ramos Lewis addresses the reasons. As we move toward having an approved COVID-19 vaccine, it is important to understand that for many, it will take time to feel comfortable and confident in getting the vaccine. While the politicization of the vaccine is to blame for some of that delay, the increased reluctance of people to get a COVID-19 vaccine runs much deeper than politics.

## Diagnostics

Oved K, Olmer L, Shemer-Avni Y, et al. **Multi-center nationwide comparison of seven serology assays reveals a SARS-CoV-2 non-responding seronegative subpopulation.** EClinical Med November 19, 2020. Full-text: <https://doi.org/10.1016/j.eclinm.2020.100651>

Serology assays from Roche, Abbott, Diasorin, BioMerieux, Beckman-Coulter, Siemens, and Mt. Sinai ELISA were used to analyze negative samples from 2391 individuals representative of the Israeli population, and 698 SARS-CoV-2 PCR positive patients. Immunoassay sensitivities were between 81,5% - 89,4% while specificities were between 97,7% - 100%, resulting in a profound impact on the expected Positive Predictive Value in low (< 15%) prevalence scenarios. No meaningful increase was detected in the false positive rate in children compared to adults. A positive correlation between disease severity and antibody titers, and no decrease in antibody titers in the first 8 weeks after PCR positivity was observed. The authors also identified a subgroup of symptomatic SARS-CoV-2 positive patients (~5%), who remained seronegative across a wide range of antigens, isotypes, and technologies.



## Clinical

Van den Borst B, Peters JB, Brink M, et al. **Comprehensive health assessment three months after recovery from acute COVID-19**. *Clin Infect Dis* 21 November 2020, ciaa1750. Full-text: <https://doi.org/10.1093/cid/ciaa1750>

More on “long COVID-19”. All patients discharged after COVID-19 from the Radboud University Medical Centre, Nijmegen, The Netherlands, were consecutively invited to a multidisciplinary outpatient facility. Also, non-admitted patients with mild disease but with symptoms persisting > 6 weeks could be referred by general practitioners. Patients underwent a standardized assessment including measurements of lung function, chest CT/X-ray, 6-minute walk test, body composition, and questionnaires. Among 124 patients (27 mild, 51 moderate, 26 severe and 20 critical), lung diffusion capacity was below the lower limit of normal in 42% of discharged patients, and 22% had low exercise capacity. Problems in mental and/or cognitive function were found in 36% of patients. Health status was generally poor, particularly in the domains of functional impairment (64%), fatigue (69%) and quality of life (72%).

Kennedy M, Helfand BKI, Gou RY, et al. **Delirium in Older Patients With COVID-19 Presenting to the Emergency Department**. *JAMA Netw Open*, November 19, 2020;3(11):e2029540. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.29540>

In this retrospective cohort study of 817 patients older than 65 years with COVID-19 presenting at emergency departments (ED) of 7 US sites, 28% had delirium at presentation, and delirium was the sixth most common of all presenting signs and symptoms. Among delirious patients, 37% had no typical COVID-19 symptoms or signs, such as cough or fever. Factors associated with delirium (with adjusted relative risk, aRR between 1.1 and 2) were older than 75 years, living in a nursing home or assisted living, had prior use of psychoactive medication, vision impairment, hearing impairment, stroke, and Parkinson’s disease. Not very surprising: delirium was associated with ICU stay (aRR 1.67) and death (aRR 1.24).

## Severe COVID-19

Fiacchini G, Tricò D, Ribechini A, et al. **Evaluation of the Incidence and Potential Mechanisms of Tracheal Complications in Patients With COVID-19**. *JAMA Otolaryngol Head Neck Surg*. Published online November 19, 2020. Full-text: <https://doi.org/10.1001/jamaoto.2020.4148>

Giacomo Fiacchini and colleagues from Pisa, Italy demonstrate a high tracheal complication rate of invasive mechanical ventilation. In their cohort study of 98 patients with COVID-19 and severe respiratory failure, the incidence of full-thickness tracheal lesions or tracheoesophageal fistulas after prolonged ( $\geq 14$  days) invasive mechanical ventilation was significantly higher in patients with COVID-19 (46,7%) than matched controls (2,2%). Attempts to prevent these lesions should be made and quickly recognized when they occur to avoid potentially life-threatening complications in ventilated patients with COVID-19.

Sun L, Hymowitz M, Pomeranz HD. **Eye Protection for Patients With COVID-19 Undergoing Prolonged Prone-Position Ventilation.** JAMA Ophthalmol. Published online November 19, 2020. Full-text: <https://doi.org/10.1001/jamaophthalmol.2020.4988>

Clinicians should also be aware of the possible presence of elevated intraocular pressure from periorbital edema due to direct compression of the eye and orbit, and optic disc edema and retinal hemorrhages, which may be associated with a hypercoagulable state, in patients in prolonged prone position. Lucy Sun and colleagues report on two patients with periorbital edema in the prone position with bilateral findings of optic disc edema and retinal hemorrhages as well as a substantial increase in intraocular pressure.

## Pregnancy

Adhikari EH, Moreno W, Zofkie AC, et al. **Pregnancy Outcomes Among Women With and Without Severe Acute Respiratory Syndrome Coronavirus 2 Infection.** JAMA Netw Open November 19, 2020;3(11):e2029256. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.29256>

Good news from Dallas, USA: in this cohort study of 252 SARS-CoV-2-positive and 3122 negative pregnant women tested in outpatient and inpatient settings at a large county medical center, adverse pregnancy outcomes were similar. Neonatal infection occurred in 3% of infants, predominantly among infants born to asymptomatic or mildly symptomatic women. Placental abnormalities were not associated with disease severity, and the rate of hospitalization was similar to rates among non-pregnant women.

## Pediatrics

Roarty C, Tonry C, McFetridge L, et al. **Kinetics and seroprevalence of SARS-CoV-2 antibodies in children.** *Lancet Infect Dis* November 19, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30884-7](https://doi.org/10.1016/S1473-3099(20)30884-7)

Antibody titers in children exposed to SARS-CoV-2 remain at a detectable level for at least 62 days.

## 23 November

### Epidemiology

Taylor CA, Boulos C, Almond D. **Livestock plants and COVID-19 transmission.** *PNAS* November 19, 2020. Full-text: <https://doi.org/10.1073/pnas.2010115117>

Livestock processing poses a particular public health risk extending far beyond meatpacking companies and their employees. The authors estimate livestock plants to be associated with 236,000 to 310,000 COVID-19 cases (6 to 8% of total US cases) and 4,300 to 5,200 deaths (3 to 4% of total US cases) as of July 21. They also illustrate potential contributions of plant size, industrial concentration, plant shutdowns, and policy actions to this phenomenon. High numbers were found among large processing facilities and large meatpacking companies. According to the authors, their results “motivate investigation into supply chains, operating procedures, and labor relations within the meatpacking industry”. They also discuss some implications. Interestingly, one was seemingly beyond the intellectual grasp of the authors: that consumers could abstain from buying meat produced by these large meatpacking companies.

### Virology

Hammer AS, Quaade ML, Rasmussen TB, Fonager J, Rasmussen M, Mundbjerg K, et al. **SARS-CoV-2 transmission between mink (Neovison vison) and humans, Denmark.** *Emerg Infect Dis* Nov 18, 2020. 2021 Feb. Full-text: <https://doi.org/10.3201/eid2702.203794>

Anne Sophie Hammer and colleagues describe the outbreaks on three Danish mink farms. A high proportion of mink were infected within a few days, which may provide major virus exposure to persons working with mink. Full-length virus genome sequencing revealed novel viral variants in mink. These variants subsequently appeared within the local human community.

## Immunology

Karki ER, Sharma BR, Tuladhar S, et al. **Synergism of TNF- $\alpha$  and IFN- $\gamma$  triggers inflammatory cell death, tissue damage, and mortality in SARS-CoV-2 infection and cytokine shock syndromes.** Cell November 18, 2020. Full-text: <https://doi.org/10.1016/j.cell.2020.11.025>

More on the cytokine storm: Rajenda Karki and colleagues evaluated the role of pro-inflammatory cytokines that are highly upregulated in patients with COVID-19 in inducing inflammatory cell death, inflammation, tissue and organ damage, and mortality. They show that the specific combination of TNF- $\alpha$  and IFN- $\gamma$  is critical for these processes. In mice, the combination of anti-TNF- $\alpha$  and anti-IFN- $\gamma$  neutralizing antibodies protected against death in SARS-CoV-2 infection and models of sepsis, hemophagocytic lymphohistiocytosis (HLH), and cytokine shock.

Hekman RM, Hume AJ, Goel RK, et al. **Actionable Cytopathogenic Host Responses of Human Alveolar Type 2 Cells to SARS-CoV-2.** Molecular Cell November 18, 2020. Full-text: <https://doi.org/10.1016/j.molcel.2020.11.028>

SARS-CoV-2 infects alveolar epithelial type 2 cells (AT2s), leading to lung injury and impaired gas exchange. As AT2 injury is central to COVID-19 pathogenesis, there is an urgent need to delineate the mechanisms of SARS-CoV-2-driven lung pathology. Primary AT2s are difficult to maintain in culture, but human induced pluripotent stem cell-derived alveolar epithelial type 2 cells (iAT2s) have been developed and extensively characterized. Using these cells, Ryan Hekman and colleagues from Boston performed a quantitative phosphoproteomic survey, demonstrating diverse host responses to infection of alveolar epithelial cells and suggesting a dynamic disease signature that evolves as the virus disrupts host programs and rewires modules. Time course analysis revealed rapid remodeling of diverse host systems, including signaling, RNA processing, translation, metabolism, nuclear integrity, protein trafficking, and cytoskeletal-microtubule organization, leading to cell cycle arrest, genotoxic stress, and innate immunity.

Karlsson AC, Humbert M, Buggert M. **The known unknowns of T cell immunity to COVID-19.** Science Immunology 18 Nov 2020: Vol. 5, Issue 53, eabe8063. Full-text: <https://doi.org/10.1126/sciimmunol.abe8063>

In their brilliant perspective, Annika C. Karlsson and colleagues from Stockholm, Sweden summarize and speculate on a specific set of questions related

to T cell immunity against respiratory viral infections, with a focus on COVID-19 severity, immunity, long-term consequences, and vaccination.

Cervia C, Nilsson J, Zurbuchen Y, et al. **Systemic and mucosal antibody responses specific to SARS-CoV-2 during mild versus severe COVID-19.** *J Allergy Clin Immunol.* 2020 Nov 19:S0091-6749(20)31623-7. Full-text: <https://doi.org/10.1016/j.jaci.2020.10.040>

Using immunoassays specific for SARS-CoV-2 spike proteins, Carlo Cervia and colleagues from Zurich, Switzerland determined SARS-CoV-2-specific IgA and IgG in sera and mucosal fluids of PCR positive patients and of negative HCWs. Serum IgA titers in mild COVID-19 cases were often transiently positive, whereas serum IgG titers remained negative or became positive 12-14 days after symptom onset. Conversely, patients with severe COVID-19 showed a highly significant increase of SARS-CoV-2-specific serum IgA and IgG titers after symptom onset. Interestingly, some HCWs with negative SARS-CoV-2-specific serum antibody titers showed SARS-CoV-2-specific IgA in mucosal fluids with virus-neutralizing capacity in some cases.

## Vaccines

Lederer K, Castaño D, Atria DG, et al. **SARS-CoV-2 mRNA vaccines foster potent antigen-specific germinal center responses associated with neutralizing antibody generation.** *Cell* November 21, 2020. Full-text: <https://doi.org/10.1016/j.immuni.2020.11.009>

A systematic comparison between two vaccine platforms, nucleoside modified mRNA lipid nanoparticle and recombinant protein formulated with the MF59-like adjuvant AddaVax (rRBD-AddaVax), evaluating quantitatively and qualitatively the germinal center (GC) responses to SARS-CoV-2 upon immunization. The authors found that SARS-CoV-2 mRNA vaccines had a superior capacity, in comparison to rRBD-AddaVax, to elicit potent SARS-CoV-2 specific GC B cell responses after the administration of a single vaccine dose. Importantly, they demonstrated that GC B cells and Tfh cells strongly correlated with the production of nAbs.

## Clinical

Manzano GS, Woods, JK, Amato AA. **Covid-19-Associated Myopathy Caused by Type I Interferonopathy.** *NEJM* November 20, 2020. Full-text: <https://doi.org/10.1056/NEJMc2031085>

Myalgias and elevated creatine kinase levels are seen in many patients. Whether the elevation in creatine kinase level is caused by viral infection of muscle, toxic effects of cytokines, or another mechanism is unclear. Giovanna S. Manzano and colleagues from Boston describe a COVID-19 patient with myopathy who had a muscle-biopsy specimen showing evidence of virus-induced type I interferonopathy.

## Treatment

Bozzi G, Mangioni D, Minoia F, et al. **Anakinra combined with methylprednisolone in patients with severe COVID-19 pneumonia and hyperinflammation: an observational cohort study.** J Allergy Clin Immunol. 2020 Nov 18:S0091-6749(20)31621-3. PubMed: <https://pubmed.gov/33220354>. Full-text: <https://doi.org/10.1016/j.jaci.2020.11.006>

IL-1 receptor antagonist anakinra is one of the cytokine-blocking agents employed for COVID-19 treatment. Of 120 patients with hyperinflammation (33% on mechanical ventilation), 65 were treated with anakinra and methylprednisolone and 55 were untreated historical controls. At 28 days, mortality was 14% in treated patients and 36% in controls ( $p = 0,005$ ). Unadjusted and adjusted risk of death was significantly lower for treated patients compared to controls (HR 0,33,  $p = 0.007$  and HR 0,18,  $p = 0,001$ , respectively). Randomized, controlled trials including use of either agent alone are needed to confirm these results.

Milewska A, Chi Y, Szczepanski A, et al. **HTCC as a Polymeric Inhibitor of SARS-CoV-2 and MERS-CoV.** J Virology November 20, 2020. Full-text: <https://doi.org/10.1128/JVI.01622-20>

The cationically modified chitosan, N-(2-hydroxypropyl)-3-trimethylammonium chitosan chloride (HTCC) is a potent inhibitor of all known human coronaviruses. Using *in vitro* and *ex vivo* models of human airway epithelium, the authors show that HTCC effectively blocks MERS-CoV and SARS-CoV-2 infection.

## 24 November

### Epidemiology

Jeong JM, Radeos MS, Shee B, et al. **COVID-19 Seroconversion in Emergency Professionals at an Urban Academic Emergency Department in New York City.** *Ann Emerg Med.* 2020 Dec;76(6):815-816. PubMed: <https://pubmed.gov/33222793>. Full-text: <https://doi.org/10.1016/j.annemergmed.2020.06.038>

Emergency professionals as a high-risk group. Between February 1, 2020, and April 30, 2020, an overwhelming number greater than 1,000 patients with a diagnosis of COVID-19 presented at an emergency department (ED) in Brooklyn, NY. Results: The overall rate of seroconversion among emergency professionals was incredibly high (46%). Rates for attending physicians, emergency medicine residents, and physician assistants were 64%, 36%, and 29%, respectively.

### Prevention

Xu J, Xiao X, Zhang W, et al. **Air-Filtering Masks for Respiratory Protection from PM2.5 and Pandemic Pathogens.** *One Earth* Volume 3, ISSUE 5, P574-589, November 20, 2020. Full-text: <https://doi.org/10.1016/j.oneear.2020.10.014>

Air-filtering masks, also known as respirators, protect wearers from inhaling fine particulate matter (PM2.5) in polluted air, as well as airborne pathogens. Fibrous medium, used as the filtration layer, is the most essential component of an air-filtering mask. This comprehensive review gives an overview of the development of fibrous media for air filtration.

### Vaccine

Sun W, Leist SR, McCroskery S, et al. **Newcastle disease virus (NDV) expressing the spike protein of SARS-CoV-2 as a live virus vaccine candidate.** *EBioMedicine* November 21, 2020. Full-text: <https://doi.org/10.1016/j.ebiom.2020.103132>

The Newcastle disease virus vector vaccine has some advantages similar to those of other viral vector vaccines. The NDV vector can be amplified in embryonated chicken eggs, which allows for high yields and low costs per dose. Also, the NDV vector is not a human pathogen, therefore the delivery of the foreign antigen would not be compromised by any pre-existing immunity in humans. Weina Sun and colleagues describe NDV vector vaccines expressing

the spike protein of SARS-CoV-2 in its wild type format or a membrane-anchored format lacking the polybasic cleavage site. The NDV vector vaccines elicited high levels of antibodies that are neutralizing when the vaccine is given intramuscularly in mice. Importantly, these COVID-19 vaccine candidates protect mice from a mouse-adapted SARS-CoV-2 challenge with no detectable viral titer and viral antigen in the lungs. The results suggested that the NDV vector expressing either the wild type S or membrane-anchored S without the polybasic cleavage site could be used as live vector vaccine against SARS-CoV-2.

McClung N, Chamberland M, Kinlaw K, et al. **The Advisory Committee on Immunization Practices' Ethical Principles for Allocating Initial Supplies of COVID-19 Vaccine — United States, 2020.** MMWR Morb Mortal Wkly Rep. ePub: 23 November 2020. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6947e3>

Four ethical principles will assist the Advisory Committee on Immunization Practices (ACIP) in formulating recommendations for the initial allocation of COVID-19 vaccine: 1) maximizing benefits and minimizing harms; 2) promoting justice; 3) mitigating health inequities; and 4) promoting transparency. Read how application of ethical principles to four candidate groups for initial COVID-19 vaccine allocation is planned in the US.

## Immunology

Rodda LB, Netland JH, Shehata L, et al. **Functional SARS-CoV-2-specific immune memory persists after mild COVID-19.** Cell November 23, 2020. Full-text: <https://doi.org/10.1016/j.cell.2020.11.029>

Even mild COVID-19 elicits memory lymphocytes that persist and display functional hallmarks of antiviral immunity. Lauren Rodda found that three months after mildly symptomatic COVID-19, 15 recovered individuals had formed an expanded arsenal of SARS-CoV-2-specific immune memory B-cells (MBCs) that exhibited protective antiviral functions. Recovered individuals had increased neutralizing antibodies, IgG+ classical MBCs with BCRs that formed neutralizing antibodies, Th1 cytokine-producing CXCR5+ circulating T follicular helper(Tfh) cells and CXCR5- non-Tfh cells, proliferating CXCR3+ CD4+memory cells and IFN- $\gamma$ -producing CD8+ T cells. These components of immune memory have all been associated with protection from other viruses in humans.



Prado-Vivar B, Becerra-Wong M, Guadalupe JJ, et al. **A case of SARS-CoV-2 reinfection in Ecuador.** *Lancet* November 23, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30910-5](https://doi.org/10.1016/S1473-3099(20)30910-5)

A 46-year-old man from Quito, Ecuador, presenting with a second infection, only 2 months after the first episode. Phylogenetic analysis revealed that the first infection variant belonged to clade 20A and lineage B1.p9, whereas the second infection variant belonged to clade 19B and lineage A.1.1. Of note, the second episode was more severe.

## Clinical

Perrot L, Hemon M, Busnel JM, et al. **First flare of ACPA-positive rheumatoid arthritis after SARS-CoV-2 infection.** *Lancet Rheumatology*, November 23, 2020. Full-text: [https://doi.org/10.1016/S2665-9913\(20\)30396-9](https://doi.org/10.1016/S2665-9913(20)30396-9)

The first definitive case of ACPA-positive rheumatoid arthritis developing after SARS-CoV-2 infection (ie, with samples taken before and after arthritis onset) in a 60-year-old woman from Marseille, France, with infection as a potential trigger for epitope spreading and onset of clinical rheumatoid arthritis symptoms.

## Comorbidities

Yu B, Li C, Sun Y, et al. **Insulin treatment is associated with increased mortality in patients with COVID-19.** *Cell Metabolism* November 23, 2020. Full-text: <https://doi.org/10.1016/j.cmet.2020.11.014>

Oops! In this retrospective study on 689 patients with COVID-19 and Type 2 diabetes from Wuhan, China, insulin treatment was associated with a significant increase in mortality (27.2% vs. 3.5%; adjusted HR, 5.38). Further analysis showed that insulin treatment was associated with enhanced systemic inflammation and aggravated injuries of vital organs. However, this was a retrospective observation which could not establish a causal effect relationship between insulin treatment and high mortality. Moreover, there were significant differences in several baseline characteristics and laboratory indices at admission (for examples, SpO<sub>2</sub>, NT-proBNP and albumin), which may contribute to the different severity and outcome observed in patients treated with insulin.

## Collateral

Morgan L, Protopopova A, Birkler RID, et al. **Human–dog relationships during the COVID-19 pandemic: booming dog adoption during social isolation.** *Humanit Soc Sci Commun* 7, 155 (2020). Full-text: <https://doi.org/10.1057/s41599-020-00649-x>

Good news (for dogs) from Israel: the stricter the social isolation became during the COVID-19 pandemic, the greater the interest in dog adoption. Dog abandonment has decreased and the rates of dog adoptions improved significantly; the demand for adoptable dogs and the requests to serve as foster families increased significantly, and accordingly, the length of stay of dogs at the shelter was significantly shorter.

## Pediatrics

Bailey LC, Razzaghi H, Burrows EK, et al. **Assessment of 135 Patients Tested for Severe Acute Respiratory Syndrome Coronavirus 2 Across the United States.** *JAMA Pediatr.* 2020 Nov 23. PubMed: <https://pubmed.gov/33226415>. Full-text: <https://doi.org/10.1001/jamapediatrics.2020.5052>

□794 Pediatric

In this large cohort study of 135,794 US pediatric patients, SARS-CoV-2 infection rates were low (5374 = 4% were infected), and clinical manifestations were typically mild. Black, Hispanic, and Asian race/ethnicity; adolescence and young adulthood; and nonrespiratory chronic medical conditions were associated with identified infection. Among the 5374 patients with positive test results, 359 (7%) were hospitalized for respiratory, hypotensive, or COVID-19–specific illness. Of these, 99 (28%) required intensive care unit services, and 33 (9%) required mechanical ventilation. The case fatality rate was 0.2% (8 of 5374). The number of patients with a diagnosis of Kawasaki disease in early 2020 was 40% lower (259 vs 433 and 430) than in 2018 or 2019.

## 25 November

### Epidemiology

Bajema KL, Wiegand RE, Cuffe K, et al. **Estimated SARS-CoV-2 Seroprevalence in the US as of September 2020.** *JAMA Intern Med* November 24, 2020. Full-text: <https://doi.org/10.1001/jamainternmed.2020.7976>

In this repeated, cross-sectional study of 177,919 residual clinical specimens, the estimated percentage of persons in a US jurisdiction with detectable

SARS-CoV-2 antibodies ranged from fewer than 1% to 23%. Over 4 sampling periods in 42 of 49 jurisdictions with calculated estimates, fewer than 10% of people had detectable SARS-CoV-2 antibodies.

Kennedy BS, Richeson RP, Houde AJ. **Risk Factors for SARS-CoV-2 in a Statewide Correctional System.** N Eng J Med November 24, 2020. Full-text: <https://doi.org/10.1056/NEJMc2029354>

Mass testing by RT-PCR among 10,304 incarcerated persons in the Connecticut (US) statewide correctional system revealed that by far the strongest risk factor for SARS-CoV-2 infection was dormitory housing (odds ratio, 35.3). Social distancing may be more challenging in such settings than in cells that house one or two inmates.

Liu M, Thomadsen R, Yao S. **Forecasting the spread of COVID-19 under different reopening strategies.** Sci Rep 10, 20367 (2020). Full-text: <https://doi.org/10.1038/s41598-020-77292-8>

Using a modified susceptible-infected-recovered (SIR) model in the United States, the authors found that the incidence of COVID-19 spread is concave in the number of infectious individuals, as would be expected if people have inter-related social networks. This concave shape has a significant impact on forecasted COVID-19 cases. The number of COVID-19 cases would only have an exponential growth for a brief period at the beginning of the contagion event or right after a re-opening, but would quickly settle into a prolonged period of time with stable, slightly declining levels of disease spread. In contrast, if social distancing is eliminated, there will be a massive increase in the cases.

## Transmission

Sun K, Wang W, Gao L, et al. **Transmission heterogeneities, kinetics, and controllability of SARS-CoV-2.** Science 24 Nov 2020: eabe2424. Full-text: <https://doi.org/10.1126/science.abe2424>

Using detailed information on 1178 SARS-CoV-2 infected individuals along with their 15,648 contacts in Hunan, China, Kaiyuan Sun and colleagues dissected the behavioral and clinical drivers of SARS-CoV-2 transmission. They also evaluated the plausibility of SARS-CoV-2 control through individual and population-based interventions. Of note, 80% of secondary infections traced back to 15% of SARS-CoV-2 primary infections. Transmission risk scales positively with the duration of exposure and the closeness of social interactions and is modulated by demographic and clinical factors. Modeling indicates

SARS-CoV-2 control requires the synergistic efforts of case isolation, contact quarantine, and population-level interventions, owing to the specific transmission kinetics of this virus.

## Immunology

Omer SB, Yildirim I, Forman HP. **Herd Immunity and Implications for SARS-CoV-2 Control**. JAMA November 24, 2020; 324(20):2095-2096. Full-text: <https://doi.org/10.1001/jama.2020.20892>

Saad B. Omer and colleagues discuss herd immunity in the context of the COVID-19 pandemic and explain the herd immunity threshold as a function of transmissibility ( $R_0$ ), the role of an effective vaccine and vaccination program in sustaining herd immunity, and the risks of an infection-based herd immunity approach. Assuming that less than 10% of the population has been infected so far, with an infection-induced immunity lasting 2 to 3 years (duration unknown), infection-induced herd immunity is not realistic at this point to control the pandemic.

## Vaccine

Ma X, Zou F, Yu F, et al. **Nanoparticle Vaccines Based on the Receptor Binding Domain (RBD) and Heptad Repeat (HR) of SARS-CoV-2 Elicit Robust Protective Immune Responses**. Immunity November 25, 2020. Full-text: <https://doi.org/10.1016/j.immuni.2020.11.015>

A promising new vaccination approach: Xiancai Ma and colleagues from Guangdong, China developed nanoparticle vaccines by covalently conjugating the self-assembled 24-mer ferritin to the receptor binding domain (RBD) and/or heptad repeat (HR) subunits of spike (S) protein. Compared to monomer vaccines, nanoparticle vaccines elicited more robust neutralizing antibodies and cellular immune responses. hACE2 transgenic mice vaccinated with RBD and/or RBD-HR nanoparticles exhibited reduced viral load in the lungs after SARS-CoV-2 challenge. RBD-HR nanoparticle vaccines also promoted neutralizing antibodies and cellular immune responses against other coronaviruses. The nanoparticle vaccination of rhesus macaques induced neutralizing antibodies, and T and B cell responses prior to boost immunization; these responses persisted for longer than three months.

## Clinical

Bilinski A, Emanuel EJ. **COVID-19 and Excess All-Cause Mortality in the US and 18 Comparison Countries.** JAMA 2020; 324(20):2100-2102. Full-text: <https://doi.org/10.1001/jama.2020.20717>

Compared with other countries, the US experienced high COVID-19-associated mortality and excess all-cause mortality into September 2020. After the first peak in early spring, US death rates from COVID-19 and from all causes remained exceptionally high. This may have been a result of several factors, including weak public health infrastructure and a decentralized, inconsistent US response to the pandemic.

Fodoulian L, Tuberosa J, Rossier D, et al. **SARS-CoV-2 receptors and entry genes are expressed in the human olfactory neuroepithelium and brain.** iScience November 24, 2020. Full-text: <https://doi.org/10.1016/j.isci.2020.101839>

More on anosmia: Leon Fodoulian and colleagues from Geneva, Switzerland asked whether specific cells present in the human olfactory neuroepithelium may represent targets for SARS-CoV-2, by looking at the molecular players involved in infection, both at the RNA and protein levels. They found that sustentacular cells, which maintain the integrity of olfactory sensory neurons, express ACE2 and TMPRSS2. These cells represent a potential way in for SARS-CoV-2 in a neuronal sensory system that is in direct connection with the brain.

## Treatment

Simonovich VA, Burgos Pratz LD, Scibona P, et al for the PlasmAr Study Group. **A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia.** N Eng J Med, November 24, 2020. Full-text: <https://doi.org/10.1056/NEJMoa2031304>

A crushing failure for convalescent plasma (CP): this study from Argentina randomly assigned 338 hospitalized adult patients with severe COVID-19 pneumonia in a 2:1 ratio to receive CP or placebo. No significant differences were observed in clinical status or overall mortality and prespecified subgroup analyses failed to suggest any credible subgroup effects. Moreover, the trial ensured that more than 95% of the transfused CP units had a total anti-SARS-CoV-2 antibody titer of at least 1:800 and that the plasma volume infused had a correction factor according to the participant's weight. The au-

thors “believe the use of CP as a standard of care in such patients should be reevaluated”. Well said.

Fan H, Hong B, Luo Y et al. **The effect of whey protein on viral infection and replication of SARS-CoV-2 and pangolin coronavirus in vitro.** Sig Transduct Target Ther 5, 275 (2020). Full-text: <https://doi.org/10.1038/s41392-020-00408-z>

Human breastmilk inhibits SARS-CoV-2 virus infection in Vero E6 and A549 cell lines. Huaghao Fan and colleagues show for the first time that whey protein from human breastmilk effectively inhibited SARS-CoV-2 by blocking viral attachment and viral replication at entry and even post-entry. Moreover, human whey protein inhibited infectious virus production, as proved by a plaque assay. Whey protein from different species, such as cow and goat, also showed anti-coronavirus properties. Commercial bovine formula milk also showed similar anti-SARS-CoV-2 activity.

## 26 November

### Transmission

Scudellari M. **How Iceland hammered COVID with science.** Nature 2020, published 25 November. Full-text: <https://www.nature.com/articles/d41586-020-03284-3>

In this semi-interview with Kári Stefánsson, the founder and chief executive of [deCODE genetics](#), Megan Scudellari describes how a private company and health authorities worked hand-in-hand, sharing ideas, data, laboratory space and staff. This collaboration, coupled with [Iceland's](#) diminutive size, has put the country in the enviable position of knowing practically every move the virus has made. The teams have tracked the health of every person who has tested positive for SARS-CoV-2, sequenced the genetic material of each viral isolate and screened more than half of the island's 368.000 residents for infection. A tiny world laboratory.

van Dorp L, Richard D, Tan CCS, et al. **No evidence for increased transmissibility from recurrent mutations in SARS-CoV-2.** Nat Commun 11, 5986 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19818-2>

As yet no evidence for increased transmissibility of SARS-CoV-2. After analyzing 46.723 SARS-CoV-2 genomes isolated from patients worldwide, Lucy van Dorp, François Balloux and colleagues did not identify a single recurrent mu-

tation in this set convincingly associated with increased viral transmission. Instead, recurrent mutations seem to be primarily induced by host immunity through RNA editing mechanisms, and likely tend to be selectively neutral, with no or only negligible effects on virus transmissibility.

## Prevention

Mina MJ, Parker R, Larremore DB. **Rethinking Covid-19 Test Sensitivity — A Strategy for Containment.** *N Engl J Med* 2020; 383:e120. Full-text: <https://doi.org/10.1056/NEJMp2025631>

Do we really need a highly sensitive SARS-CoV-2 test? Yes, if we want to make a diagnosis of SARS-CoV-2 infection. No, if we want to prevent as many transmission events as possible. In this brilliant *Perspective*, Michael Mina, Roy Parker and Daniel Larremore advocate the massive use of cheap (< 5 US\$) and rapid [lateral-flow antigen tests](#) which can be produced in the tens of millions or more per week, and could be performed at home. Note that lateral-flow antigen tests have limits of detection that are 100 or 1000 times higher than that of the PCR tests; however, this is largely inconsequential if your goal is to identify people who are currently transmitting SARS-CoV-2. Find out more about ‘COVID filter’, the ‘long tail of RNA positivity’ and the economic burden of thousands of people being sent to 10-day quarantines after positive RNA tests despite having already passed the transmissible stage of infection.

Kuehn BM. **Hand Hygiene Gaps Identified.** *JAMA.* 2020 Nov 24;324(20):2021. PubMed: <https://pubmed.gov/33231672>. Full-text: <https://doi.org/10.1001/jama.2020.22227>

Men, young adults, and White people are more likely than other groups to be too stupid to wash their hands properly. Bridget Kuehn reminds us of a pair of surveys published in *MMWR* ([Haston 2020](#); [Czeisler 2020](#), [presented 21 June](#)) that found serious gaps in hand hygiene practices by race, age, and sex. Hand washing or using an alcohol-based hand sanitizer after touching shopping carts, gas pumps, automated teller machines, etc. – tell your boys, tell your men, tell your white neighbors.

Gallagher JE, Sukriti KC, Johnson IG, et al. **A systematic review of contamination (aerosol, splatter and droplet generation) associated with oral surgery and its relevance to COVID-19.** *BDJ Open* 6, 25 (2020). Full-text: <https://doi.org/10.1038/s41405-020-00053-2>

The SARS-CoV-2 pandemic has impacted the delivery of dental care and has led to re-evaluation of infection control standards. After exploring the evidence on bioaerosols in dentistry, the authors conclude that “a risk of contamination (microbiological, visible and imperceptible blood) to patients, dental team members and the clinical environment is present during oral surgery procedures, including routine extractions.” Our recommendation: schedule your dentist appointments between COVID-19 waves.

## Immunology

Woolsey C, Borisevich V, Prasad AN, et al. **Establishment of an African green monkey model for COVID-19 and protection against re-infection.** *Nat Immunol* (2020). Full-text: <https://doi.org/10.1038/s41590-020-00835-8>

In this model, the authors demonstrate that African green monkeys (AGMs) mimic several aspects of human disease, including pronounced viral replication and pulmonary lesions. SARS-CoV-2 was detected in mucosal samples, including rectal swabs, as late as 15 days after exposure. Marked inflammation and coagulopathy in blood and tissues were prominent features. Antibody and cellular responses contributed to rapid clearance after re-challenge with an identical strain at 35 days after first exposure.

## Genetics

Ray JG, Schull MJ, Vermeulen MJ, Alison LP. **Association Between ABO and Rh Blood Groups and SARS-CoV-2 Infection or Severe COVID-19 Illness.** *Ann Intern Med* 2020, published 24 November. Full-text: <https://doi.org/10.7326/M20-4511>

To determine whether ABO and Rh blood groups are associated with risk for SARS-CoV-2 infection and severe COVID-19 illness, the authors analyzed 225,556 persons, mean age of 54 years. The O and Rh- blood groups were associated with a slightly lower risk for SARS-CoV-2 infection as well as severe COVID-19 illness or death.



## Clinical

Piazza G, Morrow DA. **Diagnosis, Management, and Pathophysiology of Arterial and Venous Thrombosis in COVID-19.** JAMA. 2020 Nov 23. PubMed: <https://pubmed.gov/33226423>. Full-text: <https://doi.org/10.1001/jama.2020.23422>

Thrombotic complications (myocardial infarction, ischemic stroke, venous thromboembolism, etc.) may occur in up to a third of critically ill patients with COVID-19. After a short discussion of the current evidence, Gregory Piazza and David Morrow conclude that thromboprophylaxis should be considered for all hospitalized patients with COVID-19 in the absence of contraindications.

## Pregnancy

Rasmussen SA, Lyerly DA, Jamieson DJ. **Delaying Pregnancy during a Public Health Crisis — Examining Public Health Recommendations for Covid-19 and Beyond.** N Engl J Med 2020; 383:2097-2099. Full-text: <https://doi.org/10.1056/NEJMp2027940>

Pregnant women with COVID-19 don't seem to be at increased risk for death, although they may have a [higher risk of being admitted to an intensive care unit and of requiring mechanical ventilation](#). Should that be a reason for postponing pregnancy? Sonja Rasmussen, Anne Lyerly and Denise Jamieson dig into their experience with HIV, H1N1 and Zika and conclude that a recommendation to avoid pregnancy during a public health emergency should meet several criteria. Find out which ones here.

## Education

Rubin EJ, Baden LR, Morrissey S. **New Studies of Covid-19 Transmission.** Audio interview (30:16). N Engl J Med 2020; 383: e138. Access: <https://doi.org/10.1056/NEJMe2034094>

The editors look at new studies of disease transmission in closed environments and provide updates on convalescent plasma and hydroxychloroquine.

## 27 November

### Treatment

WHO 20201120. **WHO recommends against the use of remdesivir in COVID-19 patients.** WHO 2020, published 20 November. Full-text: <https://www.who.int/news-room/feature-stories/detail/who-recommends-against-the-use-of-remdesivir-in-covid-19-patients>

First nail in the remdesivir coffin. On 20 November, WHO issued a conditional recommendation against the use of remdesivir (brand name: Veklury) in hospitalized patients, regardless of disease severity, as there is currently no evidence that remdesivir improves survival and other outcomes in these patients. Evidence from over 7000 patients across 4 trials suggests no important effect on mortality, need for mechanical ventilation, time to clinical improvement, and other patient-important outcomes. Happy France (see below, *Covid-19: comment Gilead a vendu son remdésivir à l'Europe!*)

### Epidemiology

Mavragani A, Gkillas K. **COVID-19 predictability in the United States using Google Trends time series.** Sci Rep 10, 20693 (2020). Full-text: <https://doi.org/10.1038/s41598-020-77275-9>

How will you monitor and forecast regional outbreaks as they happen or even before they happen? By using Google Trends. Amaryllis Mavragani and Konstantinos Gkillas from the University of Stirling in Scotland present a model that exhibits strong COVID-19 predictability. The authors conclude that Google Trends offers a solid foundation for quantitative analysis with respect to the monitoring and predictability of COVID-19 and suggest that these approaches may flatten epidemic curves, help in allocating health resources, and increase the effectiveness and preparedness of health care systems.

### Immunology

Perez-Potti A, Lange J, Buggert M. **Deciphering the ins and outs of SARS-CoV-2-specific T cells.** Nat Immunol 2020, published 26 November. Full-text: <https://doi.org/10.1038/s41590-020-00838-5>

Marcus Buggert, André Perez-Potti and Joshua Lange comment on the paper by Nelde A, Bilich T, Heitmann JS, et al. who characterized HLA-specific peptide targets from SARS-CoV-2 in convalescent patients and identify cross-reactive epitopes which were probably induced by common cold coronaviruses in non-infected individuals [SARS-CoV-2-derived peptides define heterolo-

gous and COVID-19-induced T cell recognition. *Nat Immunol* 2020, published 30 September. PubMed: <https://pubmed.gov/32999467>. Full-text: <https://doi.org/10.1038/s41590-020-00808-x>. This was one of the first studies to indicate that a more polyclonal T cell response may be critical in protection against SARS-CoV-2.

## Pathogenesis

Wei C, Wan L, Yan Q, et al. **HDL-scavenger receptor B type 1 facilitates SARS-CoV-2 entry.** *Nat Metab* 2020, published 26 November. Full-text: <https://doi.org/10.1038/s42255-020-00324-0>

Could high-density lipoprotein (HDL) **scavenger receptor B type 1** (SR-B1) facilitate ACE2-dependent entry of SARS-CoV-2? That is the statement by Hui Zhong, Congwen Wei, finding that the S1 subunit of SARS-2-S binds to cholesterol and possibly to HDL components and facilitates SARS-CoV-2 cellular attachment, entry and infection. SARS-CoV-2 entry is inhibited by silencing SR-B1 expression and by SR-B1 antagonists. Blockade of the cholesterol-binding site on SARS-2-S1 with a monoclonal antibody inhibited HDL-enhanced SARS-CoV-2 infection.

## Vaccine

Wang J. **New strategy for COVID-19 vaccination: targeting the receptor-binding domain of the SARS-CoV-2 spike protein.** *Cell Mol Immunol* 2020, published 26 November. Full-text: <https://doi.org/10.1038/s41423-020-00584-6>

Junzhi Wang comments on a study by Yang J, Wang W, Chen Z et al. [A vaccine targeting the RBD of the S protein of SARS-CoV-2 induces protective immunity. *Nature* 2020, published 29 July. Full-text: <https://doi.org/10.1038/s41586-020-2599-8>] we presented on **30 July**. The authors show that a recombinant spike receptor-binding domain (RBD) protein of SARS-CoV-2 prepared from insect cells could induce a potent functional antibody response in mice, rabbits and non-human primates as early as 7 or 14 days after a single dose injection. Even one dose of the vaccine generated viral neutralizing activity. The vaccine protected non-human primates from live SARS-CoV-2 challenge 28 days after the first vaccination.

## Clinical

Bellan M, Patti G, Hayden E, et al. **Fatality rate and predictors of mortality in an Italian cohort of hospitalized COVID-19 patients.** *Sci Rep* 10, 20731 (2020). Full-text: <https://doi.org/10.1038/s41598-020-77698-4>

In March and April 2020, almost 30% of all patients (504/1697) hospitalized in three hospitals in Northern Italy died. In this 126-author paper by Pier Paolo Sainaghi, Mattia Bellan and colleagues, age, a diagnosis of cancer, and the baseline PaO<sub>2</sub>/FiO<sub>2</sub> ratio were independent predictors of mortality.

Hubiche T, Cardo-Leccia N, Le Duff F, et al. **Clinical, Laboratory, and Interferon-Alpha Response Characteristics of Patients With Chilblain-like Lesions During the COVID-19 Pandemic.** *JAMA Dermatol* 2020, published 25 November. Full-text: <https://doi.org/10.1001/jamadermatol.2020.4324>

In this series of 40 consecutive patients with chilblain-like lesions, Thierry Passeron, Thomas Hubiche and colleagues found that none had a positive RT-PCR test, and only 12 (30%) had positive COVID-19 serologic results. Common findings included increased D-dimers, lymphocytic inflammation, vascular damage on skin biopsy results, and a significant interferon-alpha response compared with patients with PCR-positive, acute COVID-19 infection. The authors conclude that chilblain-like lesions observed during the COVID-19 pandemic represent manifestations of a viral-induced type I interferonopathy.

## Education

Centor R. **A Primer on COVID-19 Vaccines.** Audio interview (29:19). *Ann Intern Med* 2020, published 24 November. Access: <https://doi.org/10.7326/A19-0044>

In this episode, Robert Cento discusses the COVID-19 vaccines under development with Paul Goepfert.

## Society

Green A. **A tribute to some of the doctors who died from COVID-19.** *Lancet* 2020, published 28 November. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32478-8](https://doi.org/10.1016/S0140-6736(20)32478-8)

“The global COVID-19 death toll stands at more than 1.3 million. Among the lives lost have been those of healthcare workers, who have had crucial roles throughout the response. As the virus spread, many doctors provided treat-

ment for a disease they little understood, while others contributed to accelerated research on potential treatments and vaccines. An Obituary published in *The Lancet* pays tribute to some of these doctors who died from COVID-19. Whilst it is not possible to honour all of the health workers who have died from COVID-19, the short obituaries serve as a tribute to the many other health workers who have died in the pandemic.”

## French

If you read French, read Barnéoud L. **Covid-19 : comment Gilead a vendu son remdésivir à l'Europe.** *Le Monde* 2020, published 27 November. Full-text: [https://www.lemonde.fr/planete/article/2020/11/27/covid-19-comment-gilead-a-vendu-son-remdesivir-a-l-europe\\_6061300\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/27/covid-19-comment-gilead-a-vendu-son-remdesivir-a-l-europe_6061300_3244.html)

Un contrat de 900 millions de dollars a été passé avec la Commission, alors même que le laboratoire Gilead connaissait les résultats négatifs d'un essai clinique de l'OMS. La France est le seul pays à ne pas avoir passé commande.

## 28 November

### Epidemiology

Muiry R, Parsons V, Madan I. **Risks posed by COVID-19 to healthcare workers.** *Occup Med* 2020, published 28 November. Full-text: <https://doi.org/10.1093/occmed/kqaa191>

What is the exact nature of the risks posed by SARS-CoV-2 to healthcare workers? Rupert Muiry, Vaughan Parsons and Ira Madan summarize the current literature, including consideration of broader biopsychosocial morbidities.

### Transmission

Cunningham L, Nicholson PJ, O'Connor J, McFadden JP. **Cold working environments as an occupational risk factor for COVID-19.** *Occup Med* 2020, published 28 November. Full-text: <https://doi.org/10.1093/occmed/kqaa195>

Employers and their occupational health and safety professionals should consider work in cold environments to be an independent occupational risk factor for developing COVID-19. Follow Louise Cunningham et al. on their tour in cold environments.

## Vaccine

Editors. **The COVID vaccine challenges that lie ahead.** Nature. 2020 Nov;587(7835):522. PubMed: <https://pubmed.gov/33235368>. Full-text: <https://doi.org/10.1038/d41586-020-03334-w>

Large clinical trials of four vaccine candidates are showing remarkable promise, with three exceeding 90% efficacy – all unexpectedly high. None reported worrying safety signals and one has shown promise in older adults who are particularly vulnerable to SARS-CoV-2 but sometimes respond less well to vaccines. But, there remains a lot of work to do for researchers and clinicians.

Cohen J. **After dosing mix-up, latest COVID-19 vaccine success comes with big question mark.** Science 2020, published 25 November. Full-text: <https://www.sciencemag.org/news/2020/11/after-dosing-mix-latest-covid-19-vaccine-success-comes-big-question-mark>

Callaway E. **Why Oxford's positive COVID vaccine results are puzzling scientists.** Nature 2020, published 23 November. Full-text: <https://www.nature.com/articles/d41586-020-03326-w>

Preliminary data from the AstraZeneca vaccine are puzzling. Two full doses given a month apart would be 62% effective, but a half dose followed by a full dose would be 90% effective. Now researchers are trying desperately to instill meaning into these results. Let Jon Cohen and Ewen Callaway explain, sort of.

Editors. **Nanomedicine and the COVID-19 vaccines.** Nat. Nanotechnol 2020, published 27 November. Full-text: <https://doi.org/10.1038/s41565-020-00820-0>

If approved, BNT162b2 (BioNTech/Pfizer) and mRNA-1273 (Moderna/NIH), credited in press releases with sky-rocketing efficacy, would be the first messenger RNA (mRNA)-based vaccines to be used in large populations. mRNA vaccines use nanotechnology platforms to deliver the genetic sequence of specific viral proteins to the host cells. Find more about the founding principles of nanomedicine in this short editorial.

## Diagnostics

Alexandersen S, Chamings A, Bhatta TR. **SARS-CoV-2 genomic and subgenomic RNAs in diagnostic samples are not an indicator of active replication.** *Nat Commun* 11, 6059 (2020). Full-text: <https://doi.org/10.1038/s41467-020-19883-7>

In patients with mild or moderate SARS-CoV-2 infection, a positive RT-PCR test 10 days or more after the onset of symptoms is generally not considered proof of infectiousness. But why do tests continue to be positive? Now, Soren Alexandersen, Anthony Chamings and Tarka Raj Bhatta provide a preliminary answer. Subgenomic RNAs, like virion RNA, are rather stable and are likely protected from nucleases by cellular membranes. This information may pave the way for development of better strategies to define active SARS-CoV-2 infection as opposed to extended presence of what most likely represent highly stable virus genomic and subgenomic RNAs present in, and at least in part protected by, cellular membranes. The message for national Health Services: Don't lock your citizens down for weeks and weeks.

## Clinical

Wehbe RM, Sheng J, Dutta S, et al. **DeepCOVID-XR: An Artificial Intelligence Algorithm to Detect COVID-19 on Chest Radiographs Trained and Tested on a Large US Clinical Dataset.** *Radiology*. 2020 Nov 24:203511. PubMed: <https://pubmed.gov/33231531>. Full-text: <https://doi.org/10.1148/radiol.2020203511>

Artificial intelligence (AI) is a significant threat to radiologists and radiology as a specialty. Here, Ramsey Wehbe et al. show that an AI algorithm detected COVID-19 on chest radiographs with a performance similar to a consensus of experienced thoracic radiologists. See also the editorial by van Ginneken B. **The Potential of Artificial Intelligence to Analyze Chest Radiographs for Signs of COVID-19 Pneumonia.** *Radiology*. 2020 Nov 24:204238. PubMed: <https://pubmed.gov/33236962>. Full-text: <https://doi.org/10.1148/radiol.2020204238>

## Collateral Effects

Clark JJ, Dwyer D, Pinwill N, Clark P, Johnson P, Hackshaw A. **The effect of clinical decision making for initiation of systemic anticancer treatments in response to the COVID-19 pandemic in England: a retrospective analysis.** *Lancet Oncol* 2020, published 27 November. Full-text: [https://doi.org/10.1016/S1470-2045\(20\)30619-7](https://doi.org/10.1016/S1470-2045(20)30619-7)

During the 2020 spring lockdown and immediately thereafter, there was an important reduction in systemic anti-cancer treatment initiation in England: 32% in April and 10% in May. In June, the number of registrations for new systemic anti-cancer treatments increased by 15% compared to the 6 pre-COVID months (September, 2019, to February, 2020). James Clark et al. recommend continuing to assess the effects of delaying treatment initiation for advanced cancers and neoadjuvant therapies.

## Society

Guglielmi G. **Italian labs shape-shift to fight the pandemic.** Nature Italy 2020, published 21 November. Full-text: <https://www.nature.com/articles/d43978-020-00026-x>

In Italy, one of the early epicenters of the COVID pandemic, scientists from all fields have re-focused expertise and equipment to study the virus. Go on a short trip to this peninsula in the Mediterranean.

## 29 November

### Epidemiology

Trieu MC, Bansal A, Madsen A, et al. **SARS-CoV-2-specific neutralizing antibody responses in Norwegian healthcare workers after the first wave of COVID-19 pandemic: a prospective cohort study.** J Infect Dis. 2020 Nov 28;jjaa737. PubMed: <https://pubmed.gov/33247924> . Full-text: <https://doi.org/10.1093/infdis/jjaa737>

A low number of SARS-CoV-2-seropositive HCWs in a low prevalence setting. In this study from Norway, 607 HCW were evaluated pre- and post-the first COVID-19 pandemic wave, using a 2-step ELISA. Exposure history, COVID-19-like symptoms and serum samples were collected. Only 32 HCW (5.3%) had spike-specific antibodies (11 seroconverted with  $\geq 4$ -fold increase, 21 were seropositive at baseline). The infection rate was only 1,7-fold higher in HCW with COVID-19 patient-exposure (2,4%) than in HCW with no exposure (1,4%).

Santos-Hövenner C, Neuhauser HK, Schaffrath Rosario A, et al, CoMoLo Study Group. **Serology- and PCR-based cumulative incidence of SARS-CoV-2 infection in adults in a successfully contained early hotspot (CoMoLo study), Germany, May to June 2020.** Euro Surveill. 2020;25(47):pii=2001752. <https://doi.org/10.2807/1560-7917.ES.2020.25.47.2001752>



After a large church concert on March 1 and the first detected infection on March 9, the southern German community of Kupferzell in the federal state Baden-Württemberg faced a steep increase of SARS-CoV-2 infections. The cumulative incidence of 1.760 per 100.000 by the end of April was one of the highest in Germany. The authors set out to analyze the SARS-CoV-2 seroprevalence in a random sample of this community from 20 May to 9 June. Results: 12%. This study confirmed that even in areas with high COVID-19 prevalence, only a small proportion of the population is infected.

## Prevention

Vogel G, Couzin-Frankel J. **Grade: incomplete.** Science 27 November 2020: Vol. 370, Issue 6520, pp. 1023-1027. Full-text: <https://doi.org/10.1126/science.370.6520.1023>

Schools around the world are again the site of a large, and largely uncontrolled, experiment. Scrutiny of school openings in countries where the virus is resurgent paints a complex picture of the risks and how they might be managed. In their well-balanced article, Gretchen Vogel and Jennifer Couzin-Frankel summarize the main questions. How common are school outbreaks? (answer: less common than initially feared, although data are sparse). Do open schools change risk perception? (answer: probably). How much fresh air is enough? (answer: we don't know, but high-quality carbon dioxide monitors may help) Does testing make a difference? (answer: yes, but it takes up potentially scarce resources and can give a false picture). Should schools stay open as cases surge? (answer: let's better think about what we need to do to keep schools open).

## Immunology

Bowman ER, Cameron CMA, Avery A, et al. **Levels of Soluble CD14 and Tumor Necrosis Factor Receptors 1 and 2 may be predictive of death in Severe Coronavirus Disease 2019 (COVID-19).** J Inf Dis. Full-text: <https://doi.org/10.1093/infdis/jiaa744>

Emily Bowman and colleagues from Cleveland measured serum biomarkers in 14 uninfected individuals and in 44 individuals with mild, moderate, or critical COVID-19 disease. Levels of monocyte activation (sCD14 and FABP4) and inflammation (TNFR1 and 2) were increased in COVID-19 individuals, regardless of disease severity. Among patients with critical disease, individuals who recovered from COVID-19 had lower levels of TNFR1 and TNFR2 at hospital

admission compared to the levels in patients with critical disease who ultimately died.

## Vaccine

Wadman M. **Public needs to prep for vaccine side effects.** *Science* 27 November 2020: Vol. 370, Issue 6520, pp. 1022. Full-text: <https://doi.org/10.1126/science.370.6520.1022>

Expect a rough night after vaccination: A subset of people may face intense, if transient, side effects, called reactogenicity. In this interesting article, Meredith Wadman argues that transparency is key. Rather than minimizing the chance of fever, vaccine administrators could alert people that they may experience a fever that can feel severe but is temporary.

## Clinical

Pastor-Barriuso PR, Pérez-Gómez B, Hernán MA, et al. **Infection fatality risk for SARS-CoV-2 in community dwelling population of Spain: nationwide seroepidemiological study.** *BMJ* 2020, published 27 November. Full-text: <https://doi.org/10.1136/bmj.m4509>

In this large study from Spain, SARS-CoV-2 infections were derived from the estimated seroprevalence by a chemiluminescent microparticle immunoassay for IgG antibodies in 61.098 participants in the ENE-COVID nationwide survey between 27 April and 22 June 2020. The overall infection fatality risk (IFR) was 0,8% for confirmed COVID-19 deaths and 1,1% for excess deaths. IFR was higher in men than in women (1,1 versus 0,6%). The IFR increased sharply in the elderly age groups, ranging from 1,5% (60-70 years) to 11,6% (80+) in men, and from 0,53 (60-70) to 4,62 (80+) in women.

## Severe COVID-19

Knouhuizen SA, Aday A, Lee WM. **Ketamine-Induced Sclerosing Cholangitis (KISC) in a Critically Ill Patient with COVID-19.** *Hepatology* 23 November 2020. Full-text: <https://doi.org/10.1002/hep.31650>

Prior reports of recreational ketamine abuse have been associated with findings of secondary sclerosing cholangitis. The authors report here a novel presentation of the syndrome in association with prolonged ketamine use in the intensive care unit.

## Collateral damage (and benefits)

Simões D, Stengaard AR, Combs L, The EuroTEST COVID-19 impact assessment consortium of partners. **Impact of the COVID-19 pandemic on testing services for HIV, viral hepatitis and sexually transmitted infections in the WHO European Region, March to August 2020.** Euro Surveill 2020;25(47):pii=2001943. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.47.2001943>

The pandemic has had considerable impact on testing for HIV, viral hepatitis and STIs in the WHO European Region. Preliminary results show that 95% of respondents from 34 countries reported testing less than half the expected number of people during the first months of the COVID-19 pandemic between March and May 2020. This continued, although to a lesser degree, between June and August 2020, when measures were less strict in most countries.

Sullivan SG, Carlson S, Cheng AC, et al. **Where has all the influenza gone? The impact of COVID-19 on the circulation of influenza and other respiratory viruses, Australia, March to September 2020.** Euro Surveill. 2020;25(47). Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.47.2001847>

In Australia, influenza activity was at an all-time low during the southern hemisphere's 2020 winter. The 2020 pandemic restrictions may substantially ameliorate winter respiratory pathogen epidemics in 2021 and beyond.

## Pediatrics

Perrine CG, Chiang KV, Anstey EH, et al. **Implementation of Hospital Practices Supportive of Breastfeeding in the Context of COVID-19 — United States, July 15–August 20, 2020.** MMWR Morb Mortal Wkly Rep 2020;69:1767–1770. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6947a3>

Women with suspected or confirmed COVID-19 who are separated from their newborns and whose newborns are not feeding directly at the breast might need timely, professional, breastfeeding support. CDC conducted a COVID-19 survey (July 15–August 20, 2020) among 1,344 hospitals to assess current practices and breastfeeding support while in hospital. Among mothers with suspected or confirmed COVID-19, 14,0% of hospitals discouraged and 6,5% prohibited skin-to-skin care; 37,8% discouraged and 5,3% prohibited rooming-in; 20,1% discouraged direct breastfeeding but allowed it if the mother chose; and 12,7% did not support direct breastfeeding, but encouraged feeding of expressed breast milk. In response to the pandemic, 17,9% of hospitals re-

ported reduced in-person lactation support, and 72,9% reported discharging mothers and their newborns < 48 hours after birth.

## 30 November

### Epidemiology

Vos ERA, den Hartog G, Schepp RM, et al. **Nationwide seroprevalence of SARS-CoV-2 and identification of risk factors in the general population of the Netherlands during the first epidemic wave.** J Epidemiol Community Health. 2020 Nov 28;jech-2020-215678. PubMed: <https://pubmed.gov/33249407>. Full-text: <https://doi.org/10.1136/jech-2020-215678>

During the first wave of the epidemic in April 2020, overall seroprevalence in the Netherlands was 2,8% (95% CI 2.1 to 3.7), with no differences between sexes or ethnic background, and regionally ranging between 1,3 and 4,0%. This is in striking contrast with the 30-fold lower number of reported cases.

### Immunology

Perreault J, Tremblay T, Fournier MJ, et al. **Waning of SARS-CoV-2 RBD antibodies in longitudinal convalescent plasma samples within 4 months after symptom onset.** Blood. 2020 Nov 26;136(22):2588-2591. PubMed: <https://pubmed.gov/33001206>. Full-text: <https://ashpublications.org/blood/article/136/22/2588/463996/Waning-of-SARS-CoV-2-RBD-antibodies-in>

Anti-RBD antibody response in 15 CCP donors who donated at least 4 times, during a time interval after symptom onset ranging from 33 to 77 days for the first donation to 66 to 114 days for the last donation. Interestingly, the decrease during a period of about 20 days (considering the mean and median of third and fourth quartiles, both of 76 and 95 days, respectively) was reminiscent of the plasma immunoglobulin G half-life of 21 days. This suggests that *de novo* synthesis of anti-RBD antibodies stopped between the third and fourth quartiles in all CCP donors.

Self WH, Tenforde MW, Stubblefield WB, et al. **Decline in SARS-CoV-2 Antibodies After Mild Infection Among Frontline Health Care Personnel in a Multistate Hospital Network — 12 States, April–August 2020.** *MMWR Morb Mortal Wkly Rep* 2020;69:1762–1766. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6947a2>

Among 156 frontline health care personnel who had positive SARS-CoV-2 antibody test results in spring 2020, 94% experienced a decline at repeat testing approximately 60 days later, and 28% sero-reverted to below the threshold of positivity. A higher percentage of those with low baseline antibody levels sero-reverted (65%) than did those with high baseline titers (7%). These results suggest that a substantial proportion of persons infected with SARS-CoV-2 might have negative serologic test results in the months following infection.

## Vaccine

MacPherson A, Hutchinson N, Schneider O, et al. **Probability of Success and Timelines for the Development of Vaccines for Emerging and Reemerged Viral Infectious Diseases.** *Ann Int Med* 24 November 2020. Full-text: <https://doi.org/10.7326/M20-5350>

If a SARS-CoV-2 vaccine is licensed within 18 months of the start of the pandemic, it will mark an unprecedented achievement for non-influenza viral vaccine development. The authors took a look at other vaccines for emerging and re-emerged viral infectious diseases at ClinicalTrials.gov: in total, 606 clinical trials that formed part of 220 distinct development trajectories were identified. The probability of vaccines progressing from Phase II to licensure within 10 years was 10,0%, with most approvals representing H1N1 or H5N1 vaccines. The average timeline from Phase II to approval was 4,4 years. The probabilities of advancing from Phase I to II, Phase II to III, and Phase III to licensure within the total available follow-up time were 38,2%, 38,3%, and 61,1%, respectively.

## Clinical

Bowles KH, McDonald M, Barró Y. **Surviving COVID-19 After Hospital Discharge: Symptom, Functional, and Adverse Outcomes of Home Health Recipients.** *Ann Int Med* 24 November 2020. Full-text: <https://doi.org/10.7326/M20-5206>

A retrospective observational cohort from New York City, evaluating 1409 patients with COVID-19 admitted to home health care (HHC) between 1 April

and 15 June 2020 after hospitalization. After an average of 32 days in HHC, 94% of patients were discharged and most achieved statistically significant improvements in symptoms and function. Eleven patients (1%) died, 137 (10%) were re-hospitalized, and 23 (2%) remain hospitalized. Comorbid conditions of heart failure and diabetes, as well as characteristics present at admission (male gender, white ethnicity), identified patients at greatest risk for an adverse event.

Merello M, Bhatia KP, Obeso JA. **SARS-CoV-2 and the risk of Parkinson's disease: facts and fantasy.** *Lancet Neurology* November 27, 2020. Full-text: [https://doi.org/10.1016/S1474-4422\(20\)30442-7](https://doi.org/10.1016/S1474-4422(20)30442-7)

In this well-balanced review, Marcelo Merello, Kailash Bhatia, Jose Obeso argue that the causal association of SARS-CoV-2 infection with the development of Parkinson's disease is not supported by robust evidence yet. The authors are concerned about unjustified claims and speculations anticipating a future high incidence of Parkinson's disease, secondary to the SARS-CoV-2 pandemic. A coordinated international effort to investigate viral effects is essential and should be based on well-designed prospective studies.

Lersy F, Benotmane I, Helms J, et al. **Cerebrospinal fluid features in COVID-19 patients with neurologic manifestations: correlation with brain MRI findings in 58 patients.** *J Infect Dis.* 2020 Nov 29:jiaa745. PubMed: <https://pubmed.gov/33249438>. Full-text: <https://doi.org/10.1093/infdis/jiaa745>

In this single-center study, the authors describe neurological manifestations in 58 patients, regarding cerebrospinal fluid (CSF) analysis and neuroimaging findings. Protein and albumin levels in CSF were increased in 38% and 23%, respectively. 40% of patients displayed an elevated albumin quotient suggesting impaired blood-brain barrier integrity. A CSF-specific IgG oligoclonal band was found in five (11%) cases, suggesting an intrathecal synthesis of IgG, and 26 (55%) patients presented identical oligoclonal bands in serum and CSF. Only four (7%) patients harbored a positive SARS-CoV-2 RT-PCR in CSF.

Ioanno GN, Liang P, Locke E, et al. **Cirrhosis and SARS-CoV-2 infection in US Veterans: risk of infection, hospitalization, ventilation and mortality.** *Hepatology* 21 November 2020. Full-text: <https://doi.org/10.1002/hep.31649>

Among 88,747 patients tested for SARS-CoV-2 between January and mid-May in the US Veterans Affairs (VA) national healthcare system, cirrhosis was as-

sociated with a 1,7-fold increase in mortality in patients with SARS-CoV-2 infection.

### Collateral damage

Singhai R, Tahrani AA, Ludwig C, et al. **Global 30-day outcomes after bariatric surgery during the COVID-19 pandemic (GENEVA): an international cohort study.** *Lancet Diabetes Endocrinology* November 27, 2020. Full-text: [https://doi.org/10.1016/S2213-8587\(20\)30375-2](https://doi.org/10.1016/S2213-8587(20)30375-2)

This international cohort study GENEVA investigated the outcomes of bariatric and metabolic surgery (BMS) performed in 2116 adults ( $\geq 18$  years) between May 1 and July 10 from 133 hospitals in 38 countries. Overall, 30-day morbidity and mortality following BMS during the COVID-19 pandemic with locally appropriate perioperative COVID-19 protocols in place seemed to be similar to pre-pandemic levels. Of the ten patients with symptomatic post-operative COVID-19, none needed ventilation and none died.

### Treatment

Mishra GP, Mulani J. **Corticosteroids for COVID-19: the search for an optimum duration of therapy.** *Lancet Resp Med* November 26, 2020. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30530-0](https://doi.org/10.1016/S2213-2600(20)30530-0)

According to this comment by Gyanshankar P Mishra and Jasmin Mulani, corticosteroids seem to be a double-edged sword and need to be used judiciously, considering the risk-benefit ratio, as a short-course (up to 10 days) therapeutic agent in a select group of patients with COVID-19 for whom a survival benefit has been reported. Extended courses of steroids may be detrimental.

### German

If you read German, read Dinklage F, Ehmann A, Erdmann E, Klack M, Mast M, Stahnke J, Tröger J, Vallentin C, Blickle P. **So schnell verbreitet sich das Coronavirus in Innenräumen.** *Die Zeit* 2020, published 26 November. Full-text: <https://www.zeit.de/wissen/gesundheit/2020-11/coronavirus-aerosole-ansteckungsgefahr-infektion-hotspot-innenraeume> | English version: <https://www.zeit.de/wissen/gesundheit/2020-11/coronavirus-aerosols-infection-risk-hotspot-interiors>

Ob daheim, im Klassenzimmer oder Restaurant: Unser Rechner zeigt, wann sich Menschen in geschlossenen Räumen infizieren können. Testen Sie, wie sicher Ihre Umgebung ist.

## Spanish

If you read Spanish, read Domínguez N, Galocha A. **ARN, la molécula que puede sacarnos de esta pandemia.** El País 2020, published 29 November. Full-text: <https://elpais.com/ciencia/2020-11-28/arn-la-molecula-que-puede-sacarnos-de-esta-pandemia.html>

Dos de las vacunas más eficaces contra la covid se basan en un compuesto sin el que la vida en la Tierra no podría existir. Su aprobación puede ser el comienzo de una nueva era de tratamientos contra el cáncer, enfermedades raras y vacunas universales.

Lipovetsky G. **Son tiempos tristes: las discotecas están cerradas, ya no nos besamos.** El País 2020, published 28 November. Full-text: <https://elpais.com/ideas/2020-11-28/son-tiempos-tristes-las-discotecas-estan-cerradas-ya-no-nos-besamos.html>

El universo de la seducción está en peligro con la pandemia, escribe para 'Ideas' el filósofo francés Gilles Lipovetsky. Pero prevalecerá: nos gusta demasiado.

Altares G. **Mi hermano Juan: 50 días en coma por el coronavirus.** El País 2020, published 29 November. Full-text: <https://elpais.com/sociedad/2020-11-27/vivir-para-contar-la-covid-19.html>

Durante los meses más duros de la pandemia Juan Altares sufrió todas las complicaciones de una enfermedad entonces desconocida. Así vivió una familia el día a día de un paciente crítico.

de Miguel R. **Los hospitales ingleses recibirán las primeras dosis de la vacuna contra el coronavirus a partir del 7 de diciembre.** El País 2020, published 28 November. Full-text: <https://elpais.com/sociedad/2020-11-28/los-hospitales-ingleses-recibiran-las-primeras-dosis-de-la-vacuna-contr-el-coronavirus-a-partir-del-7-de-diciembre-segun-the-guardian.html>

La Agencia Reguladora de Medicamentos y Productos Sanitarios del Reino Unido aún no ha dado luz verde a la inmunización, pero se espera que lo haga la semana que viene.



## French

If you read French, read **Covid-19 : la Haute Autorité de santé préconise une stratégie de vaccination en cinq étapes**. Le Monde 2020, published 30 November. Full-text :

[https://www.lemonde.fr/planete/article/2020/11/30/covid-19-la-haute-autorite-de-sante-va-rendre-ses-conclusions-sur-l-acces-prioritaire-au-vaccin\\_6061587\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/30/covid-19-la-haute-autorite-de-sante-va-rendre-ses-conclusions-sur-l-acces-prioritaire-au-vaccin_6061587_3244.html)

Selon la Haute Autorité de santé, les personnes âgées résidant en Ehpad doivent être vaccinées en priorité « à l'arrivée des toutes premières doses », « compte tenu du nombre limité de doses qui seront disponibles au démarrage de la campagne de vaccination ».

Stromboni C. « **Pendant ce temps, on ne sait pas comment le cancer évolue** » : les « déprogrammés » de la deuxième vague du Covid-19 entre colère et résignation. Le Monde 2020, published 30 November. Full-text : [https://www.lemonde.fr/planete/article/2020/11/29/pendant-ce-temps-on-ne-sait-pas-comment-le-cancer-evolue-les-deprogrammes-de-la-deuxieme-vague-du-covid-19-entre-colere-et-resignation\\_6061525\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/29/pendant-ce-temps-on-ne-sait-pas-comment-le-cancer-evolue-les-deprogrammes-de-la-deuxieme-vague-du-covid-19-entre-colere-et-resignation_6061525_3244.html)

Sous la pression de la crise épidémique, les hôpitaux ont mis à l'arrêt une partie de leur activité, dans une proportion moindre qu'au printemps, mais suscitant la même anxiété chez les malades concernés par les reports.

Delacroix G. **A Pune, en Inde, un vaccin anti-Covid est déjà produit par millions de doses**. Le Monde 2020, published 28 November. Full-text : [https://www.lemonde.fr/planete/article/2020/11/28/a-pune-en-inde-un-vaccin-anti-covid-est-deja-produit-par-millions-de-doses\\_6061440\\_3244.html](https://www.lemonde.fr/planete/article/2020/11/28/a-pune-en-inde-un-vaccin-anti-covid-est-deja-produit-par-millions-de-doses_6061440_3244.html)

Depuis plusieurs semaines, le Serum Institute of India fabrique le vaccin AstraZeneca au rythme de 6 millions de flacons par mois. Reportage chez le plus grand producteur au monde.

Bernard P. « **Le Covid-19 est un terrible révélateur des fractures sanitaires de la planète** ». Le Monde 2020, published 28 November. Full-text : [https://www.lemonde.fr/idees/article/2020/11/28/le-covid-19-agit-comme-un-terrible-revelateur-des-fractures-sanitaires-de-la-planete\\_6061439\\_3232.html](https://www.lemonde.fr/idees/article/2020/11/28/le-covid-19-agit-comme-un-terrible-revelateur-des-fractures-sanitaires-de-la-planete_6061439_3232.html)

Les habitants des pays pauvres risquent d'être les derniers servis en vaccin anti-Covid-19, mais aussi de subir le dramatique retour des maladies «

classiques » induit par cette épidémie, observe Philippe Bernard, éditorialiste au « Monde », dans sa chronique.

# December 2020

## 1 December

### Virology

Popa A, Genger JW, Nicholson MD. **Genomic epidemiology of superspreading events in Austria reveals mutational dynamics and transmission properties of SARS-CoV-2.** *Science Translational Medicine* 23 November 2020: eabe2555. Full-text: <https://doi.org/10.1126/scitranslmed.abe2555>

Alexandra Popa, Andreas Bergthaler and colleagues from Vienna identified major SARS-CoV-2 clusters during the first wave of infections in Austria and performed deep whole-genome sequencing of 572 virus samples. Their genomic epidemiology analysis enabled the retrospective identification of SARS-CoV-2 chains of transmission and international hotspots. Taking advantage of a well-described and independently confirmed transmission network with 39 transmission events, the authors also found that the number of viral particles transmitted from one individual to another that contributed productively to the infection was on average higher than 1000. This suggests that social distancing and mask wearing may be effective even when they cannot prevent the spread of all viral particles.

### Immunology

Bacher P, Rosati E, Esser D, et al. **Low avidity CD4+ T cell responses to SARS-CoV-2 in unexposed individuals and humans with severe COVID-19.** *Immunity* November 26, 2020. Full-text: <https://doi.org/10.1016/j.immuni.2020.11.016>

Interesting work, arguing against a protective role for CCCoV (common cold coronavirus) reactive T cells in SARS-CoV-2 infection. Petra Bacher from UKSH (Kiel, Germany) and colleagues employed antigen-specific T cell enrichment to characterize SARS-CoV-2-specific T cells from 55 healthy donors and 56 COVID-19 patients including their avidity and clonality as well as their cross-reactivity to CCCoV and other viruses. First, pre-existing T cell memory was common in humans, correlated with the size of the CD4+ memory repertoire rather than with CCCoV-specific memory, and displayed only low functional avidity. Second, robust CD4+ T cell responses against CCCoV were prevalent in the population; however, T cells reacting to CCCoV were not present among SARS-CoV-2-specific T cells in COVID-19 patients. Third, in severe

COVID-19 patients, SARS-CoV-2-specific CD4<sup>+</sup> T cells also displayed low functional avidity and TCR clonality, although their frequencies increased with disease severity.

Salahudeen AA, Choi SS, Rustagi A et al. **Progenitor identification and SARS-CoV-2 infection in human distal lung organoids.** Nature November 24, 2020. Full-text: <https://doi.org/10.1038/s41586-020-3014-1>

The distal lung contains terminal bronchioles and alveoli that facilitate gas exchange. This work by Ameen A. Salahudeen, Shannon S. Choi and colleagues from Chicago helps to study these cells. The authors have established a long-term feeder-free, chemically defined culture of distal lung progenitors as organoids derived from single adult human alveolar epithelial type II (AT2) cells. Their culture experiments identified unsuspected basal cell functional heterogeneity and established a facile *in vitro* organoid model for human distal lung infections including COVID-19-associated pneumonia.

## Vaccine

Sanchez-Felipe L, Vercruyssen T, Sharma S et al. **A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate.** Nature December 1, 2020. Full-text: <https://doi.org/10.1038/s41586-020-3035-9>

Yellow Fever 17D (YF17D) is a small RNA live-attenuated virus with limited vector capacity. The YF17D vaccine is known to rapidly induce broad multi-functional innate, humoral and cell-mediated immune responses that may result in life-long protection following a single vaccine dose in nearly all vaccinees. These favorable characteristics translate also to vectored vaccines based on the YF17D backbone. Consequently, YF17D is used as vector in two licensed human vaccines, generated by swapping genes encoding the YF17D surface antigens for those of Japanese encephalitis or dengue viruses. Here, the authors describe the discovery of a live virus-vectored SARS-CoV-2 vaccine candidate using the YF17D vaccine as vector to express a non-cleavable prefusion form of the SARS-CoV-2 Spike antigen. Safety, immunogenicity and efficacy after a single dose are shown in several animal models such as hamsters, mice and macaques.

## Transmission

Bulfone TC, Malekinejad M, Rutherford, et al. **Outdoor Transmission of SARS-CoV-2 and Other Respiratory Viruses, a Systematic Review.** J Inf Dis November 29, 2020. Full-text: <https://doi.org/10.1093/infdis/jiaa742>

According to this review, existing evidence supports the widely held belief that the risk of SARS-CoV-2 transmission is lower outdoors. Moreover, historical evidence gleaned from influenza outbreaks further support the lower risk of transmission outdoors. However, there are significant gaps in our understanding of specific pathways. It is important to note that infections are possible outdoors and the advantage may be overtaken by relaxed mitigation efforts (think of the White House outbreak on September 26).

Yoon Y, Choi G-J, Kim JY, Kim K-R, Park H, Chun JK, et al. **Childcare exposure to severe acute respiratory syndrome coronavirus 2 for 4-year-old pre-symptomatic child, South Korea.** *Emerg Infect Dis* 2020 November 30, 2020. Full-text: <https://doi.org/10.3201/eid2702.203189>

An epidemiologic investigation of potential exposure of a presymptomatic child who attended a childcare center in South Korea: a 4-year-old child, probably infected by his grandmother, attended the center during the pre-symptomatic period (February 19–21, 2020). Fever developed on February 22, and he was given a diagnosis of SARS-CoV-2 infection on February 27. At the center, 190 persons were identified as contacts; 44 (23.2%) were defined as close contacts (37 children and 7 adults). All 190 persons were negative for SARS-CoV-2 on days 8–9 after the last exposure. This investigation adds indirect evidence of potentially low infectivity in a childcare setting with exposure to a presymptomatic child.

## Clinical

Mackey K, Ayers CK, Kondo KK. **Racial and Ethnic Disparities in COVID-19-Related Infections, Hospitalizations, and Deaths.** *Annals Int Medicine* 1 December 2020. Full-text: <https://doi.org/10.7326/M20-6306>

Differences in health care access and exposure risk may be driving higher infection and mortality rates. This systematic review revealed that African-American/Black and Hispanic populations experience disproportionately higher rates of SARS-CoV-2 infection, hospitalization, and COVID-19-related mortality compared with non-Hispanic White populations, but not higher case-fatality rates (moderate- to high-strength evidence). Asian populations experience similar outcomes to non-Hispanic White populations (low-strength evidence). Outcomes for other racial/ethnic groups have been insufficiently studied. Health care access and exposure factors may underlie the observed disparities more than susceptibility due to co-morbid conditions (low-strength evidence).

## Treatment

Young B, Tan TT, Leo YS. **The place for remdesivir in COVID-19 treatment.** Lancet Inf Dis November 26, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30911-7](https://doi.org/10.1016/S1473-3099(20)30911-7)

Is there is a place for remdesivir? Last week, the WHO said no (<https://www.who.int/news-room/feature-stories/detail/who-recommends-against-the-use-of-remdesivir-in-covid-19-patients>). In their comment on current data, Barnaby Young and colleagues from Singapore are not that strict. They believe that the natural history of COVID-19 suggests a window of opportunity for antivirals before fulminant inflammation sets in. However, they conclude that “for now, remdesivir is an important COVID-19 treatment option only in selected patient groups”.

Dangerfield TL, Huang NZ, Johnson KA. **Remdesivir is effective in combating COVID-19 because it is a better substrate than ATP for the viral RNA-dependent RNA polymerase.** iScience November 27, 2020. Full-text: <https://doi.org/10.1016/j.isci.2020.101849>

Tyler L. Dangerfield and colleagues compared binding and incorporation parameters for nucleoside analogs such as remdesivir relative to their natural counterparts (ATP). The specificity constant for remdesivir triphosphate incorporation was higher than that for competing ATP. Would be nice to see this effect *in vivo*.

Sörgel F, Nalin JJ, Hagman H, et al. **Pharmacokinetics of remdesivir in a COVID-19 patient with end-stage renal disease on intermittent haemodialysis.** Journal of Antimicrobial Chemotherapy November 30,2020. Full-text: <https://doi.org/10.1093/jac/dkaa500>

Jan Rybniker from Cologne and colleagues report the pharmacokinetics of remdesivir and its metabolites and the treatment outcome in a patient on renal replacement therapy without residual renal function suffering from severe COVID-19.

## 2 December

### Epidemiology

Guerriero M, Bisoffi Z, Poli A, Micheletto C, Conti A, Pomari C. **Prevalence of SARS-CoV-2, Verona, Italy, April–May 2020.** Emerg Infect Dis. 2021 Jan. Full-text: <https://doi.org/10.3201/eid2701.202740>

In Veneto, Italy, Verona was the province with the most cases and deaths caused by SARS-CoV-2. Massimo Guerriero and colleagues estimated the prevalence of active or past infection among randomly selected participants > 10 years of age from Verona. Of 1515 participants, 2,6% tested positive by a serologic assay and 0,7% by PCR. The total prevalence was 3,0%, suggesting 7051 cumulative cases (4,6 times higher than the official count).

### Immunology

Agarwal V, Venkatakrishnan AJ, Puranik A et al. **Long-term SARS-CoV-2 RNA shedding and its temporal association to IgG seropositivity.** Cell Death Discov. 6, 138 December 2, 2020. Full-text: <https://doi.org/10.1038/s41420-020-00375-y>

A retrospective analysis of 851 SARS-CoV-2-positive patients with at least two positive PCR tests. The mean lower bound of viral RNA shedding was 17,3 days (SD: 7,8), and the mean upper bound of viral RNA shedding from 668 patients transitioning to confirmed PCR-negative status was 22,7 days (SD: 11,8). Some seropositive patients actively shed viral RNA (14 of 90 patients).

### Vaccine

Behr MA, Divangahi M, Schurr E. **Lessons from BCG for SARS-CoV-2 vaccine candidates.** J Infect Dis 2020, published 30 November. Full-text: <https://doi.org/10.1093/infdis/jiaa637>

A note of caution: according to Marcel Behr and colleagues from Montréal, developers of SARS-CoV-2 vaccines should consider some of the lessons from a 'new' vaccine introduced in 1921, where BCG introduced to great fanfare had no measurable effect on the global epidemic, despite evidence of protection at the individual level.

## Diagnostics

Klumpp-Thomas C, Kalish H, Hicks J, et al. **D614G Spike Variant Does Not Alter IgG, IgM, or IgA Spike Seroassay Performance.** *J Infect Dis* 2020, published 1 December. Full-text: <https://doi.org/10.1093/infdis/jiaa743>

Does an individual exposed to one variant of a virus have cross-reactive memory to the second? Probably yes. Carleen Klumpp-Thomas and colleagues from NIH analyzed the serologic ELISA reactivity of both variants and found that antibodies from 88 donors from a high-incidence population reacted toward both the original spike and the D614 spike variant. This suggests that use of the full spike protein construct should not impact seroassay performance or “miss” seropositive samples. However, the fact that D614 and G614 both elicited seropositivity is perhaps expected, given that the human immune response is polyclonal.

Myhre PL, Prebensen C, Strand H, et al. **Growth Differentiation Factor 15 Provides Prognostic Information Superior to Established Cardiovascular and Inflammatory Biomarkers in Unselected Patients Hospitalized With COVID-19.** *Circulation* 2020 Dec;142(22):2128-2137. PubMed: <https://pubmed.gov/33058695>. Full-text: <https://doi.org/10.1161/CIRCULATIONAHA.120.050360>

Growth differentiation factor 15 (GDF-15) is a member of the transforming growth factor  $\beta$  superfamily. Expression in pathological states is highly regulated through several pathways including inflammation, oxidative stress, and hypoxia and elevated concentrations of circulating GDF-15 have been identified in multiple disease entities. Among 123 hospitalized COVID-19 patients from Oslo, Norway, GDF-15 was elevated in the majority of patients. Higher concentrations were associated with SARS-CoV-2 viremia, hypoxemia, and worse outcome. The prognostic value of GDF-15 was additional and superior to established cardiovascular and inflammatory biomarkers.

Rieser M, Wirth L, Pollmeier L, et al. **Serum protein profiling reveals a specific upregulation of the immunomodulatory protein progranulin in COVID-19.** *J Inf Dis* November 29, 2020. Full-text: <https://doi.org/10.1093/infdis/jiaa741>

Another biomarker. The immunomodulatory protein progranulin (GRN) is a pleiotropic growth factor and immunoregulatory molecule expressed in a broad range of tissues and cell types such as epithelia, bone marrow and various immune cells including T cells, DCs, monocytes and macrophages. In a



prospective single-center registry, Marina Rieser and colleagues from Freiburg, Germany included 24 SARS-CoV-2 positive patients and 61 patients with “similar symptoms and severity of disease but negative for SARS-CoV-2” (cancer, cardiac disease, and others) admitted to the emergency department and compared their serum protein expression profiles. Of note, no differences in IL-6 expression between SARS-CoV-2-positive and -negative patients were observed. In contrast, a specific upregulation of GRN was found which was associated with COVID-19 severity. Among the proteins showing the most significant positive correlation with GRN were GDF-15, urokinase-type plasminogen activator (uPA) and urokinase-type plasminogen activator receptor (uPAR).

## Clinical

Cao A, Rohaut B, Guennec LL, et al. **Severe COVID-19-related encephalitis can respond to immunotherapy.** *Brain* December 2, 2020. Full-text: <https://doi.org/10.1093/brain/awaa337>

See title (“can” respond). The authors report a case series of five patients with severe COVID-19-related encephalitis (impaired consciousness/unresponsive and mechanically ventilated) treated by therapeutic plasma exchanges and corticosteroids. The dramatic improvement in three of five patients “reinforces the hypothesis of an immune-related mechanism”.

## Collateral damage

Perez S, Innes GK, Walters MS, et al. **Increase in Hospital-Acquired Carbapenem-Resistant *Acinetobacter baumannii* Infection and Colonization in an Acute Care Hospital During a Surge in COVID-19 Admissions — New Jersey, February–July 2020.** *MMWR Morb Mortal Wkly Rep.* ePub: 1 December 2020. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6948e1>

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) causes health care-associated infections that are challenging to contain and often linked to infection prevention and control breaches. What a mess: colleagues from a New Jersey hospital report on a cluster of 34 CRAB cases (26 isolates harbored the gene encoding the OXA-23 carbapenemase) that peaked during a surge in COVID-19 hospitalizations. The authors conclude that strategies to preserve continuity of care led to deviations in IPC practices; CRAB cases decreased when normal operations resumed.

Armitaage R, Nellums B. **Antibiotic prescribing in general practice during COVID-19.** Lancet December 01, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30917-8](https://doi.org/10.1016/S1473-3099(20)30917-8)

Richard Armitage and Laura B Nellums comment on the number of antibiotic prescriptions made in UK general practice between April 1, and Aug 31, 2020. The number was 15% lower than in the corresponding period in 2019. However, given the decrease in absolute number of appointments over this time, this number of prescriptions was 7% higher than expected, supporting evidence that antibiotic prescribing rates are higher in remote consultations than during in-person appointments.

## Pediatrics

Lee EH, Kepler KL, Geevarughese A, et al. **Race/Ethnicity Among Children With COVID-19–Associated Multisystem Inflammatory Syndrome.** JAMA Netw Open November 30, 2020;3(11):e2030280. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.30280>

Distribution of race/ethnicity among 223 MIS-C cases reported to the New York City (NYC) Department of Health and Mental Hygiene: compared with White children, the authors observed a higher incidence of MIS-C among Black (IRR, 3.2) and Hispanic (IRR, 1.7) children. Black (IRR, 1.7) and Hispanic (IRR, 2.1) children had higher COVID-19 hospitalization rates compared with White children. It remains unclear whether this finding represents a phenomenon distinct from the increased burden of COVID-19 in Black and Hispanic communities.

## 3 December

### Transmission

Manna A. **Be Aware of Droplets and Bubbles.** Ann Intern Med 2020, published 1 December. Web page: <https://doi.org/10.7326/G20-0114>

No comment.

### Vaccine

WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation. **Placebo-Controlled Trials of Covid-19 Vaccines — Why We Still Need Them.** N Engl J Med 2020, published 2 December. Full-text: <https://doi.org/10.1056/NEJMp2033538>

In this *Perspective*, the participants in a World Health Organization *ad hoc* consultation on the next steps for COVID-19 vaccine evaluation recommend on how to proceed clinically as the first commercial vaccines increasingly become available. **Yes**, continue with placebo-controlled trials (the bedrock of modern clinical decision-making) because we still need more data on longer-term safety and duration of protection; on whether waning of vaccine-induced protection may lead to vaccine-enhanced disease if a vaccinee becomes infected after exposure to SARS-CoV-2; on information on protection against clinically severe forms of COVID-19; and knowledge of any associations between the degree of protection and the recipient's age or co-existing conditions. **No**, refrain from observational studies which are subject to substantial biases and are much less amenable to unambiguous interpretation.

Branswell H. **The Covid-19 vaccines are a marvel of science. Here's how we can make the best use of them.** STAT 2020, published 2 December. Full-text: <https://www.statnews.com/2020/12/02/how-society-can-make-the-most-of-covid-19-vaccines/>

Will 95% efficacy vaccines show the way to a straight road back to Normalville? Or will the route back be a meandering country lane with detours and potholes? Pothole 1: Vaccine skepticism. Pothole 2: Pregnant women. Pothole 3: Children. Pothole 4: How to continue important Phase III randomized trials while vaccines are already on the market? Pothole 5: Understanding SARS-CoV-2 transmission by vaccinated individuals. Have enough time before starting this long-read article.

## Diagnostics

Dugdale CM, Anahtar MN, Chiosi JJ, et al. **Clinical, laboratory, and radiologic characteristics of patients with initial false-negative SARS-CoV-2 nucleic acid amplification test results.** Open Forum Infect Dis 2020, published 24 November. Full-text: <https://doi.org/10.1093/ofid/ofaa559>

People with COVID-19 symptoms who have a negative PCR test should be re-tested within two weeks, especially in areas with sustained community transmission of SARS-CoV-2. This is the message Caitlin Dugdale and colleagues from the Massachusetts General Hospital, Boston, after finding 60 positives of 2699 subjects (2,2%) on a second test. Most of these subjects had symptoms (52/60; 87%) and chest radiography (19/32; 59%) consistent with COVID-19. A total of 60% had their initial test either  $\leq 1$  day ( $n = 18$ ) or  $> 7$  days ( $n = 18$ ) after symptom onset.

## Treatment

WHO Solidarity Trial Consortium. **Repurposed Antiviral Drugs for Covid-19 – Interim WHO Solidarity Trial Results.** N Engl J Med 2020, published 2 December. Full-text: <https://doi.org/10.1056/NEJMoa2023184>

Harrington DP, Baden LR, Hogan JW (Editorial). **A Large, Simple Trial Leading to Complex Questions.** N Engl J Med 2020, published 2 December. Full-text: <https://doi.org/10.1056/NEJMe2034294>

Remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay. This is the interim result of the WHO Solidarity Trial which of 11,330 adults at 405 hospitals in 30 countries. 2750 were randomly assigned to receive remdesivir, 954 to hydroxychloroquine, 1411 to lopinavir (without interferon), 2063 to interferon (including 651 to interferon plus lopinavir), and 4088 to no trial drug. Death occurred in 301 of 2743 patients receiving remdesivir and in 303 of 2708 receiving the control. In the accompanying editorial, David Harrington, Lindsey Baden, and Joseph Hogan try to save the day for remdesivir; however, it is clear that the drug plays in an altogether different league than the powerful anti-HIV and anti-HCV drugs. Also, in future pandemics we will remember that repurposing old antiviral drugs was not successful.

## Drug Development

Cox RM, Wolf JD, Plemper RK. **Therapeutically administered ribonucleoside analogue MK-4482/EIDD-2801 blocks SARS-CoV-2 transmission in ferrets.** Nat Microbiol 2020, published 3 December. Full-text: <https://doi.org/10.1038/s41564-020-00835-2>

Molnupiravir (MK-4482/EIDD-2801) is able to mitigate SARS-CoV-2 infection and block transmission when therapeutically administered to ferrets. The drug, initially developed as an inhibitor of influenza viruses, is currently in Phase II/III clinical trials (NCT04405570 and NCT04405739).

Wang G, Yang ML, Duan ZL, et al. **Dalbavancin binds ACE2 to block its interaction with SARS-CoV-2 spike protein and is effective in inhibiting SARS-CoV-2 infection in animal models.** Cell Res 2020, published 1 December. Full-text: <https://doi.org/10.1038/s41422-020-00450-0>

Dalbavancin is a once-a-week antibiotic (plasma half-life: 5–7 days) with activity against a broad range of Gram-positive pathogens, including methicil-

lin-resistant *Staphylococcus aureus* (MRSA) and which has been approved for the treatment of acute bacterial skin and skin structure infections. Here, Ren Lai, Gan Wang and colleagues show that the drug effectively prevented SARS-CoV-2 replication in Vero E6 cells with an EC<sub>50</sub> of ~12 nM. In both mouse and rhesus macaque models, viral replication and histopathological injuries caused by SARS-CoV-2 infection were significantly inhibited by dalbavancin administration.

## Education

Rubin EJ, Baden LR, Morrissey S. **Caring for Hospitalized Patients with Covid-19.** Audio interview (18:39). N Engl J Med 2020; 383: e140. Access: <https://doi.org/10.1056/NEJMe2034472>

The editors discuss the WHO's Solidarity study and the changing recommendations for the care of hospitalized patients.

## Beyond Corona

Callaway E. **'It will change everything': DeepMind's AI makes gigantic leap in solving protein structures.** Nature 2020, published 30 November. Full-text: <https://www.nature.com/articles/d41586-020-03348-4>

Google's deep-learning program for determining the 3D shapes of proteins might transform biology. Is it truly a game changer? Will it change medicine, research and bioengineering, as suggests Andrei Lupas from MPI Tübingen? Follow Ewen Callaway on this tour around the AI-biology interface.

## 4 December

Planning the 6<sup>th</sup> edition. No Top 10.

## 5 December

### Epidemiology

Podewils LJ, Burket TL, Mettenbrink C, et al. **Disproportionate Incidence of COVID-19 Infection, Hospitalizations, and Deaths Among Persons Identifying as Hispanic or Latino — Denver, Colorado March–October 2020.** MMWR Morb Mortal Wkly Rep 2020;69:1812–1816. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6948a3>

COVID-19 disproportionately affected Hispanic persons in Denver, US. Overall, the proportions of COVID-19 cases (55%), hospitalizations (62%), and deaths (51%) among Hispanic adults were approximately double the proportion of Hispanic adults in the Denver community (24,9%). Among adults with COVID-19, Hispanic persons reported larger household sizes and more known COVID-19 household exposure, working in essential industries, working while ill, and delays in testing after symptom onset.

Horton R. **Offline: COVID-19—what have we learned so far?** Lancet 2020, published 5 December. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32584-8](https://doi.org/10.1016/S0140-6736(20)32584-8)

Richard Horton, the Lancet Editor-in-Chief, briefly discusses what we have discovered in 2020 and how these discoveries might inform our future.

## Transmission

Patterson EI, Elia G, Grassi A, et al. **Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy.** Nat Commun 11, 6231 (2020). Full-text: <https://doi.org/10.1038/s41467-020-20097-0>

A pre-print paper we presented on [27 July](#) has now been published in Nat Commun. In the final version, Nicola Decaro and colleagues describe SARS-CoV-2 infection in 919 companion animals in northern Italy at the height of the spring 2020 epidemic. Although no animals tested PCR positive, 3,3% of dogs and 5,8% of cats had measurable SARS-CoV-2 neutralizing antibody titers, with dogs from COVID-19 positive households being significantly more likely to test positive than those from COVID-19 negative households. From their experience, the authors conclude that it is unlikely that infected pets play an active role in SARS-CoV-2 transmission to humans. Only under special circumstances, such as the high animal population densities encountered on infected mink farms, might animal-to-human transmission be more likely.

## Vaccine

Ledford H, Cyranoski D, Van Noorden R. **The UK has approved a COVID vaccine — here's what scientists now want to know.** Nature 2020, published 3 December. Full-text: <https://www.nature.com/articles/d41586-020-03441-8>

The Pfizer-BioNTech vaccine has passed safety and efficacy tests — but scientists still have many questions about how this and other vaccines will perform as they're rolled out to millions of people.

Danaiya Usher A. **South Africa and India push for COVID-19 patents ban.** Lancet 2020, published 5 December. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32581-2](https://doi.org/10.1016/S0140-6736(20)32581-2)

South Africa and India want the World Trade Organization to temporarily suspend intellectual property rights so that COVID-19 vaccines and other new technologies are accessible for poor countries. Right on.

Widge AT, Rouphael NG, Jackson LA. **Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination.** N Engl J Med 2020, published 3 December. Full-text: <https://doi.org/10.1056/NEJMc2032195>

The correlates of protection against SARS-CoV-2 infection are not yet established. In this short letter, Alicia Widge et al. report the results of immunogenicity studies 3 months after the second vaccination with mRNA-1273. (The 57 days results were published by Jackson et al. in July and Anderson et al. in September.) The data shows that mRNA-1273 produced high levels of binding and neutralizing antibodies that declined slightly over time but they remained elevated in all participants 3 months after the booster vaccination. The authors conclude that mRNA-1273 has the potential to provide durable humoral immunity. Studies of vaccine-induced B cells are ongoing.

Dooling K, McClung N, Chamberland M, et al. **The Advisory Committee on Immunization Practices' Interim Recommendation for Allocating Initial Supplies of COVID-19 Vaccine — United States, 2020.** MMWR Morb Mortal Wkly Rep. ePub: 3 December 2020. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6949e1>

Over the coming weeks and months, demand for vaccines will exceed supply. In the initial phase of the COVID-19 vaccination program, both health care personnel and residents of long-term care facilities should be offered priority vaccination.

## Severe COVID

Bramante CT, Ingraham NE, Murray TA, et al. **Metformin and risk of mortality in patients hospitalised with COVID-19: a retrospective cohort analysis.** Lancet Healthy Longevity 2020, published 3 December. Full-text: [https://doi.org/10.1016/S2666-7568\(20\)30033-7](https://doi.org/10.1016/S2666-7568(20)30033-7)

Metformin for women with obesity or type 2 diabetes who are hospitalized for COVID-19? This is the suggestion of a retrospective cohort analysis by Carolyn Bramante from the University of Minnesota. Metformin was associated with decreased mortality in women by Cox proportional hazards (HR 0.785, 95% CI 0.650–0.951) and propensity matching (OR 0.759, 95% CI 0.601–0.960,  $p = 0.021$ ). If these findings are reproduced in prospective studies, the safe and inexpensive drug might be used for prevention of COVID-19 mortality. There was no significant reduction in mortality among men.

See also the comment by Dardano A, Del Prato S. **Metformin: an inexpensive and effective treatment in people with diabetes and COVID-19?** *Lancet Healthy Longevity* 2020, published 3 December. Full-text: [https://doi.org/10.1016/S2666-7568\(20\)30047-7](https://doi.org/10.1016/S2666-7568(20)30047-7)

Ceulemans LJ, Van Slambrouck J, De Leyn, P, et al. **Successful double-lung transplantation from a donor previously infected with SARS-CoV-2.** *Lancet Respir Med* 2020 published 1 December. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30524-5](https://doi.org/10.1016/S2213-2600(20)30524-5)

Laurens Ceulemans from the University Hospitals Leuven, Belgium, report a successful double-lung transplantation from a donor exposed to SARS-CoV-2 who had mild COVID-19-like symptoms 3 months earlier. The lungs were successfully transplanted without viral transmission to the recipient, as shown by repetitive bronchoalveolar lavage and serology after transplantation.

See also the Video abstract: [https://www.thelancet.com/cms/10.1016/S2213-2600\(20\)30524-5/attachment/9385e393-669b-466b-b39e-c756b87ea947/mmc1.mp4](https://www.thelancet.com/cms/10.1016/S2213-2600(20)30524-5/attachment/9385e393-669b-466b-b39e-c756b87ea947/mmc1.mp4) and the comment by Meyer KC. **Risks of lung transplantation in the SARS-CoV-2 era.** *Lancet Respir Med* 2020 published 1 December. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30561-0](https://doi.org/10.1016/S2213-2600(20)30561-0)

## Society

Mair S. **Neoliberal economics, planetary health, and the COVID-19 pandemic: a Marxist ecofeminist analysis.** *Lancet Planetary Health* 2020, published in December 2020. Full-text: [https://doi.org/10.1016/S2542-5196\(20\)30252-7](https://doi.org/10.1016/S2542-5196(20)30252-7)

The global capitalist economy has unprecedented productive capacity. Might it also use this capacity to create the conditions that improve and maintain people's health? If you want to explore key concepts from the ecological, feminist, and Marxist perspectives of the economy, this *Personal View* by Simon Mair is for you.



## Spanish

If you read Spanish, read Sampedro J. **El mundo rico se vacunará en 2021**. El País 2020, published 3 December. Full-text: <https://elpais.com/opinion/2020-12-02/el-mundo-rico-se-vacunara-en-2021.html>

Los países en desarrollo tendrán que esperar dos años más.

Ansede M, Galocha A. **Las enormes diferencias entre las vacunas de Pfizer, Moderna y Oxford**. El País 2020, published 24 November. Full-text: <https://elpais.com/ciencia/2020-11-23/las-diferencias-abismales-entre-las-vacunas-de-pfizer-moderna-y-oxford.html>

Los tres candidatos más avanzados contra la covid se distinguen en factores como su precio, que varía entre tres y 21 euros por dosis, y su temperatura de conservación.

Sevillano EG. **“Autorizar la vacuna de emergencia es correr un riesgo que no parece justificado”** – El País 2020, published 3 December. Full-text: <https://elpais.com/sociedad/2020-12-02/autorizar-la-vacuna-de-emergencia-es-correr-un-riesgo-que-no-parece-justificado.html>

“En una situación en la que no parece que vayamos a peor, en adelantar en una semana o dos la vacunación tendría que haber un beneficio potencial muy grande”, dice César Hernández, jefe del Departamento de Medicamentos de Uso Humano de la Aemps.

Moreno C. **Malentendidos, desconexión con el resto del equipo, ansiedad: la cara oculta del teletrabajo**. El País 2020, published 30 November. Full-text: [https://retina.elpais.com/retina/2020/11/30/tendencias/1606759678\\_037855.html](https://retina.elpais.com/retina/2020/11/30/tendencias/1606759678_037855.html)

Tener la oficina en casa conlleva retos para los que no nos habían preparado. Y quizá haya que ir preparándose para convivir mucho tiempo con ellos.

## French

If you read French, read Dagorn G. **Comment fonctionnent les futurs vaccins contre le Covid-19**. Le Monde 2020, published 4 December. Full-text: [https://www.lemonde.fr/les-decodeurs/article/2020/12/04/comment-fonctionnent-les-futurs-vaccins-contre-le-covid-19\\_6062151\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2020/12/04/comment-fonctionnent-les-futurs-vaccins-contre-le-covid-19_6062151_4355770.html)

On compte aujourd'hui 237 projets de vaccins contre le Covid-19 dans le monde, développés selon des techniques très différentes. Voici comment ils agissent.

Damgé M, Parienté J, Audureau W, Maad A, Aubert R. **Combien de vaccins ? Quand seront-ils disponibles ? Seront-ils obligatoires ? Peuvent-ils mettre fin à l'épidémie de Covid -19 ?** Full-text : [https://www.lemonde.fr/les-decodeurs/article/2020/12/01/combien-de-vaccins-quand-seront-ils-disponibles-seront-ils-obligatoires-peuvent-ils-mettre-fin-l-epidemie-de-covid-19-nos-reponses-a-vos-questions\\_6061795\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2020/12/01/combien-de-vaccins-quand-seront-ils-disponibles-seront-ils-obligatoires-peuvent-ils-mettre-fin-l-epidemie-de-covid-19-nos-reponses-a-vos-questions_6061795_4355770.html)

Nos réponses à vos questions.

## 6 December

### Virology

Wang K, Chen W, Zhang Z, et al. **CD147-spike protein is a novel route for SARS-CoV-2 infection to host cells.** Sig Transduct Target Ther 5, 283 (2020). Full-text: <https://doi.org/10.1038/s41392-020-00426-x>

Might there be a hitherto clandestine loophole for SARS-CoV-2 to enter into human cells? Here, Zhi-Nan Chen, Ke Wang and co-authors wonder that although angiotensin-converting enzyme 2 (ACE2) – the receptor which mediates the infection of cells by binding to the spike protein – is expressed in the lung, kidney, and intestine, its expressing levels are rather low, especially in the lung. They describe an interaction between the host cell receptor CD147 and the SARS-CoV-2 spike protein. The loss of CD147 or blocking CD147 in Vero E6 and BEAS-2B cell lines by anti-CD147 antibody meplazumab inhibited SARS-CoV-2 amplification. The authors suggest that a novel viral entry route via the CD147-spike protein might provide a new target for developing drugs against SARS-CoV-2.

### Transmission

Alsved M, Matamis A, Bohlin R, et al. **Exhaled respiratory particles during singing and talking.** Aerosol Research Letters 2020, published 17 September. Full-text: <https://doi.org/10.1080/02786826.2020.1812502>

Aerosols are emitted from breathing, talking, coughing and sneezing. Over time, normal breathing can generate more viable viral aerosol than even coughing! In this study, Jacob Löhndal, Malin Alsved and colleagues investi-

gated aerosol and droplet emissions during singing, as compared to talking and breathing. As expected, normal singing generated significantly more aerosol particles than normal talking and loud singing produced more particles than normal singing. (*Advice of the Editors: Get vaccinated – and then wait 57 days – before you go back to your weekly choir sessions.*)

## Immunology

McMahan K, Yu J, Mercado NB, et al. **Correlates of protection against SARS-CoV-2 in rhesus macaques.** Nature 2020, published 4 December. Full-text: <https://doi.org/10.1038/s41586-020-03041-6>

Dan Barouch, Katherine McMahan and colleagues from Harvard show that adoptive transfer of purified IgG from convalescent macaques protects naïve recipient rhesus macaques against SARS-CoV-2 challenge in a dose dependent fashion; relatively low antibody titers were sufficient for protection against SARS-CoV-2 in rhesus macaques whereas higher antibody titers were required for therapy of SARS-CoV-2 infection in macaques. Depletion of CD8+ T cells in convalescent animals partially depletes the protective efficacy of natural immunity against SARS-CoV-2 re-challenge.

Starr TN, Greaney AJ, Addetia A, et al. **Prospective mapping of viral mutations that escape antibodies used to treat COVID-19.** bioRxiv 2020, posted 1 December. Full-text: <https://doi.org/10.1101/2020.11.30.405472>

Jesse Bloom, Tyler Starr and colleagues from the Fred Hutchinson Cancer Research Center in Seattle, US, mapped SARS-CoV-2 mutation that could prevent binding by the three monoclonal antibodies LY-CoV016 (Eli Lilly; which is different from bamlanivimab [LY-CoV555]) and casirivimab and imdevimab (REGN-COV2). They identified a single amino-acid mutation that fully escapes the REGN-COV2 cocktail. Please note: *these findings have not yet been peer reviewed.*

## Pathogenesis

Simoneau CR, Ott M. **Modeling Multi-organ Infection by SARS-CoV-2 Using Stem Cell Technology.** Cell Stem Cell 2020, published 3 December. Full-text: <https://doi.org/10.1016/j.stem.2020.11.012>

COVID-19 is a multi-organ disease causing characteristic complications. In this mini-review, Camille Simoneau and Melanie Ott from the Gladstone Institute of Virology, San Francisco, show that stem cell models of various organ systems—most prominently, lung, gut, heart, and brain—are at the forefront

of studies aimed at understanding the role of direct infection in COVID-19 multi-organ dysfunction. A perfect reading for the weekend!

## Diagnosics

Wang D, He S, Wang X, et al. **Rapid lateral flow immunoassay for the fluorescence detection of SARS-CoV-2 RNA.** Nat Biomed Eng 2020, published 3 December. Full-text: <https://doi.org/10.1038/s41551-020-00655-z>

The authors describe an inexpensive amplification-free nucleic acid immunoassay for the fluorescence detection of SARS-CoV-2 RNA in less than an hour. In a multi-hospital randomized double-blind trial involving 734 samples (593 throat swabs and 141 sputum), the assay achieved sensitivities of 100% and specificities of 99% for both types of sample.

Larremore DB, Toomre D, Parker R. **Modeling the effectiveness of olfactory testing to limit SARS-2-CoV transmission.** medRxiv 2020, posted 2 December. Full-text: <https://doi.org/10.1101/2020.11.30.20241174>

Olfactory dysfunction – hyposmia or anosmia – occurs in up to 80% of SARS-CoV-2 infected individuals if standardized olfactory dysfunction test is performed, even in those who remain otherwise asymptomatic. Here, the authors from the University of Colorado Boulder suggest that mass-produced, low-cost and self-administered olfactory tests might reduce the spread of SARS-CoV-2. Interesting approach but attention: *this is just a model.*

## Severe COVID

Kaeuffer C, Le Hyaric C, Fabacher T, et al. **Clinical characteristics and risk factors associated with severe COVID-19: prospective analysis of 1,045 hospitalised cases in North-Eastern France, March 2020.** Eurosurveill 2020, published 3 December. Full-text: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.48.2000895>

This non-interventional prospective study (1045 adult COVID-19 patients hospitalized in two different hospitals in Alsace, France: Strasbourg University Hospital and Mulhouse Hospital in March 2020) presents a wealth of data. Advanced age, being male, inflammation parameters and dyspnea were associated with the development of severe disease and death. Being overweight or obese was associated with severe disease only, whereas co-morbidities such as chronic kidney disease, diabetes and immunosuppression increased the risk of death.

## Beyond Corona

Mitchell MJ, Billingsley MM, Haley RM, et al. , **M.J., Billingsley, M.M., Haley, R.M. et al. Engineering precision nanoparticles for drug delivery.** Nat Rev Drug Discov (2020). Full-text: <https://doi.org/10.1038/s41573-020-0090-8>

In recent years, nanoparticles have been developed to navigate biological barriers – systemic, microenvironmental and cellular – that are heterogeneous across patient populations and diseases. In this 294-citation review, Robert Langer, Michael Mitchell and colleagues discuss advances in nanoparticle design. Optimized drug delivery in a personalized manner might ultimately have an impact on patient outcome.

## Press

Zimmer K, Weiland N. **Many Trial Volunteers Got Placebo Vaccines. Do They Now Deserve the Real Ones?** The New York Times 2020, published 2 December. Full-text: <https://www.nytimes.com/2020/12/02/health/covid-vaccine-placebo-group.html>

Some vaccine experts worry that “unblinding” the trials and giving all of the volunteers vaccines would tarnish the long-term results. See also **Placebo-Controlled Trials of Covid-19 Vaccines — Why We Still Need Them.** N Engl J Med 2020, published 2 December. Full-text: <https://doi.org/10.1056/NEJMp2033538>

## Spanish

If you read Spanish, read Grasso D, Llaneras K, Zafra M. **Aislar rápido y cortar contagios: cómo los test de antígenos están cambiando la pandemia.** El País 2020, published 5 December. Full-text: <https://elpais.com/sociedad/2020-12-05/aislar-rapido-y-cortar-contagios-como-los-test-de-antigenos-estan-cambiando-la-pandemia.html>

Estas pruebas se están convirtiendo en un arma clave en la segunda ola y ya se usan como análisis de referencia en hospitales y primaria. Son lo bastante sensibles para detectar personas contagiosas.

## French

Remember the paper **COVID-19 Outbreak Associated with a 10-Day Motorcycle Rally in a Neighboring State — Minnesota, August–September 2020** that we presented on 21 November? If you read French, read Le Bars S. **Une**

**troisième vague de Covid-19 au milieu de nulle part : le Dakota du Sud, terrain fertile pour l'épidémie.** Le Monde 2020, published 5 December. Full-text : [https://www.lemonde.fr/m-le-mag/article/2020/12/05/le-dakota-du-sud-un-terrain-fertile-pour-le-covid-19\\_6062267\\_4500055.html](https://www.lemonde.fr/m-le-mag/article/2020/12/05/le-dakota-du-sud-un-terrain-fertile-pour-le-covid-19_6062267_4500055.html)

Cet Etat américain, rural et conservateur, dont les habitants « n'aiment pas qu'on se mêle de leurs affaires », est majoritairement réfractaire à toute mesure sanitaire. Au nom de la liberté. (Ndlr : *Nous devrions peut-être leur expliquer le vrai sens de la parole liberté.*)

## 7 December

### Prevention

Bahethi RR, Liu BY, Asriel B, et al. **The COVID-19 Student Workforce at the Icahn School of Medicine at Mount Sinai: A Model for Rapid Response in Emergency Preparedness.** Acad Med. 2020 Dec 1. PubMed: <https://pubmed.gov/33264110>. Full-text: <https://doi.org/10.1097/ACM.0000000000003863>

From March 15, 2020 to June 14, 2020, student volunteers recorded 29.602 hours (2277 hours per week) in 7 different task forces which operated at 7 different hospitals throughout the health system. Volunteers included students from all years of medical school as well as PhD, master's, and nursing students.

Ghram A, Briki W, Mansoor H, Al-Mohannadi AS, Lavie CJ, Chamari K. **Home-based exercise can be beneficial for counteracting sedentary behavior and physical inactivity during the COVID-19 pandemic in older adults.** Postgrad Med. 2020 Dec 4. PubMed: <https://pubmed.gov/33275479>. Full-text: <https://doi.org/10.1080/00325481.2020.1860394>

Lockdowns, quarantine and self-isolation are periods characterized by cessation of outdoor exercise. To avoid the harmful effects of periods of not doing exercise, physical activity (PA) could be prescribed to older adults, which is of great importance for breaking their sedentary lifestyle and improving their immunity. The authors discuss the importance of performing PA to reduce the harmful effects of COVID-19.

### Clinical

Mikulski TR, Johnson SR, Fraenkel L, et al. **American College of Rheumatology Guidance for the Management of Rheumatic Disease in Adult Patients During the COVID-19 Pandemic: Version 3.** *Arthritis Rheumatol.* 2020 Dec 5. PubMed: <https://pubmed.gov/33277981>. Full-text: <https://doi.org/10.1002/art.41596>

This document provides guidance to rheumatology providers on the management of adult rheumatic disease in the context of the COVID-19 pandemic.

### Comorbidities

Gulersen M, Staszewski C, Grayver E, et al. **Coronavirus Disease 2019 (COVID-19)-Related Multisystem Inflammatory Syndrome in a Pregnant Woman.** *Obstet Gynecol.* 2020 Dec 3. PubMed: <https://pubmed.gov/33278275>. Full-text: <https://doi.org/10.1097/AOG.0000000000004256>

Case report of a woman at 28 weeks gestation, diagnosed with COVID-19 4 weeks prior, and admitted with chest pain. Evaluation indicated myocarditis and marked elevations of inflammatory markers consistent with multisystem inflammatory syndrome in adults. Treatment with intravenous immunoglobulin and corticosteroids was associated with a favorable outcome.

Fernandez CE, Franz CK, Ko JH, et al. **Imaging Review of Peripheral Nerve Injuries in Patients with COVID-19.** *Radiology.* 2020 Dec 1:203116. PubMed: <https://pubmed.gov/33258748>. Full-text: <https://doi.org/10.1148/radiol.2020203116>

Peripheral nerve injury can occur in COVID-19 patients secondary to post-infectious inflammatory neuropathy, prone positioning-related stretch/compression injury, systemic neuropathy, or nerve entrapment from hematoma. MR neurography and high-resolution ultrasound are excellent diagnostic tools for peripheral nerve injury. For COVID-19 patients and survivors with neuromuscular complications, imaging of peripheral nerves can aid medical decision-making, rehabilitative care, and patient/family counseling.

## Pediatrics

Zimmermann P, Curtis N. **Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections.** Arch Dis Child. 2020 Dec 1;archdischild-2020-320338. PubMed: <https://pubmed.gov/33262177>. Full-text: <https://doi.org/10.1136/archdischild-2020-320338>

Compared with older adults, severe or fatal COVID-19 disease is much less common in infants, children and young adults. In this review, the authors discuss proposed hypotheses for the age-related difference in severity of COVID-19. The observed age-gradient seems to most closely parallel changes in immune and endothelial/clotting function.

## Collateral Effects

Heaton HA, Luke A, Sztajnkrzyer MD, Clements CM, De Moraes AG, Raukar NP. **Best Practices in Managing Cardiac Arrest in the Emergency Department During the COVID-19 Pandemic.** Mayo Clin Proc. 2020 Dec;95(12):2704-2708. PubMed: <https://pubmed.gov/33276842>. Full-text: <https://doi.org/10.1016/j.jmayocp.2020.10.009>

Patients with COVID-19 are at increased risk of cardiac complications including cardiac arrest. Of admitted patients, almost 30% may have evidence of myocardial injury with mortality among hospitalized patients as high as 70%. The resuscitation of these patients requires a conscious effort to minimize the spread of SARS-CoV-2. The authors present a best-practice model based on four guiding principles: (1) reduce the risk of exposure to the entire health care team; (2) decrease the number of aerosol-generating procedures; (3) use a small resuscitation team to limit potential exposure; and (4) consider early termination of resuscitative efforts.

Fuady A, Houweling TAJ, Richardus JH. **COVID-19 and Tuberculosis-Related Catastrophic Costs.** Am J Trop Med Hyg. 2020 Dec 2. PubMed: <https://pubmed.gov/33269683>. Full-text: <https://doi.org/10.4269/ajtmh.20-1125>

Interruptions of TB control programs could potentially prolong diagnostic delays and worsen TB treatment outcomes. In addition, the upcoming economic recession could lead to a reduction of income and a rise in unemployment rates in TB-affected households. All of these factors increase the risk of TB incidence and the economic impact on TB-affected households.



Indini A, Cattaneo M, Ghidini M, et al. **Triage process for the assessment of coronavirus disease 2019-positive patients with cancer: The ONCOVID prospective study.** *Cancer.* 2020 Dec 3. PubMed: <https://pubmed.gov/33270908>. Full-text: <https://doi.org/10.1002/cncr.33366>

General measures to keep COVID-19-free cancer divisions have been adopted worldwide. In this prospective clinical trial, the authors evaluated the efficacy of triage to identify COVID-19 among patients with cancer. Of 562 enrolled patients, 6 (1%) were diagnosed with COVID-19, of whom 4 (67%) had the disease detected through telehealth triage, and 2 patients (33%) without suspect symptoms at triage had the disease detected later. The authors conclude that telehealth triage was helpful in detecting suspect patients and to keep a COVID-19-free cancer center. The overall incidence of COVID-19 diagnosis (1%) and antibody positivity (13%) in patients with suspect symptoms was similar to that observed in the general population.

Peach E, Rutter M, Lanyon P, et al. **Risk of death among people with rare autoimmune diseases compared to the general population in England during the 2020 COVID-19 pandemic.** *Rheumatology (Oxford).* 2020 Dec 4:keaa855. PubMed: <https://pubmed.gov/33271595>. Full-text: <https://doi.org/10.1093/rheumatology/keaa855>

The risk of all-cause death is more prominently heightened during COVID-19 among people with rare autoimmune rheumatic diseases (RAIRD) than among the general population. This is a result of an analysis which included 168,691 people with a recorded RAIRD diagnosis alive on 01/03/2020. The age-standardized mortality rate (ASMR) among people with RAIRD was 1.44 times higher than the average ASMR during the same months of the previous 5 years, whereas in the general population of England it was 1.38 times higher. The authors suggest quantifying how much risk is due to COVID-19 and how much is due to a disruption to healthcare services.

## 8 December

### Epidemiology

Haag C, Höglinger M, Moser A, et al. **Social mixing and risk exposures for SARS-CoV-2 infections in elderly persons.** *Swiss Med Wkly.* 2020 Dec 5;150:w20416. PubMed: <https://pubmed.gov/33277915>. Full-text: <https://doi.org/10.4414/sm.w.2020.20416>

Although many elderly persons continued to follow the recommended preventive measures during the transitional phase between the two pandemic waves, social mixing with younger persons constitutes a way for transmission of infections across age groups. In this large survey from Switzerland, about one quarter of all elderly were still strictly adhering to social distancing and preventive measures. In contrast, a minority of 10% of the elderly had many social contacts and were lacking adherence to preventive measures. The remaining groups seemed to fall in between: while they did have multiple personal contacts, they did maintain the recommended distance. Thus, preventive measures remain important among all age groups.

Balabdaoui F, Mohr D. **Age-stratified discrete compartment model of the COVID-19 epidemic with application to Switzerland.** *Sci Rep.* 2020 Dec 4;10(1):21306. PubMed: <https://pubmed.gov/33277545>. Full-text: <https://doi.org/10.1038/s41598-020-77420-4>

A discrete modeling framework is proposed to capture the dynamics of highly age-sensitive epidemics and to evaluate the effect of social contact patterns on the load of hospitals and their intensive care units. According to the authors, there should be sufficient time for governments to take corrective measures in case they detect a significant increase in hospitalizations after relaxing the lockdown. Even though the second wave may not lead to a collapse of the healthcare system in Switzerland, it is still important to maintain the overall reproduction number always below one to avoid any silent multiplication of the total number of fatalities.

## Transmission

Muller N, Kunze M, Steitz F, et al. **Severe Acute Respiratory Syndrome Coronavirus 2 Outbreak Related to a Nightclub, Germany, 2020.** *Emerg Infect Dis.* 2020 Dec 2;27(2). PubMed: <https://pubmed.gov/33263514>. Full-text: <https://doi.org/10.3201/eid2702.204443>

Club X is located in a basement in Berlin, Germany. The area accessible to guests is 150 m<sup>2</sup> with a height of 3 m. Ventilation of the space is ensured by a mechanical air exhaust and supply system and maintenance was performed according to the manufacturer's instructions. To avoid noise pollution in the surrounding neighborhood, windows are usually closed during events. On February 29, Club X held an event attended by 300 guests and an index patient who had self-reported initial symptoms one day before attending event. Results: 74 reported cases were linked to the outbreak. Staff members were

particularly affected (attack rate 56%) and likely caused sustained viral transmission after an event at the club. This outbreak illustrates the potential for superspreader events and supports current club closures.

## Immunology

Wajnberg A, Amanat F, Firpo A, et al. **Robust neutralizing antibodies to SARS-CoV-2 infection persist for months.** *Science*. 2020 Dec 4;370(6521):1227-1230. PubMed: <https://pubmed.gov/33115920>. Full-text: <https://doi.org/10.1126/science.abd7728>

Ania Wajnberg and colleagues used a cohort of 30,082 infected individuals with mild to moderate COVID-19 symptoms screened at Mount Sinai Health System in New York City to determine the robustness and longevity of the anti-SARS-CoV-2 antibody response. They found that neutralizing antibody titers against the SARS-CoV-2 spike protein persisted for at least 5 months after infection. The authors plan to follow this cohort over a longer period of time.

Singh H, Choudhari R, Nema V, Khan AA. **ACE2 and TMPRSS2 polymorphisms in various diseases with special reference to its impact on COVID-19 disease.** *Microb Pathog*. 2020 Dec 2:104621. PubMed: <https://pubmed.gov/33278516>. Full-text: <https://doi.org/10.1016/j.micpath.2020.104621>

There are diversities in distribution of ACE2 and TMPRSS2 polymorphisms among different populations. According to this systematic review, analyzing the genetic variants and expression of ACE2 and TMPRSS2 genes in a population may provide the genetic marker for susceptibility or resistance against the coronavirus infection. This might be useful for identifying susceptible population groups for targeted interventions and for making relevant public health policy decisions.

## Prevention

Mitze T, Kosfeld R, Rode J, Wälde K. **Face masks considerably reduce COVID-19 cases in Germany.** Proc Natl Acad Sci U S A. 2020 Dec 3:202015954. PubMed: <https://pubmed.gov/33273115>. Full-text: <https://doi.org/10.1073/pnas.2015954117>

Face masks became mandatory at different points in time across different regions in Germany. Timo Mitze and colleagues compared the rise in infections in regions with masks and regions without masks. Weighing various estimates, they concluded that face masks reduced the daily growth rate of reported infections by around 47%.

## Clinical

Lani-Louzada R, Ramos CDVF, Cordeiro RM, Sadun AA. **Retinal changes in COVID-19 hospitalized cases.** PLoS One. 2020 Dec 3;15(12):e0243346. PubMed: <https://pubmed.gov/33270751>. Full-text: <https://doi.org/10.1371/journal.pone.0243346>

Surprisingly, of the 25 patients with severe or critical disease in this study from Brazil, only three (12%) manifested convincing retinal changes (micro-hemorrhages, flame-shaped hemorrhage and nerve fiber layer infarcts). These retinal changes were likely secondary to clinical intercurrents or comorbidities.

## Collateral damage

Friedman J, Beletsky L, Schriger DL. **Overdose-Related Cardiac Arrests Observed by Emergency Medical Services During the US COVID-19 Epidemic.** JAMA Psychiatry December 3, 2020. 2020. Full-text: <https://doi.org/10.1001/jamapsychiatry.2020.4218>

The authors leveraged a large, national US EMS database to characterize emergent trends in overdose mortality fueled by the pandemic. They describe a large-magnitude, national surge in overdose-related cardiac arrest during the initial months of the COVID-19 epidemic in the US. Peak rates in May 2020 were more than double the baseline from 2018 and 2019, and overall 2020 values were elevated by approximately 50%. Results suggest that the fallout from the COVID-19 pandemic—perhaps especially social isolation—is sharply accelerating fatal overdose trends.

## Treatment

Butt JH, Gerds TA, Schou M, et al. **Association between statin use and outcomes in patients with coronavirus disease 2019 (COVID-19): a nationwide cohort study.** *BMJ Open.* 2020 Dec 4;10(12):e044421. PubMed: <https://pubmed.gov/33277291>. Full-text: <https://doi.org/10.1136/bmjopen-2020-044421>

In this observational cohort study using data from Danish nationwide registries, 843/4842 (17%) COVID-19 patients redeemed a prescription of statins in the 6 months prior to COVID-19 diagnosis. Recent statin exposure was not associated with an increased or decreased risk of all-cause mortality or severe infection. The results were consistent across subgroups of age, sex and presumed indication for statin therapy. Among patients with statin exposure, there was no difference between statin drug or treatment intensity with respect to outcomes.

Spagnuolo V, Guffanti M, Galli L, et al. **Viral clearance after early corticosteroid treatment in patients with moderate or severe covid-19.** *Sci Rep.* 2020 Dec 4;10(1):21291. PubMed: <https://pubmed.gov/33277573>. Full-text: <https://doi.org/10.1038/s41598-020-78039-1>

In this retrospective analysis on 280 patients admitted to the San Raffaele Hospital (Milan, Italy) with moderate/severe COVID-19, time to negativization of nasopharyngeal swabs was similar in steroid and non-steroid users. According to multivariate analysis, SARS-CoV-2 clearance was associated with age  $\leq 70$  years, a shorter duration of symptoms at admission, a baseline PaO<sub>2</sub>/FiO<sub>2</sub>  $> 200$  mmHg, and a lymphocyte count at admission  $> 1.0 \times 10^9/L$ . SARS-CoV-2 clearance was not associated with corticosteroid use.

## French

If you read French, read Collectif. « **Vous ne vouliez pas occuper cette dernière place en réanimation...** » : l'hommage ému de soignants à « **Denise** », une patiente âgée morte du Covid-19 – *Le Monde* 2020, published 7 December. Full-text : [https://www.lemonde.fr/idees/article/2020/12/07/covid-19-madame-nous-n-oublions-jamais-que-vous-nous-avez-demande-de-nous-occuper-des-patients-qui-avaient-des-chances-de-s-en-sortir\\_6062434\\_3232.html](https://www.lemonde.fr/idees/article/2020/12/07/covid-19-madame-nous-n-oublions-jamais-que-vous-nous-avez-demande-de-nous-occuper-des-patients-qui-avaient-des-chances-de-s-en-sortir_6062434_3232.html)

Dans une adresse émue à Denise que « *Le Monde* » publie, trois réanimateurs et une sociologue évoquent leur admiration pour cette patiente âgée, décédée

des suites du Covid-19 et qui avait choisi de ne pas occuper le dernier lit disponible en réanimation.

Piarroux R, Riou B. « **Malgré le vaccin, le risque d'une troisième vague de Covid-19 dans les mois qui viennent existe toujours** » – Le Monde 2020, published 7 December. Full-text : [https://www.lemonde.fr/idees/article/2020/12/07/covid-19-malgre-le-vaccin-le-risque-existe-toujours-de-devoir-affronter-une-troisieme-vague-dans-les-mois-qui-viennent\\_6062446\\_3232.html](https://www.lemonde.fr/idees/article/2020/12/07/covid-19-malgre-le-vaccin-le-risque-existe-toujours-de-devoir-affronter-une-troisieme-vague-dans-les-mois-qui-viennent_6062446_3232.html)

Il faudra du temps pour contrôler l'épidémie alors que les conditions de propagation du virus persistent, expliquent Renaud Piarroux et Bruno Riou, l'épidémiologiste et le directeur du centre de crise de l'Assistance publique.

Herzberg N, Hecketsweiler. **Covid-19 : la saga du vaccin à ARN messenger désormais dans le sprint final**. Le Monde 2020, published 30 November. Full-text : [https://www.lemonde.fr/sciences/article/2020/11/30/covid-19-la-saga-du-vaccin-a-arn-messenger-dans-le-sprint-final\\_6061695\\_1650684.html](https://www.lemonde.fr/sciences/article/2020/11/30/covid-19-la-saga-du-vaccin-a-arn-messenger-dans-le-sprint-final_6061695_1650684.html)

Contre toute attente, c'est une technologie encore jamais éprouvée sur l'homme qui a permis de proposer le plus rapidement des solutions vaccinales contre le SARS-CoV-2, via les projets de Pfizer/BioNTech et de Moderna. Retour sur une course de vitesse lancée il y a plusieurs décennies.

## 9 December

### Immunology

Galani IE, Rovina N, Lampropoulou V, et al. **Untuned antiviral immunity in COVID-19 revealed by temporal type I/III interferon patterns and flu comparison**. Nat Immunol. 2020 Dec 4. PubMed: <https://pubmed.gov/33277638>. Full-text: <https://doi.org/10.1038/s41590-020-00840-x>

A central paradigm of immunity is that interferon (IFN)-mediated antiviral responses precede pro-inflammatory ones, optimizing host protection and minimizing collateral damage. This brilliant work suggests that this paradigm might not apply for COVID-19. By investigating temporal IFN and inflammatory cytokine patterns in 32 moderate-to-severe patients, Ioanna-Evdokia Galani from Athens, Greece and colleagues show here that IFN- $\lambda$  and type I IFN production are both diminished and delayed, induced only in a fraction of

patients as they became critically ill. On the contrary, pro-inflammatory cytokines such as tumor necrosis factor (TNF), interleukin (IL)-6 and IL-8 were produced before IFNs in all patients and persisted for a prolonged time. By comparison, in 16 patients with influenza, IFN- $\lambda$  and type I IFN were induced earlier, robustly, at higher levels and independently of disease severity, whereas pro-inflammatory cytokines were only acutely produced. These data point to an un-tuned antiviral response in COVID-19, contributing to persistent viral presence, hyperinflammation and respiratory failure. Fantastic work (take a look at the beautiful figures) which is among the 10 most important COVID-19 immunology papers of the year.

Poston D, Weisblum Y, Wise H, et al. **Absence of SARS-CoV-2 neutralizing activity in pre-pandemic sera from individuals with recent seasonal coronavirus infection.** Clin Infect Dis. 2020 Dec 3:ciaa1803. PubMed: <https://pubmed.gov/33270134>. Full-text: <https://doi.org/10.1093/cid/ciaa1803>

Daniel Poston and colleagues measured neutralizing activity against SARS-CoV-2 in pre-pandemic sera from 37 Scottish patients with prior PCR-confirmed seasonal coronavirus infection. While neutralizing activity against seasonal coronaviruses was detected in nearly all sera, cross-reactive neutralizing activity against SARS-CoV-2 was undetectable. This data argues against a broad role for pre-existing protective humoral immunity against SARS-CoV-2.

Zheng J, Wang Y, Li K, Meyerholz DK, Allamargot C, Perlman S. **SARS-CoV-2-induced immune activation and death of monocyte-derived human macrophages and dendritic cells.** J Infect Dis. 2020 Dec 5:jiaa753. PubMed: <https://pubmed.gov/33277988>. Full-text: <https://doi.org/10.1093/infdis/jiaa753>

Infection of macrophages and dendritic cells potentially plays a major role in COVID-19 pathogenesis, even in the absence of productive infection. Jian Zheng and colleagues from Iowa demonstrate that SARS-CoV-2 infection of human monocyte-derived macrophages (MDMs) and dendritic cells (MDDCs) was abortive but induced the production of multiple antiviral and pro-inflammatory cytokines. Despite the lack of efficient replication in MDMs, SARS-CoV-2 induced profound IFN-mediated cell death of host cells. Macrophage activation and death was not enhanced by exposure to low levels of

convalescent plasma, suggesting that antibody-dependent enhancement of infection does not contribute to cell death.

## Diagnosics

Yang S, Stanzione N, Uslan DZ, Garner OB, de St Maurice A. **Clinical and Epidemiologic Evaluation of Inconclusive COVID-19 PCR Results Using a Quantitative Algorithm**. Am J Clin Pathol. 2020 Dec 4:aqaa251. PubMed: <https://pubmed.gov/33274731>. Full-text: <https://doi.org/10.1093/ajcp/aqaa251>

Most PCR assays are designed to detect two or more specific target gene regions. An inconclusive result can rarely occur when only one of the targets is detected (< 1%). Shangxin Yang developed a quantitative algorithm to assess and interpret inconclusive PCR results, by combining laboratory, clinical, and epidemiologic data. They determined 5 (28%) of 18 (CDC assay) and 20 (39%) of 51 (TaqPath assay) cases to be false positive. Lowering the cycle threshold cut-off from 40 to 37 in the TaqPath assay resulted in a dramatic reduction of the false-positive rate to 14%. Testing of asymptomatic individuals was associated with a significantly higher probability of having a false-positive result.

Hodges G, Pallisgaard J, Schjerning Olsen AM, et al. **Association between biomarkers and COVID-19 severity and mortality: a nationwide Danish cohort study**. BMJ Open. 2020 Dec 2;10(12):e041295. PubMed: <https://pubmed.gov/33268425>. Full-text: <https://doi.org/10.1136/bmjopen-2020-041295>

In a large study from Denmark, analyzing all patients aged  $\geq 18$  years admitted to hospital with COVID-19 from 27th of February to 1st of May 2020, with available biochemistry data, of the 1310 patients admitted to hospital (54,6% men; median age 73,6 years), 352 (26,9%) experienced the composite endpoint and 263 (20,1%) died. Elevated levels of CRP, leucocytes, procalcitonin, urea, troponins and D-dimer, and low levels of eGFR were associated with higher standardized absolute risk of death/ICU admission within 30 days.

## Clinical

Stavem K, Ghanima W, Olsen MK, Gilboe HM, Einvik G. **Persistent symptoms 1.5-6 months after COVID-19 in non-hospitalised subjects: a population-based cohort study**. Thorax. 2020 Dec 3:thoraxjnl-2020-216377. PubMed: <https://pubmed.gov/33273028>. Full-text: <https://doi.org/10.1136/thoraxjnl-2020-216377>



The authors from Norway conducted a postal survey at the end of June 2020 among non-hospitalized patients, about 1–4 months after the positive PCR test. Of the 451 subjects (48%) who responded to the survey, > 50% (women 53%, men 67%) had no symptoms 1.5–6 months after symptom onset while 16% reported dyspnea, 12% loss/disturbance of smell, and 10% loss/disturbance of taste. Co-morbidities and a high symptom load during the acute phase were associated with persistent symptoms. At 1.5–6 months, however, there was no difference in symptoms according to length of time since COVID-19 onset. Note that these patients were non-hospitalized.

Arnold DT, Hamilton FW, Milne A, et al. **Patient outcomes after hospitalisation with COVID-19 and implications for follow-up: results from a prospective UK cohort.** *Thorax.* 2020 Dec 3;thoraxjnl-2020-216086. PubMed: <https://pubmed.gov/33273026>. Full-text: <https://doi.org/10.1136/thoraxjnl-2020-21608633271595>

Hospitalized patients may differ. In this observational study from the UK, at 8–12 weeks post-admission, 163 survivors were invited to a systematic clinical follow-up. Of 131 participants, 110 attended the follow-up clinic. Most (74%) had persistent symptoms (notably breathlessness and excessive fatigue) and limitations in reported physical ability. However, clinically significant abnormalities in chest radiograph, exercise tests, blood tests and spirometry were less frequent (35%), especially in patients not requiring supplementary oxygen during their acute infection (7%).

## Treatment

Ahmed S, Karim MM, Ross AG, et al. **A five-day course of ivermectin for the treatment of COVID-19 may reduce the duration of illness.** *Int J Infect Dis.* 2020 Dec 2;S1201-9712(20)32506-6. PubMed: <https://pubmed.gov/33278625>. Full-text: <https://doi.org/10.1016/j.ijid.2020.11.191>

Ivermectin, an inexpensive, over-the-counter medicine, is widely used as a preventative against COVID-19 in many South/Latin American countries. However, the evidence that ivermectin protects from COVID-19 is scant. This group from Bangladesh conducted a randomized, double-blind, placebo-controlled trial of oral ivermectin alone or in combination with doxycycline compared with placebo among 72 hospitalized patients. Virological clearance was earlier in the 5-day ivermectin treatment arm versus the placebo group (9,7 days vs. 12,7 days;  $p = 0.02$ ); but not in the ivermectin + doxycycline arm (11,5 days;  $p = 0.27$ ). There were no severe adverse drug events recorded in

the study. According to the authors, “larger trials will be needed to confirm these preliminary findings”.

Honjo K, Russel RM, Li R, et al. **Convalescent Plasma-Mediated Resolution of COVID-19 in a Patient with Humoral Immunodeficiency**. *Cell Rep Med* December 05, 2020. Full-text: <https://doi.org/10.1016/j.xcrm.2020.100164>

Interesting case report. Convalescent plasma (CP) is widely used to treat COVID-19, but without formal evidence of efficacy. Here, Kazuhito Honjo and colleagues report the beneficial effects of CP in a severely ill COVID-19 patient with prolonged pneumonia and CLL, who was unable to generate an antiviral antibody response of her own. On day 33 after becoming symptomatic, the patient received CP containing high-titer neutralizing antibodies, defervesced and improved clinically within 48 hours, and was discharged on day 37. Hence, when present in sufficient quantities, NABs to SARS-CoV-2 may have clinical benefit even if administered relatively late in the disease course.

## Pediatrics

Stowe J, Smith H, Thurland T, et al. **Stillbirths During the COVID-19 Pandemic in England, April-June 2020**. *JAMA*. Published online December 7, 2020. Full-text: <https://doi.org/10.1001/jama.2020.21369>

Julia Stowe and colleagues used national and regional hospitalization data in England to assess the risk of stillbirths during the COVID-19 pandemic. Contrasting previous reports from single hospitals, there was no evidence of any increase in stillbirths regionally or nationally when compared with the same months in the previous year and despite variable community SARS-CoV-2 incidence rates in different regions. This data is reassuring given the concerns about patients, including pregnant women, receiving fewer services or being hesitant to access health care during the pandemic.

## French

If you read French, read Lemarié A, Cazi E. **Covid-19 : à l'hôpital, l'épineuse question du « tri » des patients**. *Le Monde* 2020, published 8 December. Full-text : [https://www.lemonde.fr/planete/article/2020/12/07/covid-19-a-l-hopital-l-epineuse-question-du-tri-des-patients\\_6062435\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/07/covid-19-a-l-hopital-l-epineuse-question-du-tri-des-patients_6062435_3244.html)

Avec l'épidémie due au coronavirus, les situations où les soignants ont dû prioriser les malades à prendre en charge se sont multipliées, au-delà des services de réanimation.

Thibault H. **Covid-19 : comment une traque méthodique et intrusive a permis à la Corée du Sud de maîtriser le virus.** Le Monde 2020, published 8 December. Full-text :

[https://www.lemonde.fr/planete/article/2020/12/08/covid-19-comment-une-traque-methodique-et-intrusive-a-permis-a-la-coree-du-sud-de-maitriser-le-virus\\_6062564\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/08/covid-19-comment-une-traque-methodique-et-intrusive-a-permis-a-la-coree-du-sud-de-maitriser-le-virus_6062564_3244.html)

Ce pays de 52 millions d'habitants est parvenu à limiter le bilan à 549 morts depuis le début de la pandémie, tout en maintenant la liberté de circulation.

Audureau W. **Covid-19 : comparer les restrictions en France à celles d'autres pays donne une image déformée de la réalité.** Le Monde 2020, published 8 December. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2020/11/30/covid-19-gare-aux-comparaisons-hatives-entre-les-restrictions-en-france-et-dans-d-autres-pays\\_6061696\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2020/11/30/covid-19-gare-aux-comparaisons-hatives-entre-les-restrictions-en-france-et-dans-d-autres-pays_6061696_4355770.html)

La stratégie sanitaire de la France est souvent opposée à celle d'autres pays, comme l'Argentine, l'Espagne et la Suède. Des parallèles périlleux.

## 10 December

### Prevention

Chan NC, Li K, Hirsh J. **Peripheral Oxygen Saturation in Older Persons Wearing Nonmedical Face Masks in Community Settings.** JAMA December 8, 2020. 2020; 324(22):2323-2324. Full-text: <https://doi.org/10.1001/jama.2020.21905>

Some people still claim on social media that masks can cause hypoxia and are therefore dangerous. Please forget this nonsense. Noel C. Chan provided participants aged 65 years or older with a 3-layer plane-shaped disposable non-medical face mask with ear loops (Boomcare DY95 model) and a portable pulse oximeter. In their cross-over study on 25 subjects, wearing a 3-layer nonmedical face mask was not associated with a decline in oxygen saturation.

## Epidemiology

Ismail SA, Saliba V, Bernal JL, et al. **SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England.** *Lancet Inf Dis* December 08, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30882-3](https://doi.org/10.1016/S1473-3099(20)30882-3)

In this prospective, cross-sectional analysis of educational settings in England that had re-opened after the first national lockdown, SARS-CoV-2 infections and outbreaks were uncommon. Among 55 outbreaks (at least two epidemiologically linked cases, with sequential cases diagnosed within 14 days in the same educational setting), probable direction of transmission was staff-to-staff in 26, staff-to-student in 8, student-to-staff in 16 outbreaks, and student-to-student in 5 outbreaks. The risk of an outbreak increased by 72% (95% CI 28–130) for every five cases per 100.000 population increase in community incidence, emphasizing the importance of controlling community transmission to protect educational settings. Interventions should focus on reducing transmission in and among staff.

See also the comment by Flasche S, Edmunds JW. **The role of schools and school-aged children in SARS-CoV-2 transmission.** *The Lancet Infectious Diseases.* December 8, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30927-0](https://doi.org/10.1016/S1473-3099(20)30927-0)

## Immunology

Fu Y, Li Y, Guo E, et al. **Dynamics and Correlation Among Viral Positivity, Seroconversion, and Disease Severity in COVID-19: A Retrospective Study.** *Ann Intern Med.* 2020 Dec 8. PubMed: <https://pubmed.gov/33284684>. Full-text: <https://doi.org/10.7326/M20-3337>

A huge study on viral kinetics that may enrich our understanding of the various patterns of SARS-CoV-2 positivity and the disease course: In 2142 patients with laboratory-confirmed COVID-19, the viral positivity rate peaked within the first 3 days. The median duration of viral positivity was 24,0 days (95% CI, 18,9 to 29,1 days) in critically ill patients and 18,0 days (CI, 16,8 to 19,1 days) in non-critically ill patients. Being critically ill was an independent risk factor for longer viral positivity. In patients with laboratory-confirmed COVID-19, the IgM-positive rate was 19,3% in the first week, peaked in the fifth week (81,5%), and then decreased steadily to around 55% within 9 to 10 weeks. The IgG-positive rate was 44,6% in the first week, reached 93,3% in the fourth week, and then remained high.

## Vaccine

Voysey M, Clemens SA, Madhi SA, et al. **Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK.** *Lancet* December 08, 2020. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32661-1](https://doi.org/10.1016/S0140-6736(20)32661-1)

60-70% protection: this is what we can probably expect from inactivated vaccines. This important paper describes the first interim safety and efficacy data for a viral vector coronavirus vaccine, ChAdOx1 nCoV-19 (AZD1222, developed at Oxford University), evaluated in four trials across three continents. Between April 23 and Nov 4, 2020, 23,848 participants were recruited and vaccinated: 1077 in COV001 (UK), 10,673 in COV002 (UK), 10,002 in COV003 (Brazil), and 2096 in COV005 (South Africa). The vaccine showed significant vaccine efficacy of 70,4% after two doses and protection of 64,1% after at least one standard dose, against symptomatic disease. Across all four studies, the vaccine had a good safety profile with serious adverse events and adverse events of special interest balanced across the study arms. The efficacy of 90,0% seen in those who received a low dose as prime in the UK by error (COV002, read how this dosing error happened and about the implications) was intriguingly high compared with the other findings in the study. However, this has to be confirmed. Moreover, pre-specified sub-group analyses (elderly, those with comorbidities) were not included in this report. Of note, the ChAdOx1 vaccine can be easily administered in existing healthcare systems (in contrast to mRNA vaccines), stored at ‘fridge temperature’ (2-8 °C) and distributed via existing logistics.

Knoll MD, Wonodi C. **Oxford–AstraZeneca COVID-19 vaccine efficacy.** *Lancet* December 08, 2020. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32623-4](https://doi.org/10.1016/S0140-6736(20)32623-4)

In their comment on the ChAdOx1 paper, Maria Deloria Knoll and Chizoba Wonodi are enthusiastic: “Despite the outstanding questions and challenges in delivering these vaccines, it is hard not to be excited about these findings”. They believe that “perhaps by this time next year, we can celebrate the global control of SARS-CoV-2, in person”. We’ll see.

Pfizer / BioNTech. **Vaccines and Related Biological Products Advisory Committee Meeting December 10, 2020.** FDA submission 2020, published 8 December 2020. PDF: 1) [FDA document](#) – 2) [Sponsor document](#)

On December 10, Pfizer and its partner, the German company BioNTech, will be publicly reviewed by the FDA. Find here two documents (53 and 92 pages, respectively) which go into the details of the Phase III trial on 44.000 volunteers recruited in the United States, Brazil and Argentina. Among the first 170 infected persons, 162 had received the placebo and 8 the vaccine – an effectiveness of 95%. The documents disclose more details about protection after the first vaccine dose as well as the protection of elderly people, obese people and those suffering from co-morbidities. There seem to have been no significant differences between the vaccinees and the placebo group in the few serious complications recorded. However, moderate side effects were recorded after the second injection: headache, fatigue, muscle pain and chills affected up to 50% of the vaccinees, particularly those under 55 years old.

## Clinical

Lazzeroni D, Concari P, Moderato L. **Simultaneous COVID-19 in Homozygous Twins.** *Ann Intern Med.* 2020 Dec 8. PubMed: <https://pubmed.gov/33284682>. Full-text: <https://doi.org/10.7326/L20-1207>

Interesting case report: on 9 March 2020, male twins from Italy who were 60 years old and considered homozygous because of their appearances and other personal characteristics, were diagnosed with SARS-CoV-2 infection (probably transmitted by the same index patient). Despite a similar viral load at diagnosis, both twins had very different clinical courses (one with mild-to-moderate disease, one with critical COVID-19, requiring mechanical ventilation). Bottom line: everyone is unique (even homozygous twins).

## Collateral

Pun KY, Kok AA, Eikelenboom M. **The mental health impact of the COVID-19 pandemic on people with and without depressive, anxiety, or obsessive-compulsive disorders: a longitudinal study of three Dutch case-control cohorts.** *Lancet Psychiatry* December 08, 2020. Full-text: [https://doi.org/10.1016/S2215-0366\(20\)30491-0](https://doi.org/10.1016/S2215-0366(20)30491-0)

Between April 1 and May 13, 2020, online questionnaires were distributed among ongoing cohorts from the Netherlands, including people with (n = 1181) and without (n = 336) depressive, anxiety, or obsessive-compulsive disorders. People without depressive, anxiety, or obsessive-compulsive disorders showed a greater increase in symptoms during the COVID-19 pandemic, whereas individuals with the greatest burden on their mental health tended to show a slight symptom decrease.

## Comorbidities

Trapani S, Masiero L, Puoti F, et al. **Incidence and outcome of SARS-CoV-2 infection on solid organ transplantation recipients: A nationwide population-based study.** Am J Transplant. 2020 Dec 5. PubMed: <https://pubmed.gov/33278850>. Full-text: <https://doi.org/10.1111/ajt.16428>

Registry case data from Italy: the cumulative incidence of SARS-CoV-2 infection in solid organ transplantation recipients (SOTRs) is three times higher than that estimated for the Italian population, highlighting that SOTRs are more at risk of infection than non-SOTRs. The 30- and 60-day cumulative incidence of mortality of COVID+ SOTRs was twice as high when compared to non-SOTRs.

## French

If you read French, read Herzberg N, Aeberhardt C. **Covid-19 : les surprises et les enseignements des essais des vaccins d'AstraZeneca et de Pfizer.** Le Monde 2020, published 9 December. Full-text : [https://www.lemonde.fr/planete/article/2020/12/09/covid-19-les-surprises-et-les-enseignements-des-essais-des-vaccins-d-astrazeneca-et-de-pfizer\\_6062692\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/09/covid-19-les-surprises-et-les-enseignements-des-essais-des-vaccins-d-astrazeneca-et-de-pfizer_6062692_3244.html)

La revue « The Lancet » a publié les résultats complets du laboratoire britannique, tandis que la FDA a rendu publics ceux du groupe américain.

Pineau E. **Vaccins contre le Covid-19 : médecins et scientifiques demandent plus de transparence.** Le Monde 2020, published 9 December. Full-text : [https://www.lemonde.fr/planete/article/2020/12/09/covid-19-medecins-et-scientifiques-demandent-plus-de-transparence-sur-les-etudes-des-vaccins\\_6062691\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/09/covid-19-medecins-et-scientifiques-demandent-plus-de-transparence-sur-les-etudes-des-vaccins_6062691_3244.html)

Des vaccins élaborés en pleine pandémie due au coronavirus, une campagne de vaccination de masse amorcée sans données scientifiques exhaustives... Pour de nombreux spécialistes, la situation est inédite.

## 11 December

### Transmission

Becker AD, Grantz KH, Hegde ST, et al. **Development and dissemination of infectious disease dynamic transmission models during the COVID-19 pandemic: what can we learn from other pathogens and how can we move forward?** Lancet Digital Health 2020, published 7 December. Full-text: [https://doi.org/10.1016/S2589-7500\(20\)30268-5](https://doi.org/10.1016/S2589-7500(20)30268-5)

Transmission models offer a systematic way to investigate transmission dynamics and produce predictions that integrate assumptions about biological, behavioral, and epidemiological processes. These models also generate possible trajectories of disease burden, evaluate the effectiveness of intervention strategies, and estimate key transmission variables. In this review, the authors highlight key aspects of the history of infectious disease dynamic models. Learn more about malaria, HIV/AIDS, measles, rubella, foot and mouth disease and Ebola.

### Immunology

Fajgenbaum DC, June CH. **Cytokine Storm.** N Engl J Med 2020; 383:2255-2273. Full-text: <https://doi.org/10.1056/NEJMra2026131>

David Fajgenbaum and Carl June remind us that 2020 marks 10 years since the first description of a cytokine storm that developed after chimeric antigen receptor (CAR) T cell therapy and 27 years since the term was first used in the literature to describe the engraftment syndrome of acute graft-versus-host disease after allogeneic hematopoietic stem-cell transplantation. Follow them on their suspense-packed narrative. The 19-page review for your weekend.

### Vaccine

Polack FP, Thomas SJ, Kitchin N, et al. **Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine.** N Engl J Med 2020, published 10 December. Full-text: <https://doi.org/10.1056/NEJMoa2034577>

Safety and efficacy findings from the phase 2/3 trial evaluating the safety, immunogenicity, and efficacy of 30 µg of the Pfizer/BioNTech vaccine candidate BNT162b2. A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Reactogenicity was generally mild or moderate, and reactions were less common and milder in older adults than in younger adults. A must-read.



Keech C, Albert G, Cho I, et al. **Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine.** *N Engl J Med* 2020; 383:2320–2332. Full-text: <https://doi.org/10.1056/NEJMoa2026920>

The first Phase I-II results of NVX-CoV2373 (Novavax), a recombinant nanoparticle vaccine. Cheryl Keech et al. evaluated the safety and immunogenicity of the vaccine in 131 adults using 5- $\mu$ g and 25- $\mu$ g doses, with or without Matrix-M1 adjuvant. Reactogenicity was absent or mild in the majority of participants and more common with adjuvant. The addition of adjuvant resulted in enhanced immune responses, was antigen dose-sparing, and induced CD4+ T cell responses that were biased toward a Th1 phenotype. The two-dose 5- $\mu$ g adjuvant regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic COVID-19 patients (8344 and 983, respectively). NVX-CoV2373 is composed of trimeric full-length SARS-CoV-2 spike glycoproteins and a Matrix-M1 adjuvant.

## Clinical

Meyerowitz EA, Richterman A, bogoch I, Low N, Cevik M. **Towards an accurate and systematic characterisation of persistently asymptomatic infection with SARS-CoV-2.** *Lancet Infect Dis* 2020, published 7 December. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30837-9](https://doi.org/10.1016/S1473-3099(20)30837-9)

Transmission of SARS-CoV-2 from individuals without symptoms is a major force driving pandemics. Eric Meyerowith and colleagues describe three methodological issues that hinder attempts to estimate the proportion of asymptomatic or pre-symptomatic individuals. First, incomplete symptom assessment may overestimate the asymptomatic fraction; second, studies with inadequate follow-up misclassify pre-symptomatic individuals; and third, serological studies might identify people with previously unrecognised infection, but reliance on poorly defined antibody responses and retrospective symptom assessment might result in misclassification. Discover the answers to these issues.

## Comorbidities

Fancourt D, Steptoe A, Feifei Bu. **Trajectories of anxiety and depressive symptoms during enforced isolation due to COVID-19 in England: a longitudinal observational study.** *Lancet Psychiatry* 2020, published 9 December. Full-text: [https://doi.org/10.1016/S2215-0366\(20\)30482-X](https://doi.org/10.1016/S2215-0366(20)30482-X)

Several studies suggest that mental health deteriorated in many countries before and during lockdowns. The authors show that the highest levels of depression and anxiety occurred in the early stages of lockdown but declined fairly rapidly, possibly because individuals adapted to circumstances.

FAI2R / SFR / SNFMI / SOFREMIP / CRI / IMIDIATE consortium and contributors. **Severity of COVID-19 and survival in patients with rheumatic and inflammatory diseases: data from the French RMD COVID-19 cohort of 694 patients.** Ann Rheum Dis. 2020 Dec 2:annrheumdis-2020-218310. PubMed: <https://pubmed.gov/33268442>. Full-text: <https://doi.org/10.1136/annrheumdis-2020-218310>

Large French database, including patients with inflammatory rheumatic and musculoskeletal diseases (iRMD). Of 694 adults, 438 (63%) developed mild (not hospitalized), 169 (24%) moderate (hospitalized non-ICU) and 87 (13%) severe (ICU/deceased) disease. In multivariable imputed analyses, the variables associated with severe infection were age, male gender, hypertension and higher BMI. Use of corticosteroids (OR=1.97), mycophenolate mofetil (OR=6.6) and rituximab (OR=4.21) were also risk factors.

## Pediatrics

Millen GC, Arnold R, Cazier JB, et al. **Severity of COVID-19 in children with cancer: Report from the United Kingdom Paediatric Coronavirus Cancer Monitoring Project.** Br J Cancer 2020, published 10 December. Full-text: <https://doi.org/10.1038/s41416-020-01181-0>

Children with cancer with SARS-CoV-2 infection do not appear at increased risk of severe infection compared to the general pediatric population. This is reassuring result of a retrospective and prospective observational study of all children in the UK under 16 diagnosed with cancer. Between 12 March 2020 and 31 July 2020, Gerard Millen et al identified 54 cases: 15 (28%) were asymptomatic, 34 (63%) had mild infections and 5 (10%) moderate, severe or critical infections. No patients died and only three patients required intensive care support due to COVID-19. The estimated incidence of hospital identified SARS-CoV-2 infection in children with cancer under 16 was 3%.

## Collateral Effects

Mackie SL, Brouwer E, Conway R, et al. **Clinical pathways for patients with giant cell arteritis during the COVID-19 pandemic: an international perspective.** Lancet Rheumatol 2020, published 8 December. Full-text: ???

Giant cell arteritis, a common primary systemic vasculitis affecting older people, presents acutely as a medical emergency and requires rapid specialist assessment and treatment to prevent irreversible vision loss. The authors show that during the COVID-19 pandemic, patients might be involved in the reshaping of clinical services.

## Education

Rubin EJ, Baden LR, Barocas JA, Morrissey S. **SARS-CoV-2 Vaccination and Vulnerable Populations**. Audio interview (39:49). N Engl J Med 2020; 383: e143. Access: <https://doi.org/10.1056/NEJMe2034906>

The editors discuss who should be first in line as COVID-19 vaccines are rolled out.

## Spanish

If you read Spanish, read Agudo A. **Choque entre el norte y el sur por las patentes covid-19**. El País 2020, published 10 December. Full-text: <https://elpais.com/planeta-futuro/2020-12-10/choque-entre-el-norte-y-el-sur-por-las-patentes-covid-19.html>

India y Sudáfrica lideran una petición ante la Organización Mundial del Comercio para que se suspenda temporalmente la propiedad intelectual sobre tecnologías, medicamentos y vacunas contra el nuevo coronavirus mientras dure la pandemia; 99 países les apoyan, el mundo rico se resiste

## French

If you read French, read Illouz E. « **Croire à la science ou pas est devenu une question éminemment politique, sans doute celle qui va décider de l'avenir du monde** » - Le Monde 2020, published 10 December. Full-text: [https://www.lemonde.fr/idees/article/2020/12/10/eva-illouz-croire-a-la-science-ou-pas-est-devenu-une-question-eminemment-politique-sans-doute-celle-qui-va-decider-de-l-avenir-du-monde\\_6062819\\_3232.html](https://www.lemonde.fr/idees/article/2020/12/10/eva-illouz-croire-a-la-science-ou-pas-est-devenu-une-question-eminemment-politique-sans-doute-celle-qui-va-decider-de-l-avenir-du-monde_6062819_3232.html)

La sociologue Eva Illouz retrace l'histoire du complotisme et analyse les causes profondes de l'importance qu'il a prise cette dernière décennie, jusqu'à remettre en question « le pari que les démocraties ont fait sur la liberté d'expression et sur la force de la vérité ».

## German

If you read German, read Fischer S. **Wir haben uns den Lockdown redlich verdient.** Der Spiegel 2020, published 10 December. Full-text: <https://www.spiegel.de/politik/deutschland/corona-wir-haben-uns-den-lockdown-redlich-verdient-kommentar-a-41252d4b-baf8-4d11-bd07-ae97312803a0>

Zu hohe Infektionszahlen, zu viele Tote – und jeder Tag zählt. Eigentlich müssten wir sofort das öffentliche Leben herunterfahren. Aber jetzt soll erst mal das Weihnachtsgeschäft laufen, und dann sehen wir weiter: in den Abgrund.

## 12 December

### Epidemiology

Amendola A, Bianchi S, Gori M, Colzani D, Canuti M, Borghi E, et al. **Evidence of SARS-CoV-2 RNA in an oropharyngeal swab specimen, Milan, Italy, early December 2019.** Emerg Infect Dis 2020, published 8 December. Full-text: <https://doi.org/10.3201/eid2702.204632>

Elisabetta Tanzi, Antonella Amendola and colleagues from the University of Milan identified SARS-CoV-2 RNA in an oropharyngeal swab specimen collected from a child with suspected measles in early December 2019, more than two months before the first identified SARS-CoV-2 case in Italy. The authors cautiously conclude that “long-term, unrecognized spread of SARS-CoV-2 in northern Italy would help explain, at least in part, the devastating impact and rapid course of the first wave of COVID-19 in Lombardy.”

Pouwels KB, House T, Pritchard E, et al. **Community prevalence of SARS-CoV-2 in England from April to November, 2020: results from the ONS Coronavirus Infection Survey.** Lancet Public Health 2020, published 10 December. Full-text: [https://doi.org/10.1016/S2468-2667\(20\)30282-6](https://doi.org/10.1016/S2468-2667(20)30282-6)

Seroprevalence for SARS-CoV-2 continues to be low in England. After randomly collecting samples from individuals aged 2 years and older living in private households in England, the percentage of people testing positive for SARS-CoV-2 initially decreased between April 26 and June 28, 2020, from 0.40% to 0.06%, followed by low levels during July and August, 2020, before substantially increasing at the end of August, 2020, with percentages testing positive above 1% from the end of October, 2020. Age (young adults, particularly those aged 17–24 years) was an important initial driver in the second

wave. For example, the estimated percentage of individuals testing positive was more than six times higher in those aged 17–24 years than in those aged 70 years or older at the end of September, 2020. More than half of infections were in asymptomatic individuals.

## Prevention

Siva N. **Experts call to include prisons in COVID-19 vaccine plans.** *Lancet* 2020, published 12 December. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32663-5](https://doi.org/10.1016/S0140-6736(20)32663-5)

In any given week more than 200,000 people are booked into jails across the USA, and the same number leave each week. US prisons are SARS-CoV-2 hubs, says the author, “people go to court, go back to their prison, and often people get moved to another prison once they have been sentenced.” Consider prisoners an important group in vaccine prioritization.

## Vaccine

Rubin EJ, Longo DL. **SARS-CoV-2 Vaccination — An Ounce (Actually, Much Less) of Prevention** (Editorial). *N Engl J Med* 2020, published 10 December. Full-text: <https://doi.org/10.1056/NEJMe2034717>

Before December 2020, no existing vaccines had been shown to be effective against infection with any beta-coronavirus; strategies to increase the speed of vaccine development had never been tested; and no vaccines based on mRNA technologies had yet been approved. Now, with the paper by [Polack et al.](#) that we presented yesterday, all this has been done and the NEJM editors qualify it as a triumph that holds the promise of saving uncounted lives. Rightly, they continue questioning: “Will unexpected safety issues arise when the number grows to millions and possibly billions of people? Will side effects emerge with longer follow-up? Implementing a vaccine that requires two doses is challenging. What happens to the inevitable large number of recipients who miss their second dose? How long will the vaccine remain effective? Does the vaccine prevent asymptomatic disease and limit transmission? And what about the groups of people who were not represented in this trial, such as children, pregnant women, and immunocompromised patients of various sorts?” The story will continue...

Singh JA, Upshur EG. **The granting of emergency use designation to COVID-19 candidate vaccines: implications for COVID-19 vaccine trials.** *Lancet Infect Dis* 2020, published 8 December. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30923-3](https://doi.org/10.1016/S1473-3099(20)30923-3)

In the next weeks, SARS-CoV-2 candidate vaccines will be granted emergency use authorizations after only months of clinical experience. The authors caution that emergency use designations could inadvertently threaten ongoing vaccine research that is yet to define immunological correlates of protection against COVID-19, which could vary according to the vaccine platform, individual characteristics, age groups, and population subset.

## Diagnostics

Topol EJ. **Is my cough COVID-19?** *Lancet* 2020, published 12 December. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32589-7](https://doi.org/10.1016/S0140-6736(20)32589-7)

Imagine that even if you have no symptoms of COVID-19, the sound of your forced cough transmitted to your smartphone or smart speaker then processed by an algorithm, could provide a 98.5% accurate diagnosis. Here, Eric Topol describes this science fiction scenario while commenting on a study by Laguarda et al. [Laguarda J, Hueto F, Subirana B. **Covid-19 artificial intelligence diagnosis using only cough recordings.** *IEEE Open J Eng Med Biol* 2020, published 29 September. Full-text: <https://doi.org/10.1109/OJEMB.2020.3026928>], who trained their MIT Open Voice model and built a data collection pipeline of COVID-19 cough recordings through their website ([opensigma.mit.edu](https://opensigma.mit.edu)) between April and May 2020 and created the largest audio COVID-19 cough dataset reported to date with 5320 subjects. Result: COVID-19 sensitivity of 98.5% with a specificity of 94.2% (AUC: 0.97). For asymptomatic subjects it achieves sensitivity of 100% with a specificity of 83.2%.

## Pediatrics

Young TK, Shaw KS, Shah JK, et al. **Mucocutaneous Manifestations of Multi-system Inflammatory Syndrome in Children During the COVID-19 Pandemic.** *JAMA Dermatol* 2020, published 9 December. Full-text: <https://doi.org/10.1001/jamadermatol.2020.4779>

In this case series of 25 hospitalized children (11 girls [44%]; median age, 3 years [range, 0.7-17 years]) with suspected MIS-C during the COVID-19 pandemic, Vikash Oza, Trevor Young and colleagues identify a wide spectrum of

mucocutaneous findings. Although protean and transient in nature, these mucocutaneous features serve as important clues in the recognition of MIS-C.

Ronchi A, Pietrasanta C, Zavattoni M, et al. **Evaluation of Rooming-in Practice for Neonates Born to Mothers With Severe Acute Respiratory Syndrome Coronavirus 2 Infection in Italy.** *JAMA Pediatr* 2020, published 7 December. Full-text: <https://doi.org/10.1001/jamapediatrics.2020.5086>

See also the comment by Kaufman DA, Puopolo M. **Infants Born to Mothers With COVID-19—Making Room for Rooming-in.** *JAMA Pediatr* 2020, published 7 December. Full-text: <https://doi.org/10.1001/jamapediatrics.2020.5100>

### Collateral Effects

Kapur N, Clements C, Appleby L, et al. **Impact of the Covid-19 pandemic on the frequency of primary care-recorded mental illness and self-harm episodes in the UK: population-based cohort study of 14 million individuals.** *Lancet Psychiatry* 2020, published 10 December. Full-text: [https://doi.org/10.1016/S2215-0366\(20\)30528-9](https://doi.org/10.1016/S2215-0366(20)30528-9)

Self-harm often precedes suicide and can be used as a proxy outcome to identify how the pandemic has affected population mental health. As yet, there is no indication that the pandemic has caused self-harm rates to increase in the UK. The authors cite a study of 1500 general practices in the UK which found that the recorded incidence of self-harm was 38% lower in April, 2020, than the rate expected on the basis of previous years (Carr MJ, Steeg S, Webb RT, et al). Primary care contact for mental illness and self-harm before, during and after the peak of the COVID-19 pandemic in the UK: cohort study of 13 million individuals. *Lancet Public Health* (in press)). This decrease was particularly marked in women, people younger than 45 years, and those from the most deprived quintile of practices.

### Press

Nogrady B. **How kids' immune systems can evade COVID.** *Nature* 2020, published 10 December. Full-text: <https://www.nature.com/articles/d41586-020-03496-7#ref-CR1>

Young children account for only a small percentage of COVID-19 infections. Kids' immune systems might simply be better equipped to eliminate SARS-CoV-2 than those of adults.

## Spanish

If you read Spanish, read Guimón P. **Estados Unidos, a un paso de empezar la vacunación masiva contra la covid.** El País 2020, published 11 December. Full-text: <https://elpais.com/sociedad/2020-12-10/estados-unidos-a-un-paso-de-empezar-la-vacunacion-masiva-contra-la-covid.html>

El panel de expertos de la FDA recomienda la autorización del uso de emergencia de la vacuna de Pfizer-BioNTech, que se espera se realice en las próximas horas o días.

## French

If you read French, read **Covid-19 : le vaccin de Sanofi et GSK ne sera prêt qu'à la fin de 2021.** Le Monde, published 11 December. Full-text : [https://www.lemonde.fr/planete/article/2020/12/11/covid-19-le-vaccin-de-sanofi-et-gsk-ne-sera-pret-qu-a-la-fin-de-2021\\_6062993\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/11/covid-19-le-vaccin-de-sanofi-et-gsk-ne-sera-pret-qu-a-la-fin-de-2021_6062993_3244.html)

Ce retard est dû à une réponse immunitaire insuffisante chez l'adulte. La disponibilité du vaccin est désormais attendue au quatrième trimestre 2021 si le plan de développement est terminé avec succès.

## German

If you read German, read Schumann F, Simmank J. **"Es gibt keinen Druck für das Virus, tödlicher zu werden"** – Die Zeit 2020, published 10 December. Full-text: <https://www.zeit.de/wissen/gesundheit/2020-12/emma-hodcroft-richard-neher-coronavirus-mutation-erbgut>

Emma Hodcroft und Richard Neher verfolgen, wie Sars-CoV-2 mutiert. Im Virus-Erbgut lesen sie, wie gefährlich es wird, wo es herkam und warum es kaum verschwinden wird.

## 13 December

### Epidemiology

Buss LF, Prete Jr A, Abraham CMM, et al. **Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic.** Science 2020, published 8 December. Full-text: <https://doi.org/10.1126/science.abe9728>



Brazil has experienced one of the world's most rapidly-growing COVID-19 epidemics, with the Amazon being the worst hit region. Here, Ester Sabino, Nuno Faria, Lewis Buss and colleagues show that one month after the epidemic peak in **Manaus**, capital of Amazonas state, 44% of the population had detectable IgG antibodies. Correcting for cases without a detectable antibody response and antibody waning, the authors estimate a 66% attack rate in June, rising to 76% in October. The authors conclude that when poorly controlled, COVID-19 can infect a high fraction of the population causing high mortality.

Geoghegan JL, Ren X, Storey M, et al. **Genomic epidemiology reveals transmission patterns and dynamics of SARS-CoV-2 in Aotearoa New Zealand.** Nat Commun 11, 6351 (2020). Full-text: <https://doi.org/10.1038/s41467-020-20235-8>

New Zealand is one of a handful of countries that aimed to eliminate coronavirus disease 19 (COVID-19). Here, Jemma L. Geoghegan generated 649 SARS-CoV-2 genome sequences from infected patients with samples collected during the 'first wave', representing 56% of all confirmed cases in this time period. The authors found that only 19% of virus introductions into New Zealand resulted in ongoing transmission of more than one additional case. They conclude that ongoing genomic surveillance should be an integral part of the national response to monitor any re-emergence of the virus, particularly when border restrictions might eventually be eased.

## Transmission

Lemieux JE, Siddle KJ, Shaw BM, et al. **Phylogenetic analysis of SARS-CoV-2 in Boston highlights the impact of superspreading events.** Science 2020, published 10 December. Full-text: <https://doi.org/10.1126/science.abe3261>

Understanding the role of superspreading events in transmission is critical for prioritizing public health interventions. Here, Jacob Lemieux et al. report the analysis of 772 complete SARS-CoV-2 genomes from early in the Boston area epidemic. They found numerous introductions of the virus, a small number of which led to most cases. Find more about two superspreading events in a skilled nursing facility and at an international business conference and varying transmission dynamics in superspreading events.

## Clinical

Soltan ASS, Kouchaki S, Zhu T, et al. **Rapid triage for COVID-19 using routine clinical data for patients attending hospital: development and prospective validation of an artificial intelligence screening test.** *Lancet Digital Health* 2020, published 11 December. Full-text: [https://doi.org/10.1016/S2589-7500\(20\)30274-0](https://doi.org/10.1016/S2589-7500(20)30274-0)

The early clinical course of COVID-19 can be difficult to distinguish from other illnesses driving presentation to hospital and PCR testing can take up to 72 h. Here, David Clifton, Andrew Soltan and colleagues from Radcliffe, Oxford, trained linear and non-linear machine learning classifiers to distinguish patients with COVID-19 from pre-pandemic controls. Their models excluded COVID-19 with high-confidence by use of clinical data routinely available within 1 h of presentation to hospital. The authors suggest that their approach could be rapidly scalable, fitting within the existing laboratory testing infrastructure and standard of care of hospitals in high-income and middle-income countries.

## Treatment

Kalil A, Patterson TF, Mehta AK, et al. **Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19.** *N Engl J Med* 2020, published 11 December. Full-text: <https://doi.org/10.1056/NEJMoa2031994>

Baricitinib plus remdesivir was superior to remdesivir alone in reducing recovery time and accelerating improvement in clinical status among hospitalized adults with COVID-19, notably among those receiving high-flow oxygen or noninvasive ventilation. This is the result of double-blind, randomized, placebo-controlled trial involving 1033 patients. The 216 patients receiving high-flow oxygen or noninvasive ventilation at enrollment had a time to recovery of 10 days with combination treatment (n=103) and 18 days with control (n=103) (rate ratio for recovery, 1.51; 95% CI, 1.10 to 2.08). The 28-day mortality was 5.1% in the combination group and 7.8% in the control group (hazard ratio for death, 0.65; 95% CI, 0.39 to 1.09). We still need better drugs.

**An EUA for Bamlanivimab—A Monoclonal Antibody for COVID-19.** *JAMA* 2020, published 11 December. Full-text: <https://doi.org/10.1001/jama.2020.24415>

JAMA published a *Medical Letter* about the investigational neutralizing IgG1 monoclonal antibody bamlanivimab (LY-CoV555; Lilly) which has been granted an FDA Emergency Use Authorization (EUA) for treatment of recently di-

agnosed mild to moderate COVID-19 in patients who are  $\geq 12$  years old, weigh at least 40 kg, and are at high risk for progressing to severe disease and/or hospitalization. See also the FDA fact sheet of bamlanivimab at <https://www.fda.gov/media/143603/download>.

### Comorbidities

Bhaskaran K, Rentsch CT, MacKenna B, et al. **HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform.** *Lancet HIV* 2020, published 11 December. Full-text: [https://doi.org/10.1016/S2352-3018\(20\)30305-2](https://doi.org/10.1016/S2352-3018(20)30305-2)

Should people with HIV in the UK be at increased risk of COVID-19 mortality? This would be the suggestion of a retrospective cohort study by Ben Goldacre, Krishnan Bhaskaran and colleagues who analyzed the data of 17 282 905 adults, of whom 27 480 (0.16%) had HIV recorded. 14,882 COVID-19 deaths occurred during the study period, with 25 among people with HIV. People living with HIV had higher risk of COVID-19 death than those without HIV after adjusting for age and sex: hazard ratio (HR) 2.90 (95% CI 1.96–4.30;  $p < 0.0001$ ). In a comment, Laura Waters and Anton Pozniak urge for caution in interpreting the results of this study. (Waters LJ, Pozniak AL. **COVID-19 death in people with HIV: interpret cautiously.** *Lancet HIV* 2020, published 11 December. Full-text: [https://doi.org/10.1016/S2352-3018\(20\)30332-5](https://doi.org/10.1016/S2352-3018(20)30332-5).) They emphasize a low absolute mortality of less than 0.1% and recall that 23 (92%) of 25 people with HIV who died had comorbidities.

### Pediatrics

O'Leary ST, Trefren L, Roth H, et al. **Number of Childhood and Adolescent Vaccinations Administered Before and After the COVID-19 Outbreak in Colorado.** *JAMA Pediatr* 2020, published 7 December. Full-text: <https://doi.org/10.1001/jamapediatrics.2020.4733>

As a consequence of the social distancing measures, medical visits to primary care physicians have dropped, including preventive visits and scheduled vaccinations. In Colorado, after March 15 (weeks 12-18), the mean immunization rate dropped 31% for individuals aged 0 to 2 years, 78% for those aged 3 to 9 years, and 82% for those aged 10 to 17 years.

## Beyond Corona

Marshall M. **How the first life on Earth survived its biggest threat — water.** Nature 2020, published 9 December. Full-text: <https://www.nature.com/articles/d41586-020-03461-4>

Living things depend on water, but it breaks down DNA and other key molecules. So how did the earliest cells deal with the water paradox? In this *News Feature*, Michael Marshall goes back to the beginning of life. Listen also to the Nature podcast at 00:46: **A shallow start to life on Earth?** – <https://www.nature.com/articles/d41586-020-03512-w> | It's long been thought that life on Earth first appeared in the oceans. However, the chemical complexities involved in creating biopolymers in water has led some scientists to speculate that shallow pools on land were actually the most likely location for early life.

## 14 December

### Prevention

Brainard J, Jones NR, Lake IR, Hooper L, Hunter PR. **Community use of face masks and similar barriers to prevent respiratory illness such as COVID-19: a rapid scoping review.** Euro Surveill. 2020 Dec;25(49):2000725. PubMed: <https://pubmed.gov/33303066>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.49.2000725>

Everything You Always Wanted to Know About Face Masks\* (\*But Were Afraid to Ask). Does wearing face masks reduce primary respiratory infection risk by only 6–15%? See also the comment by Cowling BJ, Leung GM. **Face masks and COVID-19: don't let perfect be the enemy of good.** Euro Surveill. 2020 Dec;25(49):2001998. PubMed: <https://pubmed.gov/33303063>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.49.2001998>

Pavelka M, Van-Zandvoort K, Abbott S, et al. **The effectiveness of population-wide, rapid antigen test based screening in reducing SARS-CoV-2 infection prevalence in Slovakia.** medRxiv 2020, posted 4 December. Full-text: <https://doi.org/10.1101/2020.12.02.20240648>

On 31 October, Slovakia deployed around 20 thousand medical staff and 40 thousand non-medical personnel to administer up to 4 million SARS-CoV-2 tests in 2 days. Here the authors report the results of the mass testing where rapid antigen tests were used to screen the whole population and to isolate infectious cases together with their household members. Prevalence of de-

tected infections decreased by 58% (95% CI: 57-58%) within one week in the 45 counties that took part in two rounds of mass testing. See also the comments at <https://www.sciencemediacentre.org/expert-reaction-to-a-pre-print-looking-at-population-wide-rapid-antigen-testing-for-sars-cov-2-in-slovakia/>

## Immunology

Guthmiller JJ, Wilson PC. **Remembering seasonal coronaviruses.** Science. 2020 Dec 11;370(6522):1272-1273. PubMed: <https://pubmed.gov/33303605>. Full-text: <https://doi.org/10.1126/science.abf4860>

In November, two groups (Shrock 2020 and Ng 2020; we presented the papers on 30 September and 9 November) showed that individuals exposed and unexposed to SARS-CoV-2 have cross-reactive serum antibodies against the spike protein of SARS-CoV-2 and seasonal HCoVs. Jenna Guthmiller and Patrick Wilson discuss the studies more in depth. They conclude by highlighting the need for further research into how SARS-CoV-2 antibody responses are shaped by previous exposures to seasonal HCoVs and how this immunity can be harnessed to provide protection.

The papers cited above: 1) Ng KW, Faulkner N, Cornish GH, et al. **Preexisting and de novo humoral immunity to SARS-CoV-2 in humans.** Science 06 Nov 2020. Full-text: <https://doi.org/10.1126/science.abe1107> – 2) Shrock E, Fujimura E, Kula T, et al. **Viral epitope profiling of COVID-19 patients reveals cross-reactivity and correlates of severity.** Science 29 Sep 2020. Full-text: <https://doi.org/10.1126/science.abd4250>

## Pathogenesis

Hennessy EJ, FitzGerald GA. **Battle for supremacy: nucleic acid interactions between viruses and cells.** J Clin Invest. 2020 Dec 8;144227. PubMed: <https://pubmed.gov/33290272>. Full-text: <https://doi.org/10.1172/JCI144227>

The variability in the clinical response to infection with SARS-CoV-2 reflects differences in host genetics and/or immune response. In this review, Elizabeth Hennessy and Garret FitzGerald examine the influence of viruses on the host epigenome and consider how variation in the epigenome may contribute to heterogeneity in the response to SARS-CoV-2.

## Vaccine

Noval Rivas M, Ebinger JE, Wu M, et al. **BCG vaccination history associates with decreased SARS-CoV-2 seroprevalence across a diverse cohort of healthcare workers.** J Clin Invest. 2020 Nov 19:145157. PubMed: <https://pubmed.gov/33211672>. Full-text: <https://doi.org/10.1172/JCI145157>

A history of BCG vaccination was associated with decreased seroprevalence of anti-SARS-CoV-2 IgG and reduced reported COVID-19-related clinical symptoms in a cohort of healthcare workers in Los Angeles. Of the 6201 HCWs, 29,6% reported a history of BCG vaccination whereas 68,9% did not receive BCG vaccination. Seroprevalence of anti-SARS-CoV-2 IgG as well as incidence of self-reported clinical symptoms associated with COVID-19 were significantly decreased among HCWs with a history of BCG vaccination compared to those without BCG vaccination.

See also the comment by Netea MG, van der Meer JW, van Crevel R. **BCG vaccination in healthcare providers and the protection against COVID-19.** J Clin Invest. 2020 Dec 11:145545. PubMed: <https://pubmed.gov/33306484>. Full-text: <https://doi.org/10.1172/JCI145545>

## Comorbidities

Lee SC, Son KJ, Han CH, et al. **Impact of comorbid asthma on severity of coronavirus disease (COVID-19).** Sci Rep 10, 21805 (2020). Full-text: <https://doi.org/10.1038/s41598-020-77791-8>

Asthma may not be a risk factor for poor prognosis of COVID-19. In a nationwide retrospective cohort study, Seon Cheol Park, Sang Chul Lee and colleagues from South Korea selected 7272 adult COVID-19 patients, 686 of whom had a history of asthma. After adjusting for age, sex, and the Charlson comorbidity score, asthma was not a significant risk factor for respiratory failure or mortality among all COVID-19 patients (odds ratio [OR] = 0,99,  $p = 0,997$  and OR = 1,06,  $p = 0,759$ ). Only a history of acute exacerbation in the previous year before COVID-19 was a significant risk factors for death (OR = 2,63,  $P = 0,043$ ).

Culha MG, Demir O, Sahin O, et al. **Sexual attitudes of healthcare professionals during the COVID-19 outbreak.** Int J Impot Res 2020. Full-text: <https://doi.org/10.1038/s41443-020-00381-9>

Sporadic episodes of sexual dysfunction? Don't worry, it's COVID. The reassuring news has just been published by Mehmet Gökhan Çulha and colleagues in a short summary of an online survey among 185 healthcare professionals. Sexual desire, weekly sexual intercourse/masturbation number, foreplay

time, sexual intercourse time – everything decreased. When factors affecting sexual dysfunction were analyzed as univariate and multivariate, sexual dysfunction was shown to be significantly more common in males and alcohol users. Time to put the bottle aside and get vaccinated.

Colombier S, Mahendiran T, Niclauss L, Kirsch M. **Cardiac arrest and COVID-19: inflammation, angiotensin-converting enzyme 2, and the destabilization of non-significant coronary artery disease—a case report.** *European Heart Journal* 2020, published 12 December. Full-text: <https://doi.org/10.1093/ehjcr/ytaa475>

The authors describe the case of a 60-year-old COVID-19 patient whose inaugural presentation was a refractory cardiac arrest secondary to the destabilization of known, non-significant coronary artery disease. This case illustrates several potential mechanisms that are thought to drive the cardiac complications seen in COVID-19.

Diller GP, Gatzoulis MA, Broberg CS, et al. **Coronavirus disease 2019 in adults with congenital heart disease: a position paper from the ESC working group of adult congenital heart disease, and the International Society for Adult Congenital Heart Disease.** *Eur Heart J* 2020, published 12 December. Full-text: <https://doi.org/10.1093/eurheartj/ehaa960>

In this position paper, the authors discuss the impact of COVID-19 on ACHD patients, focusing on pathophysiology, risk stratification for work, self-isolation, hospitalization, impact on pregnancy, psychosocial health, and longer-term implications for the provision of ACHD care.

Palumbo MV, Rambur B, McKenna LP. **Living at Home with Dementia Now More Complicated with COVID-19.** *Health Social Work* 2020, published 13 December. Full-text: <https://doi.org/10.1093/hsw/hlaa029>

Living at home with dementia is complicated, even more so during the SARS-CoV-2 pandemic. In this article Mary Val Palumbo, Betty Rambur and Lori P McKenna describe that unpredictability is heightened; that grief associated with dementia progression because of relationship changes, loss of emotional support, decreased financial support, increased dependency, and loss of future plans has intensified; and that fear of contracting the virus has exacerbated stress for single, largely homebound family caregivers.

## Spanish

If you read Spanish, read Salas J, Zafra M. **Cómo frenar al coronavirus en Navidad.** El País 2020, published 13 December. Full-text: <https://elpais.com/ciencia/2020-12-12/como-reducir-riesgos-en-navidad.html>

Estas fiestas serán peligrosas y se espera que aumenten los contagios por COVID. Pero hay alternativas para minimizar los problemas que pueden surgir en cada situación. Piense bien su celebración y aplique las restricciones que le proponemos.

Estefanía J. **La vacuna, bien público global.** El País 2020, published 11 December. Full-text: <https://elpais.com/ideas/2020-12-11/la-vacuna-bien-publico-global.html>

Sería mejor vacunar en paralelo en todos los países que hacerlo en función de su riqueza.

## German

If you read German, read Simmank J, Schumann F, Fischer L. **Die USA haben eine Impfung – was kann sie?** Die Zeit 2020, published 12 December. Full-text: <https://www.zeit.de/wissen/gesundheit/2020-12/corona-impfstoff-biontech-usa-wirksamkeit-nebenwirkungen-europa-faq>

Die erste Impfung gegen Covid-19 wird in den USA zugelassen. Wie funktioniert sie, was wissen wir bisher über Wirksamkeit und Nebenwirkungen – und wann folgt Europa?

## 15 December

### Epidemiology

**Tracking the Coronavirus at U.S. Colleges and Universities.** The New York Times 2020, published 11 December. Full-text: <https://www.nytimes.com/interactive/2020/us/covid-college-cases-tracker.html>



Harmon A. **Superspreading Boston biotech conference in February is linked to 1.9 percent of all U.S. cases.** The New York Times 2020, published 11 December. Full-text:

<https://www.nytimes.com/2020/12/11/world/superspreading-boston-biotech-conference-in-february-is-linked-to-1-9-percent-of-all-us-cases.html>

A short summary of the study by Lemieux JE et al. we presented two days ago (Lemieux JE, Siddle KJ, Shaw BM, et al. **Phylogenetic analysis of SARS-CoV-2 in Boston highlights the impact of superspreading events.** Science 2020, published 10 December. Full-text: <https://doi.org/10.1126/science.abe3261>). As many as 300.000 coronavirus cases across the United States can be traced to a two-day conference in Boston convened by the drug company Biogen.

## Virology

Swann H, Sharma H, Preece B, et al. **Minimal system for assembly of SARS-CoV-2 virus like particles.** Sci Rep 10, 21877 (2020). Full-text: <https://doi.org/10.1038/s41598-020-78656-w>

Non-infectious virus-like particles (VLPs) displaying essential viral proteins can be used to study the structural properties of the SARS-CoV-2 virions and because of their maximum immunogenicity are also vaccine candidates. Here, Saveez Saffarian, Heather Swann and colleagues demonstrate that non-infectious SARS-CoV-2 virus-like particles (VLPs) can be assembled by co-expressing the viral proteins S, M and E in mammalian cells.

## Pathogenesis

Hernández Cordero AI, Li X, Yang CX, et al. **Gene expression network analysis provides potential targets against SARS-CoV-2.** Sci Rep 10, 21863 (2020). Full-text: <https://doi.org/10.1038/s41598-020-78818-w>

Cell entry of SARS-CoV-2 is facilitated by host cell angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2). Here, the authors show that dozens of genes are co-expressed with ACE2 and TMPRSS2, many of which have plausible links to COVID-19 pathophysiology and might potentially be targetable with existing drugs.

## Vaccine

Oliver S, Gargano J, Marin M, et al. **The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine — United States, December 2020.** *MMWR Morb Mortal Wkly Rep.* ePub: 13 December 2020. Full-text: <http://dx.doi.org/10.15585/mmwr.mm6950e2>

On December 12, 2020, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Pfizer-BioNTech COVID-19 vaccine in persons aged  $\geq 16$  years for the prevention of COVID-19. Mass vaccinations in the US started two days later.

## Diagnostics

Lean FZX, Lamers MM, Smith SP, et al. **Development of immunohistochemistry and in situ hybridisation for the detection of SARS-CoV and SARS-CoV-2 in formalin-fixed paraffin-embedded specimens.** *Sci Rep* 10, 21894 (2020). Full-text: <https://doi.org/10.1038/s41598-020-78949-0>

Have you ever needed to detect SARS-CoV and SARS-CoV-2 viral products in formalin-fixed paraffin-embedded (FFPE) specimens? Fabian Lean and colleagues show you how. The authors conclude that the diverse techniques for virus detection and control material generation could be applied to investigations of coronavirus pathogenesis and therapeutic research in animal models.

## Genetics

Berber B, Aydin C, Kocabas F, et al. **Gene editing and RNAi approaches for COVID-19 diagnostics and therapeutics.** *Gene Ther* (2020). Full-text: <https://doi.org/10.1038/s41434-020-00209-7>

RNA interference (RNAi) mechanism has been used for the silencing of genes that are related to cancer, viral infections, and autoimmune diseases. In this review, Cihan Tastan, Burak Berber and colleagues discuss molecular biology approaches that could revolutionize the diagnostics of viral infections and therapies to fight COVID-19 in a highly specific, stable, and efficient way.

## Treatment

Buckland MS, Galloway JB, Fhogartaigh CN, et al. **Treatment of COVID-19 with remdesivir in the absence of humoral immunity: a case report.** *Nat Commun* 11, 6385 (2020). <https://doi.org/10.1038/s41467-020-19761-2>

The authors report the case of a patient with COVID-19 and the prototypic genetic antibody deficiency X-linked agammaglobulinemia (XLA). The patient developed persistent SARS-CoV-2 pneumonitis, without progressing to multi-organ involvement. Over two independent courses of treatment, the authors observed a temporally correlated clinical and virologic response, leading to clinical resolution and viral clearance.

## Comorbidities

Keddi S, Pakpoor J, Mouselé C, et al. **Epidemiological and cohort study finds no association between COVID-19 and Guillain-Barré syndrome.** *Brain* 2020, published 14 December. Full-text: <https://doi.org/10.1093/brain/awaa433>

Some reports of Guillain-Barré syndrome (GBS) have emerged during the coronavirus disease 2019 (COVID-19) pandemic. Here, Michael Lunn, Stephen Keddie and colleagues from University College London Hospitals NHS Foundation Trust studied the epidemiology of GBS cases reported to the UK National Immunoglobulin Database from 2016 to 2019 and compared it to cases reported during the COVID-19 pandemic. The result: GBS incidence has fallen during the pandemic, which may be the influence of lockdown measures reducing transmission of GBS inducing pathogens such as *Campylobacter jejuni* and respiratory viruses.

## Collateral Effects

Ma X, Guan C, Chen R, et al. **Pathological and molecular examinations of postmortem testis biopsies reveal SARS-CoV-2 infection in the testis and spermatogenesis damage in COVID-19 patients.** *Cell Mol Immunol* (2020). Full-text: <https://doi.org/10.1038/s41423-020-00604-5>

Yesterday, we reported about sexual desire, weekly sexual intercourse/masturbation number, foreplay time, and sexual intercourse which might be somewhat decreased in COVID times (see <https://covidreference.com/top-10-december-14>). Now Shuiqiao Yuan, Xixiang Ma and colleagues from Huazhong University of Science and Technology, Wuhan, evaluated the effects of SARS-CoV-2 infection on spermatogenesis by examining the pathophysiology and molecular features of testes obtained from five male COVID-19 patients at autopsy. Their findings might provide evidence that SARS-CoV-2 can infect the testis and germ cells, indicating the potential impact of the COVID-19 pandemic on spermatogenesis and male fertility.

## Spanish

If you read Spanish, read Camarero A. **Las medidas anticovid en los colegios reducen los casos de bronquiolitis o catarros y la incidencia de piojos en los niños.** El País 2020, published 14 December. Full-text: <https://elpais.com/mamas-papas/2020-12-14/las-medidas-anticovid-en-los-colegios-reducen-los-casos-de-bronquiolitis-o-catarros-y-la-incidencia-de-piojos-en-los-ninos.html>

Mantener la distancia de seguridad y el uso de la mascarilla están produciendo un efecto beneficioso en las aulas. Los expertos destacan que se está registrando un descenso en el número de consultas pediátricas.

## French

If you read French, read Hecketsweiler C. **La deuxième vague de Covid-19 vue de l'hôpital Bichat : « Ils sont totalement à plat dans leur lit, c'est frappant »** – Le Monde 2020, published 14 December. Full-text: [https://www.lemonde.fr/planete/article/2020/12/14/la-deuxieme-vague-de-covid-19-vue-de-l-hopital-bichat-ils-sont-totalement-a-plat-dans-leurs-lits-c-est-frappant\\_6063271\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/14/la-deuxieme-vague-de-covid-19-vue-de-l-hopital-bichat-ils-sont-totalement-a-plat-dans-leurs-lits-c-est-frappant_6063271_3244.html)

Dans le service de gériatrie, douze lits sont réservés aux patients touchés par le Covid-19, qui accable d'une intense fatigue les malades très âgés, parfois complètement déboussolés.

Raybaud A. **« Ma vie amoureuse est en pause depuis un an » : sous l'effet du Covid, une jeunesse en mal de rencontres.** Le Monde 2020, published 14 December. Full-text: [https://www.lemonde.fr/campus/article/2020/12/14/ma-vie-amoureuse-est-en-pause-depuis-un-an-sous-l-effet-du-covid-une-jeunesse-en-mal-de-rencontres\\_6063373\\_4401467.html](https://www.lemonde.fr/campus/article/2020/12/14/ma-vie-amoureuse-est-en-pause-depuis-un-an-sous-l-effet-du-covid-une-jeunesse-en-mal-de-rencontres_6063373_4401467.html)

La restriction des contacts et la fermeture des lieux propices à de nouvelles relations plongent certains jeunes dans le désarroi, à un âge habituellement associé à une diversité d'expériences sexuelles et sentimentales.

Jérôme B. **Covid-19 : Dans les Ehpad, le dilemme de la vaccination.** Le Monde 2020, published 14 December. Full-text: [https://www.lemonde.fr/societe/article/2020/12/14/covid-19-dans-les-ehpad-le-dilemme-de-la-vaccination\\_6063297\\_3224.html](https://www.lemonde.fr/societe/article/2020/12/14/covid-19-dans-les-ehpad-le-dilemme-de-la-vaccination_6063297_3224.html)

Les fédérations des directeurs d'établissement pour personnes âgées plaident pour un accord écrit des résidents.

## German

If you read German, read **Medizinisches Personal hat hohes Risiko für schwere Krankheitsverläufe**. Der Spiegel 2020, published 14 December. Full-text: <https://www.spiegel.de/wissenschaft/medizin/coronavirus-risiko-fuer-schwere-covid-19-erkrankung-besonders-hoch-in-gesundheitsberufen-a-0a5c22bf-7f31-4cb0-808b-94fa503020e3>

Eine Studie hat untersucht, in welchen Berufen das Risiko hoch ist, schwer an Covid-19 zu erkranken. Demnach trifft es Ärzte, Pflegekräfte, Rettungssanitäter und Menschen in anderen sozialen Berufen.

## 16 December

### Epidemiology

Mutambudzi M, Niedwiedz C, Macdonald EB, et al. **Occupation and risk of severe COVID-19: prospective cohort study of 120 075 UK Biobank participants**. Occup Environ Med. 2020 Dec 9:oemed-2020-106731. PubMed: <https://pubmed.gov/33298533>. Full-text: <https://doi.org/10.1136/oemed-2020-106731>

Essential workers such as healthcare workers (RR 7.43, 95% CI 5.52 to 10.00), social and education workers (RR 1.84, 95% CI 1.21 to 2.82) and other essential workers (RR 1.60, 95% CI 1.05 to 2.45) appear to have a higher risk of severe COVID-19. This is the result of a prospective cohort study of 120,075 persons, (employed or self-employed, alive and aged < 65 years in 2020), of whom 271 had severe COVID-19. We need to protect them!

Althoff KN, Laeyendecker O, Li R, et al. **SARS-CoV-2 antibody status in decedents undergoing forensic postmortem examination in Maryland, May 24 to June 30, 2020**. Open Forum Infect Dis 2020, published 15 December. Full-text: <https://doi.org/10.1093/ofid/ofaa611>

Seroprevalence of SARS-CoV-2 antibodies was 10% among the subset of decedents undergoing forensic post-mortem examination in June in Maryland. Decedents of motor vehicle crashes had similar seroprevalence compared to those with a natural death (including decedents with SARS-CoV-2 infection). Decedents of motor vehicle crashes may be a sentinel surveillance population.

## Virology

Lu M, Uchil PD, Li W, et al. **Real-Time Conformational Dynamics of SARS-CoV-2 Spikes on Virus Particles.** *Cell Host Microbe.* 2020 Dec 9;28(6):880-891.e8. PubMed: <https://pubmed.gov/33242391>. Full-text: <https://doi.org/10.1016/j.chom.2020.11.001>

More on the mechanisms of S (SARS-CoV-2 spike) recognition and conformations for immunogen design. The authors apply single-molecule fluorescence (Förster) resonance energy transfer (smFRET) imaging to observe conformational dynamics of S on viral particles, showing transitions from a closed ground state to the open receptor-accessible conformation via an on-path intermediate.

See also the comment by Serrão VHB, Lee JE. **FRETing over SARS-CoV-2: Conformational Dynamics of the Spike Glycoprotein.** *Cell Host Microbe* 2020, published 9 December. Full-text: <https://doi.org/10.1016/j.chom.2020.11.008>

## Prevention

McLellan A, Godlee F. **Covid 19: Christmas relaxation will overwhelm services.** *BMJ* 2020, published 15 December. Full-text: <https://doi.org/10.1136/bmj.m4847>

Since the UK's first lockdown in March, the government has had one (perhaps only one) consistent message—protect the NHS. Now, with the number of hospital patients with COVID-19 again on the rise, and a third wave almost inevitable, the New Year is likely to see NHS trusts facing a stark choice: be overwhelmed or stop most elective and non-urgent work. Rather than lifting restrictions over Christmas as currently planned, the UK should follow the more cautious examples of Germany, Italy, and the Netherlands. To protect the NHS, the UK government must abandon plans for household mixing.

Lewis D. **Why many countries failed at COVID contact-tracing — but some got it right.** *Nature* 2020, published 14 December. Full-text: <https://www.nature.com/articles/d41586-020-03518-4>

Nine months after the World Health Organization (WHO) declared COVID-19 a pandemic, few countries are wielding contact-tracing effectively. Even rich nations have struggled with one of the most basic and important methods for controlling infectious diseases.

## Vaccine

Bubar KM, Reinhold K, Kissler SM, et al. **Model-informed COVID-19 vaccine prioritization strategies by age and serostatus.** medRxiv 2020, posted 7 December. Full-text: <https://doi.org/10.1101/2020.09.08.20190629>

Over the coming months, the supply of SARS-CoV-2 vaccine will be limited. Who should receive the first available vaccine doses? It depends. If your priority is preventing as many transmissions as possible, give the vaccine to adults aged 20-49. If you want to minimize mortality and years of life lost, vaccinate the 60+ years old.

## Severe COVID

Koehler P, Bassetti M, Chakrabarti A, et al. **Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance.** Lancet Infect Dis 2020, published 14 December. Full-text: 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30847-1](https://doi.org/10.1016/S1473-3099(20)30847-1)

SARS-CoV-2 causes direct damage to the airway epithelium, enabling *aspergillus* invasion, and azole-resistant *aspergillus* have been reported. Philipp Koehler et al. present a consensus statement on defining and managing COVID-19-associated pulmonary aspergillosis, endorsed by medical mycology societies. Among the key messages: a) Three different grades are proposed (possible, probable, and proven COVID-19-associated invasive pulmonary aspergillosis [CAPA]) to enable researchers to homogeneously classify patients in registries and interventional clinical trials; b) voriconazole or isavuconazole are recommended as first-line treatment for possible, probable, and proven CAPA.

## Collateral Effects

Jones N. **How COVID-19 is changing the cold and flu season.** Nature 2020, published 15 December. Full-text: <https://www.nature.com/articles/d41586-020-03519-3>

By mid-December, the Northern Hemisphere is usually well into the start of its annual cold and flu season — but so far this year, even as the COVID-19 pandemic surges in dozens of countries, the levels of many common seasonal infections remain extremely low. Measures meant to tame the coronavirus pandemic are quashing influenza and most other respiratory diseases, which could have wide-ranging implications.

## Beyond Corona

**Viruses, microscopy and fast radio bursts: 10 remarkable discoveries from 2020.** Nature 2020, published 14 December. Full-text: <https://www.nature.com/articles/d41586-020-03514-8>

Highlights from News & Views published this year:

1. [Fight or flight turns hair white](#) — Shayla A. Clark and Christopher D. Deppmann
2. [Matter–antimatter symmetry violated](#) — Silvia Pascoli and Jessica Turner
3. [Jet stream stops shifting as ozone layer recovers](#) — Alexey Yu. Karpechko
4. [Incest uncovered at elite prehistoric Irish burial site](#) — Alison Sheridan
5. [Satellites could soon map every tree on Earth](#) — Niall P. Hanan and Julius Y. Anchang
6. [Latent HIV gets a shock](#) — Mathias Lichterfeld
7. [Engineering a picky eater](#) — Jessica L. Zung and Carolyn S. McBride
8. [A fast radio burst in our own Galaxy](#) — Amanda Weltman and Anthony Walters
9. [Cryo-electron microscopy reaches atomic resolution](#) — Mark A. Herzik Jr
10. [Interferon deficiency can lead to severe COVID](#) — Eric Meffre and Akiko Iwasaki

**Video.** The OSIRIS-REx spacecraft touches the surface of asteroid Bennu. (This video has no sound.) Credit: NASA/Goddard/University of Arizona

[https://www.nature.com/immersive/d41586-020-03438-3/assets/KhWoVgA7OQ/a\\_samcam\\_approach\\_and\\_tag\\_37x\\_2.mp4](https://www.nature.com/immersive/d41586-020-03438-3/assets/KhWoVgA7OQ/a_samcam_approach_and_tag_37x_2.mp4)

## French

If you read French, read Bordenet C. « **Se retrouver dans la file du Secours populaire, ça donne envie de chialer** » : les nouveaux visages de la pré-carité. Le Monde 2020, published 15 December. Full-text: <https://www.lemonde.fr/economie/article/2020/12/15/se-retrouver-dans->



[la-file-du-secours-populaire-ca-donne-envie-de-chialer-les-nouveaux-visages-de-la-precarite\\_6063397\\_3234.html](https://doi.org/10.1136/bmj.m4677)

Ils sont intérimaires, intermittents du spectacle, jeunes diplômés... Privés de travail à cause de la crise, ils sont contraints de se tourner vers les banques alimentaires pour la première fois.

## 17 December

### Prevention

Xie Y, Bowe B, Maddukuri G, et al. **Comparative evaluation of clinical manifestations and risk of death in patients admitted to hospital with covid-19 and seasonal influenza: cohort study.** BMJ 15 December 2020; 371. Full-text: <https://doi.org/10.1136/bmj.m4677>

Is COVID-19 a flu (no)? Or is it more severe and deadly than seasonal influenza (yes)? Yan Xie and colleagues have compared patients admitted to hospital with COVID-19 between 1 February 2020 and 17 June 2020 (n = 3641) and seasonal influenza between 2017 and 2019 (n = 12,676). COVID-19 was associated with higher risk of acute kidney injury (odds ratio 1.52), incident renal replacement therapy (4.11), severe septic shock (4.04), vasopressor use (3.95), pulmonary embolism (1.50), deep venous thrombosis (1.50), stroke (1.62), acute myocarditis (7.82), arrhythmias and sudden cardiac death (1.76). Compared with seasonal influenza, COVID-19 was also associated with higher risk of death (HR 4.97), mechanical ventilator use (4.01), and admission to intensive care (2.41). You may use this data for discussions with COVID-19 deniers (meh, they won't believe you anyway).

Brauner JM, Mindermann S, Sharma Mm et al. **Inferring the effectiveness of government interventions against COVID-19.** Science 15 Dec 2020: eabd9338. Full-text: <https://science.sciencemag.org/content/early/2020/12/15/science.abd9338>

Jan M. Brauner and colleagues from Oxford evaluated the impact of several NPIs on the epidemic's growth in 34 European and 7 non-European countries by using a Bayesian hierarchical model. Good to know during these days of a second lockdown: closing all educational institutions, limiting gatherings to 10 people or less, and closing face-to-face businesses each reduced transmission considerably. **Interestingly, the additional effect of stay-at-home orders was comparatively small.**

## Epidemiology

Poustchi H, Darvishshiaqan M, Mohammadi Z, et al. **SARS-CoV-2 antibody seroprevalence in the general population and high-risk occupational groups across 18 cities in Iran: a population-based cross-sectional study.** Lancet Infect Dis December 15, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30858-6](https://doi.org/10.1016/S1473-3099(20)30858-6)

Seroprevalence is likely to be much higher than the reported prevalence of COVID-19 based on confirmed COVID-19 cases in Iran. The overall population weight-adjusted and test performance-adjusted prevalence of antibody seropositivity in the general population was 17.1% (95% CI 14.6–19.5). Despite high seroprevalence in a few cities, a large proportion of the population is still uninfected.

## Immunology

Rha MS, Jeong HW, Ko JH, et al. **PD-1-Expressing SARS-CoV-2-Specific CD8+ T Cells Are Not Exhausted, but Functional in Patients with COVID-19.** Immunity December 10, 2020. Full-text: <https://doi.org/10.1016/j.immuni.2020.12.002>

Min-Seok Rha and colleagues from Korea detected SARS-CoV-2-specific CD8+ T cells using MHC class I multimers and investigated their *ex vivo* phenotypes in peripheral blood mononuclear cells (PBMCs) from acute and convalescent COVID-19 patients. Notably, SARS-CoV-2-specific memory CD8+ T cells from convalescent patients exhibited a high proliferative capacity, but IFN- $\gamma$  was produced by less than half of the SARS-CoV-2-specific memory CD8+ T cell population. The authors also demonstrated that PD-1-expressing SARS-CoV-2-specific CD8+ T cells from acute and convalescent patients were not exhausted, but activated and functional. PD-1 expression on CD8+ T cells likely reflects activation, rather than exhaustion, in COVID-19.

Jørgensen J, Holter M, Christensen JC, et al. **Increased interleukin-6 and macrophage chemoattractant protein-1 are associated with respiratory failure in COVID-19.** Sci Rep 10, 21697 (2020). Full-text: <https://doi.org/10.1038/s41598-020-78710-7>

For this Norwegian COVID-19 cohort study, plasma cytokine levels at admission and follow-up during the first ten days of hospitalization were related to disease severity. A broad network of pro-inflammatory cytokines was elevated in plasma, especially pronounced in severe cases. Although the authors “did not find convincing evidence of a true cytokine storm”, combinations of

IL-6 and MCP-1 may be further explored as potential biomarkers in severe COVID-19 infection.

Zang R, Case JB, Yutuc E, et al. **Cholesterol 25-hydroxylase suppresses SARS-CoV-2 replication by blocking membrane fusion.** PNAS December 15, 2020 117 (50) 32105-32113; first published November 25, 2020. Full-text: <https://doi.org/10.1073/pnas.2012197117>

Cholesterol 25-hydroxylase (CH25H) is an interferon (IFN)-stimulated gene that shows broad antiviral activities against a wide range of enveloped viruses. Here, using an IFN-stimulated gene screen against vesicular stomatitis virus (VSV)-SARS-CoV and VSV-SARS-CoV-2 chimeric viruses, Ruochen Zang from St. Louis and colleagues identified CH25H and its enzymatic product 25-hydroxycholesterol (25HC) as potent inhibitors of SARS-CoV-2 replication. Internalized 25HC accumulates in the late endosomes and potentially restricts SARS-CoV-2 spike protein catalyzed membrane fusion via blockade of cholesterol export. Data suggest a unifying model in which 25HC results in a redistribution of cholesterol and inhibits both endosomal entry and plasma membrane fusion, which potentially explains the CH25H inhibitory activity against wild-type SARS-CoV-2.

Chen Z, Ruan P, Wang L, Nie X, Ma X, Tan Y. **T and B cell epitope analysis of SARS-CoV-2 S protein based on immunoinformatics and experimental research.** J Cell Mol Med. 2020 Dec 15. PubMed: <https://pubmed.gov/33325143> . Full-text: <https://doi.org/10.1111/jcmm.16200>

The authors used immunoinformatics to identify conservative B and T cell epitopes for S proteins of SARS-CoV-2, which might play roles in the initiation of SARS-CoV-2 infection. They identified the B cell and T cell peptide epitopes of S protein and their antigenicity, as well as the interaction between the peptide epitopes and human leucocyte antigen (HLA).

## Vaccine

Rid A, Lipsitch M, Miller FG, et al. **The Ethics of Continuing Placebo in SARS-CoV-2 Vaccine Trials.** JAMA December 14, 2020. Published online December 14, 2020. Full-text: <https://doi.org/10.1001/jama.2020.25053>

Participants who received placebo in the vaccine trials have made an essential contribution to testing vaccine safety and efficacy. This important viewpoint argues that given limited vaccine supply for at least several months,

only the participants receiving placebo who would be eligible for vaccination outside the trial should be offered access to the vaccines at this point. What did the informed consent say? Did it contemplate a EUA or other vaccines getting to market before their specific trial finishes?

Wang W, Wu Q, Yang J, et al. **Global, regional, and national estimates of target population sizes for covid-19 vaccination: descriptive study.** BMJ 15 December 2020; 371. Full-text: <https://doi.org/10.1136/bmj.m4704>

For the record: The adult population willing to be vaccinated is estimated at 3.7 billion (95% confidence interval 3.2 to 4.1 billion).

## Comorbidities

Huskamo HA, Busch AB, Uscher-Pines, et al. **Treatment of Opioid Use Disorder Among Commercially Insured Patients in the Context of the COVID-19 Pandemic.** JAMA December 15, 2020; 324(23):2440-2442. Full-text: <https://doi.org/10.1001/jama.2020.21512>

During the first 3 months of the pandemic, among patients already receiving OUD medication, there was no decrease in medication fills or clinician visits.

Liondan CE, Mankad K, Ram D. **Neuroimaging manifestations in children with SARS-CoV-2 infection: a multinational, multicentre collaborative study.** Lancet Child Adol December 15, 2020. Full-text: [https://doi.org/10.1016/S2352-4642\(20\)30362-X](https://doi.org/10.1016/S2352-4642(20)30362-X)

An international call for cases of children with encephalopathy related to SARS-CoV-2 infection and abnormal neuroimaging findings was made. In total, 38 cases from 8 different countries reviewed by a central neuroradiology panel. The most common imaging patterns were post-infectious immune-mediated acute disseminated encephalomyelitis-like changes of the brain (16 patients), myelitis (eight patients), and neural enhancement (13 patients).

## 18 December

### Virology

Baric RS. **Emergence of a Highly Fit SARS-CoV-2 Variant.** NEJM December 16, 2020. Full-text: <https://doi.org/10.1056/NEJMcibr2032888>

Brief overview on the genetic and molecular evidence for enhanced fitness of the G614 variant over ancestral strains by Ralph S. Baric, one of the world's

leading experts in the field. Fortunately, the new variant is as sensitive to the serum specimens as the D614 strain and thus should allay fears that it might escape vaccine-elicited immunity. However, there remains a critical need for proactive, rather than reactive, tracking of SARS-CoV-2 and other potential emerging coronaviruses.

## Immunology

Garcia-Beltran WF, Lam EC, Astudillo MG, et al. **COVID-19 neutralizing antibodies predict disease severity and survival.** Cell December 15, 2020. Full-text: <https://doi.org/10.1016/j.cell.2020.12.015>

Wilfredo Garcia-Beltran from Boston and colleagues examined antibody responses in 113 COVID-19 patients and found that severe cases exhibited increased inflammatory markers, lymphopenia, pro-inflammatory cytokines, and high anti-RBD antibody levels. A new finding was that patient sera were also able to neutralize the recently emerged SARS-CoV-2 mutant D614G, suggesting cross-protection from re-infection by either strain. In contrast, SARS-CoV-2 sera lacked cross-neutralization to a highly homologous bat coronavirus, WIV1-CoV, that has not yet crossed the species barrier.

Ku MW, Bourguine M, Authié P. **Intranasal Vaccination with a Lentiviral Vector Protects against SARS-CoV-2 in Preclinical Animal Models.** Cell Host Microbe December 14, 2020. Full-text: <https://doi.org/10.1016/j.chom.2020.12.010>

Min-Wen Ku from Paris and colleagues generated a lentiviral vector (LV) that elicits neutralizing antibodies against the Spike glycoprotein of SARS-CoV-2. Eliciting an immune response in the respiratory tract through an intranasal boost results in  $> 3 \log_{10}$  decrease in the lung viral load and reduces local inflammation. The vaccine also worked well in golden hamsters, designating intranasal immunization as a powerful approach against COVID-19.

Pairo-Castineira E, Clohisey S, Klaric L et al. **Genetic mechanisms of critical illness in Covid-19.** Nature (2020). Full-text: <https://doi.org/10.1038/s41586-020-03065-y>

Erola Pairo-Castineira and colleagues report the results of the GenOMICC (Genetics Of Mortality In Critical Care) genome-wide association study (GWAS) in 2244 critically ill COVID-19 patients from 208 UK intensive care units (ICUs). They scanned each person's genes, which contain the instructions for every biological process, including how to fight a virus. They have identified some

genetic differences (odds ratio of the tested risk alleles were 1.2-1.9) between patients with severe COVID-19 and the general population, revealing “robust genetic signals relating to key host antiviral defense mechanisms, and mediators of inflammatory organ damage”.

## Prevention

Salathé M, Althaus C, Anderegg N, et al. **Early evidence of effectiveness of digital contact tracing for SARS-CoV-2 in Switzerland.** *Swiss Med Wkly.* 2020 Dec 16;150:w20457. PubMed: <https://pubmed.gov/33327003>. Full-text: <https://doi.org/10.4414/smw.2020.20457>

COVID apps may work (at least in Switzerland!). By 10 September 2020, the SwissCovid app (it uses the EN framework to estimate proximity between phones) has been downloaded 2,36 million times. Marcel Salathé and colleagues estimate that digital contact tracing can show similar effectiveness at identifying infected partners of index cases as classic contact tracing, provided that both the index case and the exposed contacts use the app. These apps represent a helpful complementary tool for controlling the spread of SARS-CoV-2. Please download your local app.

## Clinical

Faust JS, Krumholz HM, Du C, et al. **All-Cause Excess Mortality and COVID-19-Related Mortality Among US Adults Aged 25-44 Years, March-July 2020.** *JAMA* December 16, 2020. Full-text: <https://doi.org/10.1001/jama.2020.24243>

According to provisional National Center for Health Statistics data, the COVID-19 pandemic was associated with increases in all-cause mortality among US adults aged 25 to 44 years from March through July of 2020. From March to July, a total of 76,088 all-cause deaths occurred among US adults aged 25 to 44 years, which was 11,899 more than expected (incident rate ratio, 1.19 [95% CI, 1.14-1.23]). Of note, only 38% of all-cause excess deaths were attributed directly to COVID-19, suggesting that COVID-19-related mortality may have been under-detected in this population.

Izurieta HS, Graham DJ, Jiao Y, et al. **Natural history of COVID-19: Risk factors for hospitalizations and deaths among >26 million U.S. Medicare beneficiaries.** *J Infect Dis* 16 December 2020. Full-text: <https://doi.org/10.1093/infdis/jiaa767>

Retrospective cohort study covering Medicare fee-for-service beneficiaries, comparing 653,966 elderly residents in nursing homes (NH) and 292,302 with end-stage renal disease (ESRD) from the primary study population of > 25 million individuals aged  $\geq$  65. COVID-related death rates (per 10,000) were much higher among elderly NH residents (275,7) and ESRD patients (60,8) than the primary study population (5,0). Regression-adjusted clinical predictors of death among the primary population included immunocompromised status (OR: 1.43), frailty index conditions such as cognitive impairment (3.16) as well as other co-morbidities including congestive heart failure (1.30). Demographic-related risk factors included male sex (1.77), older age (OR: 3.09 for 80-year-old vs. 65-year-old), and racial/ethnic minority.

### Severe COVID-19

Bharat A, Querrey M, Markov NS, et al. **Lung transplantation for patients with severe COVID-19**. *Sci Transl Med*. 2020 Dec 16;12(574):eabe4282. PubMed: <https://pubmed.gov/33257409>. Full-text: <https://doi.org/10.1126/scitranslmed.abe4282>

Ankit Bharat and colleagues from Chicago report the results of lung transplantation in three patients with non-resolving COVID-19-associated respiratory failure: a 28-year-old Latina female with neuromyelitis optica (who was treated with rituximab, patient A), a 62-year-old male with hypertension (B), and a 43-year-old man with medically controlled type 2 diabetes mellitus (C). About 4-5 months after transplantation, patients A and B reported independence in activities of daily living while patient C received care in an in-patient rehabilitation facility at month 3. SARS-CoV-2 RNA could not be detected in the explanted lungs of these patients, but fibrotic pathology and transcriptional changes resembling those of lungs from patients with pulmonary fibrosis were observed.

### Comorbidities

Agrawal M, Brenner EJ, Zhang X, et al. **Characteristics and Outcomes of IBD Patients with COVID-19 on Tofacitinib Therapy in the SECURE-IBD Registry**. *Inflammatory Bowel Diseases* 16 December 2020. Full-text: <https://doi.org/10.1093/ibd/izaa303>

Tofacitinib is a Janus kinase inhibitor (JAKi) approved for the treatment of ulcerative colitis (UC) and other immune-mediated diseases. As many JAKis, it is also evaluated in COVID-19 trials. Manasi Agrawal and colleagues here describe characteristics and outcomes of COVID-19 in 37 patients with IBD

treated with tofacitinib compared with other medications in the SECURE-IBD registry. Overall, they found no difference in COVID-19 outcomes between the two groups. Good to see: though tofacitinib at the higher dose has been associated with venous thromboembolism, none of the tofacitinib-treated patients in this cohort experienced thrombotic complications.

## 19 December

### Immunology

Duysburgh E, Mortgar L, Barbezange C, et al. **Persistence of IgG response to SARS-CoV-2.** *Lancet Infect Dis* December 17, 2020. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30943-9](https://doi.org/10.1016/S1473-3099(20)30943-9)

A rapid decline of SARS-CoV-2 IgG seropositivity or neutralizing capacity is unlikely: Among 74 (91%) HCW from Belgium who remained seropositive, median duration of antibody persistence (defined as the time between the day IgGs were last detected and the day of presumed onset of infection) is currently 168,5 (range 62–199) days. In total, 61 (82%) had neutralizing antibodies in their most recent IgG-positive serum sample.

### Vaccine

Anderson EJ, Roupheal NG, Widge AT, et al. **Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults.** *N Engl J Med*, December 17 2020; 383:2427-2438. Full-text: <https://doi.org/10.1056/NEJMoa2028436>

Moderna's messenger RNA vaccine (mRNA-1273) seems to work in older people. In this Phase I, dose-escalation, open label trial in 40 older adults, serum neutralizing activity was detected in all the participants by multiple methods after the second immunization. Solicited adverse events were dose-dependent and predominantly mild or moderate in severity.

### Transmission

Jones JM, Kracalik I, Rana MM, Nguyen A, Keller BC, Mishkin A, et al. **SARS-CoV-2 infections among recent organ recipients, March–May 2020, United States.** *Emerg Infect Dis* 2021. Full-text: <https://doi.org/10.3201/eid2702.204046>

In March 2020, US transplant centers began to report potential donor-derived SARS-CoV-2 transmission to the Organ Procurement and Transplantation Network (OPTN). For 8 potential donor-derived SARS-CoV-2 transmissions



reported to the OPTN during March–May 2020, the available evidence suggest that the most likely source of transmission was community or healthcare exposure, not the organ donor.

## Clinical

Piroth L, Cottenet J, Mariet AS, et al. **Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study.** *Lancet Resp Med* December 17, 2020. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30527-0](https://doi.org/10.1016/S2213-2600(20)30527-0)

No, again, it's not a flu. This nationwide retrospective cohort study from France included discharge summaries for all hospital admissions, comparing 89,530 patients with COVID-19 and 45,819 patients with influenza. In-hospital mortality was higher in patients with COVID-19 than in patients with influenza (16.9% vs 5.8%), with a relative risk of death of 2.9 (95% CI 2.8–3.0) and an age-standardized mortality ratio of 2.82.

François J, Collery AS, Hayek G, et al. **Coronavirus Disease 2019–Associated Ocular Neuropathy With Panuveitis.** *JAMA Ophthalmol* December 17, 2020. Full-text: <https://doi.org/10.1001/jamaophthalmol.2020.5695>

Case report of an inflammatory ocular neuritis that was associated with uveitis may have been induced by SARS-CoV-2, and resulted in permanent loss of visual acuity. It is notable that although initial disc edema was moderate to mild in this patient, it led to severe atrophy. Other viruses (eg, varicella-zoster virus) have also been reported to have this effect.

## Severe COVID-19

Kwak PE, Connors JR, Benedict PA. **Early Outcomes From Early Tracheostomy for Patients With COVID-19.** *JAMA Otolaryngol Head Neck Surg* December 17, 2020. Full-text: <https://doi.org/10.1001/jamaoto.2020.4837>

Retrospective medical record review of 148 patients requiring mechanical ventilation at a single tertiary-care medical center in New York City. Median length of stay was 40 days in those who underwent early tracheostomy (within 10 days of endotracheal intubation) and 49 days in those who underwent late tracheostomy. In a competing risks model with death as the competing risk, the late tracheostomy group was 16% less likely to discontinue mechanical ventilation (hazard ratio, 0.84; 95% CI, 0.55 to 1.28). According to the authors, their data provide an opportunity to reconsider guidelines for trache-

ostomy for patients with COVID-19, demonstrating non-inferiority of early tracheostomy.

## Long COVID-19

Baig AM. **Deleterious Outcomes in Long-Hauler COVID-19: The Effects of SARS-CoV-2 on the CNS in Chronic COVID Syndrome.** ACS Chem Neurosci. 2020 Dec 16;11(24):4017-4020. PubMed: <https://pubmed.gov/33275404>. Full-text: <https://doi.org/10.1021/acchemneuro.0c00725>

Complex clinical findings are currently addressed in COVID long-haulers, for which the more clinically related term chronic COVID syndrome (CCS) has recently been coined. This Viewpoint highlights this syndrome, the possible pathogenetic pathways involved, and the treatment approaches that can be taken to help manage COVID long-haulers in CCS.

## Comorbidities

Morales DR, Conover MM, You SC, et al. **Renin-angiotensin system blockers and susceptibility to COVID-19: an international, open science, cohort analysis.** Lancet Digital Health December 17, 2020. Full-text: [https://doi.org/10.1016/S2589-7500\(20\)30289-2](https://doi.org/10.1016/S2589-7500(20)30289-2)

In this multicenter cohort study following more than 1,3 million patients with hypertension from the USA and Spain, no clear association of increased risk of COVID-19 diagnosis, hospital admission, or subsequent complications was seen with the outpatient use of ACEI or ARB. These findings support recent recommendations that patients should not halt their ACEI or ARB therapy despite previously posited mechanisms of increased COVID-19 risk. Furthermore, the marginal difference between ACEIs and ARBs does not warrant class switching to reduce COVID-19 susceptibility.

Vijenthira A, Gong IY, Fox TA. **Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients.** Blood December 17, 2020, 136 (25): 2881-2892. Full-text: <https://doi.org/10.1182/blood.2020008824>

Systemic review and meta-analysis of 34 adult and 5 pediatric studies (3377 patients) from Asia, Europe, and North America (14 of 34 adult studies included only hospitalized patients). Adult patients with hematologic malignancy and COVID-19 found a 34% risk of death, whereas pediatric patients had a 4% risk of death. Patients on systemic anticancer therapy had a similar risk of death to patients on no treatment.

## Treatment

Weinreich DM, Sivapalasingam S, Norton T, et al. **REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19.** NEJM December 17, 2020, Full-text: <https://doi.org/10.1056/NEJMoa2035002>

Antibodies may work, but only in seronegative patients. Here, an interim analysis is presented for the two anti-spike antibodies casirivimab (REGN10933) and imdevimab (REGN10987). Both make up REGN-COV2 (and were given to Trump). This ongoing Phase I-III trial randomly assigned 275 non-hospitalized patients to receive placebo, 2,4 g or 8,0 g of REGN-COV2. The least-squares mean difference (REGN-COV2 dose groups vs. placebo group) in the time-weighted average change in viral load from day 1 through day 7 was minus 0,56  $\log_{10}$  copies/mL among patients who were serum antibody-negative at baseline and minus 0,41  $\log_{10}$  copies/mL in the overall trial population. But did this translate into a clinical benefit? Maybe. At least one medical attended visit was necessary in 3% vs. 6% (placebo) overall and in 6% vs. 15% (placebo) in serum antibody-negative at baseline.

Sheppard JP, Nicholson B, Lee J, et al. **The association between blood pressure control and Coronavirus Disease 2019 outcomes in 45,418 symptomatic patients with hypertension: An observational cohort study.** Hypertension. 2020 Dec 16. PubMed: <https://pubmed.gov/33325240>. Full-text: <https://doi.org/10.1161/HYPERTENSIONAHA.120.16472>

This study examined the association between pre-infection blood pressure (BP) control and COVID-19 outcomes using data from 460 general practices in England. Eligible patients were adults with hypertension who were diagnosed with COVID-19. A total of 4277 patients (9,4%) were diagnosed with COVID-19 and 877 died within 28 days. There was no association between BP control and COVID-19 diagnosis or hospitalization. Of note, individuals with stage 1 uncontrolled BP had lower odds of COVID-19 death (OR 0.76, 95%CI 0.62-0.92) compared to patients with well-controlled BP. However, these patients were older, had more co-morbidities and had been diagnosed with hypertension for longer, suggesting more advanced atherosclerosis and target organ damage.

## 20 December

### Virology

Miao G, Zhao H, Li Y, et al. **ORF3a of the COVID-19 virus SARS-CoV-2 blocks HOPS complex-mediated assembly of the SNARE complex required for autolysosome formation.** Development Cell December 16, 2020. Full-text: <https://doi.org/10.1016/j.devcel.2020.12.010>

Have no clue what HOPS and SNARE complexes are? Never mind. Autophagy acts as a cellular surveillance mechanism to combat invading pathogens. Viruses have evolved various strategies to block autophagy and even subvert it for their replication and release. This study reveals a mechanism by which SARS-CoV-2 evades lysosomal destruction. ORF3a, an accessory protein specific to SARS-CoV-2, greatly impairs the formation of degradative autolysosomes.

Liu K, Tan S, Niu S, et al. **Cross-species recognition of SARS-CoV-2 to bat ACE2.** PNAS December 16, 2020. 118 (1). Full-text: <https://doi.org/10.1073/pnas.2020216118>

SARS-CoV-2 may infect bats, and the extensive species diversity of bats may have profound effects on SARS-CoV-2 evolution. However, SARS-CoV-2 receptor binding domain (RBD) binds to bACE2-Rm with lower affinity than that to human ACE2 receptor (hACE2).

### Immunology

Yao C, Bora SA, Patimo T, et al. **Cell type-specific immune dysregulation in severely ill COVID-19 patients.** Cell Report December 16, 2020. Full-text: <https://doi.org/10.1016/j.celrep.2020.108590>

Changfu Yao and colleagues have added some evidence to the observation that although most immune cellular compartments have an expected hyper-inflammatory response in severe patients, several of their key pathways are dysfunctional. Moreover, immune imbalance in which dysregulation of both the innate and adaptive immune responses may be contributing to a more severe disease course. The key findings: monocyte antigen presentation pathway gene expression is lower in severe COVID-19, lymphocyte cytotoxicity pathways are reduced, and B cell activation is blunted. Interferon signaling is elevated in lymphocytes but diminished in monocytes.

Keller MD, Harris KM, Jensen-Wachspress MA, et al. **SARS-CoV-2-specific T cells are rapidly expanded for therapeutic use and target conserved regions of the membrane protein.** Blood December 17, 2020, 136 (25): 2905–2917. Full-text: <https://doi.org/10.1182/blood.2020008488>

In this report, Michael Keller and colleagues demonstrate a broadly specific T cell therapeutic targeting 3 structural proteins of SARS-CoV-2 that could be reliably expanded from the majority of convalescent donors. The authors believe that SARS-CoV-2 directed T cell immunotherapy targeting structural proteins (most importantly the membrane protein) should be feasible for the prevention or early treatment of SARS-CoV-2 infection in immunocompromised patients with blood disorders.

## Vaccine

Editorial. **COVID-19 vaccines: the pandemic will not end overnight.** The Lancet Microbe December 18, 2020. Full-text: [https://doi.org/10.1016/S2666-5247\(20\)30226-3](https://doi.org/10.1016/S2666-5247(20)30226-3)

See title. Even a global mass immunization program will not immediately end the COVID-19 pandemic. Although control over the infection's most harmful effects is expected and limiting its spread can be hoped for, it will likely be a few years before the virus can be brought under control worldwide.

## Prevention

Priesemann V, Brinkmann MM, Ciesek S, et al. **Calling for pan-European commitment for rapid and sustained reduction in SARS-CoV-2 infections.** Lancet December 18, 2020. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32625-8](https://doi.org/10.1016/S0140-6736(20)32625-8)

In their comment (which was signed by > 200 researchers), the authors urge governments throughout Europe to agree on clearly formulated common goals, coordinate their efforts, develop regionally adapted strategies to reach the goals, and thereby work resolutely towards lowering case numbers.

## Clinical

Woolf SH, Chapman DA, Lee JH. **COVID-19 as the Leading Cause of Death in the United States.** JAMA December 17, 2020. Full-text: <https://doi.org/10.1001/jama.2020.24865>

The news media dutifully report each day's increase in new cases and deaths but putting these numbers in perspective may be difficult. According to CDC

data, by October 2020, COVID-19 had become the third leading cause of death for persons aged 45 through 84 years and the second leading cause of death for those aged 85 years or older. Adults 45 years or older were more likely to die from COVID-19 than from chronic lower respiratory disease, transport accidents (eg, motor vehicle fatalities), drug overdoses, suicide, or homicide. Steven H. Woolf and colleagues argue that the *daily* US mortality rate for COVID-19 deaths is equivalent to the September 11 attacks, which claimed 2988 lives, occurring every 1.5 days, or 19 Airbus 320 jetliners, each carrying 150 passengers, crashing every day.

## Comorbidities

ERA-EDTA Council, ERACODA Working Group. **Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA.** *Nephrology Dialysis Transplantation* December 19 2020. Full-text: <https://academic.oup.com/ndt/advance-article/doi/10.1093/ndt/gfaa314/6041849>

The OpenSAFELY project analysed factors associated with COVID-19 deaths in 17 million patients. The picture that arose differs significantly from initial reports. For example, hypertension is not an independent risk factor for COVID-19 death, but renal disease very much is. Dialysis (aHR 3.69), organ transplantation (aHR 3.53) and CKD (aHR 2.52 for patients with eGFR < 30 mL/min/1.73 m<sup>2</sup>) represent three of the four co-morbidities associated with the highest mortality risk from COVID-19. The risk associated with CKD Stages 4 and 5 is higher than the risk associated with diabetes mellitus (aHR range 1.31–1.95, depending upon glycemic control) or chronic heart disease (aHR 1.17). This article defines essential action points, among which is advocating the inclusion of CKD patients in clinical trials, testing the efficacy of drugs and vaccines to prevent severe COVID-19.

## Treatment

Salama C, Han J, Yau L, et al. **Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia.** *NEJM* December 17. Full-text: <https://doi.org/10.1056/NEJMoa2030340>

In this RCT, 389 patients hospitalized with COVID-19 pneumonia who were not receiving mechanical ventilation were randomized to receive standard of care plus one or two doses of either tocilizumab (TCZ) or placebo. TCZ reduced the likelihood of progression to the composite outcome of mechanical ventilation or death (12% vs 19%), but it did not improve survival.

Dal-Ré R, Banzo R, Georgin-Lavialle S, et al. **Remdesivir for COVID-19 in Europe: will it provide value for money?** *Lancet Resp Med* December 17, 2020. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30568-3](https://doi.org/10.1016/S2213-2600(20)30568-3)

In their comment on remdesivir pricing, Rafael Dal-Ré and colleagues review the clinical data available and argue that once remdesivir becomes available in Europe, governments should agree a substantially lower price with Gilead (amid a time of high incidence of COVID-19 cases in Europe, and with remdesivir in short supply, the European Commission had signed a joint procurement contract with Gilead, with an agreed price of \$2340 for a 5-day course). Until the effectiveness of remdesivir in clinical practice is well defined in Europe, a pay-for-result agreement might also be considered.

## 21 December

### Transmission

European Centre for Disease Prevention and Control. **Threat Assessment Brief: Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom.** ECDC 2020, published 20 December. Full-text: <https://www.ecdc.europa.eu/en/publications-data/threat-assessment-brief-rapid-increase-sars-cov-2-variant-united-kingdom>

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European Centre for Disease Prevention and Control. **Rapid increase of a SARS-CoV-2 variant with multiple spike protein mutations observed in the United Kingdom.** ECDC 2020, published 20 December. Full-text: <https://www.ecdc.europa.eu/sites/default/files/documents/SARS-CoV-2-variant-multiple-spike-protein-mutations-United-Kingdom.pdf>

South East England has recently faced a rapid increase in COVID-19 cases. Analysis of viral genome sequence data showed that a large proportion of cases belonged to a new single phylogenetic cluster. The new variant is defined by multiple spike protein mutations (deletion 69-70, deletion 144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H) present as well as mutations in other genomic regions. Preliminary analysis in the UK suggests that this variant is more transmissible than previously circulating variants, with an estimated potential to increase the reproductive number (R) by 0.4 or greater with an estimated increased transmissibility of up to 70%. There is no

indication at this point of increased infection severity associated with the new variant.

## Virology

Pickering BS, Smith G, Pinette MM, et al. **Susceptibility of domestic swine to experimental infection with severe acute respiratory syndrome coronavirus 2.** *Emerg Infect Dis* December 17, 2020. Full-text: <https://doi.org/10.3201/eid2701.200339>

Domestic swine are susceptible to low levels of SARS-CoV-2 viral infection. Among 16 experimentally inoculated animals, 5 (31,3%) displayed some level of exposure or elicited an immune response to the virus. Only 1 pig in the study retained live virus, but 2 other animals had detectible RNA measured in nasal wash, and another 2 developed antibodies. Of note, Brad Pickering from the Canadian Food Inspection Agency and colleagues used a 10-fold higher viral dose for experimental infection than was used in previous studies.

## Immunology

Singh DK, Singh B, Ganatra SR. et al. **Responses to acute infection with SARS-CoV-2 in the lungs of rhesus macaques, baboons and marmosets.** *Nat Microbiol* December 18, 2020. Full-text: <https://doi.org/10.1038/s41564-020-00841-4>

Rhesus macaques, baboons and marmosets can all be infected with SARS-CoV-2 but show differential progression to COVID-19. Whereas older marmosets have a mild infection, macaques developed moderate progressive pneumonia that resolves, accompanied by a marked reduction in lung and nasal viral loads. Baboons have the most severe lung pathology, and the greatest viral load.

## Vaccine

Dai L, Gao GF. **Viral targets for vaccines against COVID-19.** *Nat Rev Immunol* 18 December 2020. Full-text: <https://doi.org/10.1038/s41577-020-00480-0>

Which viral elements are used in COVID-19 vaccine candidates, why might they act as good targets for the immune system and what are the implications for protective immunity? This review addresses these questions.



Ewer KJ, Barrett JR, Belij-Rammerstorfer S. et al. **T cell and antibody responses induced by a single dose of ChAdOx1 nCoV-19 (AZD1222) vaccine in a phase 1/2 clinical trial.** Nat Med December 18, 2020. Full-text: <https://doi.org/10.1038/s41591-020-01194-5>

A detailed description of the immune response after administration of one dose of ChAdOx1 nCoV-19 in 88 adults (ages 18-55 years). The authors define, in detail, the isotypes, subclasses and antibody avidity induced after vaccination. They also performed multiplex cytokine profiling and intracellular cytokine staining analysis, demonstrating that ChAdOx1 nCoV-19 vaccination induces a predominantly Th1-type response (that appears to be good).

## Prevention

Spaccaferri G, Larrieu S, Pouey J, et al. **Early assessment of the impact of mitigation measures to control COVID-19 in 22 French metropolitan areas, October to November 2020.** Euro Surveill 2020;25(50):pii=2001974. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.50.2001974>

In France, measures including curfew and lockdown were implemented to control the COVID-19 pandemic second wave in 2020. This study found a considerable decrease in incidence of COVID-19 cases and hospital admissions 7 to 10 days after mitigation measures were put in place, occurring earlier in metropolitan areas.

## Transmission

Sayampanathan AA, Heng CS, Pin PH, et al. **Infectivity of asymptomatic versus symptomatic COVID-19.** Lancet December 18, 2020. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32651-9](https://doi.org/10.1016/S0140-6736(20)32651-9)

Some evidence of a lower infectivity of asymptomatic patients. Andrew Sayampanathan and colleagues looked at 628 people with COVID-19 and 3790 close contacts in Singapore. Overall, 89 (2%) of 3790 close community contacts developed COVID-19 while in quarantine. Binomial regression revealed that when adjusted for age, gender, and serology of index case, the incidence of COVID-19 among close contacts of a symptomatic index case was 3.85 times higher than for close contacts of an asymptomatic index case (95% CI 2.06–7.19;  $p < 0.0001$ ).

Heinrich F, Meißner K, Langenwalder F, et al. **Postmortem stability of SARS-CoV-2 in nasopharyngeal mucosa.** Emerg Infect Dis December 16, 2020. Full-text: [https://wwwnc.cdc.gov/eid/article/27/1/20-3112\\_article](https://wwwnc.cdc.gov/eid/article/27/1/20-3112_article)

Be careful with human corpses: Fabian Heinrich and colleagues from Hamburg found that nasopharyngeal viral RNA stability in 79 corpses showed no time-dependent decrease. Maintained infectivity was supported by virus isolation up to 35 hours post-mortem. There was no correlation between the post-mortem interval (time of death until cooling at 4°C; median 17,8 hours) and the viral RNA loads of corpses. According to the authors, their data indicate potentially high infectivity of human corpses, requiring hazard assessments in professional fields concerned and careful and conscious handling.

## Comorbidities

Goodman KE, Magder LS, Baghdadi JD, et al. **Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals.** Clin Infect Dis 2020, December 19. Full-text: <https://doi.org/10.1093/cid/ciaa1787>

Among 66.646 (6,5%) admissions with a COVID-19 diagnosis across 613 US hospitals, 12.388 (18,6%) died in-hospital. In multivariable analysis, male sex was independently associated with 30% higher mortality risk (aRR, 1.30, 95% CI: 1.26 – 1.34). Of note, diabetes without chronic complications was not a risk factor at any age (aRR 1.01, 95% CI: 0.96 – 1.06), and hypertension without chronic complications was only a risk factor in younger people (20-39 year-olds) (aRR, 1.68, 95% CI: 1.17 – 2.40). Diabetes with chronic complications, hypertension with chronic complications, and obesity were risk factors in most age groups, with highest relative risks among 20-39 year-olds (respective aRRs 1.79, 2.33, 1.92;  $p \leq 0.002$ ).

Hyrich KL, Machado PM. **Rheumatic disease and COVID-19: epidemiology and outcomes.** Nat Rev Rheumatol December 18, 2020. Full-text: <https://doi.org/10.1038/s41584-020-00562-2>

According to this brief review, many questions about COVID-19 in patients with rheumatic diseases remain unanswered. These patients, when analyzed as a combined group, might have a slightly increased risk of death, although the role of disease activity and treatment was not taken into account in most studies. Chronic use of glucocorticoids at moderate or high doses is associated with hospitalization for severe COVID-19. Treatment with cytokine inhibitors

could reduce the risk of SARS-CoV-2 infection, although the mechanisms of this protective effect are not clear.

## 22 December

### Epidemiology

Aschele C, Negru M, Pastorino A, et al. **Incidence of SARS-CoV-2 Infection Among Patients Undergoing Active Antitumor Treatment in Italy.** *JAMA Oncol* December 17, 2020; Full-text: <https://doi.org/10.1001/jamaoncol.2020.6778>

Large investigation on the incidence of SARS-CoV-2 in almost 60.000 patients with cancer. The 0,68% rate of infection was relatively low. Notably, the rate remained below 1% even in areas with the greatest COVID-19 spread, partly reflecting reorganization measures implemented in medical oncology units in Italy at the onset of this outbreak, supporting the continuation of most oncologic treatments in the adjuvant and metastatic setting. Based on these data, delaying active antitumor treatment to avoid SARS-CoV-2 transmission should not be routinely recommended.

### Virology

Schoof M, Faust B, Saunders RA, et al. **An ultrapotent synthetic nanobody neutralizes SARS-CoV-2 by stabilizing inactive Spike.** *Science* 2020, Vol. 370, Issue 6523, pp. 1473-1479. Full-text: <https://doi.org/10.1126/science.abe3255>

Monoclonal antibodies that target SARS-CoV-2 must be produced in mammalian cells and need to be delivered intravenously. By contrast, nanobodies can be produced in bacteria or yeast, and their stability may enable aerosol delivery. Here, Aashish Manglik, Michael Schoof and colleagues describe nanobodies that disrupt the interaction between the SARS-CoV-2 Spike protein and the host cell receptor angiotensin-converting enzyme 2 (ACE2). Cryo-electron microscopy (cryo-EM) revealed that one nanobody, Nb6, binds Spike in a fully inactive conformation with its receptor binding domains locked into their inaccessible down state, incapable of binding ACE2.

Xiang Y, Nambulli S, Xiao Z, et al. **Versatile and multivalent nanobodies efficiently neutralize SARS-CoV-2.** *Science* 2020, Vol. 370, Issue 6523, pp. 1479-1484. Full-text: <https://doi.org/10.1126/science.abe4747>

In yet another paper on nanobodies, Yi She, Yufei Xiang and colleagues describe neutralizing nanobodies (Nbs) with picomolar to femtomolar affinities that inhibit viral infection at concentrations below the nanograms-per-milliliter level. The authors determined a structure of one of the most potent Nbs in complex with the RBD. Multivalent constructs of selected nanobodies achieved even more potent neutralization.

## Prevention

Spaccferri G, Larrieu S, Pouey J, et al. **Early assessment of the impact of mitigation measures to control COVID-19 in 22 French metropolitan areas, October to November 2020.** Euro Surveill. 2020;25(50):pii=2001974. <https://doi.org/10.2807/1560-7917.ES.2020.25.50.2001974>

To control this second SARS-CoV-2 pandemic wave, French national and local authorities implemented a series of mitigation measures in certain metropolitan areas starting mid-October, followed by a countrywide lockdown on 30 October. Here, Guillaume Spaccferri, Sophie Larrieu and colleagues assess the impact and timeliness of these measures, mainly curfews, describing COVID-19 spread and severity in the 22 French metropolitan areas. A considerable decrease in incidence and hospital admissions was observed 7 to 10 days after the measures were put in place, occurring earlier in metropolitan areas where these had first been undertaken.

Tufekci Z. **Hang On for 3 More Months.** The Atlantic 2020, published 17 December. Full-text: <https://www.theatlantic.com/ideas/archive/2020/12/wait-until-march/617410/>

Some simple advice for anyone contemplating a holiday gathering: Wait until March or Easter 2021: 4 April.

## Vaccine

Ball P. **The lightning-fast quest for COVID vaccines – and what it means for other diseases.** Nature 2020, published 18 December. Full-text: <https://www.nature.com/articles/d41586-020-03626-1>

The speedy approach used to tackle SARS-CoV-2 could change the future of vaccine science. “It shows how fast vaccine development can proceed when there is a true global emergency and sufficient resources,” says Dan Barouch, director of the Center for Virology and Vaccine Research at Harvard Medical School in Boston, Massachusetts.

Rubin EJ, Baden LR, Barocas JA, Morrissey S. **Covid-19 Vaccine Fundamentals**. Audio interview (19:46). *N Engl J Med* 2020; 383: e146. Access: <https://doi.org/10.1056/NEJMe2035370>

The editors discuss the five types of COVID-19 vaccine under study, as well as trial results of the therapeutic agent baricitinib.

## Severe COVID

Berlin DA, Gulick RM, Martinez FJ. **Severe Covid-19**. *N Engl J Med* 2020, published 17 December. Full-text: <https://doi.org/10.1056/NEJMcp2009575>

David Berlin, Roy Gulick and Fernando Martinez describe the case of a 50-year-old, previously healthy man who presented to the emergency department with 2 days of worsening dyspnea. He had fever, cough, and fatigue during the week before presentation. The authors discuss various strategies, review some guidelines for severe COVID-19 (American Thoracic Society, Infectious Diseases Society of America, National Institutes of Health, and Surviving Sepsis Campaign) and conclude with recommendations.

## Journal Feature

Gaind N. **The best science images of 2020**. *Nature*, December 2020. Full-text: <https://www.nature.com/immersive/d41586-020-03436-5/index.html>

It's almost Christmas. Let's enjoy some pictures about wafer-thin solar cells, gene-edited squids, a 30-micrometre boat and many more.

## Retractions

Oransky I, Marcus A. **The Top Retractions of 2020**. *The Scientist* 2020, published 15 December. Full-text: <https://www.the-scientist.com/news-opinion/the-top-retractions-of-2020-68284>

According to Retraction Watch in early December, 39 articles about the novel coronavirus have been retracted from preprint servers or peer-reviewed journals so far—a number we're confident will grow. (That number does not include the retraction of an article from a Johns Hopkins student newspaper claiming that COVID-19 has had “relatively no effect on deaths in the United States.”)

## 23 December

### Epidemiology

Pullano G, Di Domenico L, Sabbatini CE, et al. **Underdetection of COVID-19 cases in France threatens epidemic control.** Nature 2020, published 21 December. Full-text: <https://doi.org/10.1038/s41586-020-03095-6>

In the first 7 weeks following the end of the French lockdown on 11 May 2020, 90.000 cases (9 out of 10 cases) may not have been ascertained by the national surveillance system. Vittoria Colizza, Giulia Pullano and colleagues suggest that more aggressive, targeted and efficient testing is required to act as a pandemic-fighting tool. They warn that a coherent testing strategy will be again of critical value to avoid a third SARS-CoV-2 wave in the coming months.

See also the *NEWS AND VIEWS* comment by Shaman J. **An estimation of undetected COVID cases in France.** Nature 2020, published 21 December. Full-text: <https://www.nature.com/articles/d41586-020-03513-9>

de Gier B, de Oliveira BL, van Gaalen RD, et al. **Occupation- and age-associated risk of SARS-CoV-2 test positivity, the Netherlands, June to October 2020.** Euro Surveill December 17, 2020;25(50):pii=2001884. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.50.2001884>

This study from the Netherlands found an increased positivity to the COVID test among workers in the hospitality and public transport sectors, but also among driving instructors, hairdressers and estheticians.

### Transmission

Eisenstein M. **What's your risk of catching COVID? These tools help you to find out.** Nature 2020, published 21 December. Full-text: <https://www.nature.com/articles/d41586-020-03637-y>

Several apps have been recently launched that claim to predict the chance of infection and illness depending on what people are doing and where they are. In this *Technology Feature*, Michael Eisenstein takes a closer look.

### Prevention

Mina MJ, Andersen KG. **COVID-19 testing: One size does not fit all.** Science 2020, published 21 December. Full-text: <https://doi.org/10.1126/science.abe9187>

A one-sentence abstract by Michael Mina and Kristian Andersen: “To control the pandemic, testing should be considered a public health tool.” Discover the world of SARS-CoV-2 testing one year into the pandemic.

Swaminathan S. **The WHO’s chief scientist on a year of loss and learning.** Nature 2020, published 17 December. Full-text: <https://www.nature.com/articles/d41586-020-03556-y>

The head of scientific work at the World Health Organization reflects on the agency’s challenges and achievements as it navigates the COVID pandemic.

## Immunology

Jarjour NN, Masopust D, Jameson SC. **T cell memory: Understanding COVID-19.** Immunity 2020, published 19 December. Full-text: <https://doi.org/10.1016/j.immuni.2020.12.009>

In this *Primer*, Nicholas Jarjour, David Masopust and Stephen Jameson explain the fundamental features of T cell memory and their potential relevance for effective immunity to SARS-CoV-2.

## Vaccine

Oliver S, Gargano J, Marin M, et al. **The Advisory Committee on Immunization Practices’ Interim Recommendation for Use of Moderna COVID-19 Vaccine — United States, December 2020.** MMWR Morb Mortal Wkly Rep. ePub: 20 December 2020. DOI: <http://dx.doi.org/10.15585/mmwr.mm695152e1>

The Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the Moderna COVID-19 (mRNA-1273) vaccine. Adverse events that occur in a recipient after receipt of COVID-19 vaccine should be reported to the Vaccine Adverse Events Reporting System (VAERS). FDA requires that vaccination providers report vaccination administration errors, serious adverse events, cases of multisystem inflammatory syndrome, and cases of COVID-19 that result in hospitalization or death after administration of the COVID-19 vaccine under an EUA. Information on how to submit a report to VAERS is available at <https://vaers.hhs.gov/index.html>.

## Severe COVID

Working group for the surveillance and control of COVID-19 in Spain; Members of the Working group for the surveillance and control of COVID-19 in Spain. **The first wave of the COVID-19 pandemic in Spain: characterisation of cases and risk factors for severe outcomes, as at 27 April 2020.** Euro Surveill. 2020 Dec;25(50). PubMed: <https://pubmed.gov/33334400>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.50.2001431>

During the first pandemic wave in Spain in spring 2020, males had higher odds ratio (OR) of severe outcomes than females with regard to hospitalization, ICU admission and death. Pneumonia was associated with a 27-fold higher odds of hospitalization. Patients who presented with cardiovascular disease were more likely to have a severe outcome. Older age predicted mortality, with highest odds of death among patients  $\geq 80$  years (OR: 28.45; 95% CI: 19.85–40.78), compared with patients  $< 40$  years. Looking at predisposing conditions, chronic kidney disease had the highest OR of death.

## Society

Radwan E, Radwan A, Radwan W. **The role of social media in spreading panic among primary and secondary school students during the COVID-19 pandemic: An online questionnaire study from the Gaza Strip, Palestine.** Heliyon 2020, published 21 December. Full-text: <https://doi.org/10.1016/j.heliyon.2020.e05807>

Social media can be a global calamity in times of pandemic. Misinformation, fake news, and rumors spread on social media faster than reliable information – even faster than the virus itself. In this study, Eqbal Radwan, Afnan Radwan and Walaa Radwan (Father and sons? Cousins?) determined how social media affects the spread of panic about COVID-19 among primary and secondary school students in the Gaza Strip, Palestine. You know the answer.

## 24 December

### Epidemiology

da Silva Filipe A, Shepherd JG, Williams T, et al. **Genomic epidemiology reveals multiple introductions of SARS-CoV-2 from mainland Europe into Scotland.** Nat Microbiol 6, 112–122 (2021). Full-text: <https://doi.org/10.1038/s41564-020-00838-z>



During the first month of the SARS-CoV-2 outbreak in Scotland, 2641 cases of COVID-19 led to 1832 hospital admissions, 207 intensive care admissions and 126 deaths. Here, Emma Thomson, Ana da Silva Filipe and colleagues sequenced 1314 SARS-CoV-2 viral genomes and show that SARS-CoV-2 was introduced to Scotland on at least 283 occasions during February and March 2020. Early introductions of SARS-CoV-2 originated from mainland Europe (the majority from Italy and Spain). The authors identified subsequent early outbreaks in the community, within healthcare facilities and at an international conference. The authors conclude that the risk of multiple reintroduction events in future waves of infection remains high in the absence of population immunity.

## Virology

Li T, Liu D, Yang Y, et al. **Phylogenetic supertree reveals detailed evolution of SARS-CoV-2.** *Sci Rep* 10, 22366 (2020), published 22 December. Full-text: <https://doi.org/10.1038/s415>

The origin of SARS-CoV-2 and its evolutionary relationship is still being discussed. Here, Jie Feng, Tingting Li and colleagues applied the matrix representation with parsimony (MRP) pseudo-sequence supertree analysis to study the origin and evolution of SARS-CoV-2.

## Immunology

Malone B, Simovski B, Moliné C, et al. **Artificial intelligence predicts the immunogenic landscape of SARS-CoV-2 leading to universal blueprints for vaccine designs.** *Sci Rep* 10, 22375 (2020). Full-text: <https://doi.org/10.1038/s41598-020-78758-5>

In order to effectively combat the SARS-CoV-2 pandemic, a vaccine will need to protect the vast majority of the human population and stimulate diverse T cell responses against multiple viral targets including, but not limited to, the S protein. Here, Trevor Clancy, Brandon Malone and colleagues profiled the entire SARS-CoV-2 proteome across the most frequent 100 HLA-A, HLA-B and HLA-DR alleles in the human population and generated comprehensive epitope maps. They identified a subset of epitope hotspots that could be harnessed in a vaccine formulation to provide broad coverage across the global population.

Larsen MD, de Graaf EL, Sonneveld ME, et al. **Afucosylated IgG characterizes enveloped viral responses and correlates with COVID-19 severity.** Science 2020, published 23 December. Full-text: <https://doi.org/10.1126/science.abc8378>

Afucosylated IgG (~6% of total IgG in humans) are specifically formed against enveloped viruses but generally not against other antigens. Here, Gestur Vidarsson, Mads Delbo Larsen and colleagues report that critically ill COVID-19 patients, but not those with mild symptoms, had high levels of afucosylated IgG antibodies against SARS-CoV-2, amplifying pro-inflammatory cytokine release and acute phase responses.

## Pathogenesis

Schmidt N, Lareau CA, Keshishian H, et al. **The SARS-CoV-2 RNA-protein interactome in infected human cells.** Nat Microbiol (2020). Full-text: <https://doi.org/10.1038/s41564-020-00846-z>

Mathias Munschauer, Nora Schmidt and colleagues provide detailed molecular insights into the identity of host factors and cellular machinery that directly and specifically bind SARS-CoV-2 RNAs during infection of human cells. They integrated CRISPR perturbation data and performed genetic and pharmacological validation experiments that together suggest functional roles for 18 RNA interactome proteins in SARS-CoV-2 infections.

## Vaccine

Pollard AJ, Bijker EM. **A guide to vaccinology: from basic principles to new developments.** Nat Rev Immunol (2020). Full-text: <https://doi.org/10.1038/s41577-020-00479-7>

2021 may be the perfect time for immunologists to be involved in designing the next generation of powerful immunogens. In this review, Andrew Pollard and Else Bijker provide an overview of vaccines, immunization and related issues.

## Diagnostics

Rosado J, Pelleau S, Cockram C, et al. **Multiplex assays for the identification of serological signatures of SARS-CoV-2 infection: an antibody-based diagnostic and machine learning study.** Lancet Microbe 2020, published 21 December. Full-text: [https://doi.org/10.1016/S2666-5247\(20\)30197-X](https://doi.org/10.1016/S2666-5247(20)30197-X)

Would you like to classify individuals who were infected more than 6 months ago and measure perform serological surveys in very low transmission settings? Then measure IgG and IgM antibody responses to 1) seven SARS-CoV-2 spike or nucleoprotein antigens, 2) two antigens for the nucleoproteins of the 229E and NL63 seasonal coronaviruses, and 3) three non-coronavirus antigens up to 39 days after symptom onset from 215 adults – and start your machine learning algorithms. A paper by Michael White, Jason Rosado and colleagues from the Pasteur Institute in Paris.

## Treatment

ACTIV-3/TICO LY-CoV555 Study Group. **A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19.** N Engl J Med 2020, published 22 December. Full-text: <https://doi.org/10.1056/NEJMoa2033130>

The Lilly monoclonal antibody LY-CoV555, when co-administered with remdesivir, did not demonstrate efficacy among hospitalized patients who had COVID-19 without end organ failure. This is the result of a randomized study involving 314 hospitalized patients by Jens D. Lundgren and colleagues of the ACTIV-3/TICO LY-CoV555 Study Group.

## Pediatrics

Henderson LA, Yeung RSM. **MIS-C: early lessons from immune profiling.** Nat Rev Rheumatol (2020). Full-text: <https://doi.org/10.1038/s41584-020-00566-y>

A brief summary of what we have learned in 9 months about the multisystem inflammatory syndrome in children (MIS-C), a rare complication of SARS-CoV-2 infection.

## Beyond Corona

Steindl D, Boehmerle W, Körner R, et al. **Novichok nerve agent poisoning.** Lancet 2020, published 22 December. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32644-1](https://doi.org/10.1016/S0140-6736(20)32644-1)

Kai-Uwe Eckardt, David Steindl and colleagues report the clinical details of 44-year-old Alexei Navalny's poisoning. Two weeks after the poisoning, a laboratory of the German armed forces identified an organophosphorus nerve agent from the novichok group in blood samples collected immediately after Navalny's admission to Charité clinic in Berlin.

Editors. **A review of 2020 through Nature's editorials.** Nature 2020, published 22 December. Full-text: <https://www.nature.com/articles/d41586-020-03560-2>

Nature's first editorial of 2020 marked the beginning of what was expected to be a super-year for the environment and sustainable development. Then, on 21 January, Nature's first editorial on the coronavirus appeared.

## 25 December

### In Memoriam

Normile D, Huihui B, Hicks L, et al. **Ones we've lost.** Science. 2020 Dec 18;370(6523):1398-1401. PubMed: <https://pubmed.gov/33335047>. Full-text: <https://science.sciencemag.org/content/370/6523/1398>

### Epidemiology

Wurtzer S, Marechal V, Mouchel JM, et al. **Evaluation of lockdown effect on SARS-CoV-2 dynamics through viral genome quantification in waste water, Greater Paris, France, 5 March to 23 April 2020.** Euro Surveill. 2020 Dec;25(50). PubMed: <https://pubmed.gov/33334397>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.50.2000776>

Management of epidemics requires careful monitoring of the infected population because special measures such as lockdowns rely on this kind of information. Here, Laurent Moulin and colleagues from [Eau de Paris](#) report the analysis of raw waste water (WW) collected at the inlets of waste water treatment plants (WWTPs). They demonstrate that a quantitative detection of SARS-CoV-2 in WW reflects the circulation of the virus in the human population in Greater Paris.

### Transmission

Kemp SA, Collier DA, Datir R, et al. **Neutralising antibodies drive Spike mediated SARS-CoV-2 evasion.** medRxiv 2020, posted 19 December. Full-text: <https://doi.org/10.1101/2020.12.05.20241927>

In immune-suppressed individuals, treatment with convalescent plasma might lead to the emergence of a mutated SARS-CoV-2 strain. Here, Ravindra Gupta from the Cambridge Institute for Therapeutic Immunology and Infectious Diseases reports the case of a repeated evolutionary response by SARS-CoV-2 against antibody therapy during the course of a persistent and eventu-

ally fatal infection in an immunocompromised host. The authors describe a 69-70 deletion in the spike protein which was twice as infectious in a lentivirus model. The 69-70 deletion is also present in the new UK variant strain B.1.1.7.

Read also Kupferschmidt K. **Mutant coronavirus in the United Kingdom sets off alarms, but its importance remains unclear.** Nature 2020, published 20 December. Full-text: <https://www.sciencemag.org/news/2020/12/mutant-coronavirus-united-kingdom-sets-alarms-its-importance-remains-unclear>

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Kupferschmidt K. **U.K. variant puts spotlight on immunocompromised patients' role in the COVID-19 pandemic.** Nature 2020, published 23 December. Full-text: <https://www.sciencemag.org/news/2020/12/uk-variant-puts-spotlight-immunocompromised-patients-role-covid-19-pandemic>

## Prevention

Brown M. **Flay your fart: viral clip calls on public to alter speech to curb Covid.** The Guardian 2020, published 21 December. Full-text: <https://www.theguardian.com/culture/2020/dec/21/flay-your-fart-viral-clip-calls-on-public-to-alter-speech-to-curb-covid?utm>

A retired PR consultant and translator has produced a video suggesting the government is to ban certain sounds and letters of the alphabet because they increase the transmission of COVID-19. Instead of “please take care”, we should say “flease nake lare”, says the skit.

## Immunology

Lumley SF, O'Donnell D, Stoesser NE, et al. **Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers.** N Engl J Med 2020, published 23 December. Full-text: <https://doi.org/10.1056/NEJMoa2034545>

Christmas 2020 – good news for people with SARS-CoV-2 antibodies. In this longitudinal cohort study, there were no symptomatic infections in 1265 workers with anti-spike antibodies. Two 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. The authors conclude that the presence of anti-spike or anti-nucleocapsid IgG antibodies are associated with a substantially reduced risk of SARS-CoV-2 reinfection in the ensuing 6 months.

## Treatment

Zhang LK, Sun Y, Zeng H, et al. **Calcium channel blocker amlodipine besylate therapy is associated with reduced case fatality rate of COVID-19 patients with hypertension.** Cell Discov. 2020 Dec 22;6(1):96. PubMed: <https://pubmed.gov/33349633>. Full-text: <https://doi.org/10.1038/s41421-020-00235-0>

Might anti-hypertensive treatment with amlodipine be associated with a decreased case fatality rate of SARS-CoV-2 infection? Gengfu Xiao and Lei-Ke Zhang from Wuhan Institute of Virology, Center for Biosafety Mega-Science, report on 96 patients who only had hypertension as co-morbidity. 19 patients received amlodipine besylate, 14 received nifedipine, 8 received ARBs/ACEIs, 45 had no drug information, and 10 had no anti-hypertensive drug treatment. The numbers are too small to draw conclusions.

Esparza TJ, Martin NP, Anderson GP, Goldman ER, Brody DL. **High affinity nanobodies block SARS-CoV-2 spike receptor binding domain interaction with human angiotensin converting enzyme.** Sci Rep. 2020 Dec 22;10(1):22370. PubMed: <https://pubmed.gov/33353972>. Full-text: <https://doi.org/10.1038/s41598-020-79036-0>

Nanobodies are 12–15 kDa single-domain antibody fragments that can be delivered by inhalation and are amenable to relatively inexpensive large-scale production. Here, David Brody, Thomas Esparza and colleagues describe the nanobody candidate NIH-CoVnb-112 which binds to the SARS-CoV-2 spike protein RBD and blocks spike protein interaction with the ACE2 receptor. They are optimistic about the possibility that low-cost, stable, and safe nanobody-based therapeutics will be developed for inhaled use in the home outside of formal healthcare environments.

## Severe COVID

Jiang Y, Abudurexiti S, An MM, et al. **Risk factors associated with 28-day all-cause mortality in older severe COVID-19 patients in Wuhan, China: a retrospective observational study.** Sci Rep 10, 22369 (2020). <https://doi.org/10.1038/s41598-020-79508-3>

Studies about risk factors for increased COVID-19 mortality abound. In this retrospective study from Wuhan including 281 older patients with severe COVID-19 categorized into two age groups (60–79 years and  $\geq 80$  years), LDH had the highest predictive value for 28-day all-cause mortality.

## 26 December

### Epidemiology

Millán-Guerrero RO, Caballero-Hoyos R, Monárrez-Espino J. **Poverty and survival from COVID-19 in Mexico.** J Pub Health 2020, published 24 December. Full-text: <https://doi.org/10.1093/pubmed/fdaa228>

Individuals living in municipalities with extreme poverty had a 9% higher risk of dying than those living in municipalities classified as not poor. This is the result of a retrospective Mexican cohort study of nearly 250,000 COVID-19 patients. Mortality was 12,3% reaching 59,3% in patients with  $\geq 1$  comorbidities. Combating extreme poverty needs to be a central preventive strategy.

Niu J, Rodriguez JA, Sareli C, et al. **COVID-19 infection among first responders in Broward County, Florida, March–April 2020.** Journal of Public Health 2020, published 24 December. Full-text: <https://doi.org/10.1093/pubmed/fdaa231>

Due to job-related exposures, first responders (FRs) are at a higher risk of SARS-CoV-2 infection than the general population. Here, Paula Eckardt, Jianli Niu and colleagues from Memorial Healthcare System, Hollywood, screened a total of 3375 FRs between March and April 2020. Overall, 289 (8,6%) were positive, with the highest rates among those aged 25-49 years. Of those testing positive, 235 (81,3%) were asymptomatic.

### Transmission

Aydillo T, Gonzales-Reiche AS, Aslam S, et al. **Shedding of Viable SARS-CoV-2 after Immunosuppressive Therapy for Cancer.** N Engl J Med 2020, published 24 December. Full-text: <https://doi.org/10.1056/NEJMc2031670>

Patients with profound immunosuppression may shed viable SARS-CoV-2 for at least 2 months. This is the results of a study by Mini Kamboj, Teresa Aydillo and colleagues from Memorial Sloan Kettering Cancer Center, New York. The authors used cell cultures to detect viable virus in serially collected respiratory samples obtained from 18 recipients of hematopoietic stem cell transplants or chimeric antigen receptor (CAR) T cell therapy and 2 patients with lymphoma.

## Treatment

Trump S, Lukassen S, Anker MS, et al. **Hypertension delays viral clearance and exacerbates airway hyperinflammation in patients with COVID-19.** Nat Biotechnol 2020, published 24 December. Full-text: <https://doi.org/10.1038/s41587-020-00796-1>

ACEI treatment in patients with SARS-CoV-2 infection and hypertension might warrant further investigation. This is the suggestion by Irina Lehmann, Saskia Trump and colleagues from Charité, Berlin, who combined clinical data (n = 144) and single cell sequencing data of airway samples (n = 48) with *in vitro* experiments. The authors observed a distinct inflammatory predisposition of immune cells in patients with hypertension that correlated with critical COVID-19 progression. ACEI treatment was associated with dampened COVID-19-related hyperinflammation and with increased cell intrinsic antiviral responses.

## Severe COVID

Jorge A, D'Silva KM, Cohen A, et al. **Temporal trends in severe COVID-19 outcomes in patients with rheumatic disease: a cohort study.** Lancet Rheumatology 2020, published 23 December. Full-text: [https://doi.org/10.1016/S2665-9913\(20\)30422-7](https://doi.org/10.1016/S2665-9913(20)30422-7)

In this cohort study of patients with rheumatic and musculoskeletal diseases, Hyon Choi, April Jorge and colleagues from Massachusetts General Hospital compared 2811 patients who were diagnosed with COVID-19 during the first 90 days of the pandemic (early cohort) with 5729 patients diagnosed during the second 90 days of the pandemic (late cohort). The late cohort fared better: the risk of hospitalization, intensive care unit admission, mechanical ventilation, acute kidney injury, renal replacement therapy, and death was lower in the late cohort than in the early cohort. This finding is probably multifactorial, due to increased testing capacity allowing for detection of milder cases, improved supportive care, and improved treatments. The lesson for the future: use historical comparators cautiously in observational studies of new therapies for COVID-19!

## Comorbidities

McGurnaghan SJ, Weir A, Bishop J, et al. **Risks of and risk factors for COVID-19 disease in people with diabetes: a cohort study of the total population of Scotland.** Lancet Diabetes Endocrinol 2020, published 23 December. Full-text: [https://doi.org/10.1016/S2213-8587\(20\)30405-8](https://doi.org/10.1016/S2213-8587(20)30405-8)



Of the total Scottish population on March 1, 2020 ( $n = 5.463.300$ ), the population with diabetes was 319.349 (5,8%), 1082 (0,3%) of whom developed fatal or critical care unit treated COVID-19 by July 31, 2020. In the population without diabetes, 4081 (0,1%) of 5.143.951 people developed fatal or critical care unit-treated COVID-19. As of July 31, the overall odds ratio (OR) for diabetes, adjusted for age and sex, was 1,395 compared with the risk in those without diabetes. The OR was 2,4 in type 1 diabetes and 1,4 in type 2 diabetes. Among people with diabetes, adjusted for age, sex, and diabetes duration and type, those who developed fatal or critical care unit-treated COVID-19 were more likely to be male, live in residential care or a more deprived area, have a COVID-19 risk condition, retinopathy, reduced renal function, or worse glycemic control, have had a diabetic ketoacidosis or hypoglycemia hospitalization in the past 5 years, be on more anti-diabetic and other medication (all  $p < 0.0001$ ), and have been a smoker ( $p = 0.0011$ ).

See also the comment by Stehouwer CDA. **Observational research on severe COVID-19 in diabetes.** *Lancet Diabetes Endocrinol* 2020, published 23 December. Full-text: [https://doi.org/10.1016/S2213-8587\(20\)30432-0](https://doi.org/10.1016/S2213-8587(20)30432-0)

Tisminetzky M, Delude C, Hebert T, et al. **Multiple Chronic Conditions, and COVID-19: A literature review.** *J Gerontol* 2020, published 24 December. Full-text: <https://doi.org/10.1093/gerona/glaa320>

Nothing new in this short review about the most frequent SARS-CoV-2 comorbidities: hypertension, diabetes mellitus, cardiovascular disease, chronic pulmonary disease, and chronic kidney disease. And: men had a higher risk of dying than women. But if you want a concise literature overview, here you go.

## Collateral Effects

Silverman ME, Burgos L, Rodriguez ZI, et al. **Postpartum mood among universally screened high and low socioeconomic status patients during COVID-19 social restrictions in New York City.** *Sci Rep* 10, 22380 (2020). Full-text: <https://doi.org/10.1038/s41598-020-79564-9>

Post-partum depression, the most common complication of childbearing, is a prevalent, cross-cultural disorder. Even in the best environments, the period following childbirth represents a time of heightened stress and vulnerability for most, if not all, new parents. In this study of 516 post-partum patients, Michael Silverman et al. now demonstrate a differentiated response in the post-partum mood of those living in New York City during the COVID-19 pan-

demic... based on socioeconomic status! While those in areas with higher socioeconomic status (SES) demonstrated no change in post-partum mood after implementation of social restrictions in New York, those living in lower SES expressed improved mood over the same time period. Try to find out why.

## Education

Tambyraja AL. **New Order, New Hope**. N Engl J Med 2020, published 24 December. Full-text: <https://doi.org/10.1056/NEJMp2016142>

In this Christmas *Perspective*, Andrew Tambyraja reminds us about traditional strengths in medicine: agility and patient focus, humility and the pursuit of the greater good.

## Beyond Corona

Else H. **Climate change and COVID-19 vaccines are among the themes set to shape research**. Nature 2020, published 22 December. Full-text: <https://www.nature.com/articles/d41586-020-03651-0>

The science events to watch for in 2021: Climate comeback | COVID vaccines | Open access drive | Stem cell revamp | Crunch time for Alzheimer's drug | Mars gets busy | Long-awaited telescope launch | Ripple effect

## 27 December

### Prevention

Martin CA, Jenkins DR, Patel P, et al. **No cases of asymptomatic SARS-CoV-2 infection among healthcare staff in a city under lockdown restrictions: lessons to inform 'Operation Moonshot'**. J Pub Health 2020, published 26 December. Full-text: <https://doi.org/10.1093/pubmed/fdaa237>

Imagine inviting more than 13,000 healthcare workers (HCWs) to get SARS-CoV-2 tested. Now about 8% (n = 1150) of the workforce volunteer and you find no cases of asymptomatic SARS-CoV-2 infection. You would probably conclude, like Manish Pareek, Christopher Martin and colleagues, that voluntary testing of asymptomatic staff may not be cost-effective.

## Vaccine

Burki T. **Equitable distribution of COVID-19 vaccines.** *Lancet Infect Dis* 2021, published 1 January. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30949-X](https://doi.org/10.1016/S1473-3099(20)30949-X)

If everything goes according to plan, November 2020 will be remembered as the beginning of the end of the COVID-19 pandemic. Countries will have to ensure that they have the infrastructure for mass immunization campaigns. Those without experience in distributing influenza vaccines must learn how to establish platforms for adult vaccination. Vaccine hesitancy will have to be overcome.

Lucia VC, Kelekar A, Afonso NM. **COVID-19 vaccine hesitancy among medical students, Journal of Public Health.** *J Pub Health* 2020, published 26 December. Full-text: <https://doi.org/10.1093/pubmed/fdaa230>

Medical students are among the group of frontline healthcare providers likely to be exposed to COVID-19 patients. It is important to achieve high COVID-19 vaccination coverage rates in this group as soon as a vaccine is available. In this survey completed by 168 of 494 medical students (response rate = 34%), the vast majority had positive attitudes regarding immunizations in general and the importance of vaccines for themselves and patients. 53% indicated they would participate in a COVID-19 vaccine trial; only 23% were unwilling to take a COVID-19 vaccine immediately upon FDA approval.

## Diagnostics

Rathe JA, Hemann EA, Eggenberger J, et al. **SARS-CoV-2 Serologic Assays in Control and Unknown Populations Demonstrate the Necessity of Virus Neutralization Testing.** *J Infect Dis* 2020, published 25 December. Full-text: <https://doi.org/10.1093/infdis/jiaa797>

How does serologic antibody testing outcome link with virus neutralization of SARS-CoV-2? To answer this question, Jennifer Rathe et al. compared serum Ig levels across platforms of viral antigens and antibodies with 15 positive and 30 negative SARS-CoV-2 controls followed by viral neutralization assessment. After applying these platforms to a clinically relevant cohort of 114 individuals with unknown histories of SARS-CoV-2 infection, they confirmed that no single serologic assay provides perfect prediction for viral neutralizing ability. Spike IgG3 provided the highest accuracy for predicting serologically positive individuals with virus neutralization activity.

## Clinical

Hampshire A, Trender W, Chamberlain SR, et al. **Cognitive deficits in people who have recovered from COVID-19 relative to controls: An N=84,285 online study.** medRxiv 2020, posted 21 October. Full-text: <https://doi.org/10.1101/2020.10.20.20215863>

SARS-CoV-2 infection may exhibit cognitive deficits that persist into the recovery phase. This is what Adam Hampshire and colleagues from the Imperial College in London suggest after analyzing cognitive test data from 84,285 Great British Intelligence Test participants who completed a questionnaire regarding suspected and biologically confirmed COVID-19 infection. Deficits were most pronounced in individuals who had been hospitalized, but were also detectable in individuals with mild but biologically confirmed cases who reported no breathing difficulty. The scale of the observed deficits was substantial; for the hospitalized patients who needed ventilator support they were equivalent to the average 10-year decline in global performance between the ages of 20 to 70 – comparable to a 8.5-point difference in IQ. Let's hope that the results of this pre-print paper posted in October will be proved wrong and not be accepted for publication.

Gerkin RC, Ohla K, Veldhuizen MG, et al. **Recent smell loss is the best predictor of COVID-19 among individuals with recent respiratory symptoms.** Chemical Senses 2020, published 25 December. Full-text: <https://doi.org/10.1093/chemse/bjaa081>

Might quantified smell loss be the best predictor of COVID-19 amongst those with symptoms of respiratory illness? That's the suggestion by Valentina Parma, Richard Gerkin and colleagues after quantifying changes in chemosensory abilities in individuals with a positive (C19+; n = 4148) or negative (C19-; n = 546) COVID-19 laboratory test outcome.

## Comorbidities

Guillet H, Gallet R, Pham V, et al. **Clinical spectrum of ischaemic arterial diseases associated with COVID-19: a series of four illustrative cases.** Eur Heart J 2020, published 25 December. Full-text: <https://doi.org/10.1093/ehjcr/ytaa488>

Henri Guillet et al. from Hôpital Henri Mondor, Paris, describe four different cases of COVID-19 infection with ischemic arterial events: a myocardial infarction with high thrombus load, ischemic stroke on spontaneous throm-

basis of the aortic valve, floating thrombus with mesenteric, splenic and renal infarction, and acute limb ischemia.

Allen B, El Shahawy O, Rogers ES, et al. **Association of substance use disorders and drug overdose with adverse COVID-19 outcomes in New York City: January–October 2020**, *Journal of Public Health*. J Pub Health 2020, published 26 December. Full-text: <https://doi.org/10.1093/pubmed/fdaa241>

What do you know about the relationships between substance use disorders (SUDs), overdose and COVID-19 severity and mortality? Patients with histories of SUD and drug overdose could face disproportionate risk of critical COVID-19 illness, is the answer by Bennett Allen et al. However, the authors concede that they cannot assure whether the outcomes were due to COVID-19 or unrelated because they adjusted for few comorbidities. In particular, due to missing data, body mass index was not assessed.

## Beyond Corona

Editors. **Tuberculosis and malaria in the age of COVID-19**. *Lancet Infect Dis* 2021, published 1 January. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30946-4](https://doi.org/10.1016/S1473-3099(20)30946-4)

Tuberculosis and malaria are greater long-term threats than COVID-19 and planning of resource allocation must account for that.

## German

If you read German, read Kattwinkel T. **Covid-19 im Kopf**. *Die Zeit* 2020, published 25 December. Full-text: <https://www.zeit.de/wissen/gesundheit/2020-12/corona-langzeitfolgen-psyche-depression-konzentration-neurologie>

Vergesslich, unkonzentriert oder sogar depressiv: Eine Corona-Infektion kann Spuren im Gehirn hinterlassen. Was über neurologische Schäden bekannt ist.

## French

If you read French, read Herzberg N. **Vaccins contre le Covid-19 : les raisons d'un record de vitesse**. *Le Monde* 2020, published 23 December. Full-text : [https://www.lemonde.fr/planete/article/2020/12/23/vaccin-anti-covid-les-raisons-de-ce-record-de-vitesse\\_6064337\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/23/vaccin-anti-covid-les-raisons-de-ce-record-de-vitesse_6064337_3244.html)

Il a fallu moins d'un an pour mettre au point les premiers vaccins, au lieu de dix habituellement.

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Roucaute D. **Covid-19 : les différentes étapes de la réponse immunitaire face au coronavirus.** Le Monde 2020, published 23 December. Full-text : [https://www.lemonde.fr/planete/article/2020/12/23/les-differentes-etapes-de-la-reponse-immunitaire-face-au-coronavirus\\_6064322\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/23/les-differentes-etapes-de-la-reponse-immunitaire-face-au-coronavirus_6064322_3244.html)

Les anticorps activés par l'organisme infecté par le SARS-CoV-2 n'ont pas la même durée de vie chez les hommes et chez les femmes.

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Meyerfeld B. **Brésil : à Manaus, le mirage de l'immunité collective contre le Covid-19.** Le Monde 2020, published 23 December. Full-text : [https://www.lemonde.fr/planete/article/2020/12/23/bresil-a-manaus-le-mirage-de-l-immunite-collective\\_6064323\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/23/bresil-a-manaus-le-mirage-de-l-immunite-collective_6064323_3244.html)

Une étude estime que 76 % des habitants de la métropole amazonienne posséderaient des anticorps contre le coronavirus. Sur place, les médecins confrontés à la deuxième vague restent sceptiques.

## Spanish

If you read Spanish, read Ansede M. **Respuestas para las principales dudas sobre las vacunas contra la covid.** El País 2020, published 19 December. Full-text: <https://elpais.com/ciencia/2020-12-19/respuestas-para-las-principales-incognitas-sobre-las-vacunas-contra-la-covid.html>

Media docena de expertos responden a cuestiones como la seguridad a largo plazo de las inyecciones y la duración de la protección en los vacunados.

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Carbajosa A. **Cómo Alemania ha pasado de país ejemplar a ver cómo las muertes por covid se disparan.** El País 2020, published 19 December. Full-text: <https://elpais.com/sociedad/2020-12-16/alemania-se-asoma-al-descontrol.html>

Una mezcla de medidas demasiado suaves, tardanza en reaccionar y falsa sensación de seguridad llevan al alumno aventajado en la prevención a ser uno de los más golpeados por el virus.

## 28 December

### Transmission

Birgand G, Pfeiffer-Smadja N, Fournier S, et al. **Assessment of Air Contamination by SARS-CoV-2 in Hospital Settings.** *JAMA Netw Open* 2020;3(12):e2033232. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.33232>

Controversy remains regarding the level of air contamination from SARS-CoV-2 in hospitals. After reviewing 24 cross-sectional observational studies, the authors report that the air close to and distant from patients with coronavirus disease 2019 was frequently contaminated with SARS-CoV-2 RNA; however, few of these samples contained viable virus. High viral loads were found in toilets and bathrooms, staff areas, and public hallways.

### Prevention

Baggett TP, Scott JA, Le MH, et al. **Clinical Outcomes, Costs, and Cost-effectiveness of Strategies for Adults Experiencing Sheltered Homelessness During the COVID-19 Pandemic.** *JAMA Netw Open*. 2020;3(12):e2028195. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.28195>

A modeling study of simulated adults living in homeless shelters. Daily symptom screening with PCR testing of individuals who had positive symptom screening paired with non-hospital care site management of people with mild to moderate coronavirus disease 2019 (COVID-19) was associated with a substantial decrease in infections and lowered costs.

### Vaccine

The Pfizer–BioNTech COVID-19 vaccine, codenamed BNT162b2, is now being sold under the brand name **Comirnaty™** (INN: **Tozinameran**). Find here a summary of the product characteristics and the package leaflet if you want to be able to answer the questions of your patients: [https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information\\_en.pdf](https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf)

## Severe COVID

Asch DA, Sheils NE, Islam N, et al. **Variation in US Hospital Mortality Rates for Patients Admitted With COVID-19 During the First 6 Months of the Pandemic.** *JAMA Intern Med.* Published online December 22, 2020. Full-text: <https://doi.org/10.1001/jamainternmed.2020.8193>

COVID-19 mortality in hospitals seems to be lower when the prevalence of SARS-CoV-2 infection in their surrounding communities is lower; and hospital outcomes for patients with COVID-19 have been improving throughout the year 2020. These are the key messages of a cohort study of 38,517 adult patients by David Asch and colleagues from the University of Pennsylvania. See also the comment by Boudourakis L. **Decreased COVID-19 Mortality—A Cause for Optimism.** *JAMA Intern Med.* Published online December 22, 2020. Full-text: <https://doi.org/10.1001/jamainternmed.2020.8438>.

## Pediatrics

Edlow AG, Li JZ, Collier AY, et al. **Assessment of Maternal and Neonatal SARS-CoV-2 Viral Load, Transplacental Antibody Transfer, and Placental Pathology in Pregnancies During the COVID-19 Pandemic.** *JAMA Netw Open.* 2020;3(12):e2030455. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.30455>

Knowledge is scarce about the factors that determine SARS-CoV-2 transmission to the newborn. In this prospective cohort study including 127 pregnancies, Andrea Edlow et al. found no maternal viremia, placental infection, or vertical transmission of SARS-CoV-2. However, the authors describe also a compromised transplacental transfer of anti-SARS-CoV-2 antibodies. Discover the implications and read the comment by Jamieson DJ, Rasmussen SA. **Protecting Pregnant Women and Their Infants From COVID-19: Clues From Maternal Viral Loads, Antibody Responses, and Placentas.** *JAMA Netw Open.* 2020;3(12):e2030564. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.30564>

## Journal Feature

Callaway E, Ledford H, Viglione G, Watson T, Witze A. **COVID and 2020: An extraordinary year for science.** *Nature*, December 2020. Full-text: <https://www.nature.com/immersive/d41586-020-03437-4/index.html>

The coronavirus pandemic shaped the year in research — from vaccines and treatments to campus shutdowns and virtual meetings.



## Spanish

If you read Spanish, read Fernando de Lis P. **El año de la ciencia**. El País 2020, published 27 December. Full-text: [https://elpais.com/elpais/2020/12/22/eps/1608637752\\_983427.html](https://elpais.com/elpais/2020/12/22/eps/1608637752_983427.html)

La investigación científica resulta tan compleja que muchos sintieron que era poco relevante para su vida. Pero el virus SARS-CoV-2 cambió de golpe esta percepción. Nunca en la historia se había logrado una vacuna en tan poco tiempo. Hemos visto lo mejor y lo peor de la ciencia este 2020. ¿Mantendrá ese esencial reconocimiento y apoyo en el futuro?

El virus que lo cambió todo. Esta imagen de microscopio electrónico de barrido muestra el SARS-CoV-2 (coloreado en azul) emergiendo de la superficie de células cultivadas en laboratorio. Fotografía de NIAID.

Silva R, Alonso A, Linde P. **España se vacuna**. El País 2020, published 27 December. Full-text: <https://elpais.com/sociedad/2020-12-26/espana-se-vacuna.html>

Tras la aprobación por parte de la Agencia Europea del Medicamentos y de la Comisión Europea, el fármaco de Pfizer comienza a distribuirse en la mayor parte del territorio europeo. Un viaje ultra frío a 70 grados bajo cero desde una fábrica de Puurs (Bélgica) hasta los almacenes de cada comunidad.

Sampedro J. **La revolución del ARN**. El País 2020, published 27 December. Full-text: <https://elpais.com/ciencia/2020-12-26/la-revolucion-del-arn.html>

Así se ha gestado la innovación tecnológica radical que ha permitido desarrollar las vacunas de la COVID en un tiempo récord

## French

If you read French, read Audureau W, Maad A. **Nos conseils pour identifier les discours complotistes et ne pas tomber dans leurs pièges**. Le Monde 2020, published 22 December. Full-text: [https://www.lemonde.fr/les-decodeurs/article/2020/12/22/nos-conseils-pour-identifier-les-discours-complotistes-et-ne-pas-tomber-dans-leurs-pieges\\_6064200\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2020/12/22/nos-conseils-pour-identifier-les-discours-complotistes-et-ne-pas-tomber-dans-leurs-pieges_6064200_4355770.html)

En 2020, les discours expliquant la pandémie de Covid-19 par des complots ont séduit des millions d'adeptes. Leur succès tient moins à leur véracité qu'à des ficelles rhétoriques éprouvées. Notre guide pour les débusquer. (Netflix,

tout comme Amazon Prime Video, propose des documentaires conspirationnistes.)

Foucart S. **Les silences de la Chine, un virus repéré dès 2013, la fausse piste du pangolin...** *Enquête sur les origines du SARS-CoV-2*. Le Monde 2020, published 22 December. Full-text : [https://www.lemonde.fr/sciences/article/2020/12/22/a-l-origine-de-la-pandemie-de-covid-19-un-virus-sars-cov-2-aux-sources-toujours-enigmatiques\\_6064168\\_1650684.html](https://www.lemonde.fr/sciences/article/2020/12/22/a-l-origine-de-la-pandemie-de-covid-19-un-virus-sars-cov-2-aux-sources-toujours-enigmatiques_6064168_1650684.html)

Du pangolin à la chauve-souris, en passant par des expériences de laboratoire controversées, « Le Monde » a tenté de remonter jusqu'aux origines de l'épidémie, responsable de plus d'un million et demi de morts dans le monde.

Cabut S, Dagorn G, Maad A. **Covid-19 : neuf questions sur le nouveau variant du SARS-CoV-2 observé au Royaume-Uni**. Le Monde 2020, published 21 December. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2020/12/21/neuf-questions-sur-le-nouveau-variant-du-sars-cov-2-observe-au-royaume-uni\\_6064152\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2020/12/21/neuf-questions-sur-le-nouveau-variant-du-sars-cov-2-observe-au-royaume-uni_6064152_4355770.html)

Un variant du virus, porteur de plusieurs mutations génétiques, semble être associé à une hausse brutale du nombre de cas dans la région de Londres. Mais la preuve d'une contagiosité accrue n'a pas été faite.

## 29 December

### Virology

Mahase E. **Covid-19: What have we learnt about the new variant in the UK?** BMJ 2020, published 23 December. Full-text: <https://doi.org/10.1136/bmj.m4944>

The new SARS-CoV-2 variant has evoked scenes reminiscent of the early days of COVID-19 when much of the world banned travel to and from Wuhan, China. With large parts of south-east England locked down, Elisabeth Mahase looks at what we know so far.

## Prevention

Tinson A, Clair A. **Better housing is crucial for our health and the COVID-19 recovery.** The Health Foundation 2020, published 28 December. Full-text: <https://www.health.org.uk/publications/long-reads/better-housing-is-crucial-for-our-health-and-the-covid-19-recovery>

In this *Long read*, Adam Tinson and Amy Clair summarize why housing problems are likely to be a significant component of the SARS-CoV-2 pandemic that has led to greater risks of COVID-19 infection and serious complications for certain social groups. The authors conclude that overcrowding, poor quality and unaffordable homes are a threat to health.

## Diagnostics

Pilarowski G, Marquez C, Rubio L, et al. **Field performance and public health response using the BinaxNOW™ Rapid SARS-CoV-2 antigen detection assay during community-based testing.** Clin Infect Dis 2020, published 27 December. Full-text: <https://doi.org/10.1093/cid/ciaa1890>

SARS-CoV-2 pandemic control calls for fast, low-barrier, high-performing field assays accessible to people who will not otherwise be tested or who will receive results too late for results to make a difference. Here, Diane Havlir, Genay Pilarowski and colleagues evaluated the Abbott BinaxNOW™ COVID-19 antigen card rapid assay performance for detection of persons with high levels of virus and measured the time to isolation in a community walk-up “test and respond” program. Among 3302 persons tested by BinaxNOW™ and RT-PCR in a community setting, rapid assay sensitivity was 100%/98.5%/89% using RT-PCR Ct thresholds of 30, 35 and 0. The specificity was 99.9%. Performance was high across ages and those both with and without symptoms. Rapid results may permit immediate public health action.

## Clinical

Narang K, Szymanski LM, Kane SV, Rose CH. **Acute Pancreatitis in a Pregnant Patient With Coronavirus Disease 2019 (COVID-19).** Obstet Gynecol 2020, published 22 December. PubMed: <https://pubmed.gov/33355431>. Full-text: <https://doi.org/10.1097/AOG.0000000000004287>

Coronavirus disease 2019 may present in pregnancy with a myriad of clinical symptoms other than respiratory. Acute pancreatitis represents an infrequent complication of primary COVID-19 infection.

## Severe COVID

Feng Z, Zhao H, Kang W, et al. **Association of Paraspinal Muscle Measurements on Chest Computed Tomography with Clinical Outcomes in Patients with Severe Coronavirus Disease 2019.** *J Gerontol A Biol Sci Med Sci.* 2020 Dec 23:glaa317. PubMed: <https://pubmed.gov/33355656>. Full-text: <https://doi.org/10.1093/gerona/glaa317>

For elderly patients in intensive care units or with critical illness, skeletal muscle loss adversely affects clinical outcomes. Here, Pengfei Rong, Zhishao Feng and colleagues from Third Xiangya Hospital, Central South University, **Changsha**, report that higher paraspinal muscle radiodensity (PMD), a proxy measure of lower muscle fat deposition, may be associated with a reduced risk of disease deterioration and decreased likelihood of prolonged viral shedding among female patients with severe COVID-19.

## Collateral Effects

Gergen AK, Madsen HJ, Tilva KR, Smith JB, Weyant MJ. **Coronavirus Disease 2019 in Lung Transplant Recipients.** *Ann Thorac Surg.* 2020 Dec 18:S0003-4975(20)32134-2. PubMed: <https://pubmed.gov/33347850>. Full-text: <https://doi.org/10.1016/j.athoracsur.2020.11.032>

The authors report risk factors, clinical manifestations, and treatment course of two lung transplant recipients diagnosed with COVID-19 pneumonia. After being hospitalized and later discharged home, both patients were readmitted several days later with significant worsening of respiratory status and infectious symptoms.

Martire LM, Isaacowitz DM. **What Can We Learn About Psychological Aging By Studying Covid-19?** *The Journals of Gerontology: Series B* 2020, published 26 December. Full-text: <https://doi.org/10.1093/geronb/gbaa217>

The authors give a short overview of papers about Americans living under varying social and travel restrictions; individuals living in Sweden during a period of voluntary social distancing; individuals living in Spain during a mandatory lockdown; older age predicting better or worse functioning; the ability of elderly people to deal with adversity; and the importance of using behavioral research to reduce ageism and promote intergenerational solidarity.

## Spanish

If you read Spanish, read Sabatés R, Vande Rusten P. **21 recuerdos para 2021**. El País 2020, published 28 December. Full-text: [https://elpais.com/elpais/2020/12/11/album/1607645873\\_709495.html](https://elpais.com/elpais/2020/12/11/album/1607645873_709495.html)

El fútbol español ha intentado aportar un poco de alegría y de entretenimiento al mundo entero en este año marcado por la pandemia. Estos son los momentos que más recordaremos

Domínguez N. **La madre de la vacuna contra la covid: “En verano podremos, probablemente, volver a la vida normal”** – El País 2020, published 28 December. Full-text: <https://elpais.com/ciencia/2020-12-26/la-madre-de-la-vacuna-contra-la-covid-en-verano-podremos-probablemente-volver-a-la-vida-normal.html>

La bioquímica húngara Katalin Karikó pasó 40 años trabajando en la sombra y desarrollando avances claves para las inyecciones de Moderna y BioNTech

Bassets M. **Futuro, año cero**. El País 2020, published 28 December. Full-text: <https://elpais.com/ideas/2020-12-26/2021-ano-del-aterrizaje.html>

Tras meses fuera de órbita, en 2021 toca poner los pies en el suelo. ¿Emprenderemos la recuperación de la crisis sanitaria y económica? ¿Lucharemos seriamente contra el cambio climático? ¿Se reforzarán las fronteras y se beneficiarán los demagogos? Especialistas de la economía, el pensamiento o la geopolítica hacen sus apuestas

## French

If you read French, read Truong N. Claire Marin : « **Il va falloir peut-être admettre que 2020 nous prépare douloureusement à l'idée de devoir vivre autrement** » – Le Monde 2020, published 27 December. Full-text: [https://www.lemonde.fr/idees/article/2020/12/27/claire-marin-nous-sommes-confines-mentalement-bien-plus-encore-que-nous-ne-l-avons-ete-physiquement\\_6064576\\_3232.html](https://www.lemonde.fr/idees/article/2020/12/27/claire-marin-nous-sommes-confines-mentalement-bien-plus-encore-que-nous-ne-l-avons-ete-physiquement_6064576_3232.html)

Entretien « Les penseurs de l'intime » (5/10). Philosophe des épreuves de la vie, Claire Marin explique dans un entretien au « Monde » comment la crise sanitaire accentue les ruptures sociales, professionnelles ou familiales et nous prépare « douloureusement à vivre autrement » en 2021.

## German

If you read German, read Schöps C. **Diese Impfreaktionen sind ganz normal.** Die Zeit 2020, published 23 December. Full-text: <https://www.zeit.de/wissen/gesundheit/2020-12/corona-impfung-risiken-nebenwirkungen-fieber-immunsystem>

Arm geschwollen, Kopfschmerz, Fieber, all das kann nach der Impfung gegen das Coronavirus passieren. Sorgen muss man sich deshalb aber keineswegs machen.

## 30 December

Only openness can confound the deluge of fake narratives: [www.CovidReference.com](http://www.CovidReference.com).

## Clinical

Aziz M, Goyal H, Haghbin H, Lee-Smith WM, Gajendran M, Perisetti A. **The Association of "Loss of Smell" to COVID-19: A Systematic Review and Meta-Nnalysis.** Am J Med Sci. 2020 Nov 1:S0002-9629(20)30427-4. PubMed: <https://pubmed.gov/33349441>. Full-text: <https://doi.org/10.1016/j.amjms.2020.09.017>

Patients with olfactory dysfunction or “loss of smell” might have a milder course of the disease. This is the result of a “Systematic Review and Meta-Nnalysis” (sic!) of 51 studies with 11.074 confirmed COVID-19 patients. Let’s hope that the analysis is more accurate than the copy-editor of *The American Journal of the Medical Sciences*. 😊

## Severe COVID

Shashikumar SP, Wardi G, Paul P, et al. **Development and Prospective Validation of a Deep Learning Algorithm for Predicting Need for Mechanical Ventilation.** Chest. 2020 Dec 17:S0012-3692(20)35454-4. PubMed: <https://pubmed.gov/33345948>. Full-text: <https://doi.org/10.1016/j.chest.2020.12.009>

Can a transparent deep learning (DL) model predict the need for MV in hospitalized patients and those with COVID-19 up to 24 hours in advance? The authors used commonly available data in electronic health records as well as commonly used clinical criteria (heart rate, oxygen saturation, respiratory rate, FiO<sub>2</sub> and pH) to feed their deep learning algorithm. The model provided significant improvement over traditional clinical criteria (p < 0.001).

## Comorbidities

Shields AM, Burns SO, Savic S, Richter AG; UK PIN COVID-19 consortium. **COVID-19 in patients with primary and secondary immunodeficiency: the United Kingdom experience.** J Allergy Clin Immunol. 2020 Dec 15:S0091-6749(20)32406-4. PubMed: <https://pubmed.gov/33338534>. Full-text: <https://doi.org/10.1016/j.jaci.2020.12.620>

In comparison to the general population, adult patients with primary immunodeficiency (PID) and symptomatic secondary immunodeficiency (SID) display greater morbidity and mortality from COVID-19. This is the result of a study that enrolled 100 patients by 1 July 2020, 60 with PID, 7 with other in-born errors of immunity including autoinflammatory diseases and C1 inhibitor deficiency and 33 with SID.

## Pediatrics

Marlais M, Wlodkowski T, Al-Akash S, et al. **COVID-19 in children treated with immunosuppressive medication for kidney diseases.** Arch Dis Child. 2020 Dec 21:archdischild-2020-320616. PubMed: <https://pubmed.gov/33355203>. Full-text: <https://doi.org/10.1136/archdischild-2020-320616>

Most children with kidney disease taking immunosuppressive medication have mild disease with SARS-CoV-2 infection. This is the result of a cross-sectional study by the European Rare Kidney Disease Reference Network which included 113 children from 30 different countries. The main underlying reasons for immunosuppressive therapy: kidney transplant (47%), nephrotic syndrome (27%), systemic lupus erythematosus (10%). The authors suggest that children on immunosuppressive therapy should not be more strictly isolated than children who are not on immunosuppressive therapy.

## Collateral Effects

Mourouvaye M, Bottemanne H, Bonny G, et al. **Association between suicide behaviours in children and adolescents and the COVID-19 lockdown in Paris, France: a retrospective observational study.** Arch Dis Child. 2020 Dec 22:archdischild-2020-320628. PubMed: <https://pubmed.gov/33355154>. Full-text: <https://doi.org/10.1136/archdischild-2020-320628>

There was a 50% decrease in the incidence of suicidal behaviors in children and adolescents during the COVID-19 lockdown in Paris, France. The authors

of this retrospective observational study conducted in [Necker Hospital](#) for Sick Children, Paris (January 2018–June 2020), speculate about the reasons for this decline.

## Spanish

If you read Spanish, read Peiró P. **Cómo la polio dejó de aterrorizar al mundo y otros momentos en que la ciencia venció a la muerte.** El País 2020, published 29 December. Full-text: <https://elpais.com/sociedad/2020-12-28/como-la-polio-dejo-de-aterrozar-al-mundo-y-otros-momentos-en-que-la-ciencia-vencio-a-la-muerte.html>

De la expedición de Balmis para llevar la vacuna de la viruela por todo el mundo, a la fabricación en masa de penicilina en la segunda Guerra Mundial, la humanidad ha superado retos como los que plantea ahora la covid.

Güell O. **El toque de queda de París también ‘funciona’ en Burdeos.** El País 2020, published 29 December. Full-text: <https://elpais.com/sociedad/2020-12-28/el-toque-de-queda-de-paris-tambien-funciona-en-burdeos.html>

Una investigación en Francia revela cómo la medida benefició a ciudades donde no fue aplicada.

González B. **Razones por las que, aunque se vacune, no podrá quitarse la mascarilla.** El País 2020, published 29 December. Full-text: <https://elpais.com/buenavida/salud/2020-12-28/razones-por-las-que-aunque-te-vacunes-no-podras-quitarte-la-mascarilla.html>

Aunque el final de esta pesadilla parezca cada vez más cerca, todavía queda recorrido.

Llaneras K. **¿Adiós a un año malo? 42 buenas noticias para empezar 2021 con optimismo.** El País 2020, published 29 December. Full-text: [https://elpais.com/politica/2020/12/27/actualidad/1609093070\\_533150.html](https://elpais.com/politica/2020/12/27/actualidad/1609093070_533150.html)

Una lista de datos positivos para el año nuevo, en la 'newsletter' de Kiko Llaneras.



## French

If you understand French, listen to **Le vaccin contre le Covid-19 va-t-il nous sauver rapidement de l'épidémie ?** Le Monde 2020, published 27 December. Video : [https://www.lemonde.fr/planete/video/2020/12/27/covid-19-le-vaccin-va-t-il-nous-sauver-rapidement-de-l-epidemie\\_6064589\\_3244.html](https://www.lemonde.fr/planete/video/2020/12/27/covid-19-le-vaccin-va-t-il-nous-sauver-rapidement-de-l-epidemie_6064589_3244.html)

Pfizer, Moderna, AstraZeneca... les vaccins de ces laboratoires vont-ils assurer une immunité globale suffisante pour arrêter la transmission du coronavirus ?

Roucaute D. **La seconde vague de Covid-19 en France est plus meurtrière que la première.** Le Monde 2020, published 29 December. Video : [https://www.lemonde.fr/planete/article/2020/12/29/une-deuxieme-vague-plus-meurtriere-que-la-premiere\\_6064736\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/29/une-deuxieme-vague-plus-meurtriere-que-la-premiere_6064736_3244.html)

Si le taux de mortalité dans les hôpitaux a été divisé par deux depuis avril, près de 32 500 personnes sont mortes des suites de la maladie lors des cinq derniers mois, contre un peu moins de 30 300 entre février et juillet.

## German

If you read German, read Albrecht H. **Zwischen Euphorie und Panik.** Die Zeit, published 29 December. Full-text: <https://www.zeit.de/2021/01/corona-impfungen-virologen-mutation-grossbritannien-herdenimmunitaet-usa>

Der Beginn der Impfkampagne darf nicht täuschen: Sars-CoV-2 steckt voller Überraschungen.

## 31 December

### Vaccines

GOV.UK 20201230. **Regulatory approval of COVID-19 Vaccine AstraZeneca.** <https://www.gov.uk> 2020, published 30 December. Full-texts: <https://www.gov.uk/government/publications/regulatory-approval-of-covid-19-vaccine-astrazeneca>

On December 30, UK regulatory authorities approved the Oxford University/AstraZeneca vaccine. ChAdOx1 nCoV-19 (AZD1222) needs only normal refrigeration at 2-8°C and is far cheaper than the previously approved vaccines Comirnaty (BioNTech/Pfizer) and mRNA-1273 (Moderna).

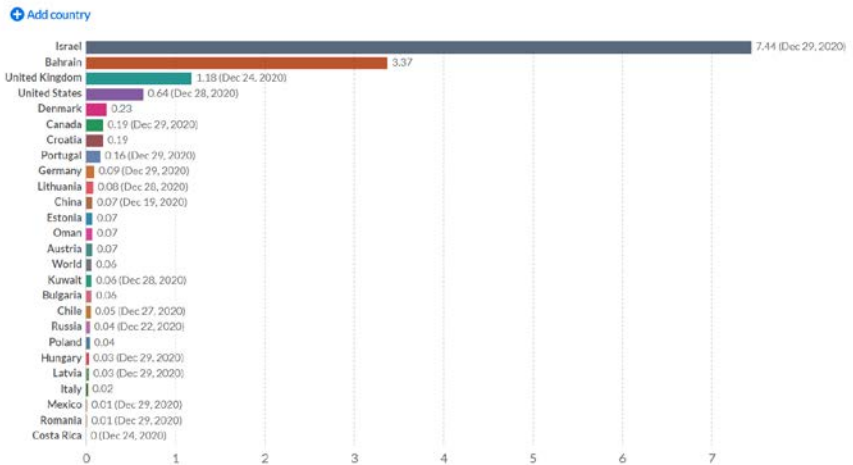
Joint Committee on Vaccination and Immunisation. **JCVI issues advice on the AstraZeneca COVID-19 vaccine.** JCVI 2020, published 30 December 2020. Full-text: <https://www.gov.uk/government/news/jcvi-issues-advice-on-the-astrazeneca-covid-19-vaccine>

The Joint Committee on Vaccination and Immunisation (JCVI) recommends that both the AstraZeneca (ChAdOx1) and the BioNTech/Pfizer (Comirnaty) vaccines are safe and provide high-levels of protection against COVID-19, including severe COVID-19. As protection is obtained around 2 weeks after the first vaccine dose, the committee recommends that vaccinating more people with the first dose is prioritized above offering others their second dose. This would provide the greatest public health benefits in the short term and save more lives. For the BioNTech/Pfizer vaccine, the second vaccine dose can be offered between 3 to 12 weeks after the first dose. (Pfizer is not amused.) For the AstraZeneca vaccine, the second dose can be offered 4 to 12 weeks after the first dose.

Our World in Data. **COVID-19 vaccination doses administered per 100 people.** 30 December 2020. Link: <https://ourworldindata.org/grapher/covid-vaccination-doses-per-capita>

COVID-19 vaccination doses administered per 100 people, Dec 30, 2020

Total number of vaccination doses administered per 100 people in the total population. This is counted as a single dose, and does not measure the number of people vaccinated (which usually requires two doses).



Source: Official data collated by Our World in Data. Dates refer to when the data was reported.

OurWorldinData.org/covid-vaccinations • CC BY

▶ Dec 14, 2020

○ Dec 30, 2020

## Prevention

Chiba H, Lewis M, Benjamin ER, et al. **"Safer at Home": The effect of the Covid-19 Lockdown on Epidemiology, Resource Utilization and Outcomes at a Large Urban Trauma Center.** J Trauma Acute Care Surg. 2020 Dec 17. PubMed: <https://pubmed.gov/33347094>. Full-text: <https://doi.org/10.1097/TA.0000000000003061>

Spring 2020 lockdown in California. At the largest trauma center in Los Angeles, there was a reduction in the automobile versus pedestrian admissions by 42,5%, motorcycle injuries by 38,7%, and bicycle accidents by 28,4%, but no significant effect on the number of motor vehicle accident admissions. There was an increase in ground level falls by 32,5%, especially in the elderly group. The absolute number of gunshot wounds increased by 6,2% and knife injuries by 39,3%. Suicides increased by 38,5%. ☹

## Pediatrics

Viner RM, Ward JL, Hudson LD, et al. **Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents.** Arch Dis Child. 2020 Dec 17:archdischild-2020-320972. PubMed: <https://pubmed.gov/33334728>. Full-text: <https://doi.org/10.1136/archdischild-2020-320972>

In case you didn't know it, there are reviews and reviews of reviews! Here is one of the latter species: fever and cough are the most common symptoms in children and young people (CYP) under age 20 years with COVID-19, with other symptoms infrequent. The conclusion of this review of reviews by Viner et al.: further research is needed. Praise be.

## Collateral Effects

Santoro GA, Grossi U, Murad-Regadas S, et al. **Delayed ColoRectal cancer care during COVID-19 Pandemic (DECOR-19): Global perspective from an international survey.** Surgery. 2020 Nov 17:S0039-6060(20)30778-9. PubMed: <https://pubmed.gov/33353731>. Full-text: <https://doi.org/10.1016/j.surg.2020.11.008>

The authors analyzed the impact of the SARS-CoV-2 pandemic on pre-operative assessment, elective surgery, and post-operative management of colorectal cancer patients, using a 35-item survey, which was answered by a total of 1051 respondents from 84 countries. The result: both diagnostic and therapeutic practices changed. Endoscopic and radiologic procedures were highly affected and elective CRC surgery was impacted for almost all re-

spondents (97,3%), with planned procedures being temporarily suspended (46,8%) or capacity reduced (50,5%).

## Spanish

If you read Spanish, read de Miguel R. **El Reino Unido se convierte en el primer país del mundo en autorizar la vacuna de Oxford y AstraZeneca.**

El País 2020, published 30 December. Full-text: <https://elpais.com/sociedad/2020-12-30/el-reino-unido-se-convierte-en-el-primer-pais-del-mundo-en-autorizar-la-vacuna-de-oxfordastrazeneca.html>

El Gobierno de Johnson anuncia que extiende el nivel 4 de Alerta Máxima impuesto en Londres a amplias zonas del centro y norte de Inglaterra. El regreso escolar de Secundaria se retrasa al 18 de enero

## French

If you read French, read Ducourtieux C. **Le Royaume-Uni donne son feu vert au vaccin Oxford-AstraZeneca.** Le Monde 2020, published 30 December.

Full-text : [https://www.lemonde.fr/international/article/2020/12/30/le-royaume-uni-donne-son-feu-vert-au-vaccin-oxford-astrazeneca\\_6064818\\_3210.html](https://www.lemonde.fr/international/article/2020/12/30/le-royaume-uni-donne-son-feu-vert-au-vaccin-oxford-astrazeneca_6064818_3210.html)

Le gouvernement britannique veut amplifier sa campagne de vaccination, tandis que les hôpitaux saturent.

**Le groupe pharmaceutique chinois Sinopharm annonce que son vaccin contre le Covid-19 est efficace à plus de 79 %.** Le Monde 2020, published 30 December. Full-text :

[https://www.lemonde.fr/planete/article/2020/12/30/covid-19-le-groupe-pharmaceutique-chinois-sinopharm-annonce-que-son-vaccin-est-efficace-a-plus-de-79\\_6064806\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/30/covid-19-le-groupe-pharmaceutique-chinois-sinopharm-annonce-que-son-vaccin-est-efficace-a-plus-de-79_6064806_3244.html)

Sinopharm n'a pas précisé si les essais cliniques étaient achevés pour ce premier vaccin, qui fait l'objet d'une demande d'homologation auprès des autorités chinoises.

## German

If you read German, read Schulz B. **“Die erleben gerade Furchtbares”** – Die Zeit 2020, published 30 December. Full-text:

<https://www.zeit.de/politik/ausland/2020-12/coronavirus-grossbritannien-impfungen-infektionszahlen-gesundheitssystem-nhs>

In Großbritannien wird massenhaft geimpft, aber die Corona-Fälle steigen weiter rasant. Das Gesundheitssystem kollabiert, Intensivstationen suchen freiwillige Helfer.

Römer J. **Studien liefern erste Erkenntnisse zur Gefahr durch die Corona-Mutation.** Der Spiegel 2020, published 30 December. Full-text: <https://www.spiegel.de/wissenschaft/mensch/grossbritannien-corona-mutation-fuehrt-nicht-haeufiger-zu-schweren-verlaeufen-a-8c22d51c-bea3-4aa3-aea4-67fdadea2e93>

Eine Studie zeigt: Die auch in Deutschland entdeckte Corona-Variante B.1.1.7 verursacht schwere Erkrankungen nicht häufiger als andere Viruslinien. Aber ein Grund zur Entwarnung ist das nicht.

# January 2021

## 1 January

### Vaccines

Baden LR, El Sahly HM, Essink B, et al. **Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine.** N Engl J Med 2020, published 30 December. Full-text: <https://doi.org/10.1056/NEJMoa2035389>

Finally – after press releases, an emergency use authorization and the start of mass vaccinations – the scientific paper by Lindsey Baden et al.! Nothing new: the mRNA-1273 vaccine developed by Moderna and the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases (NIAID), within the National Institutes of Health (NIH), has more than 90% efficacy at preventing COVID-19 illness, including severe disease. Moderate-to-severe systemic side effects, such as fatigue, myalgia, arthralgia, and headache, were noted in about 50% of participants in the mRNA-1273 group after the second dose. These side effects were transient, starting about 15 hours after vaccination and resolving in most participants by day 2, without sequelae. The incidence of serious adverse events reported throughout the entire trial was similar for mRNA-1273 and placebo. Importantly, mRNA-1273 did not show evidence in the short term of enhanced respiratory disease after infection, a concern that had emerged from animal models used in evaluating SARS and Middle East Respiratory Syndrome (MERS) vaccine constructs. The authors rightly conclude that the safety of the mRNA-1273 vaccine regimen seems to be reassuring.

Castells MC, Phillips EJ. **Maintaining Safety with SARS-CoV-2 Vaccines.** N Engl J Med 2020, published 30 December. Full-text: <https://doi.org/10.1056/NEJMra2035343>

On December 8, 2020, within 24 hours after the start of the U.K. mass vaccination program for health care workers and elderly adults, the program reported probable cases of anaphylaxis in two women, 40 and 49 years of age, who had known food and drug allergies and were carrying auto-injectable epinephrine. One week later, a 32-year-old female health care worker in Alaska who had no known allergies presented with an anaphylactic reaction within 10 minutes after receiving the first dose of the vaccine. Since then, several more cases of anaphylaxis associated with the Pfizer mRNA vaccine have been

reported in the United States after vaccination of almost 2 million health care workers, and the incidence of anaphylaxis associated with the Pfizer SARS-CoV-2 mRNA vaccine appears to be approximately 10 times as high as the incidence reported with all previous vaccines, at approximately 1 in 100,000, as compared 1 in 1,000,000. Mariana Castells and Elizabeth Phillips explain what is at stake: “It is critical that we focus on safe and efficient approaches to implementing mass vaccination. In the future, these new vaccines may mark the beginning of an era of personalized vaccinology in which we can tailor the safest and most effective vaccine on an individual and a population level.” Happy New Year!

## Comorbidities

Hoffmann C, Casado JL, Härter G, et al. **Immune deficiency is a risk factor for severe COVID-19 in people living with HIV.** *HIV Med.* 2020 Dec 27. PubMed: <https://pubmed.gov/33368966>. Full-text: <https://doi.org/10.1111/hiv.13037>

In people living with HIV (PLWH), immune deficiency is a possible risk factor for severe COVID-19, even in the setting of HIV virologic suppression. There is no evidence for a protective effect of PIs or tenofovir alafenamide. This is the result of a multi-center cohort study which evaluated risk factors for morbidity and mortality of COVID-19 in PLWH infected with SARS-CoV-2 in three countries. Patients with severe COVID-19 had a lower current CD4 T cell count and a lower CD4 T cell nadir, compared with patients with mild-to-moderate COVID-19. In a multivariate analysis, the only factor associated with risk for severe COVID-19 was a current CD4+ T cell count of < 350/ $\mu$ l (adjusted odds ratio 2.85, 95% confidence interval 1.26-6.44,  $p = 0.01$ ). The only factor associated with mortality was a low CD4 T cell nadir.

## Epidemiology

Public Health England. **Investigation of novel SARS-COV-2 variant: Variant of Concern 202012/01.** UK Government 2020, updated 28 December. Full-text: <https://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201>

The investigation into the new SARS-CoV-2 variant which has spread rapidly within the UK. The authors found that the new variant substantially increases transmissibility.

## Clinical

Nasomsong W, Luvira V, Phiboonbanakit D. **Case Report: Dengue and COVID-19 Coinfection in Thailand.** Am J Trop Med Hyg. 2020 Dec 15. PubMed: <https://pubmed.gov/33331264>. Full-text: <https://doi.org/10.4269/ajtmh.20-1340>

The authors report a 50-year-old Thai woman who presented with acute high-grade fever, vomiting, and myalgia for 1 day. RT-PCR of the nasopharyngeal swab detected SARS-CoV-2, and RT-PCR of the blood detected dengue virus serotype 2.

## Collateral Effects

Rattka M, Dreyhaupt J, Winsauer C, et al. **Effect of the COVID-19 pandemic on mortality of patients with STEMI: a systematic review and meta-analysis.** Heart. 2020 Dec 17:heartjnl-2020-318360. PubMed: <https://pubmed.gov/33334863>. Full-text: <https://doi.org/10.1136/heartjnl-2020-318360>

In this meta-analysis, the authors assessed outcomes of 50.123 patients from 10 studies. Did the analyzed data show that acute and timely medical care of these patients had been maintained during the pandemic in most countries? Yes, they did. Consequently, despite a significant reduction in overall admission rates of patients with STEMI during the COVID-19 pandemic (incidence rate ratio = 0.789, 95% CI 0.730 to 0.852,  $I^2=77%$ ,  $p < 0.01$ ), there was no significant difference in hospital mortality (OR = 1.178, 95% CI 0.926 to 1.498,  $I^2=57%$ ,  $p = 0.01$ ) compared with patients with STEMI admitted before the outbreak.

## French

If you read French, read Hecketsweiler C. **Covid-19 : Le nouveau variant britannique du SARS-CoV-2, « un risque élevé » pour l'Europe.** Le Monde 2020, published 31 December. Full-text : [https://www.lemonde.fr/planete/article/2020/12/31/le-nouveau-variant-britannique-du-sars-cov-2-un-risque-eleve-pour-l-europe\\_6064879\\_3244.html](https://www.lemonde.fr/planete/article/2020/12/31/le-nouveau-variant-britannique-du-sars-cov-2-un-risque-eleve-pour-l-europe_6064879_3244.html)

Ce variant baptisé « VoC 202012/01 » présente plusieurs mutations susceptibles d'accroître sa contagiosité.



**L'Algérie va acquérir le vaccin russe Sputnik V.** Le Monde 2020, published 31 December. Full-text : [https://www.lemonde.fr/afrique/article/2020/12/31/l-algerie-va-acquerir-le-vaccin-russe-sputnik-v\\_6064899\\_3212.html](https://www.lemonde.fr/afrique/article/2020/12/31/l-algerie-va-acquerir-le-vaccin-russe-sputnik-v_6064899_3212.html)

La campagne de vaccination contre le Covid-19 est censée commencer en janvier dans le pays qui prévoit d'acquérir 500 000 doses.

## 2 January

### Prevention

Madas BG, Fűri P, Farkas Á, et al. **Deposition distribution of the new coronavirus (SARS-CoV-2) in the human airways upon exposure to cough-generated droplets and aerosol particles.** Sci Rep 2020, published 31 December. Full-text: <https://doi.org/10.1038/s41598-020-79985-6>

Severe, potentially fatal pneumonia supposes that SARS-CoV-2 reaches the **acinar airways**. What if we reduced the number of viruses getting there? After characterizing the deposition distribution of SARS-CoV-2 in the airways upon exposure to cough-generated droplets and aerosol particles, Balázs Madas et al. found that the number of viruses deposited in the extra-thoracic airways is about 7 times higher than in the acinar airways. The authors hypothesize that most cases of COVID-19 pneumonia might be preceded by SARS-CoV-2 infection of the upper airways and that without the enhancement of viral load in the upper airways, COVID-19 would be much less dangerous. Ergo, we should use the period between the onset of initial symptoms and the potential clinical deterioration to block or significantly reduce the transport of virus towards the acinar airways, for example with non-specific treatment forms like disinfection of the throat and nasal and oral mucosa. In any case, recommend the authors, use a tissue or cloth in order to absorb droplets and aerosol particles emitted by your own coughs and sneezes... before re-inhalation! Even if you are alone in quarantine.

### Clinical

Shapiro J, McDonald TB. **Supporting Clinicians during Covid-19 and Beyond — Learning from Past Failures and Envisioning New Strategies.** N Engl J Med 2020, published 31 December. Full-text: <https://doi.org/10.1056/NEJMp2024834>

Clinicians are facing important emotional stressors during the COVID-19 pandemic, including grief from seeing so many patients die, fears of contracting

the virus and infecting their family members, and anger over health care disparities and other systems failures. Jo Shapiro and Timothy McDonald show the way medical institutions should follow to design emotional-support programs that clinicians will embrace. The last of four suggestions: institutional leadership should be accountable for clinicians' well-being. Leaders should empower clinicians to speak up about unsafe, highly stressful or morally challenging workplace conditions and ensure that concerns are listened to and, whenever possible, acted on.

## Severe COVID

Maximous S, Brotherton BJ, Achilleos A, et al. **Pragmatic Recommendations for the Management of COVID-19 Patients with Shock in Low- and Middle-Income Countries.** *Am J Trop Med Hyg.* 2020 Dec 21. PubMed: <https://pubmed.gov/33350378>. Full-text: <https://doi.org/10.4269/ajtmh.20-1105>

The authors suggest using Sequential Organ Failure Assessment (qSOFA) and point-of-care ultrasound (POCUS) for evaluation purposes to use fluid therapy, norepinephrine and low-dose corticosteroids depending on etiology. The authors also recommend avoiding the routine use of central venous or arterial catheters and using simple bedside measures such as capillary refill time to address targets of resuscitation.

## Comorbidities

Fernandez-Ruiz R, Paredes J, Niewold TB. **COVID-19 in patients with Systemic Lupus Erythematosus: Lessons learned from the inflammatory disease.** *Transl Res.* 2020 Dec 19:S1931-5244(20)30302-9. PubMed: <https://pubmed.gov/33352298>. Full-text: <https://doi.org/10.1016/j.trsl.2020.12.007>

The authors review the literature to date on COVID-19 in patients with systemic lupus erythematosus (SLE) and provide an in-depth review of current research in the area, including immune pathway activation, epidemiology, clinical features, outcomes, and the psychosocial impact of the pandemic in patients with SLE.

## Collateral Effects

Van Haren RM, Delman AM, Turner KM, et al. **Impact of the COVID-19 Pandemic on Lung Cancer Screening Program and Subsequent Lung Cancer.** *J Am Coll Surg.* 2020 Dec 12;S1072-7515(20)32525-4. PubMed: <https://pubmed.gov/33346080>. Full-text: <https://doi.org/10.1016/j.jamcollsurg.2020.12.002>

Low-dose computed tomography (LDCT) screening reduces lung cancer mortality by at least 20%. At the University of Cincinnati, COVID-19 caused significant disruption in lung cancer screening, leading to a decrease in new patients screened and an increased proportion of nodules suspicious for malignancy once screening resumed.

## Education

Rubin EJ, Baden LR, Barocas JA, Morrissey S. **A Look at Covid-19 Prevention and Care in 2020.** Audio interview (26:46). *N Engl J Med* 2020; 383: e147. Access: <https://doi.org/10.1056/NEJMe2036225>

The editors discuss the new mRNA-1273 vaccine against SARS-CoV-2, along with other studies of native and exogenous antibodies.

## 3 January

### Epidemiology

Duca LM, Xu L, Price SF, McLean C. **COVID-19 Stats: COVID-19 Incidence, by Age Group — United States, March 1–November 14, 2020.** *MMWR Morb Mortal Wkly Rep* 2021;69:1664. <http://dx.doi.org/10.15585/mmwr.mm695152a8>

### Prevention

Rolfes MA, Grijalva CG, Zhu Y, et al. **Implications of Shortened Quarantine Among Household Contacts of Index Patients with Confirmed SARS-CoV-2 Infection - Tennessee and Wisconsin, April–September 2020.** *MMWR Morb Mortal Wkly Rep.* 2021 Jan 1;69(5152):1633-1637. PubMed: <https://pubmed.gov/33382676>. Full-text: <https://doi.org/10.15585/mmwr.mm695152a1>

One of your household members is diagnosed with SARS-CoV-2 infection. Is a 7-day quarantine enough (7 days after the symptom onset of the index patient) even if you are asymptomatic and have a negative laboratory test result?

Not always, because 19% of people in your situation will experience symptoms or receive positive test results in the following week. The recommendation by Melissa Rolfes, et al.: persons released from quarantine before 14 days should continue to avoid close contact and wear masks when around others until 14 days after their last exposure.

Okyere I, Chuku EO, Ekumah B, et al. **Physical distancing and risk of COVID-19 in small-scale fisheries: a remote sensing assessment in coastal Ghana.** Sci Rep. 2020 Dec 29;10(1):22407. PubMed: <https://pubmed.gov/33376254>. Full-text: <https://doi.org/10.1038/s41598-020-79898-4>

Fish landing sites along the Ghana coast could be transmission hotspots. To get a clearer picture, Isaac Okyere et al. employed an unmanned aerial vehicle. Aerial measurements taken at times of peak landing beach activity indicated that the highest proportion of people, representing 56%, 48%, 39% and 78% in [Elmina](#), [Winneba](#), [Apam](#) and [Mumford](#) respectively, were located at distances of less than one meter from their nearest neighbor.

## Vaccine

Editorial. **Messengers of hope.** Nat Biotechnol. 2020 Dec 29;1. PubMed: <https://pubmed.gov/33376248>. Full-text: <https://doi.org/10.1038/s41587-020-00807-1>

Emergency Use Authorizations for two mRNA COVID-19 vaccines represent a turning point in the pandemic. They also herald a new era for vaccinology – an era where vaccines are designed on computers, iteratively optimized in discovery and manufactured on demand – all without expensive and finicky cell culture.

Oliver S, Gargano J, Marin M, et al. **The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Moderna COVID-19 Vaccine — United States, December 2020.** MMWR Morb Mortal Wkly Rep 2021;69:1653-1656. Full-text: <http://dx.doi.org/10.15585/mmwr.mm695152e1>

Use of all COVID-19 vaccines authorized under an EUA should be implemented in conjunction with ACIP's interim recommendations for allocating initial supplies of COVID-19 vaccines. Before vaccination, the [EUA Fact Sheet](#) should be provided to recipients and caregivers. Providers should counsel Moderna COVID-19 vaccine recipients about expected local and systemic reactogenicity.

## Clinical

Heming M, Li X, Räuber S, et al. **Neurological Manifestations of COVID-19 Feature T Cell Exhaustion and Dedifferentiated Monocytes in Cerebrospinal Fluid.** *Immunity* 2020, published 22 December. Full-text: <https://doi.org/10.1016/j.immuni.2020.12.011>

Neuro-COVID – headache and neuroinflammatory or cerebrovascular disease – are frequent in patients with severe COVID-19. Here, Gerd Meyer zu Hörste, Michael Heming and colleagues identified specific immune alterations in the CSF of neuro-COVID patients featuring an increase of de-differentiated monocytes and exhausted T cells. They observed an IFN response in neuro-COVID that was attenuated compared with viral encephalitis. Severe neuro-COVID exhibited a broad clonal T cell expansion and curtailed IFN response compared with mild neuro-COVID.

## Treatment

Padhi AK, Shukla R, Saudagar P, Tripathi T. **High-Throughput Rational Design of the Remdesivir Binding Site in the RdRp of SARS-CoV-2: Implications for Potential Resistance.** *iScience* 2020, published 26 December. Full-text: <https://doi.org/10.1016/j.isci.2020.101992>

SARS-CoV-2 can undergo positive selection and attain remdesivir resistance with very few mutations. This is the result of a study that generated a total of 100,000 mutations and provided insight into the functional outcomes of mutations in the remdesivir binding site in the nsp12 subunit of RdRp.

## Severe COVID

Lee MH, Perl DP, Nair G, et al. **Microvascular Injury in the Brains of Patients with Covid-19.** *N Engl J Med* 2020, published 30 December. Full-text: <https://doi.org/10.1056/NEJMc2033369>

Avindra Nath, Myoung-Hwa Lee and colleagues from the US National Institute of Neurological Disorders and Stroke in Bethesda observed multifocal microvascular injury in the brain and olfactory bulbs in the brains of 13 patients. They found no evidence of viral infection after PCR with multiple primer sets, RNA sequencing of several areas of the brain, and RNA *in situ* hybridization and immunostaining.

## Press

Tufekci Z. **The Mutated Virus Is a Ticking Time Bomb**. The Atlantic 2020, published 31 December. Full-text: <https://www.theatlantic.com/science/archive/2020/12/virus-mutation-catastrophe/617531/>

A new variant of the coronavirus, known as B.1.1.7, is spreading across the globe. It is thought that this variant will not decrease vaccine efficacy much, if at all. There is no evidence for more severe COVID-19 either. All good and no cause for alarm? Maybe not.

## 4 January

### Epidemiology

Maeda JM, Nkengasong JN. **The puzzle of the COVID-19 pandemic in Africa**. Science 2021, published 1 January. Full-text: <https://doi.org/10.1126/science.abf8832>

As of 22 November 2020, the continent of Africa, comprising 1,3 billion people, had recorded two million cases of COVID-19 and 50,000 deaths, representing ~ 3.6% of total global cases. Why? Justin Maeda and John Nkengasong comment on a paper we previously presented on **13 November**: Uyoga S, Adetifa IMO, Karanja HK, et al. **Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Kenyan blood donors**. Science 2020, published 11 November. Full-text: <https://doi.org/10.1126/science.abe1916> | In April-June 2020, the crude prevalence of anti-SARS-CoV-2 IgG among blood donors in Kenya was 5.6% (174/3098). It was highest in urban counties, Mombasa (8.0%), Nairobi (7.3%) and Kisumu (5.5%). Of note, Kenya had reported only 341 deaths by the end of that period. The authors conclude that the sharp contrast between the reported COVID-19 cases and deaths suggests that the disease might be attenuated in Africa.

### Transmission

Sun K, Gu L, Ma L, Duan Y. **Atlas of ACE2 gene expression reveals novel insights into transmission of SARS-CoV-2**. Heliyon 2020, published 25 December. Full-text: <https://doi.org/10.1016/j.heliyon.2020.e05850>

Could cats and dogs serve as intermediate hosts of SARS-CoV-2 infection? Here, Kun Sun from Shenzhen, China, describe the conservation of ACE2 and

its expression pattern among various mammalian species that are close to human beings. Let's keep an eye on cats and dogs.

## Prevention

Storm N, McKay LGA, Downs SN, et al. **Rapid and complete inactivation of SARS-CoV-2 by ultraviolet-C irradiation.** Sci Rep. 2020 Dec 30;10(1):22421. PubMed: <https://pubmed.gov/33380727>. Full-text: <https://doi.org/10.1038/s41598-020-79600-8>

SARS-CoV-2 is able to survive on surfaces for extended periods of time. Although contact with surfaces contaminated with droplets generated by infected persons through exhaling, talking, coughing and sneezing is not the major driver of SARS-CoV-2 transmission (the main driver is speaking to and coughing, shouting and sneezing at people), it would be useful to inactivate SARS-CoV-2 on contaminated surfaces. Here, Anthony Griffiths, Nadia Storm and colleagues describe the almost instantaneous inactivation of SARS-CoV-2 in both wet and dry format using radiation generated by a commercially available ultraviolet (UV)-C light source at 254 nm.

## Vaccines

CDC 20201231. **Interim considerations: preparing for the potential management of anaphylaxis after COVID-19 vaccination.** Vaccines & Immunizations 2020, last reviewed: December 31, 2020. Full-text: <https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/anaphylaxis-management.html>

Anaphylaxis has been reported following COVID-19 vaccination. The incidence of anaphylaxis associated with the Pfizer SARS-CoV-2 mRNA vaccine appears to be approximately 10 times as high as the incidence reported with all previous vaccines, at approximately 1 in 100,000, as compared 1 in 1,000,000 (Castells 2020). The CDC recommends that appropriate medical treatment for severe allergic reactions must be immediately available in the event that an acute anaphylactic reaction occurs following administration of an mRNA COVID-19 vaccine. In particular, persons without **contraindications to vaccination** who receive an mRNA COVID-19 vaccine be observed after vaccination for the following time periods:

- 30 minutes: Persons with a history of an immediate allergic reaction of any severity to a vaccine or injectable therapy and persons with a history of anaphylaxis due to any cause.
- 15 minutes: All other persons

## Diagnostics

Barclay RA, Akhrymuk I, Patnaik A, et al. **Hydrogel particles improve detection of SARS-CoV-2 RNA from multiple sample types.** Sci Rep. 2020 Dec 30;10(1):22425. PubMed: <https://pubmed.gov/33380736>. Full-text: <https://doi.org/10.1038/s41598-020-78771-8>

To improve detection of SARS-CoV-2 when used with CDC-recommended assays, researchers from [Ceres Nanosciences](#) developed affinity-capture hydrogel particles (Nanotrap particles) that capture and concentrate the virus prior to RNA purification. A 5-min Nanotrap particle capture step substantially increases the sensitivity of SARS-CoV-2 RT-PCR assays when used in conjunction with either commercial RNA extraction kits or a simple heat and detergent extraction method in both saliva and transport medium samples. Furthermore, the authors identified viral RNA in several diagnostic remnant samples that previously had tested negative for SARS-CoV-2.

## Severe COVID

Park J, Kim H, Kim SY, et al. **In-depth blood proteome profiling analysis revealed distinct functional characteristics of plasma proteins between severe and non-severe COVID-19 patients.** Sci Rep. 2020 Dec 29;10(1):22418. PubMed: <https://pubmed.gov/33376242>. Full-text: <https://doi.org/10.1038/s41598-020-80120-8>

The authors found 76 previously unreported proteins which could be novel prognostic biomarker candidates. Their plasma proteome signatures highlighted the role of neutrophil activation, complement activation, platelet function, and T cell suppression as well as pro-inflammatory factors upstream and downstream of interleukin-6, interleukin-1B, and tumor necrosis factor.

## Collateral Effects

Kosten TR, Petrakis IL. **The Hidden Epidemic of Opioid Overdoses During the Coronavirus Disease 2019 Pandemic.** JAMA Psychiatry. 2020 Dec 30. PubMed: <https://pubmed.gov/33377967>. Full-text: <https://doi.org/10.1001/jamapsychiatry.2020.4148>

An unexpected tragedy of the coronavirus disease 2019 (COVID-19) pandemic is increased opioid and fentanyl overdoses, since many factors could have helped in reducing opioid use disorder (OUD) and overdoses during the pan-



demic. Follow Thomas Kosten and Ismene Petrakis on this short trip through drug addiction and society's response.

## French

If you read French, read Mazaurette M. **Au lit, les hommes aussi font leur âge.** Le Monde 2021, published 2 January. Full-text : [https://www.lemonde.fr/m-perso/article/2021/01/02/au-lit-les-hommes-aussi-font-leur-age\\_6065054\\_4497916.html](https://www.lemonde.fr/m-perso/article/2021/01/02/au-lit-les-hommes-aussi-font-leur-age_6065054_4497916.html)

Le mythe d'une éternelle jeunesse sexuelle flatte l'ego masculin mais invisibilise les effets du vieillissement, explique la chroniqueuse de La Matinale Maïa Mazaurette, qui observe que tout se passe comme si seules les femmes subissaient les assauts du temps.

## German

If you read German, read Böhm A. **Reiche zuerst.** Die Zeit 2020, published 29 December. Full-text: <https://www.zeit.de/2021/01/corona-impfstoff-pharmaindustrie-logistik-reichtum-armut>

Reiche Länder teilen seit Monaten den größten Teil der Vakzinen unter sich auf. Regierungen wohlhabender Staaten, die 14 Prozent der Weltbevölkerung repräsentieren, haben sich schon jetzt über die Hälfte aller Impfstoffdosen gesichert, die bereits in der Produktion sind oder demnächst auf den Markt kommen.

## 5 January

### Vaccine

De Vrieze J. **Suspicious grow that nanoparticles in Pfizer's COVID-19 vaccine trigger rare allergic reactions.** Science 2020, published 21 December (sorry for being late!). Full-text: <https://www.sciencemag.org/news/2020/12/suspicious-grow-nanoparticles-pfizer-s-covid-19-vaccine-trigger-rare-allergic-reactions>

Severe allergy-like reactions in at least eight people who received the COVID-19 vaccine produced by Pfizer and BioNTech over the past 2 weeks may be due to a compound in the packaging of the messenger RNA (mRNA) that forms the vaccine's main ingredient, scientists say. A similar mRNA vaccine developed by Moderna, which was authorized for emergency use in the United States on Friday, also contains the compound, polyethylene glycol (PEG).

## Clinical

Rabin R. **Some Covid Survivors Haunted by Loss of Smell and Taste.** The New York Time 2021, published 2 January. Full-text: <https://www.nytimes.com/2021/01/02/health/coronavirus-smell-taste.html>

As the coronavirus claims more victims, a once-rare diagnosis is receiving new attention from scientists, who fear it may affect nutrition and mental health. Not peer-reviewed, not even from a medical journal, but worth reading.

Hoehl S, Kreutzer E, Schenk B, et al. **Longitudinal testing for respiratory and gastrointestinal shedding of SARS-CoV-2 in day care centres in Hesse, Germany.** Clin Infect Dis 2021, published 3 January. Full-text: <https://doi.org/10.1093/cid/ciaa1912>

Detection of either respiratory or gastrointestinal shedding of SARS-CoV-2 RNA in children and staff members attending day-care centers. This is the result of a longitudinal study over a period of 12 weeks from June to September 2020 to screen children and staff from day-care centers in the state of Hesse, Germany. 859 children (ages 3 months to 8 years) and 376 staff members from 50 day-care centers participated. The authors caution that the study was conducted at a time when activity of other respiratory pathogens was also low in Hesse, Germany, and children with symptoms of upper respiratory infection, other than runny nose only, were excluded from attending day care due to restricts set in place during pandemic.

## Severe COVID

Maltezou HC, Raftopoulos V, Vorou R, et al. **Association between upper respiratory tract viral load, comorbidities, disease severity and outcome of patients with SARS-CoV-2 infection.** J Infect Dis 2021, published 3 January. Full-text: <https://doi.org/10.1093/infdis/jiaa804>

Upper respiratory tract (URT) viral load could be used to identify patients at higher risk for morbidity or severe outcome. This is the result of a study that included 1122 patients (mean age: 46 years), both asymptomatic and symptomatic patients, either hospitalized or cared for in the community. Helena Maltezou et al. categorized URT as high, moderate or low. A high URT viral load was more often detected in patients with COVID-19 than in asymptomatic patients. Patients with the following co-morbidities more often had high URT viral load than moderate or low URT viral load: chronic cardiovascular

disease, hypertension, chronic pulmonary disease, immunosuppression, obesity, and chronic neurological disease (p values < 0.05 for all comparisons). A high SARS-CoV-2 URT viral load was significantly associated with an increased risk for intubation or a fatal outcome in the course of COVID-19, as well as with prolonged disease severity.

## Collateral Effects

COVIDSurg Collaborative. **Head and neck cancer surgery during the COVID-19 pandemic: An international, multicenter, observational cohort study.** *Cancer*. 2020 Dec 21. PubMed: <https://pubmed.gov/33345297>. Full-text: <https://doi.org/10.1002/cncr.33320>

Head and neck cancer surgery in the COVID-19 era appears safe even when surgery is prolonged and complex. This is the result of an international, observational cohort study comprised of 1137 consecutive patients with head and neck cancer undergoing primary surgery with curative intent in 26 countries. The overall 30-day mortality was 1.2%. Twenty-nine patients (3%) tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) within 30 days of surgery; 13 of these patients (44.8%) developed severe respiratory complications, and 3 (10.3%) died. There were significant correlations with an advanced tumor stage and admission to critical care.

Note of the editor: The original text said: “and 3.51 (10.3%) died.” Too much alcohol during pre-Christmas proof-reading?

Seitlinger J, Wollbrett C, Mazzella A, et al. **Safety and feasibility of thoracic malignancy surgery during the COVID-19 pandemic.** *Ann Thorac Surg*. 2020 Dec 14:S0003-4975(20)32115-9. PubMed: <https://pubmed.gov/33333085>. Full-text: <https://doi.org/10.1016/j.athoracsur.2020.12.001>

Maintaining surgical oncologic activity in the era of the COVID-19 pandemic seems safe and feasible, with low postoperative morbidity and mortality. The authors collected data on thoracic malignancy surgeries from January 1 to April 30, 2020, including patients from high-volume thoracic surgery departments in Nancy, Strasbourg, Freiburg, Milano, Torino and Montreal. In the cohort of 731 patients, 9 cases (1.2%) of COVID-19 were confirmed by PCR, including 5 in-hospital contaminants. The total number of deaths was 22 (3%). Only one death was related to COVID-19 (0,14%).

## COVID History

Watts J. **A cardiac arrest showed me what dying feels like. How should I live in Life 2.0?** The Guardian 2020, published 28 December. Full-text: <https://www.theguardian.com/commentisfree/2020/dec/28/cardiac-arrest-dying>

I realized I was dying about half an hour earlier. My heart had gone loco during a kick-around on Tooting Common, South London. I suddenly felt tired and asked to go on the bench for a rest. Then I keeled over. I remember being confused at finding myself lying on the grass and too weak to move.

## French

If you read French, read Mraffko C. **Israël a lancé au pas de course la vaccination contre le Covid-19.** Le Monde 2021, published 4 January. Full-text : [https://www.lemonde.fr/international/article/2021/01/04/israel-s-est-lance-dans-une-course-folle-a-la-vaccination-contre-le-covid-19\\_6065106\\_3210.html](https://www.lemonde.fr/international/article/2021/01/04/israel-s-est-lance-dans-une-course-folle-a-la-vaccination-contre-le-covid-19_6065106_3210.html)

Déjà plus de 10 % de la population a reçu une première injection. Le premier ministre, Benyamin Nétanyahou, en campagne pour sa réélection, espère ainsi contrebalancer sa gestion désastreuse de la crise sanitaire.

Sénecat A, Sanchez L. **Covid-19 : six questions pour comprendre les lenteurs de la vaccination en France.** Le Monde 2021, published 4 January. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2021/01/04/covid-19-six-questions-pour-comprendre-les-lenteurs-de-la-vaccination-en-france\\_6065175\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2021/01/04/covid-19-six-questions-pour-comprendre-les-lenteurs-de-la-vaccination-en-france_6065175_4355770.html)

Quelle est la stratégie française ? Pourquoi si peu de vaccinés depuis le 27 décembre ? Que font les autres pays ?

## 6 January

### Transmission

ECDC 20201223. **COVID-19 in children and the role of school settings in transmission - first update.** ECDC 2020, published 23 December. Full-text: <https://www.ecdc.europa.eu/en/publications-data/children-and-school-settings-covid-19-transmission>

An update on the role of children in the transmission of SARS-CoV-2 and the role of schools in the COVID-19 pandemic, based on experience in the EU from

August through December 2020. The document also addresses transmission to and from staff in school settings, school-related mitigation measures including risk communication, testing, contact tracing and the efficacy of partial and full school closures.

Children’s Task and Finish Group. **Update to 4th Nov 2020 paper on children, schools and transmission.** UK Government 2020, published 17 December. Full-text:

[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/948617/s0998-tfc-update-to-4-november-2020-paper-on-children-schools-transmission.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/948617/s0998-tfc-update-to-4-november-2020-paper-on-children-schools-transmission.pdf) +

[https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/935102/sage-65-meeting-covid-19-s0863.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/935102/sage-65-meeting-covid-19-s0863.pdf)

This paper presents evidence for increased transmission occurring among school children when schools are open, particularly in children of secondary school age (high confidence). Multiple data sources show a reduction in transmission in children following schools closing for half-term, and transmission rates increasing again following the post-half-term return to school.

## Pathogenesis

Henkel M, Weikert T, Marston K, et al. **Lethal COVID-19: Radiological-Pathological Correlation of the Lungs.** Radiol Cardiothorac Imaging 2020. Full-text: <https://doi.org/10.1148/ryct.2020200406>

A report of 14 patients who died from RT-PCR confirmed COVID-19. All patients underwent ante-mortem CT and autopsy. A significant proportion of ground glass opacities (GGO) correlates with the pathologic processes of diffuse alveolar damage, capillary dilatation and congestion and microthrombosis. Maurice Henkel, Thomas Weikert and colleagues conclude that these results underline the importance of vascular alterations as a key pathophysiological driver in lethal COVID-19.

## Clinical

Tillett RL, Sevinsky JR, Hartley PD, et al. **Genomic evidence for reinfection with SARS-CoV-2: a case study.** Lancet Infect Dis. 2021 Jan;21(1):52-58. PubMed: <https://pubmed.gov/33058797>. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30764-7](https://doi.org/10.1016/S1473-3099(20)30764-7)

Re-infections with SARS-CoV-2 are possible, but don’t seem to be the rule within the first 9 months after the original infection. As a matter of fact, we

don't currently see an epidemic of re-infections in people who were infected during the spring of 2020. Here, Marc Pandori, Richard Tillett and colleagues present the case of a 25-year-old man who presented to health authorities on two occasions with symptoms of viral infection, once at a community testing event in April 2020, and a second time to primary care then hospital at the end of May and beginning of June 2020. The authors show that the patient was infected by SARS-CoV-2 on two separate occasions by a genetically distinct virus.

See also the comment by Iwasaki A. **What reinfections mean for COVID-19.** *Lancet Infect Dis.* 2021 Jan;21(1):3-5. PubMed: <https://pubmed.gov/33058796>. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30783-0](https://doi.org/10.1016/S1473-3099(20)30783-0)

## Treatment

McCullough PA, Alexander PE, Armstrong R, et al. **Multifaceted highly targeted sequential multidrug treatment of early ambulatory high-risk SARS-CoV-2 infection (COVID-19).** *Rev Cardiovasc Med.* 2020 Dec 30;21(4):517-530. PubMed: <https://pubmed.gov/33387997>. Full-text: <https://doi.org/10.31083/j.rcm.2020.04.264>

Prompt early initiation of sequenced multi-drug therapy (SMDT) is a widely and currently available solution to stem the tide of hospitalizations and death. Here, Peter McCullough et al. present a multi-pronged therapeutic approach that includes 1) adjuvant nutraceuticals, 2) combination intracellular anti-infective therapy, 3) inhaled/oral corticosteroids, 4) antiplatelet agents/anticoagulants, 5) supportive care including supplemental oxygen, monitoring, and telemedicine.

## Severe COVID

Le Breton C, Besset S, Freitas-Ramos S, et al. **Extracorporeal membrane oxygenation for refractory COVID-19 acute respiratory distress syndrome.** *J Crit Care.* 2020 Dec;60:10-12. PubMed: <https://pubmed.gov/32731100>. Full-text: <https://doi.org/10.1016/j.jcrc.2020.07.013>

Extra-corporeal membrane oxygenation (ECMO) in patients with severe COVID-19 has been associated with high mortality rates. Here, Jean-Damien Ricard, D. Roux, C. Le Breton and colleagues report on 13 patients who required VV-ECMO (femoro-jugular cannulation). All 13 patients were weaned from ECMO after a median of 13 days (range 3 to 34). Two patients died while still on mechanical ventilation. As of June 28th, 2020 all surviving patients were weaned from the ventilator after a median duration of 29 days (range 20

to 51) and were discharged alive from the ICU after a mean stay of 34 days (range 23 to 55). The authors conclude that ECMO should be an integral part of intensive care for properly selected COVID-19 patients without life-threatening co-morbidities.

## 7 January

### Epidemiology

Veldhoen M, Simas JP. **Endemic SARS-CoV-2 will maintain post-pandemic immunity.** Nat Rev Immunol (2021). Full-text: <https://doi.org/10.1038/s41577-020-00493-9>

Marc Veldhoen and J. Pedro Simas predict that the maintenance of population immunity will not depend on continued vaccinations but on the endemic presence of SARS-CoV-2. The authors offer an intriguing long-term perspective: “Endemic SARS-CoV-2 will ensure maintenance of seroprevalence and mucosal immunity in the population, which will increase over time in new generations. As such, most infected individuals will ultimately endure a largely asymptomatic or mild course of disease, although similarly to the other common cold HCoVs, SARS-CoV-2 may cause fatalities in extremely vulnerable elderly or immunocompromised individuals.”

Ives AR, Bozzuto C. **Estimating and explaining the spread of COVID-19 at the county level in the USA.** Commun Biol 4, 60 (2021). Full-text: <https://doi.org/10.1038/s42003-020-01609-6>

Different states and counties in the USA, and different countries in the world, have experienced COVID-19 epidemics differently. Here, Anthony Ives and Claudio Bozzuto put numbers on these differences in the USA. The authors show that most of the high inter-county variance is explained by four factors ( $R^2 = 0.70$ ): the timing of the outbreak, population size, the population density, and spatial location. Their recommendation for the future: design public health interventions at the county level.

### Transmission

Davies NG, Barnard RC, Jarvis CI, et al. **Estimated transmissibility and severity of novel SARS-CoV-2 Variant of Concern 202012/01 in England.** medRxiv 2020, posted 26 December. Full-text: <https://doi.org/10.1101/2020.12.24.20248822>

Nicolas Davies et al. estimate that the novel SARS-CoV-2 variant emerged in southeast England in November 2020, is 56% more transmissible (95% credible interval across three regions 50-74%) than preexisting variants of SARS-CoV-2. The author did **not** find evidence that VOC 202012/01 resulted in greater or lesser severity of disease than pre-existing variants. However, the increase in transmissibility is likely to lead to a large increase in incidence, with COVID-19 hospitalizations and deaths projected to reach higher levels in 2021 than were observed in 2020.

## Immunology

Röltgen K, Powell AE, Wirz OF, et al. **Defining the features and duration of antibody responses to SARS-CoV-2 infection associated with disease severity and outcome.** *Sci Immunol.* 2020 Dec 7;5(54):eabe0240. PubMed: <https://pubmed.gov/33288645>. Full-text: <https://doi.org/10.1126/sciimmunol.abe0240>

Outpatients and asymptomatic individuals might have higher ratios of spike protein receptor-binding domain-specific IgG versus nucleoprotein-targeted IgG antibodies than hospitalized patients. This is the result of a study by Scott Boyd, Katharina Röltgen and colleagues who analyzed 983 longitudinal plasma samples from 79 hospitalized COVID-19 patients and 175 SARS-CoV-2-infected outpatients and asymptomatic individuals. Plasma antibody increases correlated with decreases in viral RNAemia, but antibody responses in acute illness were insufficient to predict inpatient outcomes.

## Treatment

Meduri GU, Annane D, Confalonieri M, et al. **Pharmacological principles guiding prolonged glucocorticoid treatment in ARDS.** *Intensive Care Med.* 2020 Dec;46(12):2284-2296. PubMed: <https://pubmed.gov/33150472>. Full-text: <https://doi.org/10.1007/s00134-020-06289-8>

In this review, Gianfranco Umberto Meduri et al. examine the pharmacological principles guiding glucocorticoids (GC) treatment in ARDS that demonstrates how each component of the treatment protocol is relevant to achieve optimal results. The authors integrate current clinical pharmacology knowledge of various GCs, including hydrocortisone, methylprednisolone and dexamethasone. Find more about the dosage, timing of initiation, mode of administration, duration, and tapering.



## Severe COVID

Contou D, Fraissé M, Pajot O, Tirolien JA, Mentec H, Plantefève G. **Comparison between first and second wave among critically ill COVID-19 patients admitted to a French ICU: no prognostic improvement during the second wave?** Crit Care. 2021 Jan 4;25(1):3. PubMed: <https://pubmed.gov/33397421>. Full-text: <https://doi.org/10.1186/s13054-020-03449-6>

During the first wave of the SARS-CoV-2 pandemic in Spring 2020, intensive care physicians discovered specificities of severe COVID-19 including the need for deep sedation and neuromuscular blockade, the increased risk of thrombotic and hemorrhagic events, the prolonged duration of mechanical ventilation with high rate of delirium, and the beneficial effects of early administration of glucocorticoids. Here, Damien Contou et al. report their experience during the second SARS-CoV-2 wave in Autumn 2020. Their sobering discovery: compared to the first wave, less patients required invasive mechanical ventilation, thrombotic events were less frequent and the delay between ICU admission and tracheal intubation was longer. However, ICU mortality (50% vs. 52%,  $p = 0.96$ ) and duration of ICU stay did not differ between the two waves. The Kaplan–Meier survival analysis did not show a significant difference between the two waves ( $p = 0.90$ , log-rank test).

## Collateral Effects

Evans DP, Hawk SR, Ripkey CE. **Domestic Violence in Atlanta, Georgia Before and During COVID-19.** Violence Gend 2020, published 11 December. Full-text: <https://doi.org/10.1089/vio.2020.0061>

Cumulative counts of domestic crimes were higher during the COVID-19 period of 2020 than in the preceding two years suggesting increased occurrence of domestic violence, especially during shelter-in-place orders. This is the result of an analysis of 30 weeks of crime data collected from the Atlanta Police Department (APD). Dabney Evans, Shila René Hawk and Carrie Ripkey found that a spike in domestic crimes was recorded after city and statewide shelter-in-place orders. The authors summarize that the “co-occurring pandemics of COVID-19 and domestic violence come amidst a period of racial justice reckoning in the United States and that both have a disproportionate impact on Black, Indigenous, and People of Color. As the country grapples with how to deal with health and safety concerns related to the pandemic, and the unacceptable harms being perpetrated by police, a public health approach is strongly warranted to address both universal health care and violence prevention.”

## French

If you read French, read Delfraissy JF, Duault LA, Benamouzig D, et al. **Le clone anglais «VUI-UK » – Anticiper une reprise épidémique en janvier.** Conseil scientifique COVID-19 2020, published 22 December. Full-text : <https://afpa.org/recommandation/covid-19-note-dalerte-conseil-scientifique/>

Les données actuelles fournies par les autorités britanniques rapportent une augmentation du risque de transmission ( $R_0$  augmenté de +0.4 en comparaison des autres virus), avec une augmentation modérée de la « charge virale » estimée à partir des valeurs de RT-PCR (augmentation de 0.66 log soit 2 Ct en moins), mais aucune différence n'est notée à ce jour en termes de pathogénicité (manifestations cliniques, durée de la maladie) ou d'échappement à la réponse immunitaire des personnes déjà infectées au cours de deux premières vagues.

Herzberg N. **Les vaccins anti-Covid évitent-ils la transmission du SARS-CoV-2 ?** Le Monde 2021, published 6 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/06/les-vaccins-anti-covid-evitent-ils-la-transmission-du-sars-cov-2\\_6065356\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/06/les-vaccins-anti-covid-evitent-ils-la-transmission-du-sars-cov-2_6065356_3244.html)

Les essais ont montré leur efficacité à combattre les symptômes du Covid, mais on ignore encore s'ils peuvent bloquer la contamination d'autres personnes.

Bettinelli M, Castele AV. **Covid-19, paludisme, sida : l'immense bilan humain de pandémies toujours actives.** Full-text : [https://www.lemonde.fr/planete/video/2020/12/20/covid-19-paludisme-sida-l-immense-bilan-humain-de-pandemies-toujours-actives\\_6064005\\_3244.html](https://www.lemonde.fr/planete/video/2020/12/20/covid-19-paludisme-sida-l-immense-bilan-humain-de-pandemies-toujours-actives_6064005_3244.html)

Un an après la première alarme sur l'apparition d'un « virus inconnu », finalement reconnu comme un nouveau coronavirus et dont la maladie qu'il provoque fut baptisée « Covid-19 », la planète déplore des dizaines de millions de contaminations, et plus d'1,6 million de morts. Au même moment, d'autres pandémies, parfois vieilles de plusieurs milliers d'années, continuent de faucher des milliers de vies.

Kauffmann S. « **Ce qui se passe depuis quatre ans aux Etats-Unis est grave, on le savait ; ce qui s'y passe depuis deux mois est gravissime** » - Le Monde 2021, published 6 January. Full-text : [https://www.lemonde.fr/idees/article/2021/01/06/ce-qui-se-passe-depuis-quatre-ans-aux-etats-unis-est-grave-on-le-savait-ce-qui-s-y-passe-depuis-deux-mois-est-gravissime\\_6065311\\_3232.html](https://www.lemonde.fr/idees/article/2021/01/06/ce-qui-se-passe-depuis-quatre-ans-aux-etats-unis-est-grave-on-le-savait-ce-qui-s-y-passe-depuis-deux-mois-est-gravissime_6065311_3232.html)

En refusant de quitter le pouvoir après les élections, Donald Trump expose, dans une ultime offensive destructrice, la fragilité du système américain. Une leçon pour toutes les démocraties, estime Sylvie Kauffmann, éditorialiste au « Monde ».

## 8 January

### Epidemiology

Kirby T. **New variant of SARS-CoV-2 in UK causes surge of COVID-19**. Lancet Respir Med 2021, published 5 January. Full-text: [https://doi.org/10.1016/S2213-2600\(21\)00005-9](https://doi.org/10.1016/S2213-2600(21)00005-9)

The UK remains one of the most badly affected countries. As of 6 January 2021, it had recorded more than 2,8 million cases of SARS-CoV-2 infection and almost 80.000 deaths. Driven by the new variant's increased infectiousness, the UK has recently reported more than 60.000 cases a day, and there are fears that the pandemic may get very much worse before it gets better. The only hope now is that deaths and hospitalizations will plummet as the number of elderly and vulnerable people receiving a vaccine sharply increases in the coming weeks.

### Pathogenesis

Meinhardt J, Radke J, Dittmayer C, et al. **Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19**. Nat Neurosci (2020). Full-text: <https://doi.org/10.1038/s41593-020-00758-5>

Given the neurological symptoms observed in a large majority of individuals with COVID-19, does SARS-CoV-2 penetrate into the CNS? Here Frank Hepner, Jenny Meinhardt and colleagues demonstrate the presence of SARS-CoV-2 RNA and protein in anatomically distinct regions of the nasopharynx and brain. Watch SARS-CoV-2 crossing the neural-mucosal interface in olfactory mucosa (exploiting the close vicinity of olfactory mucosal, endothelial and nervous tissue), following neuroanatomical structures and penetrating

defined neuroanatomical areas including the primary respiratory and cardiovascular control center in the medulla oblongata.

See also the comment by Yates D. **A CNS gateway for SARS-CoV-2.** *Nat Rev Neurosci* (2021). Full-text: <https://doi.org/10.1038/s41583-020-00427-3>

## Immunology

Dan JM, Mateus J, Kato Y, et al. **Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection.** *Science* 2021, published 6 January. Full-text: <https://doi.org/10.1126/science.abf4063>

After Year 1 of the SARS-CoV-2 pandemic, we realize that although millions of people were infected during spring 2020, there is no sizeable epidemic of re-infections. This observation suggests that SARS-CoV-2 infection might confer a solid immunity. Now, Shane Crotty, Alessandro Sette, Daniela Weiskopf, Jennifer Dan and colleagues publish in *Science* the pre-print paper we presented on **13 November**. The authors analyzed multiple compartments of circulating immune memory to SARS-CoV-2 in 188 COVID-19 cases, including 43 cases at > 6 months post-infection. The result: Spike-specific memory B cells were more abundant at 6 months than at 1 month post symptom onset. SARS-CoV-2-specific CD4<sup>+</sup> T cells and CD8<sup>+</sup> T cells declined with a half-life of 3-5 months. These findings might suggest that after SARS-CoV-2 infection (or after vaccination), the vast majority of people could be protected from severe COVID-19 for years. Read also the NYTimes article by Mandavilli A. **Immunity to the Coronavirus May Last Years, New Data Hint.** *The New York Times* 2020, published 17 November. Full-text: <https://www.nytimes.com/2020/11/17/health/coronavirus-immunity.html>

Widge AT, Roupheal NG, Jackson LA, et al. **Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination.** *N Engl J Med* 2021; 384:80-82. Full-text: <https://doi.org/10.1056/NEJMc2032195>

Correlates of protection against SARS-CoV-2 infection in humans are not yet established. Here, Alicia Widge et al. describe immunogenicity data 119 days after the first vaccination in 34 healthy adult participants. Despite a slight expected decline in titers of binding and neutralizing antibodies, mRNA-1273 might have the potential to provide durable humoral immunity.

## Vaccine

CDC 20210106. **Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Pfizer-BioNTech COVID-19 Vaccine — United States, December 14–23, 2020.** MMWR Morb Mortal Wkly Rep. ePub: 6 January 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7002e1>

One case of anaphylaxis in 100.000 vaccine recipients of the BioNTech/Pfizer vaccine Comirnaty. That is the result of the 10 days of monitoring (14-23 December) by the Vaccine Adverse Event Reporting System which detected 21 cases of anaphylaxis after administration of a reported 1.893.360 first doses of the vaccine (11,1 cases per million doses). Note that 71% of these occurred within 15 minutes of vaccination. Screen recipients for contraindications and precautions; have the necessary supplies available to manage anaphylaxis; implement the recommended post-vaccination observation periods; and immediately treat suspected cases of anaphylaxis with intramuscular injection of epinephrine! For detailed insight, check also Castells MC, Phillips EJ. **Maintaining Safety with SARS-CoV-2 Vaccines.** N Engl J Med 2020, published 30 December. Full-text: <https://doi.org/10.1056/NEJMra2035343> which we presented on 1 January.

Iacobucci G, Mahase E. **Covid-19 vaccination: What's the evidence for extending the dosing interval?** BMJ 2021, published 6 January. Full-text: <https://doi.org/10.1136/bmj.n18>

On 30 December the four UK chief medical officers announced that the second doses of the COVID vaccines should be given towards the end of 12 weeks rather than in the previously recommended 3-4 weeks. German authorities will issue a similar recommendation soon. Gareth Iacobucci and Elisabeth Mahase look at the questions this has raised.

## Treatment

Libster R, Marc PG, Wappner D, et al. **Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults.** N Engl J Med 2021, published 6 January. Full-text: <https://doi.org/10.1056/NEJMoa2033700>

Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults might reduce the progression of COVID-19. This is the result of a randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against SARS-CoV-2 by Fernando P. Polack, Romina Libster and colleagues. The authors randomized 160 patients. 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;  $p = 0.03$ ). Relative risk reduction: 48%.

Salama C, Han J, Yau L, et al. **Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia.** *N Engl J Med* 2021; 384:20-30. Full-text: <https://doi.org/10.1056/NEJMoa2030340>

In hospitalized patients with COVID-19 pneumonia who were not receiving mechanical ventilation, tocilizumab did not improve survival, but it reduced the likelihood of progression to the composite outcome of mechanical ventilation or death. This is the result of a trial that randomized 249 patients into the tocilizumab group and 128 patients into the placebo group. Shalini Mohan, Carlos Salama and colleagues report that death from any cause by day 28 occurred in 10,4% of the patients in the tocilizumab group and 8,6% of those in the placebo group.

## Collateral Effects

Sarvey D, Welsh JW. **Adolescent substance use: Challenges and opportunities related to COVID-19.** *J Subst Abuse Treat.* 2020 Nov 24:108212. PubMed: <https://pubmed.gov/33272731>. Full-text: <https://doi.org/10.1016/j.jsat.2020.108212>

Adolescent substance use is a significant and largely undertreated public health concern. The COVID-19 pandemic has exacerbated many pre-existing risk factors for adolescent substance use, such as early life stress, social isolation, school connections, and boredom. Here, Dana Sarvey and Justine Welsh give a short overview of changing risk and protective factors for substance use and potential opportunities during the pandemic. They recommend that practitioners should consider any and all means of reaching out to these youth and their families and addressing other co-occurring psychiatric symptoms, such as depression and anxiety.

## Beyond Corona

Smith D. **Fears mount that final 13 days pose a security threat.** *The Guardian* 2021, published 7 January. Full-text: <https://www.theguardian.com/us-news/2021/jan/07/donald-trump-final-13-days-security-threat-politicians-activists-warn>

“Twitter at one point decided he shouldn’t be able to have access to his Twitter, and yet this is someone who has access to our launch nuclear launch codes. There’s an incongruity there.”

## French

Ducourtieux C. **Possibilité de « mélange » vaccinal et délai de douze semaines entre deux injections : le pari britannique contre le Covid-19.** Le Monde 2021, published 7 January. Full-text : [https://www.lemonde.fr/international/article/2021/01/07/covid-19-le-pari-vaccinal-britannique\\_6065503\\_3210.html](https://www.lemonde.fr/international/article/2021/01/07/covid-19-le-pari-vaccinal-britannique_6065503_3210.html)

Le Royaume-Uni s’est lancé dans une course de vitesse contre le virus et son variant apparu dans le Kent, à l’heure où la mortalité causée par la pandémie reste très importante.

## 9 January

### Epidemiology

Leung K, Shum MH, Leung GM, Lam TT, Wu JT. **Early transmissibility assessment of the N501Y mutant strains of SARS-CoV-2 in the United Kingdom, October to November 2020.** Euro Surveill. 2021 Jan;26(1). PubMed: <https://pubmed.gov/33413740>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.26.1.2002106>

Two new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lineages carrying the amino acid substitution N501Y in the receptor-binding domain (RBD) of the spike protein have spread rapidly in the United Kingdom (UK) during late autumn 2020. Tommy Lam, Joseph Wu, Kathy Leung and colleagues explain that 501Y Variant 2 (*also named B.1.1.7, 20B/501Y.V1 and VOC-202012/01*) is estimated to present an  $R_0$  1.75 times higher than 501N, meaning it is 75% more transmissible compared with the 501N strain.

du Plessis L, McCrone JT, Zarebski AE, et al. **Establishment and lineage dynamics of the SARS-CoV-2 epidemic in the UK.** Science 2021, published 8 January. Full-text: <https://doi.org/10.1126/science.abf2946>

In early 2020, pre-lockdown, high travel volumes and few restrictions on international arrivals led to the establishment and co-circulation of >1000 identifiable UK transmission lineages, jointly contributing to accelerated epidemic growth that quickly exceeded national contact tracing capacity. The authors

reveal the fine-scale genetic lineage structure of this early epidemic through analysis of 50,887 SARS-CoV-2 genomes, including 26,181 from the UK sampled throughout the country's first wave of infection.

Yang DD, Ouldali N, Gajdos V, et al. **Common pediatric respiratory infectious diseases may serve as an early predictor for SARS-CoV-2 new wave of infections.** Clin Infect Dis. 2020 Sep 7:ciaa1359. PubMed: <https://pubmed.gov/32894752>. Full-text: <https://doi.org/10.1093/cid/ciaa1359>

Lockdowns lead to a decrease in the common cold, bronchiolitis, acute otitis media, and acute gastroenteritis (AGE) in children. Having found that, François Angoulvant, David Yang and colleagues were curious to know what would happen *after* the end of the lockdown and analyzed a total of 908.887 pediatric emergency visits from 6 academic hospitals over the last three years. As expected, two weeks after the lockdown, observed values reached expected values for the common cold, bronchiolitis, and acute asthma exacerbation. There was one surprise, though: there was no increase in AGE after the end of lockdown. The authors suggest continued regular handwashing and the use of alcohol-based sanitizers as an explanation for this finding. They conclude that the positive lessons learned from SARS-CoV-2, especially handwashing and social distancing, should not be forgotten after the pandemic.

## Virology

Lauring AS, Hodcroft EB. **Genetic Variants of SARS-CoV-2—What Do They Mean?** JAMA 2021, published 6 January. Full-text: <https://doi.org/10.1001/jama.2020.27124>

The emergence of the new “UK variant”—lineage B.1.1.7—has raised widespread concern. Adam Lauring and Emma Hodcroft explain virus evolution and the genomic epidemiology of SARS-CoV-2. They conclude that it is possible that mutations in spike that are “good” for the virus right now could also make it less fit in the context of population-level immunity in the future. Defining these dynamics, and their potential influence on vaccine effectiveness, will require large-scale monitoring of SARS-CoV-2 evolution and host immunity for a long time to come.



## Transmission

Oude Munnink BB, Sikkema RS, Nieuwenhuijse DF, et al. **Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans.** Science. 2021 Jan 8;371(6525):172-177. PubMed: <https://pubmed.gov/33172935>. Full-text: <https://doi.org/10.1126/science.abe5901>

We know that humans can infect animals with SARS-CoV-2, for example, cats and dogs, hamsters and rabbits. Here, Oude Munnink and colleagues show that that mink-to-human transmission also occurred. See also the perspective by Zhou P, Shi ZL. **SARS-CoV-2 spillover events.** Science. 2021 Jan 8;371(6525):120-122. PubMed: <https://pubmed.gov/33414206>. Full-text: <https://doi.org/10.1126/science.abf6097>

## Prevention

Davidson BL, Tapson VF, Irwin RS, French CL, Elliott CG, Levi M. **Commentary: Pharyngeal Antisepsis to Reduce COVID-19 Pneumonia.** Am J Med. 2020 Dec 15;S0002-9343(20)31114-1. PubMed: <https://pubmed.gov/33338507>. Full-text: <https://doi.org/10.1016/j.amjmed.2020.12.001>

Might “washing your throat” with a pharyngeal antisepsis before sleeping, when healthy adults of all ages aspirate material from above the larynx, help protect individuals against COVID-19 pneumonia? Find out why Bruce Davidson et al think it may.

## Vaccine

Callaway E. **Could new COVID variants undermine vaccines? Labs scramble to find out.** Nature 2021, published 8 January. Full-text: <https://www.nature.com/articles/d41586-021-00031-0>

Researchers race to determine why variants identified in Britain and South Africa spread so quickly and whether they’ll compromise vaccines.

Graph

## Diagnostics

Watson J, Richter A, Deeks J. **Testing for SARS-CoV-2 antibodies.** BMJ 2020. PubMed: <https://pubmed.gov/32900692>. Full-text: <https://doi.org/10.1136/bmj.m3325>

Everything you always wanted to know about pre-test probability, test sensitivity and test specificity\* (\*But Were Afraid to Ask). Jessica Watson and Alex Richter have prepared an interactive page where you can define any of these values. Get a feel for it.

## Treatment

Alschuler L, Chiasson AM, Horwitz R, et al. **Integrative medicine considerations for convalescence from mild-to-moderate COVID-19 disease.** Explore (NY). 2020 Dec 23:S1550-8307(20)30417-1. PubMed: <https://pubmed.gov/33358750>. Full-text: <https://doi.org/10.1016/j.explore.2020.12.005>

Could convalescence from mild-to-moderate (MtoM) COVID-19 disease be supported by integrative medicine (IM) strategies? Lise Alschuler et al. suggest adoption of an anti-inflammatory diet, supplementation with vitamin D, glutathione, melatonin, cordyceps, astragalus and garlic have potential utility. If you are also interested in osteopathic manipulation, qigong, breathing exercises and aerobic exercise, you should read this paper with 146 references.

## Education

Rubin EJ, Baden LR, Barocas JA, Morrissey S. **Planning for the SARS-CoV-2 Vaccine Rollout.** Audio interview (26:52). N Engl J Med 2021; 384:e13. Access: <https://doi.org/10.1056/NEJMe2100295>

The editors discuss how health care organizations are planning vaccine rollout and uptake both among their staff and in their communities.

## French

If you read French, read Larousserie D et al. **Covid-19 : l'efficacité des vaccins mise au défi des nouveaux variants du virus.** Le Monde 2021, published 8 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/08/les-vaccins-au-defi-des-nouveaux-variants\\_6065556\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/08/les-vaccins-au-defi-des-nouveaux-variants_6065556_3244.html)

Des chercheurs américains ont montré en laboratoire qu'une mutation présente dans le variant sud-africain du SARS-CoV-2 affaiblissait sensiblement le pouvoir des anticorps de patients contaminés par la souche dominante. Des variants déjà retrouvés en France.

## German

If you read German, read Beyer S. **US-Philosophin zum Angriff aufs Kapitol: »Er ist ein Faschist«** – Der Spiegel 2021, published 8 January. Full-text: <https://www.spiegel.de/politik/ausland/angriff-aufs-us-kapitol-jetzt-muessen-wir-die-dinge-beim-namen-nennen-trump-ist-ein-faschist-a-d9a4ff0f-6ea6-4672-b3ed-15f78be82219>

Wodurch ist denn der Begriff des Faschismus definiert? Gehen wir es mal durch: Unterstützung paramilitärischer Gruppen. Angriffe auf den freien Journalismus. Dämonisierung von politischen Gegnern und Intellektuellen im Allgemeinen. Die Nostalgie für eine mythische, meist ländliche, jedenfalls nicht urbane Vergangenheit. Die Idee, dass einige Volksgruppen echt national sind und andere nicht. Der Versuch, eine unabhängige Justiz zu unterminieren. Die Propagandatechnik, eine Lüge so oft zu wiederholen, dass sie irgendwann für wahr gehalten wird. All das hat er getan! Somit ist er ein Faschist.

## 10 January

### Prevention

Brainard J, Jones NR, Lake IR, Hooper L, Hunter PR. **Community use of face masks and similar barriers to prevent respiratory illness such as COVID-19: a rapid scoping review**. Euro Surveill. 2020 Dec;25(49):2000725. PubMed: <https://pubmed.gov/33303066>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.49.2000725>

Does wearing face masks reduce primary respiratory infection risk by only 6–15%? See also the comment by Cowling BJ, Leung GM. **Face masks and COVID-19: don't let perfect be the enemy of good**. Euro Surveill. 2020 Dec;25(49):2001998. PubMed: <https://pubmed.gov/33303063>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2020.25.49.2001998>

### Pathogenesis

Wei C, Wan L, Yan Q, et al. **HDL-scavenger receptor B type 1 facilitates SARS-CoV-2 entry**. Nat Metab. 2020 Dec;2(12):1391-1400. PubMed: <https://pubmed.gov/33244168>. Full-text: <https://doi.org/10.1038/s42255-020-00324-0>

Could high-density lipoprotein (HDL) **scavenger receptor B type 1 (SR-B1)** facilitate ACE2-dependent entry of SARS-CoV-2? That is the statement by Hui

Zhong, Congwen Wei, finding that the S1 subunit of SARS-2-S binds to cholesterol and possibly to HDL components and facilitates SARS-CoV-2 cellular attachment, entry and infection. SARS-CoV-2 entry is inhibited by silencing SR-B1 expression and by SR-B1 antagonists. Blockade of the cholesterol-binding site on SARS-2-S1 with a monoclonal antibody inhibited HDL-enhanced SARS-CoV-2 infection.

See also the comment by Di Guardo G. **SARS-CoV-2-Cholesterol Interaction: A Lot of Food for Thought.** Pathogens 2021, 10(1), 32- Full-text: <https://doi.org/10.3390/pathogens10010032>

## Vaccines

Wood S, Schulman K. **Beyond Politics — Promoting Covid-19 Vaccination in the United States.** N Engl J Med 2021, published 6 January. Full-text: <https://doi.org/10.1056/NEJMms2033790>

In France, some 60% of the population is skeptic about getting vaccinated. In search of inspiration, French authorities should take a look at this paper by Stacy Wood & Kevin Schulman. They should be ready to revise their marketing skills. Communication needs to become more a part of regular science.

EMA 20201221. **Comirnaty.** European Medicines Agency 2020, published 23 December. Full-text:

<https://www.ema.europa.eu/en/medicines/human/EPAR/comirnaty>

Find the 32-page product information of the EMA.

EMA 20210106. **COVID-19 Vaccine Moderna.** European Medicines Agency 2021, published 6 January. Full-text:

<https://www.ema.europa.eu/en/medicines/human/summaries-opinion/covid-19-vaccine-moderna>

Find the product information as approved by the CHMP on 6 January 2021, pending endorsement by the European Commission.

Garde D. **‘I haven’t even told my wife’.** Stat 2020. Full-text: <https://www.statnews.com/2020/12/15/inside-the-frantic-and-secretive-sprint-to-name-the-covid-19-vaccines/>

Naming a vaccine is almost always a matter of threading semantic needles, branding experts said, where the goal is to evoke positive vibes without irking the world’s more conservative regulatory bodies. And it takes time.

## Clinical

Huang C, Huang L, Wang Y, et al. **6-month consequences of COVID-19 in patients discharged from hospital: a cohort study.** *Lancet* 2021, 8 January. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32656-8](https://doi.org/10.1016/S0140-6736(20)32656-8)

At 6 months after acute infection, more than 70% of COVID-19 survivors in Wuhan, China, were troubled with fatigue or muscle weakness, sleep difficulties, and anxiety or depression. This is the result of a cohort study of discharges from [Jin Yin-tan Hospital](#) between 7 January and 29 May 2020. Bin Cao, Chaolin Huang and colleagues enrolled 1733 of 2469 discharged patients with COVID-19 (median age 57 years, 52% men). Fatigue or muscle weakness (63%) and sleep difficulties (26%) were the most common symptoms. Anxiety or depression was reported among 23% of patients. 13% of patients without acute kidney injury and with normal eGFR at the acute phase had decreased eGFR at follow-up. Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations. See also the comment by Cortinovis M, Perico N, Remuzzi G. **Long-term follow-up of recovered patients with COVID-19.** *Lancet* 2021, published 8 January. Full-text: [https://doi.org/10.1016/S0140-6736\(21\)00039-8](https://doi.org/10.1016/S0140-6736(21)00039-8)

## Treatment

Hashimoto K. **Repurposing of CNS drugs to treat COVID-19 infection: targeting the sigma-1 receptor.** *Eur Arch Psychiatry Clin Neurosci.* 2021 Jan 5. PubMed: <https://pubmed.gov/33403480>. Full-text: <https://doi.org/10.1007/s00406-020-01231-x>

Traditional central nervous system (CNS) drugs that have a high affinity at the sigma-1 receptor (i.e., fluvoxamine, donepezil, ifenprodil) for the treatment of SARS-CoV-2-infected patients? In this review, Kenji Hashimoto discusses the brief history of the sigma-1 receptor and its role in SARS-CoV-2 replication in cells.

## Collateral Effects

Adeniji N, Carr RM, Aby ES, Catana AM, Wegermann K, Dhanasekaran R. **Socioeconomic Factors Contribute to the Higher Risk of COVID-19 in Racial and Ethnic Minorities with Chronic Liver Diseases (CLD)**. *Gastroenterology*. 2020 Nov 20:S0016-5085(20)35438-X. PubMed: <https://pubmed.gov/33227281>. Full-text: <https://doi.org/10.1053/j.gastro.2020.11.035>

Recent studies have shown that patients with chronic liver disease (CLD) in general, and especially those with decompensated cirrhosis and alcohol-related liver disease, are at higher risk COVID-19-related mortality. In this multi-center US cohort study, Renumathy Dhanasekaran, Nia Adeniji and colleagues included 909 patients with CLD and COVID-19 from 21 US centers. They show that non-Hispanic Blacks (NHB) and Hispanics are disproportionately represented in patients with CLD who acquire COVID-19. Both non-Hispanic Blacks and Hispanics had lower household income, lower rates of private insurance, and Hispanics had higher rates of being uninsured. Additionally, the authors show that both NHB and Hispanics had a higher likelihood of living in multifamily housing and in neighborhoods with higher rates of poverty and overcrowding than non-Hispanic Whites.

## Journal Feature

Glausiusz J. **Rethinking travel in a post-pandemic world**. *Nature* 2021, published 5 January. Full-text: <https://www.nature.com/articles/d41586-020-03649-8>

Climate scientists recommend ways to boost the value of virtual conferences and reduce carbon footprints even when travel curbs ease.

## French

If you read French, read Santi P. **Covid-19 : après leur hospitalisation, trois patients sur quatre présenteraient des symptômes durables, selon une étude chinoise**. *Le Monde* 2021, published 9 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/09/covid-19-fatigue-faiblesse-musculaire-atteintes-renales-ou-pulmonaires-trois-patients-sur-quatre-presenteraient-des-symptomes-durables\\_6065727\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/09/covid-19-fatigue-faiblesse-musculaire-atteintes-renales-ou-pulmonaires-trois-patients-sur-quatre-presenteraient-des-symptomes-durables_6065727_3244.html)

« The Lancet » a publié samedi **une étude** portant sur une cohorte de plus de 1 700 patients chinois hospitalisés au printemps 2020, qui montre que 76 % d'entre eux souffraient encore, six mois plus tard, d'au moins un symptôme.

## 11 January

### Epidemiology

Charron N, Lapuente V, Rodriguez-Pose A. **Uncooperative Society, Uncooperative Politics or Both? How Trust, Polarization and Populism Explain Excess Mortality for COVID-19 across European regions.** The Quality of Government (QoG) Institute 2020 (December). Full-text: <https://gupea.ub.gu.se/handle/2077/67189>

Why have some places performed better than others in the fight against COVID-19? The authors found that societal polarization played a significant role. When the divide in political trust between supporters and opponents of incumbent governments within societies is high, the authors observe consistently higher COVID-19-related excess mortality deaths during the first wave of the pandemic. They also find that regions with a political elite less supportive of European integration are regions where excess deaths have been significantly higher. *Vive l'Europe!*

### Virology

Greaney AJ, Loes AN, Crawford KHD, et al. **Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies.** bioRxiv 2021, posted 4 January. Full-text: <https://doi.org/10.1101/2020.12.31.425021>

Jesse Bloom, Allison Greaney and colleagues comprehensively mapped how mutations to the SARS-CoV-2 RBD affected binding by the antibodies in convalescent human serum. One major finding is that serum antibody binding is predominantly affected by mutations at just a few dominant epitopes in the RBD. The most important site is E484, where neutralization by some sera is reduced > 10-fold by several mutations, including one in emerging viral lineages in South Africa and Brazil. *Don't miss this pre-print paper.*

Andreano E, Piccini G, Licastro D, et al. **SARS-CoV-2 escape *in vitro* from a highly neutralizing COVID-19 convalescent plasma.** bioRxiv. 2020 Dec 28:2020.12.28.424451. PubMed: <https://pubmed.gov/33398278>. Full-text: <https://doi.org/10.1101/2020.12.28.424451>

If constantly pressured, SARS-CoV-2 virus has the ability to escape even a potent polyclonal serum targeting multiple neutralizing epitopes. By Rino Rappuoli, Emanuele Andreano and colleagues.

## Transmission

Swadi T, Geoghegan JL, Devine T, et al. **Genomic Evidence of In-Flight Transmission of SARS-CoV-2 Despite Predeparture Testing.** Emerg Infect Dis. 2021 Jan 5;27(3). PubMed: <https://pubmed.gov/33400642>. Full-text: <https://doi.org/10.3201/eid2703.204714>

SARS-CoV-2 transmission may occur on aircraft and the risk may be increased during long-distance flights. Joep de Ligt, Tara Swadi and colleagues from New Zealand describe an air travel cluster where among the 7 eventually-infected passengers, 2 were probably index case-patients infected before the flight, 4 were probably infected during the flight, and the remaining passenger was probably infected while in New Zealand under “managed isolation and quarantine”. All 7 passengers were seated in aisle seats within 2 rows of where the presumed index case-patient(s) were seated.

## Vaccine

Xie X, Zou J, Fonte-Garfias CR, et al. **Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera.** bioRxiv 2021, posted 7 January. Full-text: <https://doi.org/10.1101/2021.01.07.425740>

Recent SARS-CoV-2 variants in the United Kingdom and South Africa have multiple mutations in their S glycoproteins, which are key targets of viral neutralizing antibodies. These rapidly spreading variants share the spike N501Y substitution. Pei-Yong Shi, Philip R. Dormitzer and Xuping Xie generated isogenic N501 and Y501 SARS-CoV-2. Sera of participants in a previously reported trial of the mRNA-based COVID-19 vaccine BNT162b2 had equivalent neutralizing titers to the N501 and Y501 viruses.

## Clinical

Nehme M, Braillard O, Alcoba G, et al. **COVID-19 Symptoms: Longitudinal Evolution and Persistence in Outpatient Settings.** Ann Intern Med. 2020 Dec 8:M20-5926. PubMed: <https://pubmed.gov/33284676>. Full-text: <https://doi.org/10.7326/M20-5926>

In this cohort of 669 persons (mean age 43, 60% women, 24,6% health care workers, 68,8% with no underlying risk factors), symptoms persisted in one third of ambulatory patients 30 to 45 days after diagnosis. Fatigue, dyspnea, and loss of taste or smell were the main persistent symptoms.



Salmon-Ceron D, Slama D, De Broucker T, et al. **Clinical, virological and imaging profile in patients with prolonged forms of COVID-19: A cross-sectional study.** J Infect. 2020 Dec 4:S0163-4453(20)30762-3. PubMed: <https://pubmed.gov/33285216>. Full-text: <https://doi.org/10.1016/j.jinf.2020.12.002>

Cross-sectional mono-center survey on 70 consecutive patients presenting with an initial symptomatic COVID-19 infection who developed prolonged COVID symptoms defined as persistent symptoms (> 2 months after the first day of the initial episode) or resurgent symptoms (at least 3 weeks after the 1st episode). Median age was 45 (range 23–75), 78,6% were female. The authors classify the characteristics of late symptoms in 7 main categories:

- Major fatigue or exhaustion for 51 patients (72,9%)
- Neurological symptoms, in 54 (77,1%), divided into neuro-cognitive disorders (such as memory, mood or attention disorders), headaches, sensory disturbances (such as balance disorders, tingling, burning sensations and neurogenic pains), or others (swallowing or speech disorders, thermoregulation disorders).
- Cardiothoracic symptoms in 50 patients (71,4%): chest pain and tightness, palpitations, cough, dyspnea.
- Muscular or/and articular pains for 20 (25,7%).
- ENT symptoms: persistent or recurrent anosmia, hyposmia and/or dysgeusia for 21 (30%).
- Gastro-intestinal symptoms for 17 (24,3%): diarrhea, nausea/vomiting, epigastric or abdominal pain.
- Skin and vascular symptoms in 10 (14,4%).

Pun BT, Badenes R, La Calle GH, et al. **Prevalence and risk factors for delirium in critically ill patients with COVID-19 (COVID-D): a multicentre cohort study.** Lancet Respir Health 2021, published 8 January. Full-text: [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30552-X/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30552-X/fulltext)

Acute brain dysfunction was highly prevalent and prolonged in critically ill patients with COVID-19. Now, Brenda Pun, Rafael Badenes and colleagues publish the results of a cohort study on 2088 patients treated in 69 adult intensive care units (ICUs) across 14 countries. Benzodiazepine use and lack of family visitation were identified as modifiable risk factors for delirium. The

authors conclude that their data present an opportunity to reduce acute brain dysfunction in patients with COVID-19.

## Comorbidities

Marjot T, Moon AM, Cook JA, et al. **Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: An international registry study.** *J Hepatol.* 2020 Oct 6:S0168-8278(20)33667-9. PubMed: <https://pubmed.gov/33035628>. Full-text: <https://doi.org/10.1016/j.jhep.2020.09.024>

No comment needed. The key messages presented at the beginning of the paper:

- Patients with cirrhosis experience high rates of hepatic decompensation and death following SARS-CoV-2 infection.
- Mortality increased in stepwise fashion according to Child-Pugh class.
- Other risk factors for death included advancing age and alcohol-related liver disease.
- Mortality risk was higher in patients with advanced cirrhosis than propensity-score-matched controls without liver disease.
- The majority of deaths in patients with cirrhosis were from COVID-19-related lung disease.

## Spanish

If you read Spanish, read Ansele M. **Un caldo de cultivo para variantes del virus que escapan de las vacunas.** *El País* 2021, published 10 January. Full-text: <https://elpais.com/ciencia/2021-01-09/el-peor-escenario-posible-nuevas-variantes-del-virus-que-escapen-de-las-vacunas.html>

La expansión fuera de control del coronavirus y el retraso de la segunda dosis vacunal pueden favorecer la aparición de mutantes resistentes.

Alessi G. **Brasil, una trinchera especialmente letal para los enfermeros que luchan contra la covid-19.** *El País* 2021, published 9 January. Full-text: <https://elpais.com/america/internacional/2021-01-09/brasil-una-trinchera-especialmente-letal-para-los-enfermeros-que-luchan-contra-la-covid-19.html>

Un tercio de los 1.500 sanitarios fallecidos en todo el mundo trabajaba en el gigante sudamericano. A la falta inicial de equipos de protección se suma el agotamiento y la llegada de personal inexperto.

## 12 January

### Virology

Chen Y, Li S, Wu W, Geng S, Mao M. **Distinct mutations and lineages of SARS-CoV-2 virus in the early phase of COVID-19 pandemic and subsequent global expansion.** bioRxiv 2021, published 8 January. Full-text: <https://doi.org/10.1101/2021.01.05.425339>

Mao Mao, Yan Chen and colleagues analyzed 4013 full-length SARS-CoV-2 genomes from different continents over a 14-week timespan since the outbreak in Wuhan. 2954 unique nucleotide substitutions were identified with 31 of the 4013 genomes remaining as ancestral type, and 952 (32,2%) mutations recurring in more than one genome. The authors used the same approach to analyze 261.350 full-length SARS-CoV-2 genomes available in the GISAID database as of 25 December 2020. They suggest that viral genotypes can be utilized as molecular barcodes in combination with epidemiologic data to monitor the spreading routes of the pandemic and evaluate the effectiveness of control measures.

Zahradnik J, Marciano S, Shemesh M, et al. **SARS-CoV-2 RBD in vitro evolution follows contagious mutation spread, yet generates an able infection inhibitor.** bioRxiv 2021, posted 8 January. Full-text: <https://www.biorxiv.org/content/10.1101/2021.01.06.425392v2>

SARS-CoV-2 is constantly evolving, with more contagious mutations spreading rapidly, in particular in England and South Africa. Here, Gideon Schreiber, Jiří Zahradník and colleagues show that the naturally selected mutations S477N, E484K, and N501Y of the Spike protein RBD, which show higher infectivity, were also selected by yeast surface display affinity maturation already in the first round, giving rise to the South African, E484K, N501Y, and British variants that bind ACE2 13 and 3,5-fold tighter than RBD-WT.

### Prevention

Meidan D, Schulmann N, Cohen R, et al. **Alternating quarantine for sustainable epidemic mitigation.** Nat Commun 12, 220 (2021). Full-text: <https://doi.org/10.1038/s41467-020-20324-8>

To ease the potentially devastating socioeconomic consequences of pharmaceutical interventions, social distancing, lock-downs and mobility restrictions, Baruch Barzel, Dror Meidan and colleagues, propose an alternative alternating quarantine strategy: at any moment, half of the population re-

mains under lockdown while the other half continues to be active - maintaining a routine of weekly alternation of activity and quarantine. This regime would minimize infectious interactions, as it allows only half of the population to interact for just half of the time. Dramatic reduction in transmission despite sustaining socioeconomic continuity at ~50% capacity?

## Pathogenesis

Grant RA, Morales-Nebreda L, Markov NS, et al. **Circuits between infected macrophages and T cells in SARS-CoV-2 pneumonia.** Nature 2021, published 11 January. Full-text: <https://doi.org/10.1038/s41586-020-03148-w>

SARS-CoV-2 might cause a slowly unfolding, spatially limited alveolitis in which alveolar macrophages harboring SARS-CoV-2 and T cells form a positive feedback loop that drives persistent alveolar inflammation. This is the result of a study that collected bronchoalveolar lavage fluid samples from 88 patients with SARS-CoV-2-induced respiratory failure and 211 patients with known or suspected pneumonia from other pathogens and subjected them to flow cytometry and bulk transcriptomic profiling.

## Vaccine

Bordon, Y. **Immune readouts from the Oxford COVID-19 vaccine.** Nat Rev Immunol 2021, published 11 January. Full-text: <https://doi.org/10.1038/s41577-021-00503-4>

Yvonne Bordon comments on two recent reports from the Oxford COVID-19 vaccine team which detail the immune outcomes observed in a Phase I/II trial of their ChAdOx1 nCoV-19 vaccine. In one of the papers we presented on [21 December](#), the authors give a detailed description of the immune response after administration of one dose of ChAdOx1 nCoV-19 in 88 adults (ages 18-55 years) ([Ewer 2020](#)). They define the isotypes, subclasses and antibody avidity induced after vaccination. They also performed multiplex cytokine profiling and intracellular cytokine staining analysis, demonstrating that ChAdOx1 nCoV-19 vaccination induces a predominantly Th1-type response (that appears to be good). See also Barrett JR, Belij-Rammerstorfer S, Dold C, et al. **Phase 1/2 trial of SARS-CoV-2 vaccine ChAdOx1 nCoV-19 with a booster dose induces multifunctional antibody responses.** Nat Med. 2020 Dec 17. PubMed: <https://pubmed.gov/33335322>. Full-text: <https://doi.org/10.1038/s41591-020-01179-4>

## Clinical

McGonagle D, Bridgewood C, Ramanan AV, Meaney JFM, Watad A. **COVID-19 vasculitis and novel vasculitis mimics**. *Lancet Rheumatology* 2021, published 7 January. Full-text: [https://doi.org/10.1016/S2665-9913\(20\)30420-3](https://doi.org/10.1016/S2665-9913(20)30420-3)

In this Viewpoint article, Dennis McGonagle et al. highlight how imaging and post-mortem findings point to a novel vasculitis mimic related to COVID-19 that might lead to cryptogenic strokes across multivessel territories, acute kidney injury with hematuria, a skin vasculitis mimic, intestinal ischemia, and other organ ischemic manifestations.

Solomon T. **Neurological infection with SARS-CoV-2 – the story so far**. *Nat Rev Neurol* 2021, published 7 January. Full-text: <https://doi.org/10.1038/s41582-020-00453-w>

As the COVID-19 pandemic developed and neurological manifestations were reported, concern grew that SARS-CoV-2 might directly invade neuronal cells. However, research throughout the year to address this concern has revealed a different story with inflammatory processes at its center.

## Treatment

Garber K. **Hunt for improved monoclonals against coronavirus gathers pace**. *Nat Biotechnol* 39, 9–12 (2021). Full-text: <https://doi.org/10.1038/s41587-020-00791-6>

Bamlanivimab (Lilly) and the double-antibody cocktail casirivimab + imdevimab (Regeneron) have been recently given an Emergency Use Authorization (EUA) for use in high-risk COVID-19 patients with mild or moderate disease. Though both drugs represent new options for treating the coronavirus infection, neither is ideal. The future of monoclonals remains uncertain.

Cohen JB, Hanff TC, William P, et al. **Continuation versus discontinuation of renin-angiotensin system inhibitors in patients admitted to hospital with COVID-19: a prospective, randomised, open-label trial**. *Lancet Respir Health* 2021, published 7 January. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30558-0](https://doi.org/10.1016/S2213-2600(20)30558-0)

Consistent with international society recommendations, angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), inhibitors of the renin-angiotensin system, can be safely continued in patients admitted to hospital with COVID-19. A confirmation from a small

study that enrolled 152 participants randomly assigned them to either continue or discontinue renin–angiotensin system inhibitor therapy. There were 16 (21%) of 75 participants in the continuation arm versus 14 (18%) of 77 in the discontinuation arm who required intensive care unit admission or invasive mechanical ventilation, and 11 (15%) of 75 participants in the continuation group versus ten (13%) of 77 in the discontinuation group who died.

## Severe COVID

### Comorbidities

Accili D. **Can COVID-19 cause diabetes?** Nat Metab 2021 published 11 January. Full-text: <https://doi.org/10.1038/s42255-020-00339-7>

Whether a separate entity of post-COVID-19 diabetes possibly associated with lasting  $\beta$ -cell damage also exists is not yet clear.

### Spanish

If you read Spanish, read Jericó P. **Reducir la fatiga pandémica.** El País 2021, published 10 January. Full-text: [https://elpais.com/elpais/2021/01/08/eps/1610126355\\_684003.html](https://elpais.com/elpais/2021/01/08/eps/1610126355_684003.html)

Casi un año enfrentándonos al coronavirus pasa factura. El cansancio puede hacer que relajemos las medidas preventivas. Pero también hay remedio para ello.

### French

If you read French, read Gatinois C, Aeberhardt C. **Comment le français Sanofi s'est retrouvé distancé dans la course au vaccin.** Le Monde 2021, published 11 January. Full-text : [https://www.lemonde.fr/economie/article/2021/01/11/covid-19-le-destin-contrarie-du-vaccin-de-sanofi\\_6065825\\_3234.html](https://www.lemonde.fr/economie/article/2021/01/11/covid-19-le-destin-contrarie-du-vaccin-de-sanofi_6065825_3234.html)

Après des débuts prometteurs, une erreur de laboratoire a fait perdre cinq à six mois au groupe. Nouveau rebondissement, vendredi 8 janvier : sous la pression de Bercy, le groupe français pourrait mettre son outil industriel à disposition de ses concurrents les plus avancés, et dont les capacités de production sont limitées.

## 13 January

### Treatment

Salman D, Vishnubala D, Le Feuvre P, et al. **Returning to physical activity after covid-19.** *BMJ.* 2021 Jan 8;372:m4721. PubMed: <https://pubmed.gov/33419740>. Full-text: <https://doi.org/10.1136/bmj.m4721>

“Only return to exercise after at least seven days free of symptoms and begin with at least two weeks of minimal exertion. Use daily self-monitoring to track progress, including when to seek further help.” In this nice 6-page paper, David Salman and colleagues give an excellent guide to physical activity after COVID-19. Clearly, patients with ongoing symptoms or who had severe COVID-19 or a history suggestive of cardiac involvement need thorough clinical assessment.

### Epidemiology

Bagchi S, Mak J, Li Q, et al. **Rates of COVID-19 Among Residents and Staff Members in Nursing Homes – United States, May 25–November 22, 2020.** *MMWR Morb Mortal Wkly Rep.* ePub: 8 January 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7002e2>

Increases in community rates might be associated with increases in nursing home COVID-19 incidence, and nursing home mitigation strategies need to include a comprehensive plan to monitor local SARS-CoV-2 transmission and minimize high-risk exposures within facilities.

### Transmission

Volz E, Mishra W, Chand M, et al. **Transmission of SARS-CoV-2 Lineage B.1.1.7 in England: Insights from linking epidemiological and genetic data.** *medRxiv* 2021, posted 4 January. Full-text: <https://doi.org/10.1101/2020.12.30.20249034>

The new SARS-CoV-2 lineage B117 (B.1.1.7, also named VOC 202012/01), originated in England in late Summer to early Autumn 2020. Available data indicate a larger share of under 20-year-olds among reported B117 than non-B117 cases. B117 seems to have a substantial transmission advantage, with the estimated difference in reproduction numbers between B117 and non-B117 ranging between 0.4 and 0.7. Neil Ferguson, Erik Volz and colleagues note that these estimates of transmission advantage apply to a period where high levels of social distancing were in place in England; extrapolation to other transmission contexts therefore requires caution.

## Prevention

Atherstone C, Peterson ML, Malone M, et al. **Time from Start of Quarantine to SARS-CoV-2 Positive Test Among Quarantined College and University Athletes — 17 States, June–October 2020.** MMWR Morb Mortal Wkly Rep 2021;70:7–11. DOI: <http://dx.doi.org/10.15585/mmwr.mm7001a2>

Quarantine after SARS-CoV-2 exposure is critical to preventing transmission. Among young, healthy athletes, the probability of receiving positive test results after day 10 of quarantine is low. A shorter quarantine after COVID-19 exposure could increase adherence but still pose a small residual risk for transmission.

Jones A, Fialkowski V, Prinzing L, Trites J, Kelso P, Levine M. **Assessment of Day-7 Postexposure Testing of Asymptomatic Contacts of COVID-19 Patients to Evaluate Early Release from Quarantine — Vermont, May–November 2020.** MMWR Morb Mortal Wkly Rep 2021;70:12–13. DOI: <http://dx.doi.org/10.15585/mmwr.mm7001a3>

Among the persons in quarantine who tested negative at day 7 after exposure, none who were retested between days 8 and 14 were positive. Allowing asymptomatic persons to shorten quarantine with a negative test at day 7 or later has not been demonstrated to result in transmission of SARS-CoV-2.

## Immunology

Zuniga M, Gomes C, Carsons SE, et al. **Autoimmunity to the Lung Protective Phospholipid-Binding Protein Annexin A2 Predicts Mortality Among Hospitalized COVID-19 Patients.** medRxiv 2021, posted on 4 January. Full-text: <https://doi.org/10.1101/2020.12.28.20248807>

Anti-Annexin A2 antibodies were elevated among hospitalized COVID-19 patients and these levels predicted mortality. This is the message of a pre-print paper by Ana Rodriguez, Marisol Zuniga and colleagues. The authors explain that inhibition of Annexin A2 induces systemic thrombosis, cell death, and non-cardiogenic pulmonary edema and that autoimmunity to Annexin A2 might explain key clinical findings of severe COVID-19. (Annexin A2 is a phospholipid-binding protein involved in fibrinolysis, cell membrane stabilization and repair, that ensures the integrity of the pulmonary microvasculature.)



## Vaccine

Marjot T, Webb GJ, Barritt AS. **SARS-CoV-2 vaccination in patients with liver disease: responding to the next big question.** *Lancet Gastroenterol Hepatol* 2021, published 11 January. Full-text: [https://doi.org/10.1016/S2468-1253\(21\)00008-X](https://doi.org/10.1016/S2468-1253(21)00008-X)

Patients with advanced liver disease have well recognized deficiencies in innate and humoral immunity, termed cirrhosis-associated immune dysfunction (CAID). Nonetheless, given the high COVID-19-related mortality in patients with decompensated cirrhosis, it remains of utmost importance to prioritize vaccinations in this sub-group. Eleanor Barne, Thomas Marjot and colleagues express their belief that patients with advanced liver disease should be prioritized for vaccination, with the likely benefits far outweighing any potential risks. Until it is established whether patients with liver disease and transplantation achieve optimal protection after immunization, clinicians should remain vigilant for post-vaccination COVID-19 in these cohorts.

## Clinical

Chen W, Tian Y, Li Z, et al. **Potential interaction between SARS-CoV-2 and thyroid: a review.** *Endocrinology* 2021, published 11 January. Full-text: <https://doi.org/10.1210/endo/bqab004>

Certain thyroid diseases may have a negative impact on the prevention and control of COVID-19; some anti-COVID-19 agents may cause thyroid injury; and COVID-19 and thyroid disease may mutually aggravate the disease burden.

Editorial. **Vitamin D and COVID-19: why the controversy?** *Lancet Diabetes Endocrinol* 2021, published 11 January. Full-text: [https://doi.org/10.1016/S2213-8587\(21\)00003-6](https://doi.org/10.1016/S2213-8587(21)00003-6)

In December, NICE published an updated [rapid review](#) of recent studies on vitamin D and COVID-19. Their recommendations: everyone should take vitamin D supplements to maintain bone and muscle health during the autumn and winter months. Later, [new guidance](#) from the UK government allowed extremely clinically vulnerable people to opt in to receive a free 4-month supply of daily vitamin D supplements—similar to an initiative launched earlier in Scotland. Several clinical trials on vitamin D and COVID-19 outcomes are underway.

## Severe COVID

Gupta RK, Harrison WM, Ho A, et al. **Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: a prospective cohort study.** *Lancet Respir Med* 2021, published 11 January. Full-text: DOI:[https://doi.org/10.1016/S2213-2600\(20\)30559-2](https://doi.org/10.1016/S2213-2600(20)30559-2)

How would you predict the risk of clinical deterioration in acute COVID-19 cases? Mahdad Noursadeghi, Rishi K Gupta and colleagues developed and validated a prognostic model for in-hospital clinical deterioration which integrated 11 routinely available predictors: age, sex, nosocomial infection, Glasgow coma scale score, peripheral oxygen saturation (SpO<sub>2</sub>) at admission, breathing room air or oxygen therapy (contemporaneous with SpO<sub>2</sub> measurement), respiratory rate, urea concentration, C-reactive protein concentration, lymphocyte count, and presence of radiographic chest infiltrates.

## 14 January

### Epidemiology

Vang KE, Krow-Lucal ER, James AE, et al. **Participation in Fraternity and Sorority Activities and the Spread of COVID-19 Among Residential University Communities - Arkansas, August 21-September 5, 2020.** *MMWR Morb Mortal Wkly Rep.* 2021 Jan 8;70(1):20-23. PubMed: <https://pubmed.gov/33411698>. Full-text: <https://doi.org/10.15585/mmwr.mm7001a5>

In the US, the start of the 2020–21 academic year was sometimes the beginning of local epidemics. Kristyn Vang et al. describe SARS-CoV-2 transmission by on- and off-campus congregate living settings and activities. Their analysis indicates that 91% of gatherings were associated with fraternity or sorority activities. Interestingly, at one university, women accounted for 70% of COVID-19 cases although they constituted only 54% of the university's student body. Among linked gatherings, women accounted for 86% of cases. The authors speculate about possible explanations (involvement in gender-specific activities? sorority rush week?).

### Transmission

Kasloff SB, Leung A, Strong JE, et al. **Stability of SARS-CoV-2 on critical personal protective equipment.** *Sci Rep* 11, 984 (2021). Full-text: <https://doi.org/10.1038/s41598-020-80098-3>

Cotton provides the lowest environmental stability to SARS-CoV-2. When applied to 100% cotton fabric, the virus underwent rapid degradation and became undetectable by TCID<sub>50</sub> assay within 24 h. However, viable SARS-CoV-2 was recovered after 21 days on plastic, 14 days on stainless steel, 7 days on nitrile gloves and 4 days on chemical resistant gloves.

Hwang SE, Chang JH, Bumjo O, Heo J. **Possible Aerosol Transmission of COVID-19 Associated with an Outbreak in an Apartment in Seoul, South Korea, 2020.** *Int J Infect Dis.* 2020 Dec 17:S1201-9712(20)32558-3. PubMed: <https://pubmed.gov/33346125>. Full-text: <https://doi.org/10.1016/j.ijid.2020.12.035>

Indoor aerosol transmission might be underappreciated. This is the suggestion by Jongho Heo, Seo Eun Hwang and colleague who investigated a cluster of 9 COVID-19 infections in an apartment building in Seoul, South Korea. The investigation found no other possible contact between the cases than the airborne infection through a single air duct in the bathroom. All infected cases (living from the 2<sup>nd</sup> to the 11<sup>th</sup> floor of the building) were found along two vertical lines of the building, and each line was connected through a single air duct in the bathroom for natural ventilation. The authors assume that the first infected person probably released the virus during a shower in the bathroom by coughing, breathing, singing, or flushing and that SARS-CoV-2 may have combined with water vapor and became aerosols in the humid environment.

## Prevention

Fuller JA, Hakim A, Victory KR, et al. **Mitigation Policies and COVID-19–Associated Mortality — 37 European Countries, January 23–June 30, 2020.** *MMWR Morb Mortal Wkly Rep.* ePub: 12 January 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7002e4>

European countries that implemented more stringent mitigation policies by the time they reached an early mortality threshold in spring 2020 (closure of non-essential businesses, restrictions on gatherings and movement, and stay-at-home orders) tended to report fewer COVID-19–associated deaths through the end of June. These countries have saved tens of thousands of lives relative to those countries that implemented similar policies, but later. These findings suggest that earlier implementation, even by just a few weeks (even one week!), may prevent widespread transmission and large numbers of deaths.

## Immunology

Sette A, Crotty S. **Adaptive immunity to SARS-CoV-2 and COVID-19.** Cell 2021, published 12 January. Full-text: <https://doi.org/10.1016/j.cell.2021.01.007>

In this review, Alessandro Sette and Shane Crotty describe how CD4<sup>+</sup> T cells, CD8<sup>+</sup> T cells, and neutralizing antibodies all contribute to the control of SARS-CoV-2, in both non-hospitalized and hospitalized cases of COVID-19. The authors discuss the specific functions and kinetics of these adaptive immune responses, as well as their interplay with innate immunity and implications for COVID-19 vaccines and immune memory against re-infection.

Legros V, Denolly S, Vogrig M, et al. **A longitudinal study of SARS-CoV-2-infected patients reveals a high correlation between neutralizing antibodies and COVID-19 severity.** Cell Mol Immunol (2021). Full-text: <https://doi.org/10.1038/s41423-020-00588-2>

In a cohort of 140 SARS-CoV-2 individuals with confirmed SARS-CoV-2 infection, nAb titers correlated strongly with disease severity and with anti-spike IgG levels. Patients from intensive care units exhibited high nAb titers; conversely, patients with milder disease symptoms had heterogeneous nAb titers, and asymptomatic or exclusively outpatient patients had no or low nAbs. nAb activity in SARS-CoV-2-infected patients displayed a relatively rapid decline after recovery compared to individuals infected with other coronaviruses.

## Vaccine

Dolgin E. **How COVID unlocked the power of RNA vaccines.** Nature 2021, published 12 January. Full-text: <https://www.nature.com/articles/d41586-021-00019-w>

The technology could revolutionize efforts to immunize against HIV, malaria, influenza and more.

Mahase E. **How the Oxford-AstraZeneca covid-19 vaccine was made.** BMJ 2021; 372. Full-text: <https://doi.org/10.1136/bmj.n86>

Andrew Pollard has been leading the Oxford vaccine clinical trials in the UK, Brazil, and South Africa. He tells how the Oxford vaccine came to be, how dosing was worked out, and whether it will stand up to the new variants.

## Severe COVID

Supady A, Curtis JR, Abrams D, et al. **Allocating scarce intensive care resources during the COVID-19 pandemic: practical challenges to theoretical frameworks.** *Lancet Respir Med* 2021, published 12 January. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30580-4](https://doi.org/10.1016/S2213-2600(20)30580-4)

In the coming weeks, available medical resources will not always meet the increased demand for life-saving intensive care. Alexander Supady, Randall Curtis and colleagues propose that triage committees could be involved in providing policies and guidance for clinicians to help ensure equity in the application of rationing under crisis standards of care.

## Comorbidities

Möhn N, Konen FF, Pul R, et al. **Experience in Multiple Sclerosis Patients with COVID-19 and Disease-Modifying Therapies: A Review of 873 Published Cases.** *J Clin Med.* 2020 Dec 16;9(12):4067. PubMed: <https://pubmed.gov/33339436>. Full-text: <https://doi.org/10.3390/jcm9124067>

Patients without disease modifying therapies (DMTs), with previous cardiovascular diseases, or with a severe degree of disability may be at a higher risk of severe COVID-19. In this review of 873 published cases, immunosuppressive therapy itself did not appear to be a substantial risk factor. The authors argue that it might be reasonable to assume that these therapies could be protective, either directly by mitigating the cytokine storm, or indirectly by reducing the disease activity of MS.

## Spanish

If you read Spanish, read Criado MA. **Cuanto más leve es la infección por coronavirus, peor olfato.** *El País* 2021, published 13 January. Full-text: <https://elpais.com/ciencia/2021-01-12/cuanto-mas-leve-es-la-infeccion-por-coronavirus-peor-olfato.html>

Un estudio europeo muestra que muchos de los casos menos graves sufren alucinaciones olfatorias.

Sastre A. **‘La peste’ se extiende por las villas miseria de Buenos Aires.** *El País* 2021, published 11 January. Full-text: <https://elpais.com/planeta-futuro/2021-01-11/la-peste-se-extiende-por-las-villas-miseria-de-buenos-aires.html>

Crece el temor a que la segunda ola de COVID-19 arrase con las barriadas más pobres de la capital, cuyos habitantes apenas han podido resistir a los estragos de la primera. Un recorrido por algunas de ellas.

## French

If you read French, read Sénecat A. **Covid-19 : comment établir ou écarter le lien entre le vaccin et un décès ?** Le Monde 2021, published 13 January. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2021/01/13/covid-19-comment-etablir-ou-ecarter-le-lien-entre-le-vaccin-et-un-deces\\_6066110\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2021/01/13/covid-19-comment-etablir-ou-ecarter-le-lien-entre-le-vaccin-et-un-deces_6066110_4355770.html)

Plusieurs articles évoquant la mort de personnes peu après une injection alimentent la défiance envers la vaccination. Comment sont analysés ces décès et que peut-on en conclure ?

## German

If you read German, read Fischer L. **Dieses mutierte Coronavirus könnte alles ändern.** Die Zeit 2021, published 13 Januar. Full-text: <https://www.zeit.de/wissen/2021-01/corona-variante-b-1-1-7-mutation-gefahr-massnahmen-angela-merkel>

Die schneller übertragbare Corona-Variante B117 hat Deutschland erreicht. Sie könnte die Fallzahlen explodieren lassen. Warum wir die Mutante jetzt eindämmen müssten.

## 15 January

### Epidemiology

Ledford H. **COVID reinfections are unusual — but could still help the virus to spread.** Nature 2021, published 14 January. Full-text: <https://www.nature.com/articles/d41586-021-00071-6>

A large study of UK healthcare workers suggests that most people are immune for months after catching COVID-19 for the first time.

Ashby B, Best A. **Herd immunity.** Curr Biol 2021, published 12 January. Full-text: <https://doi.org/10.1016/j.cub.2021.01.006>

If you want to do some math, read this short paper and revise a concept neither Boris Johnson (how could he!) nor his advisers really understood. In

short: as immunity accumulates in a population — naturally during the course of an epidemic or through vaccination — the spread of infectious disease is limited by the depletion of susceptible hosts. In this primer, Ben Ashby and Alex Best discuss the concept of herd immunity from first principles, clarify common misconceptions, and consider the implications for disease control.

## Vaccine

Sadoff J, Le Gars M, Shukarev G, et al. **Interim Results of a Phase 1–2a Trial of Ad26.COV2.S Covid-19 Vaccine.** *N Engl J Med* 2021, published 13 January. Full-text: <https://doi.org/10.1056/NEJMoa2034201>

Hanneke Schuitemaker, Jerald Sadoff and colleagues describe the safety and immunogenicity profiles of Ad26.COV2.S. As with other SARS-CoV-2 vaccines, the most frequent adverse events were fatigue, headache, myalgia, and injection site pain. Systemic adverse events were less common in people 65 years or older than in those 18 to 55 years of age. Neutralizing-antibody titers against wild type virus were detected in 90% or more of all participants on day 29 after the first vaccine dose and reached 100% by day 57 with a further increase in titers (GMT, 288 to 488), regardless of vaccine dose or age group. Ad26.COV2.S, developed by Janssen Pharmaceutical Companies of Johnson & Johnson, is a recombinant replication-incompetent adenovirus type 26 (Ad26) vector-based COVID-19 vaccine encoding a prefusion-stabilized SARS-CoV-2 Spike immunogen.

Efrati I. **Israel to Share Vaccination Data With Pfizer as Part of Secret Deal.** *Haaretz* 2021, published 10 January. Full-text: <https://www.haaretz.com/israel-news/.premium-israel-to-share-covid-vaccine-data-with-pfizer-but-agreement-remains-secret-1.9438504>

The Israeli newspaper reports a deal between Israel and Pfizer: Pfizer will receive anonymized data about consequences of the inoculations, side effects, efficacy, and the amount of time it takes to develop antibodies, according to different types of population, age, gender, pre-existing conditions, and other factors.

## Long COVID

Venkatesan P. **NICE guideline on long COVID.** *Lancet Respir Med* 2021, published 13 January. Full-text: [https://doi.org/10.1016/S2213-2600\(21\)00031-X](https://doi.org/10.1016/S2213-2600(21)00031-X)

While discussing the NICE guidelines on *long COVID* published a few weeks ago, Priya Venkatesan gives a short overview of the condition. The guideline defines long COVID as (1) ongoing symptomatic COVID-19 for people who still have symptoms between 4 and 12 weeks after the start of acute symptoms; and (2) post-COVID-19 syndrome for people who still have symptoms for more than 12 weeks after the start of acute symptoms. Patients with new or ongoing symptoms 4 weeks or later after acute infection should receive a full blood count, kidney and liver function tests, a C-reactive protein test, and an exercise tolerance test (recording level of breathlessness, heart rate, and O<sub>2</sub> saturation). The guidelines also recommend that a chest x-ray should be offered to all patients by 12 weeks after acute infection if they have continuing respiratory symptoms. [**COVID-19 rapid guideline: managing the long-term effects of COVID-19** – NICE guideline [NG188]. Access: <https://www.nice.org.uk/guidance/NG188>]

## Treatment

Joyner MJ, Carter RD, Senefeld JW, et al. **Convalescent Plasma Antibody Levels and the Risk of Death from Covid-19**. *N Engl J Med* 2021, published 13 January. Full-text:

Patients who have not yet received mechanical ventilation may benefit from transfusion of plasma with high anti-SARS-CoV-2 IgG antibody levels. However, in this study of 3082 patients there was no effect on the risk of death among patients who had received mechanical ventilation.

Barbui T, Vannucchi AM, Alvarez-Larran A, et al. **High mortality rate in COVID-19 patients with myeloproliferative neoplasms after abrupt withdrawal of ruxolitinib**. *Leukemia* (2021). Full-text: <https://doi.org/10.1038/s41375-020-01107-y>

This study found an association between ruxolitinib and overall mortality in 40% of the 45 cases treated with this drug. This effect was due not so much to drug exposure but to its rapid discontinuation (median 0,5 days), that accounted for 75% of deaths. The authors speculate about the reasons for stopping the treatment: uncertainties about possible adverse events? risk of interactions with other drugs? missing interactions between managing physicians and referring hematologist?



## Severe COVID

Downar J, Kekewich M. **Improving family access to dying patients during the COVID-19 pandemic.** *Lancet Respir Med* 2021, published 12 January. Full-text: [https://doi.org/10.1016/S2213-2600\(21\)00025-4](https://doi.org/10.1016/S2213-2600(21)00025-4)

James Downar and Mike Kekewich propose elements of an end-of-life visitor policy: 1) Visitors (up to 4, according to the size of the room) should be allowed during normal visiting hours, 2) preferably 1 h at a time, and 3) when physical circumstances allow, one family member can remain with the patient outside of these hours. 4) Avoid cycling of visitors and 5) make visitors comply with proper infection prevention and control procedures to limit the risks to patients, staff, and to themselves.

## Pediatrics

Levin Z, Choyke K, Georgiou A, et al. **Trends in Pediatric Hospitalizations for Coronavirus Disease 2019.** *JAMA Pediatr* 2021, published 11 January. Full-text: <https://doi.org/10.1001/jamapediatrics.2020.5535>

Between May 15, 2020, and November 15, 2020, there was an increase in hospitalizations among infected children and adolescents in the US. Using data extracted from the University of Minnesota COVID-19 Hospitalization Tracking Project, Pinar Karaca-Mandic, Zachary Levin and colleagues identified 5364 patients aged 19 and under who were hospitalized in 22 US states. The cumulative average rate rose to 17,2 hospitalizations per 100.000 children in November from 2 per 100.000 children in May.

## Education

Rubin EJ, Baden LR, Morrissey S. **Covid-19 in South Africa and a New SARS-CoV-2 Variant.** Audio interview (40:45). *N Engl J Med* 2021; 384:e14. Access: <https://doi.org/10.1056/NEJMe2100736>

The editors discuss Covid-19 in Africa and the impact of a newly discovered SARS-CoV-2 variant.

## Spanish

If you read Spanish, read Sevillano EG, Abril G. **Preocupación en la UE por la expansión de la nueva variante de coronavirus.** *Le País* 2021, published 14 January. Full-text: <https://elpais.com/sociedad/2021-01-13/preocupacion-en-la-ue-por-la-expansion-de-la-nueva-variante-de-coronavirus.html>

Alemania se prepara para extender el confinamiento más allá de enero ante las “ocho o diez semanas muy duras” de contagios que prevé Merkel.

Naranjo J. **África se queda rezagada en la carrera por vacunar a la población.** Le País 2021, published 13 January. Full-text: <https://elpais.com/sociedad/2021-01-13/africa-se-queda-rezagada-en-la-carrera-por-vacunar-a-la-poblacion.html>

La falta de recursos para conseguir dosis, los problemas de aceptación y una logística compleja dificultan que el continente alcance la inmunidad de grupo el año próximo.

## French

If you read French, read Cosnard D. **Covid-19 : l'analyse des eaux usées annonce un rebond en Ile-de-France.** Le Monde 2021, published 14 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/14/covid-19-l-analyse-des-eaux-usees-annonce-un-rebond-en-ile-de-france\\_6066288\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/14/covid-19-l-analyse-des-eaux-usees-annonce-un-rebond-en-ile-de-france_6066288_3244.html)

La concentration de virus dans les eaux usées de la région a crû d'environ 50 % en trois semaines, montrent les prélèvements effectués par le réseau Obépine.

## German

If you read German, read Erdmann E, Schumann F. **Jagd auf die mutierten Coronaviren.** Die Zeit 2021, published 14 January. Full-text: <https://www.zeit.de/wissen/gesundheit/2021-01/corona-mutationen-variante-b-1-1-7-deutschland-verbretung-sequenzierung>

Neue Corona-Varianten haben Deutschland erreicht. Um rauszufinden, wie verbreitet sie sind, muss das Virenerbgut untersucht werden. Doch wird das ausreichend getan?

Theile G. **Auch die Schweiz nimmt Corona jetzt ernst.** Der Spiegel 2021, published 14 January. Full-text: <https://www.spiegel.de/politik/ausland/corona-in-der-schweiz-regierung-verkuendet-strengere-massnahmen-a-f5767103-64a9-431f-a55a-799cc081f4a2>

Der Sonderweg ist teilweise zu Ende: Britische Urlauber haben die hochansteckende Virusvariante ins Land gebracht – nun verkündet die

Schweizer Regierung einen härteren Shutdown. Skipisten bleiben aber auf. (*Sono pazzi!, Ed.*)

## 16 January

### COVID Reference

Kamps BS, Hoffmann C, et al. **COVID Reference 2021.6**. Steinhäuser Verlag 2021, 6th edition, 453 pages, published 13 January. Download: <https://covidreference.com/download>

Since the publication of COVID Reference's first edition on 29 March 2020, our website has lived an uneventful life. We have had our regular visitors – maybe you! – who read our presentation of the daily Top 10 papers or one or another PDF, in English, Spanish, Italian, Turkish or other languages. For more than 10 months, COVID Reference (CR) has been a steady source of daily, but mostly confidential information. Until last night, when the number of visitors to our website greatly increased. We don't know why and why now, but the unusual activity may convince us to go ahead with our non-profit project. Thank you for staying with us! [The CR Team](#).

### Virology

Cyranoski D. **Alarming COVID variants show vital role of genomic surveillance**. *Nature* 2021, published 15 January. Full-text: <https://www.nature.com/articles/d41586-021-00065-4>

2021 is shaping up to be the year of COVID-19 variants. In the past two months, scientists have identified several fast-spreading variants that have prompted government restrictions in many countries – and new variants are being detected more frequently.

### Transmission

van Kampen JJA, van de Vijver DAMC, Fraaij PLA, et al. **Duration and key determinants of infectious virus shedding in hospitalized patients with coronavirus disease-2019 (COVID-19)**. *Nat Commun*. 2021 Jan 11;12(1):267. PubMed: <https://pubmed.gov/33431879>. Full-text: <https://doi.org/10.1038/s41467-020-20568-4>

Quantitative RNA viral load assays and serological assays might be used in testing based strategies to discontinue or de-escalate infection prevention and control precautions. This is the result of a study by Jeroen van Kampen

and colleagues who report that infectious viral shedding is detected by virus cultures in 23 of 129 patients (17,8%) hospitalized with COVID-19. Of these, 89 patients (69,0%) were admitted to intensive care and the remaining 40 (31,0%) admitted to medium care. The median duration of shedding infectious virus was 8 days post-onset of symptoms (IQR 5–11) and dropped below 5% after 15,2 days post-onset of symptoms (95% confidence interval (CI) 13,4–17,2). Viral loads above  $7 \log_{10}$  RNA copies/mL were independently associated with isolation of infectious SARS-CoV-2 from the respiratory tract.

Johansson MA, Quandelacy TM, Kada S, et al. **SARS-CoV-2 Transmission From People Without COVID-19 Symptoms**. JAMA Netw Open. 2021 Jan 4;4(1):e2035057. PubMed: <https://pubmed.gov/33410879>. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.35057>

The identification and isolation of persons with symptomatic COVID-19 alone might not control the ongoing spread of SARS-CoV-2. This is the conclusion of a decision model by Jay Butler, Michael Johansson and colleagues who assessed multiple scenarios for the infectious period and the proportion of transmission from individuals who never had COVID-19 symptoms. Measures such as mask wearing and physical distancing might be needed to protect them and their communities for quite some time.

## Immunology

Chambers ES, Vukmanovic-Stejic M, Shih BB, et al. **Recruitment of inflammatory monocytes by senescent fibroblasts inhibits antigen-specific tissue immunity during human aging**. Nat Aging 1, 101–113 (2021). Full-text: <https://doi.org/10.1038/s43587-020-00010-6>

Senescent fibroblasts in the skin of older participants secrete an array of chemokines including CCL2 in response to tissue injury, such as that induced by injection of saline, VZV or air. Arne Akbar, Emma Chambers and colleagues show how this phenomenon can be blocked pharmacologically to boost adaptive immunity. See also the comment by Kasler H, Verdin E. **How inflammaging diminishes adaptive immunity**. Nat Aging 1, 24–25 (2021). Full-text: <https://doi.org/10.1038/s43587-020-00021-3>

## Vaccine

Tian JH, Patel N, Haupt R, et al. **SARS-CoV-2 spike glycoprotein vaccine candidate NVX-CoV2373 immunogenicity in baboons and protection in**

**mice.** Nat Commun 12, 372 (2021). Full-text: <https://doi.org/10.1038/s41467-020-20653-8>

In mice and baboons, low-dose levels of NVX-CoV2373 with Matrix-M was highly immunogenic. NVX-CoV2373, developed by Novavax, is a recombinant nanoparticle vaccine (rSARS-CoV-2) composed of trimeric full-length SARS-CoV-2 spike glycoproteins and Matrix-M1 adjuvant. Find more information about NVX-CoV2373 at <https://covidreference.com/vaccines>.

Ledford H. **How can countries stretch COVID vaccine supplies? Scientists are divided over dosing strategies.** Nature 2021, published 11 January. Full-text: <https://www.nature.com/articles/d41586-021-00001-6>

On 30 December, the United Kingdom announced that it would allow doses of two coronavirus vaccines to be administered as many as 12 weeks apart, even though, in clinical trials, the two doses of the vaccine made by Pfizer of New York City and BioNTech of Mainz, Germany, were given to participants about three weeks apart. Not everyone agrees.

## Clinical

Resende C, Bezerra JF, Teixeira de Vasconcelos RH, et al. **Spike E484K mutation in the first SARS-CoV-2 reinfection case confirmed in Brazil, 2020.** Virological 2021, posted 10 January. Full-text: <https://virological.org/t/spike-e484k-mutation-in-the-first-sars-cov-2-reinfection-case-confirmed-in-brazil-2020/584/1>

SARS-CoV-2 strains containing the Spike E484K mutation may be a source of re-infection. The authors describe the case of a 37-year-old woman without pre-existing co-morbidities, a healthcare worker (medical doctor) who had two clinical episodes of COVID-19 (June and October 2020, interval: 116 days). The second infection (with the E484K strain) was mild and evolved without complications like the first episode.

## Treatment

Anil SM, Shalev N, Vinayaka AC et al. **Cannabis compounds exhibit anti-inflammatory activity in vitro in COVID-19-related inflammation in lung epithelial cells and pro-inflammatory activity in macrophages.** Sci Rep 11, 1462 (2021). <https://doi.org/10.1038/s41598-021-81049-2>

Dope for SARS? Not yet. Although treatment with cannabis compounds CBD, CBG and THCV may have clinical value in reducing cytokine secretion in lung

epithelial cells, Hinanit Koltai, Seegehalli Anil and colleagues from the Volcani Center in Rishon LeZion, Israel, caution that the increase of macrophage-secreted IL-6 and IL-8 levels by cannabis-based treatment may potentially lead to a worsening of the “cytokine storm” identified in severe COVID-19 patients. As for now, users and healthcare personnel should avoid the use of cannabis for COVID-19 prevention or treatment.

## Collateral Effects

Morris JA, Goldacre R, Spata E, et al. **Impact of the COVID-19 pandemic on the detection and management of colorectal cancer in England: a population-based study.** Lancet Gastroenterol Hepatol 2021, published 14 January. Full-text: [https://doi.org/10.1016/S2468-1253\(21\)00005-4](https://doi.org/10.1016/S2468-1253(21)00005-4)

Eva Morris et al.

Pandemic COVID-19 waves lead to a sustained reduction in the number of people referred, diagnosed, and treated for colorectal cancer. As compared to the monthly average in 2019, in April 2020 there was a 63% reduction (from 36.274 to 13.440) in the monthly number of 2-week referrals for suspected cancer and a 92% reduction in the number of colonoscopies (from 46.441 to 3484).

## Spanish

If you read Spanish, read **Vacunar al personal sanitario cuanto antes.** El País 2021, publicated 15 January. Full-text: <https://elpais.com/opinion/2021-01-14/proteger-al-personal-sanitario.html>

Hay que flexibilizar los planes sin escatimar medios y preparar medidas extraordinarias.

Sampedro J. **El futuro de un virus histórico.** El País 2021, publicated 15 January. Full-text: <https://elpais.com/opinion/2021-01-14/proteger-al-personal-sanitario.html>

Los nuevos modelos indican que la COVID será en los próximos años una enfermedad leve de la infancia. Y los niños de hoy serán los adultos del futuro, y estarán inmunizados de un modo u otro.

## French

If you read French, read Le Bars S. **Les Etats-Unis subissent les ravages d'une pandémie de Covid-19 hors de contrôle.** Le Monde 2021, published 15 January. Full-text :

[https://www.lemonde.fr/international/article/2021/01/15/covid-19-le-sombre-hiver-parti-pour-durer-aux-etats-unis\\_6066334\\_3210.html](https://www.lemonde.fr/international/article/2021/01/15/covid-19-le-sombre-hiver-parti-pour-durer-aux-etats-unis_6066334_3210.html)

Face aux chiffres de contaminations, d'hospitalisations et de morts et à une vaccination qui patine, Joe Biden s'est engagé à « agir vite ».

Rof G, Guillou C. **Dans les restaurants clandestins : « Il fait gaffe quand même, y a toujours quelques poucaves ».** Le Monde 2021, published 15 January. Full-text :

[https://www.lemonde.fr/economie/article/2021/01/15/dans-les-restaurants-clandestins-au-moins-ici-les-clients-voient-du-monde\\_6066309\\_3234.html](https://www.lemonde.fr/economie/article/2021/01/15/dans-les-restaurants-clandestins-au-moins-ici-les-clients-voient-du-monde_6066309_3234.html)

En Ile-de-France, le bouche-à-oreille permet vite de trouver quelques restaurants qui servent, rideaux baissés, leur clientèle d'habitues. Les voisins voient bien le manège puisqu'il y a derrière une terrasse où, aux beaux jours, on fait barbecue. Ils ne disent rien : l'ambiance est moins à la délation qu'à la comisation.

## German

If you read German, read Hecking C. **Deutschland braucht die FFP2-Maskenpflicht.** Der Spiegel 2021, published 13 January. Full-text: <https://www.spiegel.de/wissenschaft/mensch/deutschland-braucht-die-ffp2-maskenpflicht-a-0a6f4051-d3f6-4eb8-9aaf-e91ec2e9e13c>

Die selbst genähte Alltagsmaske ist ein Relikt. Es wird höchste Zeit, dass wir alle professionelle Masken tragen, die auch uns selbst vor dem Virus schützen. Bezahlen muss sie der Staat.

## 17 January

### Epidemiology

Galloway SE, Paul P, MacCannell DR, et al. **Emergence of SARS-CoV-2 B.1.1.7 Lineage — United States, December 29, 2020–January 12, 2021.** MMWR Morb Mortal Wkly Rep. ePub: 15 January 2021. Full-text: <http://dx.doi.org/10.15585/mmwr.mm7003e2>

B117, a more highly transmissible variant of SARS-CoV-2 has been detected in 10 US states. CDC recommends universal and increased compliance with mitigation strategies, including distancing and masking, and ramping up the vaccination campaign. The following figure shows how a more infectious virus could lead to many more deaths. Simplified, hypothetical scenario showing the number of new deaths every six days from three different virus strains, assuming each strain started from 10.000 infections. Source: [Adam Kucharski](#), London School of Hygiene and Tropical Medicine.

Sridhar D, Gurdasani D. **Herd immunity by infection is not an option.** Science. 2021 Jan 15;371(6526):230-231. PubMed: <https://pubmed.gov/33446540>. Full-text: <https://doi.org/10.1126/science.abf7921>

A must-read by Devi Sridhar and Deepti Gurdasani. Do you remember 'herd immunity in Brazil'? On [26 September 2020](#) we presented a medRxiv post by Buss et al. with a title suggesting that herd immunity might have been reached in Brazil's Amazon region around Manaus. [Buss LF, Prete Jr CA, Abraham CMM, et al. **COVID-19 herd immunity in the Brazilian Amazon.** medRxiv 2020, posted 21 September. Full-text: <https://doi.org/10.1101/2020.09.16.20194787>.] In the meantime, the title of the paper was changed to **Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic (13 December)** and there is no herd immunity anymore in Manaus ([The Guardian](#), 14 January).

Ranzani TO, Bastos LSL, Gelli JBM, et al. **Characterisation of the first 250 000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data.** Lancet Respir Med 2021, published 15 January. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30560-9](https://doi.org/10.1016/S2213-2600(20)30560-9)

In-hospital mortality among patients younger than 60 years was 31% (4204 of 13.468) in the Brazilian Northeast versus 15% (1694 of 11.196) in the South in this retrospective analysis by Fernando Bozza, Otavio Ranzani and colleagues. In their study, the authors included 232.036 patients admitted to hospital in Brazil between 16 February and 15 August 2020. In-hospital mortality was 38% (87.515 of 232.036 patients) overall, 59% (47.002 of 79.687) among patients admitted to the ICU, and 80% (36.046 of 45.205) among those who were mechanically ventilated.



## Prevention

Barnett BS, Carlo AD, Mezzadri A, Ruwanpura KN. **The Invisible People Behind Our Masks.** *Ann Intern Med.* 2021 Jan 12. PubMed: <https://pubmed.gov/33428438>. Full-text: <https://doi.org/10.7326/M20-7421>

In our unprecedented efforts to rapidly secure large quantities of PPE, regulators have been inconsistent in addressing the unsettling truths about where some of it may originate. To contain the human cost of the pandemic, there is no doubt that we should maximize effective use of PPE, but Brian Barnett et al. argue that we must also ensure better work practices for those who enable us to wear it in the first place.

## Immunology

Lavine JS, Bjornstad ON, Antia R. **Immunological characteristics govern the transition of COVID-19 to endemicity.** *Science.* 2021 Jan 12:eabe6522. PubMed: <https://pubmed.gov/33436525>. Full-text: <https://doi.org/10.1126/science.abe6522>

In the future, SARS-CoV-2 may be no more virulent than the common cold. The question is when and what shall we do in the meantime. The authors conclusion: “Social distancing and an effective vaccine are critical for control during a virgin epidemic and the transition out of it, but once we enter the endemic phase, mass vaccination may no longer be necessary. The necessity for continual vaccination will depend on the age-dependence of the Infection Fatality Ratio (IFR). If primary infections of children are mild (CoV-1 and CoV-2), continued vaccination may not be needed as primary cases recede to mild childhood sniffles. If, on the other hand, primary infection is severe in children (as for MERS), then vaccination of children will need to be continued.”

Arce VM, Costoya JA. **SARS-CoV-2 infection in K18-ACE2 transgenic mice replicates human pulmonary disease in COVID-19.** *Cell Mol Immunol* (2021). Full-text: <https://doi.org/10.1038/s41423-020-00616-1>

Although several animal models of COVID-19 have been investigated, only a few (hamsters, ferrets, minks, cats, and non-human primates) have been found to be susceptible to the disease. Here, Victor Arce and José Costoya comment on a paper by Michael Diamond, Emma Winkler and colleagues that we presented on 29 August [Winkler ES, Bailey AL, Kafai NM, et al. **SARS-CoV-2 infection of human ACE2-transgenic mice causes severe lung inflammation and impaired function.** *Nat Immunol.* 2020 Nov;21(11):1327-1335. PubMed: <https://pubmed.gov/32839612>. Full-text:

<https://doi.org/10.1038/s41590-020-0778-2>]. The authors conclude that the severity of disease observed following SARS-CoV-2 infection in K18-hACE2 mice might provide a useful model in which to investigate pulmonary disease and test antiviral countermeasures in this species.

## Diagnostics

Butler-Laporte G, Lawandi A, Schiller I, et al. **Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2: A Systematic Review and Meta-analysis.** JAMA Intern Med. 2021 Jan 15. PubMed: <https://pubmed.gov/33449069>. Full-text: <https://doi.org/10.1001/jamainternmed.2020.8876>

Saliva instead of nasopharyngeal swab – the future of SARS-CoV-2 testing? In this review and meta-analysis, Guillaume Butler-Laporte suggest that saliva diagnostic accuracy is similar to that of nasopharyngeal swab, especially in the ambulatory setting.

Bastos ML, Perlman-Arrow S, Menzies D, Campbell JR. **The Sensitivity and Costs of Testing for SARS-CoV-2 Infection With Saliva Versus Nasopharyngeal Swabs : A Systematic Review and Meta-analysis.** Ann Intern Med. 2021 Jan 12. PubMed: <https://pubmed.gov/33428446>. Full-text: <https://doi.org/10.7326/M20-6569>

Same topic. Saliva sampling seemed to be a similarly sensitive and less costly alternative that might soon replace nasopharyngeal swabs for collection of clinical samples for SARS-CoV-2 testing.

## Clinical

Marshall M. **COVID's toll on smell and taste: what scientists do and don't know.** Nature 2021, published 14 January. Full-text: <https://www.nature.com/articles/d41586-021-00055-6>

Almost a year later, some still haven't recovered their senses of taste and smell, and for a proportion of people who have, odors are now warped: unpleasant scents have taken the place of normally delightful ones. *Nature* surveys the science behind this potentially long-lasting and debilitating phenomenon.

Starekova J, Bluemke DA, Bradham WS, et al. **Evaluation for Myocarditis in Competitive Student Athletes Recovering From Coronavirus Disease 2019 With Cardiac Magnetic Resonance Imaging.** JAMA Cardiol. 2021 Jan 14. PubMed: <https://pubmed.gov/33443537>. Full-text: <https://doi.org/10.1001/jamacardio.2020.7444>

No need for cardiac magnetic resonance imaging (MRI) to evaluate student athletes recovering from COVID-19? In a study of 145 student athletes with COVID-19 who had mild to moderate symptoms or no symptoms during acute infection, cardiac MRI findings (at a median of 15 days after a positive test result for COVID-19) were consistent with myocarditis in only 2 patients (1,4%), based on updated Lake Louise criteria.

## Treatment

Gordon AC, Mouncey PR, Al-Beidh F, et al. **Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 – Preliminary report.** medRxiv 2021, posted 9 January. Full-text: <https://doi.org/10.1101/2021.01.07.21249390>

When administered within 24 hours of commencing organ support in an intensive care unit, tocilizumab or sarilumab may reduce mortality. This is the result of a not-yet-published (pre-print) paper by Anthony Gordon et al. Death rate in the control group (n = 402) was 36%, tocilizumab (n = 353) 28%, sarilumab (n = 48) 22%.

## Spanish

If you read Spanish, read Llaneras K, Andrino B, Grasso D. **Dos millones de muertes en el mundo.** El País 2021, published 16 January. Full-text: <https://elpais.com/sociedad/2021-01-15/dos-millones-de-muertes-en-el-mundo.html>

El año 2021 llega en mitad de una pandemia que sigue elevando su factura: la cifra oficial de muertes acaba de superar los dos millones en todo el mundo. Además, el ritmo al que crecen las víctimas, lejos de reducirse, sigue acelerándose en España, Europa y prácticamente en todas partes.

Emcke C. **La lección del virus: el vínculo social importa.** El País 2021, published 15 January. Full-text: <https://elpais.com/opinion/2021-01-15/la-leccion-del-virus-el-vinculo-social-importa.html>

La pandemia ha hecho añicos la idea de la soberanía individual cultivada por el neoliberalismo.

Ansede M. **La cantidad de virus en la saliva ayuda a predecir el futuro de los pacientes con covid.** El País 2021, published 15 January. Full-text: <https://elpais.com/ciencia/2021-01-15/la-cantidad-de-virus-en-la-saliva-ayuda-a-predecir-el-futuro-de-los-pacientes-con-covid.html>

Un equipo liderado por la inmunóloga Akiko Iwasaki, en la Universidad de Yale (EE UU), sostiene que la saliva ayuda a predecir la evolución de la enfermedad mucho mejor que las muestras tomadas con hisopo nasofaríngeo.

## French

If you read French, read Heckeitsweiler C. **Entre les vaccins et les variants du Covid-19, c'est « une course contre la montre », selon le conseil scientifique.** Le Monde 2021, published 16 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/16/covid-19-face-au-variant-anglais-le-conseil-scientifique-recommande-d-accelerer-la-vaccination\\_6066465\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/16/covid-19-face-au-variant-anglais-le-conseil-scientifique-recommande-d-accelerer-la-vaccination_6066465_3244.html) + [https://solidarites-sante.gouv.fr/IMG/pdf/avis\\_conseil\\_scientifique\\_12\\_janvier\\_2021\\_actualise\\_13\\_janvier\\_2021.pdf](https://solidarites-sante.gouv.fr/IMG/pdf/avis_conseil_scientifique_12_janvier_2021_actualise_13_janvier_2021.pdf)

Pour l'instance, qui recommande d'accélérer la campagne, « les vaccins constituent un espoir pour résoudre en grande partie la pandémie, mais pas avant l'été-automne 2021 ».

Roucaute D. **« Il y a une lumière au bout du tunnel mais le tunnel est très long » : les recommandations de l'OMS pour endiguer la pandémie de Covid-19.** Le Monde 2021, published 16 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/16/passeport-vaccinal-sequencage-l-oms-donne-ses-recommandations-face-a-la-pandemie-de-covid-19\\_6066493\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/16/passeport-vaccinal-sequencage-l-oms-donne-ses-recommandations-face-a-la-pandemie-de-covid-19_6066493_3244.html)

Le comité d'urgence de l'agence onusienne s'est réuni plus tôt que prévu, jeudi, pour faire face à la flambée épidémique du début d'année.

## 18 January

### Epidemiology

Faria NR, Claro IM, Candido D, et al. **Genomic characterisation of an emergent SARS-CoV-2 lineage in Manaus: preliminary findings.** *Virological.org* 2021, posted 12 January. Full-text: <https://virological.org/t/genomic-characterisation-of-an-emergent-sars-cov-2-lineage-in-manaus-preliminary-findings/586>

A new variant (P.1, descendent of B.1.1.28) was circulating in December 2020 in Manaus, Amazonas state, and was identified in 42% (13 out of 31) of RT-PCR positive samples collected between 15 and 23 December. These findings indicate local transmission and possibly recent increase in the frequency of a new lineage from the Amazon region. P.1 contains several mutations of known biological importance such as E484K, K417T, and N501Y. Read also Kupferschmidt K. **New coronavirus variants could cause more reinfections, require updated vaccines.** *Nature* 2021, published 15 January. Full-text: <https://www.sciencemag.org/news/2021/01/new-coronavirus-variants-could-cause-more-reinfections-require-updated-vaccines>

### Immunology

Haynes WA, Kamath K, Lucas C, Shon J, Iwasaki A. **Impact of B.1.1.7 variant mutations on antibody recognition of linear SARS-CoV-2 epitopes.** *medRxiv* 2021, posted 8 January. Full-text: <https://doi.org/10.1101/2021.01.06.20248960>

The B.1.1.7 strain circulating within the UK has raised public concerns about potential for re-infection and vaccine efficacy due to possible evasion from antibody recognition. Here, Akiko Iwasaki, Winston Haynes and colleagues suggest that the mutations might not result in immune evasion for a large majority of COVID patients.

Cohen AA, Gnanapragasam PNP, Lee YE, et al. **Mosaic nanoparticles elicit cross-reactive immune responses to zoonotic coronaviruses in mice.** *Science*. 2021 Jan 12:eabf6840. PubMed: <https://pubmed.gov/33436524>. Full-text: <https://science.sciencemag.org/content/early/2021/01/11/science.abf6840>

A single immunization with mosaic-RBD-nanoparticles provides a potential strategy to protect against SARS-CoV-2 and other emerging zoonotic coronaviruses. The authors confirm that multimerization of receptor-binding do-

mains on nanoparticles enhances immunogenicity compared with soluble antigen.

Koenig PA, Das H, Liu H, et al. **Structure-guided multivalent nanobodies block SARS-CoV-2 infection and suppress mutational escape.** Science. 2021 Jan 12:eabe6230. PubMed: <https://pubmed.gov/33436526>. Full-text: <https://doi.org/10.1126/science.abe6230>

Nanobodies may represent a versatile and less costly alternative to conventional antibodies for passive immunization against SARS-CoV-2. They are efficiently produced in prokaryotic expression systems at low cost and exhibit favorable biophysical properties including high thermostability. Here, Paul-Albert König et al. from the University of Bonn, Germany, designed multivalent nanobody constructs based on epitope mapping data by SPR and X-ray crystallography, as well as extensive information on the conformation of spike:nanobody complexes determined by cryo-EM.

## Vaccine

Topol EJ. **Messenger RNA vaccines against SARS-CoV-2.** Cell 2021, published 16 January. Access: [https://www.cell.com/cell/fulltext/S0092-8674\(20\)31761-X](https://www.cell.com/cell/fulltext/S0092-8674(20)31761-X)

The first two vaccines proven to be effective for inhibiting COVID-19 illness were both mRNA, achieving 95% efficacy (and safety) among 74.000 participants (half receiving placebo) after intramuscular delivery of two shots, 3–4 weeks apart. A one-page summary by Eric Topol.

## Diagnostics

Vogl T, Leviatan S, Segal E. **SARS-CoV-2 antibody testing for estimating COVID-19 prevalence in the population.** Cell Reports Med 2021, published 14 January. Full-text: [https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(21\)00002-1](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00002-1)

ELISAs/CLIAs appear currently as the method of choice for monitoring the population-wide spread of SARS-CoV-2 in a post-lockdown world. This is the conclusion of Eran Segal, Thomas Vogl and Sigal Leviatan who review different types of antibody tests and their application for population-scale testing.

## Clinical

Lechien JR, Chiesa-Estomba CM, Beckers E, et al. **Prevalence and 6-month recovery of olfactory dysfunction: a multicentre study of 1363 COVID-19 patients.** *J Intern Med.* 2021 Jan 5. PubMed: <https://pubmed.gov/33403772>. Full-text: <https://doi.org/10.1111/joim.13209>

Olfactory dysfunction (OD) is more prevalent in mild COVID-19 forms than in moderate-to-critical forms. Of 1363 patients, 328 (24,1%) did not subjectively recover olfaction 60 days after the onset of the dysfunction. The mean duration of self-reported OD was  $21,6 \pm 17,9$  days. The higher baseline severity of objective olfactory evaluations was strongly predictive of persistent OD ( $p < 0.001$ ).

## Severe COVID

Silva J, Lucas C, Sundaram M, et al. **Saliva viral load is a dynamic unifying correlate of COVID-19 severity and mortality.** medRxiv. 2021 Jan 10:2021.01.04.21249236. PubMed: <https://pubmed.gov/33442706>. Full-text: <https://doi.org/10.1101/2021.01.04.21249236>

Saliva viral load was significantly higher in those with COVID-19 risk factors and correlated with increasing levels of disease severity and showed a superior ability over nasopharyngeal viral load as a predictor of mortality over time. This is the message by Akiko Iwasaki, Julio Silva and colleagues who studied 154 patients admitted to Yale-New Haven hospital between March and June of 2020. Saliva viral load was positively associated with many known COVID-19 inflammatory markers such as IL-6, IL-18, IL-10, and CXCL10, as well as type 1 immune response cytokines. The authors conclude that viral load measured by saliva is a dynamic unifying correlate of disease presentation, severity, and mortality over time.

## Collateral Effects

Wang J, Li Y, Musch DC, et al. **Progression of Myopia in School-Aged Children After COVID-19 Home Confinement.** *JAMA Ophthalmol.* 2021 Jan 14. PubMed: <https://pubmed.gov/33443542>. Full-text: <https://doi.org/10.1001/jamaophthalmol.2020.6239>

Home confinement during the COVID-19 pandemic may have been associated with a substantial myopic shift for younger school-aged children (6-8 years). In this cross-sectional study of 123.535 children, Xuehan Qian, Jiaying Wang and colleagues found that the prevalence of myopia increased 1,4 to 3 times

in 2020 compared with the previous 5 years. See also the comment by Klaver CCW, Polling JR, Enthoven CA. **2020 as the Year of Quarantine Myopia.** JAMA Ophthalmol. 2021 Jan 14. PubMed: <https://pubmed.gov/33443551>. Full-text: <https://doi.org/10.1001/jamaophthalmol.2020.6231>

## Society

Bleich SN, Ard JD. **COVID-19, obesity, and structural racism: Understanding the past and identifying solutions for the future.** Cell Metabol 2021, published 13 January. Full-text: [https://www.cell.com/cell-metabolism/fulltext/S1550-4131\(21\)00010-3](https://www.cell.com/cell-metabolism/fulltext/S1550-4131(21)00010-3)

Longstanding systemic inequalities – fueling unequal access to critical resources such as healthcare, housing, education, and employment opportunities – are largely responsible for the significant race disparities in obesity and COVID-19. Sara Bleich and Jamy Ard analyze lines of future action.

## Press

Levin S. **'The horror stories are countless': inside the LA hospital at the center of the Covid crisis.** The Guardian 2021, 12 January. Full-text: <https://www.theguardian.com/us-news/2021/jan/12/the-horror-stories-are-countless-inside-the-la-hospital-at-the-center-of-the-covid-crisis>

Los Angeles sees a person infected every six seconds. In a predominantly Latino neighborhood, Martin Luther King Jr community hospital faces ‘a sea of illness’.

## Spanish

If you read Spanish, read Ansede M. **De discoteca a epicentro de la lucha contra la pandemia.** El País 2021, published 17 January. Full-text: <https://elpais.com/ciencia/2021-01-16/de-discoteca-a-epicentro-de-la-lucha-contra-la-pandemia.html>

El médico argentino Fernando Polack lidera las pruebas de la vacuna de Pfizer desde una organización científica situada en un antiguo local de baile.

Ford T, Schweik CM. **La odisea de la cadena de suministro en frío y de la vacuna de la covid-19 para llegar a todas partes.** El País 2021, published 17 January. Full-text: <https://elpais.com/planeta-futuro/2021-01-16/la-odisea-de-la-cadena-de-suministro-en-frio-y-de-la-vacuna-de-la-covid-19-para-llegar-a-todas-partes.html>



En interés de la salud global y por pura justicia social, las dosis de inmunización deben distribuirse con igualdad entre las poblaciones con menos recursos. Pero en muchos países del mundo preservarlas congeladas es imposible.

## 19 January

### Epidemiology

Oliva C, Di Maddaloni F, Marcellusi A, Favato G. **Cross-regional variations of Covid-19 mortality in Italy: an ecological study.** J Public Health 2021, published 18 January. Full-text: <https://doi.org/10.1093/pubmed/fdaa248>

Four independent variables best explained the cross-regional differences in the number of deaths attributed to COVID-19: the force of infection, population density, number of elderly living in assisted facilities and the standard rate of diabetes.

Nørgaard SK, Vestergaard LS, Nielsen J, et al. **Real-time monitoring shows substantial excess all-cause mortality during second wave of COVID-19 in Europe, October to December 2020.** Euro Surveill. 2021 Jan;26(2). PubMed: <https://pubmed.gov/33446304>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2021.26.1.2002023>

No comment.

### Virology

Gravagnuolo AM, Faqih L, Cronshaw C, et al. **Epidemiological Investigation of New SARS-CoV-2 Variant of Concern 202012/01 in England.** medRxiv 2021, posted 15 January. Full-text: <https://doi.org/10.1101/2021.01.14.21249386>

The proportion in England of B117 (the new *Variant of Concern*) increased rapidly in December 2020 rising to over 70% of strong positive test results at the beginning of January 2021.

### Transmission

Mathai V, Das A, Bailey JA, Breuer K. **Airflows inside passenger cars and implications for airborne disease transmission.** Sci Adv. 2020 Dec 4;7(1):eabe0166. PubMed: <https://pubmed.gov/33277325>. Full-text: <https://doi.org/10.1126/sciadv.abe0166>

Are you afraid of driving with friends and family in your car because you remember that the transmission of SARS-CoV-2 is facilitated by exhaled droplets and aerosols suspended in air for extended periods of time? Then study the complex fluid dynamics during everyday commutes. The authors also reveal non-intuitive ways in which open windows can either increase or suppress airborne transmission. The preliminary recommendation by Varghese Mathai and colleagues: open the two windows farthest from the occupants (front right and rear left, respectively) which would give better protection to the passenger. See also the press article by Anthes E. **How to (Literally) Drive the Coronavirus Away**. The New York Times 2021, published 16 January. Full-text: <https://www.nytimes.com/2021/01/16/health/coronavirus-transmission-cars.html>

Samet JM, Prather K, Benjamin G, et al. **Airborne Transmission of SARS-CoV-2: What We Know**. Clin Infect Dis. 2021 Jan 18:ciab039. PubMed: <https://pubmed.gov/33458756>. Full-text: <https://doi.org/10.1093/cid/ciab039>

This perspective examines the potential for airborne transmission of SARS-CoV-2 using a source-to-dose framework that begins with generation of virus-containing droplets and aerosols and ends with the virus depositing in the respiratory tract of a susceptible individual. The authors ask four critical questions and summarize what we know (accepted manuscript).

Shah K, Kandre Y, Mavalankar D. **Secondary attack rate in household contacts of COVID-19 Paediatric index cases: a study from Western India**. J Public Health (Oxf). 2021 Jan 18:fdaa269. PubMed: <https://pubmed.gov/33454742>. Full-text: <https://doi.org/10.1093/pubmed/fdaa269>

The secondary attack rate (SAR) in household contacts of pediatric index cases may be as low as 1,7%. In this study from Gujarat, India, SAR was closely associated with the family size of the index cases. The authors conclude that home quarantine should be advocated for in smaller families with appropriate isolation facilities. Next week: what to do in larger families. (JOKE!)

## Immunology

Gaebler C, Wang Z, Lorenzi JCC, et al. **Evolution of antibody immunity to SARS-CoV-2**. Nature (2021). Full-text: <https://doi.org/10.1038/s41586-021-03207-w>

After recovery from SARS-CoV-2 infection, people can make potent antibodies to SARS-CoV-2 that evolve in the months after infection. These antibodies may be evolving in response to residual viral antigen hidden in the gut.

## Pathogenesis

Cheng XP, Cheng MP, Gu W, et al. **Cell-Free DNA Tissues-of-Origin by Methylation Profiling Reveals Significant Cell, Tissue and Organ-Specific injury related to COVID-19 Severity**. *Cell Med* 2021, published 16 January. Full-text: [https://www.cell.com/med/fulltext/S2666-6340\(21\)00031-3](https://www.cell.com/med/fulltext/S2666-6340(21)00031-3)

A blood test to broadly quantify cell, tissue, and organ-specific injury due to COVID-19? That's what Iwijn De Vlaminck and colleagues propose after performing cell-free DNA (cfDNA) profiling on 104 plasma samples from 33 COVID-19 patients. The authors suggest that cfDNA profiling – an easy-to-obtain molecular blood test – might provide quantifiable prognostic parameters and a more granular assessment of clinical severity at the time of presentation.

## Spanish

If you read Spanish, read Güell O, Mouzo J. **Covid persistente: las secuelas que no se van**. *El País* 2021, published 18 January. Full-text: <https://elpais.com/sociedad/2021-01-17/covid-persistente-las-secuelas-que-no-se-van.html>

El reto de tratar a muchos pacientes que sufren fatiga y otros síntomas hasta seis meses después de superar la enfermedad.

Bueno Ballesteros A. **Vacunas con firma de mujer**. *El País* 2021, published 18 January. Full-text:

[https://verne.elpais.com/verne/2021/01/15/articulo/1610729453\\_607403.html](https://verne.elpais.com/verne/2021/01/15/articulo/1610729453_607403.html)

A veces olvidamos que nuestra calidad de vida actual debe mucho a las vacunas. Y las vacunas deben también mucho a un buen puñado de mujeres.

## French

If you read French, read Bezat JM. **Covid-19 : « C'est par des biotechs que l'industrie pharmaceutique a produit un miracle : la mise au point en un an de plusieurs vaccins efficaces »**. *Le Monde* 2021, published 18 January. Full-text : <https://www.lemonde.fr/idees/article/2021/01/18/covid-19-c-est->

[par-des-biotechs-que-l-industrie-pharmaceutique-a-produit-un-miracle-la-mise-au-point-en-un-an-de-plusieurs-vaccins-efficaces\\_6066609\\_3232.html](https://www.spiegel.de/wissenschaft/corona-strategie-in-deutschland-der-schlimmste-aergste-laengste-fehler-a-d6bad65c-f7a9-43b0-b1ce-ab8ab170ba60)

Les partenariats noués entre les poids lourds et les poids légers très innovants du secteur, conjugués aux aides d'Etat et aux précommandes massives des gouvernements, ont permis cette percée scientifique.

## German

If you read German, read Stöcker C. **Der schlimmste, ärgste, längste Fehler.** Der Spiegel 2021, published 17 January. Full-text: <https://www.spiegel.de/wissenschaft/corona-strategie-in-deutschland-der-schlimmste-aergste-laengste-fehler-a-d6bad65c-f7a9-43b0-b1ce-ab8ab170ba60>

Nirgends haben Politik und RKI hierzulande mehr Fehler gemacht als beim Thema Masken. Sogar Impfstoffe waren schneller verfügbar als der einfachste wirksame Schutz für alle – ein historisches Versagen.

## 20 January

### Transmission

#### Paper of the Day

Li F, Li YY, Liu MJ, et al. **Household transmission of SARS-CoV-2 and risk factors for susceptibility and infectivity in Wuhan: a retrospective observational study.** Lancet Infect Dis 2021, published 18 January. Full-text: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30981-6/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30981-6/fulltext)

Within households, children and adolescents are less susceptible to SARS-CoV-2 infection but may be more infectious than older individuals. This is the message by Shun-Qing Xu, Fang Li and colleagues who analyzed 27.101 households with 29.578 primary cases and 57.581 household contacts. The secondary attack rate was estimated at 15.6% (95% CI 15.2–16.0), assuming a mean incubation period of 5 days and a maximum infectious period of 22 days. Pre-symptomatic cases were more infectious and individuals with asymptomatic infection less infectious than symptomatic cases.

## Epidemiology

Mervosh S, Baker M, Mazzei P, Walker M. **One Year, 400,000 Coronavirus Deaths: How the U.S. Guaranteed Its Own Failure.** The New York Times 2021, published 17 January. Full-text: <https://www.nytimes.com/2021/01/17/us/covid-deaths-2020.html>

After the White House declined to pursue a unified national COVID strategy, governors faced off against lobbyists, health experts and a restless public consumed by misinformation.

## Virology

Mahase E. **Covid-19: What new variants are emerging and how are they being investigated?** BMJ. 2021 Jan 18;372:n158. PubMed: <https://pubmed.gov/33462092>. Full-text: <https://doi.org/10.1136/bmj.n158>

What do we know about the new variant emerging from Brazil? What do we know about the South African variant? Do the current vaccines work against the Brazilian, English, and South African variants? Could the virus still mutate to escape the vaccines? Elisabeth Mahase gives the *preliminary* answers.

Corum J, Zimmer C. **Inside the B.1.1.7 Coronavirus Variant.** The New York Times 2021, published 18 January. Full-text: <https://www.nytimes.com/interactive/2021/health/coronavirus-mutations-B117-variant.html>

Rambaut A, Loman N, Pybus O, et al. **Preliminary genomic characterisation of an emergent SARS-CoV-2 lineage in the UK defined by a novel set of spike mutations.** Virological 2020, Full-text: <https://virological.org/t/preliminary-genomic-characterisation-of-an-emergent-sars-cov-2-lineage-in-the-uk-defined-by-a-novel-set-of-spike-mutations/563/1>

A paper we missed 4 weeks ago where Andrew Rambaut and colleagues describe the B117 lineage.

Tegally H, Wilkinson E, Giovanetti M, et al. **Emergence and rapid spread of a new severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) lineage with multiple spike mutations in South Africa.** Virological 2020, Full-text: doi: <https://doi.org/10.1101/2020.12.21.20248640>

Another paper we missed where Tulio de Oliveira, Houriiyah Tegally and colleagues describe the 501Y.V2 lineage characterized by eight mutations in the spike protein, including three at important residues in the receptor-binding domain (K417N, E484K and N501Y) that may have functional significance. This lineage emerged in South Africa and spread rapidly, becoming the dominant lineage within weeks in the Eastern Cape and Western Cape Provinces.

## Vaccine

Kim JH, Marks F, Clemens JD. **Looking beyond COVID-19 vaccine phase 3 trials.** Nat Med (2021). Full-text: <https://doi.org/10.1038/s41591-021-01230-y>

After Phase III vaccine trials, a comprehensive program of prevention, continued work on vaccine optimization, new vaccines, correlates, long-term safety and continued surveillance will be needed simultaneously with the steady implementation of vaccination.

Glover RE, Urquhart R, Lukawska J, Blumenthal KG. **Vaccinating against covid-19 in people who report allergies.** BMJ. 2021 Jan 18;372:n120. Pub-Med: <https://pubmed.gov/33461962>. Full-text: <https://doi.org/10.1136/bmj.n120>

A history of severe allergy does not preclude vaccination unless that allergy is to the vaccine or its components. Discover the key facts and reassure your patients.

## Clinical

Naveca F, da Costa C, Nascimento V, et al. **SARS-CoV-2 reinfection by the new Variant of Concern (VOC) P.1 in Amazonas, Brazil.** Virological 2021, posted 18 January. Full-text: <https://virological.org/t/sars-cov-2-reinfection-by-the-new-variant-of-concern-voc-p-1-in-amazonas-brazil/596>

The lineage P.1 (alias of B.1.1.28.1) is an emerging variant that harbors several amino acid mutations including S:K417T, S:E484K, and S:N501Y. Paola Resende, Felipe Naveca and colleagues describe the first confirmed case of reinfection with the P.1 lineage in a 29-year-old woman in Manaus, Amazonas, Brazil, with no history of immunosuppression, who presented two clinical episodes of COVID-19 infection within a gap of nine months.

## Beyond Corona

Rothe C (Ed.). **Clinical Cases in Tropical Medicine**. Elsevier 2022, 2nd edition, 320 pages. Link: <https://www.amazon.com/dp/0702078794/>

We almost never recommend books (why not?), but this one, by **Camilla Rothe** and more than 100 contributors, is a worthy exception. Find 103 outstanding case reports for doctors and senior medical students who already have some background knowledge in tropical medicine.

## Spanish

If you read Spanish, read Gomollón-Bel F. **El glaseado que camufla al coronavirus**. El País 2021, published 19 January. Full-text: <https://elpais.com/ciencia/2021-01-18/el-glaseado-que-camufla-al-coronavirus.html>

Una capa de azúcares recubre al patógeno y ayuda a esconderlo de nuestro sistema inmunitario. Ahora, gracias a los superordenadores, podemos verlos por primera vez y pintar una imagen del coronavirus totalmente diferente.

González B. **¿Es exagerado el miedo a que la vacuna de la covid provoque alergia?** El País 2021, published 18 January. Full-text: <https://elpais.com/buenavida/salud/2021-01-18/es-exagerado-el-miedo-a-que-la-vacuna-de-la-covid-provoque-alergia.html>

No es nada extraño que las vacunas tengan efectos secundarios. De hecho, todas los tienen, solo que unas más y otras menos. El peor efecto adverso que tiene la vacuna es no administrarla.

Sampedro J. **Vuelve Manaos**. El País 2021, published 18 January. Full-text: <https://elpais.com/ciencia/2021-01-18/vuelve-manaos.html>

No herd immunity in Manaus, Brazil.

## French

If you read French, read **Marc Gozlan**. **Covid-19 : le défi des nouveaux variants**. Réalités Biomédicales 2021, published 18 January. Full-text: <https://www.lemonde.fr/blog/realitesbiomedicales/2021/01/18/covid-19-le-defi-des-nouveaux-variants/>

Depuis quelques jours, les données concernant les variants du coronavirus SARS-CoV-2, qu'ils soient britannique, sud-africain, brésilien, voire possible-

ment américain, se succèdent à un rythme soutenu. Ces nouveaux variants du SARS-CoV-2 inquiètent les autorités dans le monde entier. En effet, certains sont plus contagieux que les variants circulant actuellement, appelés variants historiques.

## 21 January

### Treatment

#### Paper of the Day

Lopes RD, Macedo AV, Silva P, et al. **Effect of Discontinuing vs Continuing Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers on Days Alive and Out of the Hospital in Patients Admitted With COVID-19: A Randomized Clinical Trial.** JAMA January 19, 2021; 325(3):254-264. Full-text: <https://doi.org/10.1001/jama.2020.25864>

Paper of the day: does discontinuation compared with continuation of ACEIs or ARBs change anything? *No.* In this randomized open label clinical trial that included 659 patients from Brazil who were hospitalized with mild to moderate COVID-19 who were taking ACEIs or ARBs before hospital admission, the mean number of days alive and out-of-hospital for those assigned to discontinue versus continue these medications was 21,9 vs 22,9, respectively.

### Epidemiology

Gouvea-Reis FA, Oliveira PD, et al. **COVID-19 outbreak in a large penitentiary complex, April–June 2020, Brazil.** Emerg Infect Dis, March 2021. Full-text: <https://doi.org/10.3201/eid2703.204079>

Faster viral spread in overcrowded settings: the mean serial interval during this large SARS-CoV-2 outbreak at a Brazilian prison was only 2,51 days. Between April 1 and June 12, there were 1057 reported cases: 859 (81,3%) in inmates, 180 (17,1%) in prison guards, 9 (0,8%) in contracted staff, and 9 (0,8%) in health professionals. Nine patients were hospitalized, and 3 deaths were reported: 1 prison guard and 2 inmates.

### Prevention

Goyal R, Hotchkiss J, Schooley RT, et al. **Evaluation of SARS-CoV-2 transmission mitigation strategies on a university campus using an agent-based network model.** Clinical Infectious Diseases January 19, 2021. Full-text: <https://doi.org/10.1093/cid/ciab037>



Continue wearing your mask! Interesting modeling study, investigating the impact of risk mitigation interventions at the University of San Diego. The authors assessed four scenarios with varying housing, instructional, and behavioral characteristics. The main message: structural interventions for housing (singles only) and instructional changes (from in-person to hybrid with class size caps) can substantially reduce  $R_0$ , but masking and social distancing are required to reduce this to 1 or below.

Rader B, White LF, Burns MR, et al. **Mask-wearing and control of SARS-CoV-2 transmission in the USA: a cross-sectional study.** *The Lancet Digital Health* January 19, 2021. Full-text: [https://doi.org/10.1016/S2589-7500\(20\)30293-4](https://doi.org/10.1016/S2589-7500(20)30293-4)

Again, masks work. This large web platform randomly surveyed almost 400,000 US individuals aged 13 years and older, to ask about face mask wearing. A logistic model controlling for physical distancing, population demographics and other variables found that a 10% increase in self-reported mask wearing was associated with an increased odds of transmission control (odds ratio 3.53, 95% CI 2.03–6.43). Communities with high reported mask wearing and physical distancing had the highest predicted probability of transmission control.

## Diagnostics

Zhang Z, Bi Q, Fang S. **Insight into the practical performance of RT-PCR testing for SARS-CoV-2 using serological data: a cohort study.** *Lancet Microbe* January 19, 2021. [https://doi.org/10.1016/S2666-5247\(20\)30200-7](https://doi.org/10.1016/S2666-5247(20)30200-7)

Even rigorous RT-PCR testing protocols (as used in Shenzhen, China) might miss some SARS-CoV-2 infections, perhaps in part due to difficulties in determining the timing of testing in asymptomatic individuals for optimal sensitivity. In this study, 40 (4.5%) of 880 RT-PCR-negative close contacts were later found to be positive on total antibody ELISA.

## Clinical

Bravata DM, Perkins AJ, Myers LJ, et al. Association of Intensive Care Unit Patient Load and Demand With Mortality Rates in US Department of Veterans Affairs Hospitals During the COVID-19 Pandemic. *JAMA Netw Open* January 19, 2021; 4(1):e2034266. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.34266>

Again, flatten the curve! In this cohort study of 8516 patients with COVID-19 admitted to 88 US Veterans Affairs hospitals, strains on critical care capacity were associated with increased COVID-19 mortality. Among patients with COVID-19, those treated in the ICU during periods of peak COVID-19 ICU demand had a nearly 2-fold increased risk of mortality compared with those treated during periods of low demand.

Rubinson L. **Intensive Care Unit Strain and Mortality Risk Among Critically Ill Patients With COVID-19—There Is No “Me” in COVID.** JAMA Netw Open January 19, 2021;4(1):e2035041. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.35041>

Comment: Lewis Rubinson argues that, in light of the important policy implications, additional analyses are urgently needed to investigate whether this association of ICU strain and mortality is causal. If causality is supported, delineation of which care processes are suboptimally provided as ICU load and demand increase will be important to assist hospitals to support them in the hope of reducing the impact of ICU strain on mortality.

Tan CW, Tan JY, Wong WH, et al. **Clinical and laboratory features of hypercoagulability in COVID-19 and other respiratory viral infections amongst predominantly younger adults with few comorbidities.** Sci Rep 11, January 19, 2021, 1793. Full-text: <https://doi.org/10.1038/s41598-021-81166-y>

This retrospective cohort study included 182 consecutive COVID-19 and 165 non-CoV-2-respiratory virus patients (median age 37 and 35 years) admitted to Singapore General Hospital. Thrombotic rates were low and comparable in this young and otherwise healthy population. Coagulation parameters did not differ throughout the course of mild COVID-19.

## Collateral Effects

Li W, Zhang Y, Wang J, et al. **Association of Home Quarantine and Mental Health Among Teenagers in Wuhan, China, During the COVID-19 Pandemic.** JAMA Pediatr January 19, 2021. Full-text: <https://doi.org/10.1001/jamapediatrics.2020.5499>

During the COVID-19 quarantine period, more than 20% of adolescents had anxiety and depression. This is the result of an online questionnaire (using convenient sampling method) with 7890 teenagers from Wuhan. The prevalence was 21,7% (n=1708) for anxiety and 24,6% (n=1941) for depression (HADS subscale score > 7). Long-term home restrictions might have adverse

effects on mental health of adolescents because of a sharp change of lifestyle and various other stressors like fear of infection, frustration, and boredom.

Tanaka T, Okamoto S. **Increase in suicide following an initial decline during the COVID-19 pandemic in Japan.** *Nat Hum Behav* (2021). Full-text: <https://doi.org/10.1038/s41562-020-01042-z>

In Japan, monthly suicide rates declined by 14% during the first 5 months of the pandemic (February to June 2020). This could be due to a number of complex reasons, including the government's generous subsidies, reduced working hours and school closure. By contrast, monthly suicide rates increased by 16% during the second wave (July to October 2020), with a larger increase among females (37%) and children and adolescents (49%).

## French

Roucaute D. **Covid-19 : faut-il privilégier les masques de catégorie 1 face aux nouveaux variants du coronavirus ?** *Le Monde* 2021, published 20 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/20/faut-il-privilégier-les-masques-de-categorie-1-face-aux-nouveaux-variants-du-coronavirus\\_6066982\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/20/faut-il-privilégier-les-masques-de-categorie-1-face-aux-nouveaux-variants-du-coronavirus_6066982_3244.html)

Le Haut Conseil de la santé publique recommande de porter des masques en tissu ou chirurgicaux ayant une capacité de filtration supérieure à 90 %. Mais certains experts jugent que ce message introduit de la confusion.

Ducourtieux C. **Vaccination contre le Covid-19 : le Royaume-Uni meilleur élève européen mais loin d'être sorti d'affaire.** *Le Monde* 2021, published 20 January. Full-text : [https://www.lemonde.fr/international/article/2021/01/20/vaccination-contre-le-covid-19-le-royaume-uni-meilleur-eleve-europeen-mais-loin-d-etre-sorti-d-affaires\\_6066870\\_3210.html](https://www.lemonde.fr/international/article/2021/01/20/vaccination-contre-le-covid-19-le-royaume-uni-meilleur-eleve-europeen-mais-loin-d-etre-sorti-d-affaires_6066870_3210.html)

Le gouvernement britannique est très inquiet à l'idée que les efforts nationaux puissent être en partie ruinés par l'apparition d'autres variants du SARS-CoV-2 que celui observé pour la première fois sur son territoire.

If you read French, read Handweiler V. **Covid-19 : la vitamine D en question comme traitement préventif.** *Le Monde* 2021, published 20 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/20/covid-19-la-vitamine-d-en-question-comme-traitement-preventif\\_6066923\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/20/covid-19-la-vitamine-d-en-question-comme-traitement-preventif_6066923_3244.html)

Des experts et des sociétés savantes estiment qu'une supplémentation pour réduire le déficit de cette hormone pourrait aider à combattre la pandémie. Pour l'heure, aucune étude n'a apporté de preuve directe de son efficacité.

Cordier S. **Devenir parents en temps de Covid : « A partir de ses deux mois, on n'a plus vu personne »**. Le Monde 2021, published 19 January. Full-text : [https://www.lemonde.fr/societe/article/2021/01/19/comment-la-crise-sanitaire-a-modifie-l-experience-de-la-parentalite\\_6066785\\_3224.html](https://www.lemonde.fr/societe/article/2021/01/19/comment-la-crise-sanitaire-a-modifie-l-experience-de-la-parentalite_6066785_3224.html)

L'année 2020 n'a eu qu'un impact limité sur l'évolution de la natalité française, qui a poursuivi sa baisse. Reste qu'au-delà des statistiques, l'expérience de la parentalité a été largement modifiée par la crise sanitaire.

## German

If you read German, read Simmank J, Schöps C, Stockrahm S. **Ohne das Virus leben ist das Ziel**. Die Zeit 2021, published 20 January. Full-text: <https://www.zeit.de/wissen/gesundheit/2021-01/no-covid-strategie-coronavirus-initiative-lockdown/komplettansicht>

Der Lockdown ist verlängert – ohne Perspektive. Wieder reagiert die Politik nur. Eine Expertengruppe setzt auf einen Null-Fälle-Plan. "No Covid" könnte ein Ausweg sein.

## 22 January

### Epidemiology

Somekh I, Shohat T, Boker LK, Simões EAF, Somekh E. **Reopening Schools and the Dynamics of SARS-CoV-2 Infections in Israel: A Nationwide Study**. Clin Infect Dis. 2021 Jan 18:ciab035. PubMed: <https://pubmed.gov/33460434>. Full-text: <https://doi.org/10.1093/cid/ciab035>

This analysis does not support that school reopening played a major role in the resurgence of the COVID-19 curve (between March and July 2020) in Israel. Easing restrictions on large scale gatherings was the major influence on this resurgence.

Lewis D. **What new COVID variants mean for schools is not yet clear**. Nature 21 January 2021, <https://www.nature.com/articles/d41586-021-00139-3>

Read the title out loud. Dyani Lewis summarizes current knowledge. Children are no more susceptible to these lineages than adults are — and closing schools on the basis of incomplete information could have serious repercussions. The debate continues.

Priesemann V, Balling R, Brinkmann MM, et al. **An action plan for pan-European defence against new SARS-CoV-2 variants.** *Lancet* January 21, 2021. Full-text: [https://doi.org/10.1016/S0140-6736\(21\)00150-1](https://doi.org/10.1016/S0140-6736(21)00150-1)

According to Viola Priesemann and colleagues, core measures to prevent the spread of SARS-CoV-2 in Europe are:

1. Achieve and maintain low case numbers with a clear prevention strategy
2. Monitor the spread of the virus and of individual variants
3. Stop the virus before it crosses borders
4. Protect the vulnerable
5. Increase the pace of administration of vaccines

The core principles of action are to avoid importing new variants, to prevent their spread, and to improve molecular surveillance. The earlier and more effectively countries act, the earlier the restrictions can be relaxed. All types of measures ought to be coordinated and synchronized across Europe. Every additional reduction of contagion counts, as it reduces the necessary duration of strict measures more than 1:1.

Bartsch M, Bohr F, von Bredow R, et al. **Can We Stop a Super Coronavirus?** *Der Spiegel* 2021, published 19 January. Full-text: <https://www.spiegel.de/international/world/can-germany-stop-the-new-supervirus-a-e9ffc207-0015-4330-8361-b306f6053e15>

The new variants of the coronavirus are even more dangerous than those known so far. Researchers and politicians fear a sharp increase in the number of infections, with dramatic consequences like those seen in Britain. Can Germany still stop the new killers?

## Vaccine

Klass P, Ratner AJ. **Vaccinating Children against Covid-19 — The Lessons of Measles.** *NEJM* January 20, 2021. Full-text: <https://doi.org/10.1056/NEJMp2034765>

Perri Klass and Adam Ratner argue that we need to consider lessons from recent measles epidemics — not only about the power of legislative mandates, but also about their potential for sowing distrust if delivered without careful, sensitive, accurate public health messaging. Communication, people!

Connors M, Graham BS, Lane HC, Fauci AS. SARS-CoV-2 Vaccines: **Much Accomplished, Much to Learn**. *Ann Intern Med*. 2021 Jan 19. PubMed: <https://pubmed.gov/33460347>. Full-text: <https://doi.org/10.7326/M21-0111>

Progress toward effective vaccines for SARS-CoV-2 has proceeded at an unprecedented pace and it is highly likely that vaccination and its subsequent ability to prevent disease will provide critical and life-saving benefit in the coming months and may be one of our surest ways to emerge from this pandemic to a more normal society. However, acknowledging that there is still much to learn while strongly encouraging vaccination is a critical challenge facing health care today.

## Pathogenesis

Khamsi R. **Rogue antibodies could be driving severe COVID-19**. *Nature NEWS FEATURE* 19 January 2021. Full-text: <https://doi.org/10.1038/d41586-021-00149-1>

Roxanne Khamsi summarizes the growing evidence that self-attacking ‘auto-antibodies’ could be the key to understanding some of the worst cases of SARS-CoV-2 infection.

## Diagnostics

Goh YS, Chavatte JM, Jielsing AL, et al. **Sensitive detection of total anti-Spike antibodies and isotype switching in asymptomatic and symptomatic COVID-19 patients**. *Cell Reports* January 16, 2021. Full-text: <https://doi.org/10.1016/j.xcrm.2021.100193>

This flow cytometry assay based on the full-length SARS-CoV-2 S protein (SFB assay) allows the detection of a wider repertoire of antibodies such as antibodies binding to various domains and conformational epitopes of the S protein. Of note, the SFB assay was able to detect 97% of the pre-/asymptomatic infections.

Prince-Guerra JL, Almendares O, Nolen LD, et al. **Evaluation of Abbott BinaxNOW Rapid Antigen Test for SARS-CoV-2 Infection at Two Community-Based Testing Sites — Pima County, Arizona, November 3–17, 2020.** MMWR Morb Mortal Wkly Rep. ePub: 19 January 2021. Full-text: <http://dx.doi.org/10.15585/mmwr.mm7003e3>

Sensitivity of the BinaxNOW antigen test, compared with polymerase chain reaction testing, was lower when used to test specimens from asymptomatic (35,8%) than from symptomatic (64,2%) persons, but specificity was high. Sensitivity was higher for culture-positive specimens (92,6% and 78,6% for those from symptomatic and asymptomatic persons, respectively); however, some antigen test-negative specimens had culturable virus.

## Treatment

Cohen MS. **Monoclonal antibodies to disrupt progression of early Covid-19 infection.** NEJM January 21, 2021; 384: 289-91. Full-text: <https://doi.org/10.1056/NEJMe2034495>

Editorial, summarizing the two trials on the REGN-CoV-2 cocktail (casirivimab and imdevimab) and Lilly's mAb bamlanivimab. Both trials were done in outpatients with early infection and showed "some" clinical benefit. However, Myron S. Cohen from Chapel Hill considers the findings from these trials "provocative and promising". Read why.

Weinreich DM, Sivapalasingam S, Norton T, et al. **REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19.** NEJM December 17, 2020, Full-text: <https://doi.org/10.1056/NEJMoa2035002>

Chen P, Nirula A, Heller B, et al. **SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19.** N Engl J Med 2020, published 28 October. Full-text: <https://doi.org/10.1056/NEJMoa2029849>

## 23 January

### Clinical

#### Paper of the Day

Anesi GL, Jablonski J, Harhay MO, et al. **Characteristics, Outcomes, and Trends of Patients With COVID-19-Related Critical Illness at a Learning Health System in the United States.** Ann Intern Med. 2021 Jan 19. PubMed: <https://pubmed.gov/33460330>. Full-text: <https://doi.org/10.7326/M20-5327>

Is there a learning curve? Among 468 patients with COVID-19–related critical illness admitted to ICUs during the initial surge of the pandemic in the US (from 1 March to 11 May 2020), mortality seemed to decrease over time despite stable patient characteristics. Mortality decreased over time, from 43,5% (95% CI: 31,3% to 53,8%) to 19,2% (CI: 11,6% to 26,7%) between the first and last 15-day periods in the core adjusted model, whereas patient acuity and other factors did not change. Further studies are necessary to investigate causal mechanisms.

Vahidy FS, Pan AP, Ahnstedt H, et al. **Sex differences in susceptibility, severity, and outcomes of coronavirus disease 2019: Cross-sectional analysis from a diverse US metropolitan area.** PLoS One. 2021 Jan 13;16(1):e0245556. PubMed: <https://pubmed.gov/33439908> . Full-text: <https://doi.org/10.1371/journal.pone.0245556>. eCollection 2021

In this large US cohort, males were more likely to test positive for COVID-19. In hospitalized patients, males were more likely to have complications, require ICU admission and mechanical ventilation, and had higher mortality than females, independent of age.

Song E, Zhang C, Israelow B, et al. **Neuroinvasion of SARS-CoV-2 in human and mouse brain.** J Exp Med. 2021 Mar 1;218(3):e20202135. PubMed: <https://pubmed.gov/33433624>. Full-text: <https://doi.org/10.1084/jem.20202135>

Evidence for the neuro-invasive capacity of SARS-CoV-2. Akiko Iwasaki, Eric Song and colleagues demonstrate that neuronal infection can be prevented by blocking ACE2 with antibodies or by administering cerebrospinal fluid from a COVID-19 patient. In autopsies, they also detected SARS-CoV-2 in cortical neurons and noted pathological features associated with infection with minimal immune cell infiltrates.

## Vaccine

Callaway E. **Fast-spreading COVID variant can elude immune responses.** Nature News 21 January 2021. Full-text: <https://www.nature.com/articles/d41586-021-00121-z>

Ewen Callaway discusses the growing evidence that the SARS-CoV-2 variant identified in South Africa might compromise immunity sparks concerns about vaccine effectiveness.



Ella E, Vadreva KM, Jogdand H, et al. **Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial.** *Lancet Infect Dis* January 21, 2021. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30942-7](https://doi.org/10.1016/S1473-3099(20)30942-7)

In this double-blind, multi-center, randomized Phase I trial from India, the inactivated vaccine BBV152 led to tolerable safety outcomes and enhanced immune responses. Different adjuvants were also evaluated (chemisorbed imidazoquinoline onto the aluminum hydroxide gel or not). In 375 participants who were assigned to receive two doses separated by 2 weeks of BBV152 3 µg with Algel-IMDG (n = 100), 6 µg with Algel-IMDG (n = 100), or 6 µg with Algel (n = 100), or an Algel-only control (n = 75), 80% of patients in each vaccine group seroconverted, with at least a four-fold increase in binding antibody titers. Seroconversion occurred by microneutralization in 88% and 92% of the 3 and 6 µg Algel-IMDG groups but also in 8% of the control group, suggesting SARS-CoV-2 infections occurred in some participants.

Rostad CA, Anderson EJ. **Optimism and caution for an inactivated COVID-19 vaccine.** *Lancet Inf Dis* January 21, 2021. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30988-9](https://doi.org/10.1016/S1473-3099(20)30988-9)

Christina Rostad and Evan Anderson see an inactivated vaccine as a welcome addition to the COVID-19 vaccine landscape. However, they discuss the open questions and concerns regarding inactivated vaccines (i.e. antibody-dependent enhancement of infection and vaccine-associated enhanced respiratory disease). Until then, they “will wait with cautious optimism on this vaccine candidate poised to bolster worldwide equitable access to COVID-19 prevention”. Ok, let’s wait. But for how long?

Siegel CA, Melmed GY, McGovern DP, et al. **SARS-CoV-2 vaccination for patients with inflammatory bowel diseases: recommendations from an international consensus meeting.** *Gut*. 2021 Jan 20;gutjnl-2020-324000. Pub-Med: <https://pubmed.gov/33472895>. Full-text: <https://doi.org/10.1136/gutjnl-2020-324000>

The panel recommends vaccinating all patients with IBD as soon as they are able to receive the vaccine, regardless of immune-modifying therapies. The exception is for any live-attenuated virus vaccines or replication-competent viral vector vaccines that come to market.

## Collateral

Doubleday A, Choe Y, Busch Isaksen T, Miles S, Errett NA. **How did outdoor biking and walking change during COVID-19?: A case study of three U.S. cities.** PLoS One. 2021 Jan 20;16(1):e0245514. PubMed: <https://pubmed.gov/33471858>. Full-text: <https://doi.org/10.1371/journal.pone.0245514>

In Houston, bicycle use increased during lockdown. In New York, less people used their bikes. In Seattle, the results varied by trail use type. Read here why.

## Treatment

Veiga VC, Prats JAGG, Farias DLC, et al. **Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial.** BMJ. 2021 Jan 20;372:n84. PubMed: <https://pubmed.gov/33472855>. Full-text: <https://doi.org/10.1136/bmj.n84>

Bad news from this randomized, open-label trial in nine hospitals in Brazil. Patients who were receiving supplemental oxygen or mechanical ventilation and had abnormal levels of at least two serum biomarkers were randomized to receive standard of care (SOC) plus tocilizumab (TCZ) or SOC alone. 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 SOC + TCZ group (17% vs 3%).

Chen JS, Alfajaro MM, Chow RD, et al. **Non-steroidal anti-inflammatory drugs dampen the cytokine and antibody response to SARS-CoV-2 infection.** J Virol. 2021 Jan 13;JVI.00014-21. PubMed: <https://pubmed.gov/33441348>. Full-text: <https://doi.org/10.1128/JVI.00014-21>

SARS-CoV-2 infection induces COX-2 expression in cell lines, primary airway epithelial cells, and mice. Inhibition of COX-2 by NSAIDs did not affect viral entry or replication *in vitro* or *in vivo*. However, NSAID treatment impaired the production of pro-inflammatory cytokines and neutralizing antibodies in response to SARS-CoV-2 infection in mice. NSAIDs could therefore have complex effects on the host response to SARS-CoV-2.

## 24 January

### Treatment

#### Paper of the Day

Gottlieb RL, Chen P, Boscia J, et al. **Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19.** A Randomized Clinical Trial. JAMA January 21, 2021. Full-text: <https://doi.org/10.1001/jama.2021.0202>

Bamlanivimab and etesevimab are anti-spike neutralizing monoclonal antibodies that were derived from 2 separate patients who recovered from COVID-19 in North America and China, respectively. This RCT evaluated early treatment in 577 outpatients with mild-to-moderate COVID-19. There was no significant difference in change in viral load with 3 different doses of bamlanivimab monotherapy compared with placebo. However, treatment with a combination of bamlanivimab and etesevimab significantly decreased SARS-CoV-2 viral load by -0.57 log at day 11 compared with placebo. Further ongoing clinical trials will focus on assessing the clinical benefit.

The CORIMUNO-19 Collaborative group. **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.** Lancet Resp Med January 22, 2021. DOI:[https://doi.org/10.1016/S2213-2600\(20\)30556-7](https://doi.org/10.1016/S2213-2600(20)30556-7).

Anakinra is a recombinant human IL-1 receptor antagonist. This randomized open label study from France was stopped early following the recommendation of the data and safety monitoring board, after the recruitment of 116 patients: anakinra did not improve outcomes in patients with mild-to-moderate COVID-19 pneumonia.

Cavalli G, Dagna L. **The right place for IL-1 inhibition in COVID-19.** Lancet Resp Med January 22, 2021. DOI:[https://doi.org/10.1016/S2213-2600\(21\)00035-7](https://doi.org/10.1016/S2213-2600(21)00035-7)

According to Giulio Cavalli and Lorenzo Dagna, the “impression stands that IL-1 inhibition has therapeutic rationale in COVID-19”. In their comment on the CORIMUNO trial, they argue that a true test of anakinra would be in patients with more severe COVID-19, or with evidence of IL-1-mediated hyperinflammation.

Cohen J. **Monoclonal antibodies can prevent COVID-19—but successful vaccines complicate their future.** Sciencemag January 22, 2021. <https://www.sciencemag.org/news/2021/01/monoclonal-antibodies-can-prevent-covid-19-successful-vaccines-complicate-their-future>

Some thoughts on antibodies. Now that vaccines, cheaper and easier to administer, are being deployed by the millions—with priority for the most vulnerable populations—the question is what role remains for monoclonal antibodies. One potential drawback is that these antibodies could undermine the effectiveness of vaccines. According to some experts, they might be important for the elderly and other people with compromised immune systems who do not have vigorous responses to vaccines.

## Epidemiology

Quilty BJ, Clifford S, Hellewell J, et al. **Quarantine and testing strategies in contact tracing for SARS-CoV-2: a modelling study.** Lancet Public Health January 20, 2021. DOI:[https://doi.org/10.1016/S2468-2667\(20\)30308-X](https://doi.org/10.1016/S2468-2667(20)30308-X)

The main results of this modelling study: quarantine until a PCR or lateral flow antigen test on day 7 after exposure (with early release if negative) might avert as much transmission as a 14-day quarantine period. Additionally, daily repeated lateral flow antigen testing of traced contacts for 5 days, with isolation only after a positive test, might allow for the quarantine requirement to be removed with a small increase in transmission risk, which could itself be offset by increased participation and adherence to isolation. (A visual would be great here)

## Immunology

Kusnadi A, Ramírez-Suástegui C, Fajardo V, et al. **Severely ill COVID-19 patients display impaired exhaustion features in SARS-CoV-2-reactive CD8+ T cells.** Sci Immunol. 2021 Jan 21;6(55):eabe4782. PubMed: <https://pubmed.gov/33478949>. Full-text: <https://doi.org/10.1126/sciimmunol.abe4782>

This study, using single-cell transcriptome and TCR sequence analyses of > 87,000 *in vitro* activated virus-reactive CD8+ T cells and > 20,000 CD8+ T cells expressing activation markers *ex vivo*, from a total of 39 COVID-19 patients, gives important insights into CD8 T cell responses. Findings indicate that SARS-CoV-2-reactive CD8+ T cells from patients with severe COVID-19 displayed multiple features that support the generation of robust CD8+ T cell

memory responses with pro-survival properties and a lack of “restrained function” via “exhaustion” features.

## Vaccine

Bubar KM, Reinholt K, Kissler SM, et al. **Model-informed COVID-19 vaccine prioritization strategies by age and serostatus**. *Science* 21 Jan 2021:eabe6959. DOI: 10.1126/science.abe6959

Mathematical models comparing five age-stratified prioritization strategies: a highly effective transmission-blocking vaccine prioritized to adults ages 20-49 years minimized cumulative incidence, but mortality and years of life lost were minimized in most scenarios when the vaccine was prioritized to adults over 60 years old. Use of individual-level serological tests to redirect doses to seronegative individuals improved the marginal impact of each dose while potentially reducing existing inequities in COVID-19 impact.

Fitzpatrick MC, Galvani AP. **Optimizing age-specific vaccination**. *Science* 21 Jan 2021: eabg2334. DOI: 10.1126/science.abg2334

Vaccination strategies are not one size fits all. In their perspective, Meagan C. Fitzpatrick and Alison P. Galvani looked at vaccination of different age groups. Although vaccination of younger adults is projected to avert the greatest incidence, vaccinating older adults will most effectively reduce mortality.

## Pathogenesis

Hann von Weyhern C, Kaufmann I, Neff F. **Neuropathology associated with SARS-CoV-2 infection – Authors' reply**. *Lancet* January 23, 2021. DOI:[https://doi.org/10.1016/S0140-6736\(21\)00097-0](https://doi.org/10.1016/S0140-6736(21)00097-0)

Lively Discussion about various hypotheses regarding COVID-19 neuropathology (the authors report a pronounced CNS involvement with pan-encephalitis, meningitis, and brainstem neuronal cell damage in a small case series).

## Clinical

Ni YN, Wang T, Liang BM, Liang ZA. **The independent factors associated with oxygen therapy in COVID-19 patients under 65 years old**. *PLoS One*. 2021 Jan 22;16(1):e0245690. PubMed: <https://pubmed.gov/33481912>. Full-text: <https://doi.org/10.1371/journal.pone.0245690>. eCollection 2021

Oxygen therapy is highly required in COVID-19 patients under 65 years old who are admitted to hospital, but the success rate is high: among 833 COVID-19 patients under 65 years old, 29,4% had one or more co-morbidities. Oxygen therapy was required in 63,1%, and the mortality was only 2,9% among the oxygen therapy patients. Respiratory failure-related symptoms, elevated respiratory rate, low albumin and globulin levels, and fever at admission were independent risk factors for the requirement of oxygen.

## 25 January

First publication of the [Long COVID](#) chapter.

## 26 January

### Transmission

Tönshoff B, Müller B, Elling R, et al. **Prevalence of SARS-CoV-2 Infection in Children and Their Parents in Southwest Germany.** JAMA Pediatr January 22, 2021. Full-text: <https://doi.org/10.1001/jamapediatrics.2021.0001>

In a population-based sample in southwest Germany, this large-scale, multi-center, cross-sectional investigation of 4,964 participants accurately determined anti-SARS-CoV-2 seropositivity. The estimated SARS-CoV-2 seroprevalence was low in parents (1.8%) and 3-fold lower in children aged 1 to 10 years (0.6%), indicating that young children do not play a key role in SARS-CoV-2 spreading during the current pandemic (or their parents don't hug them enough! ☺).

### Immunology

Wauters E, Van Mol P, Garg AD et al. **Discriminating mild from critical COVID-19 by innate and adaptive immune single-cell profiling of bronchoalveolar lavages.** Cell Res (2021). Full-text: <https://doi.org/10.1038/s41422-020-00455-9>

Using scRNA-seq data derived from BAL, Els Wauters and colleagues from Leuven, Belgium, performed deep-immune profiling of the adaptive and innate immune cell landscape within the main locale of COVID-19 pathology. Briefly, their findings support a model wherein neutrophils execute their antiviral function in an immunologically 'controlled' fashion, regulated by T cells with good effector functions and paralleled by 'orderly' phagocytic dis-

posal of expired cells by macrophages in mild disease. In contrast, in critical disease, T cells are less abundant and dysregulated, which coupled with hyperinflammatory monocytes facilitates excessive neutrophil-based inflammation.

Shaan Lakshmanappa Y, Elizaldi SR, Roh JW et al. **SARS-CoV-2 induces robust germinal center CD4 T follicular helper cell responses in rhesus macaques.** Nat Commun 12, 541 (2021). Full-text: <https://doi.org/10.1038/s41467-020-20642-x>

According to the authors, these animal experiments add to our understanding of immune responses to SARS-CoV-2 in three significant ways. First, they demonstrate that robust Th1-Tfh responses are observed following SARS-CoV-2 infection. Second, Tfh responses focused on S and N are seen within lymph nodes, circulate throughout the peripheral blood, potentially seeding the spleen. Third, they showed that acute antibody kinetics are characterized by induction of IgG, predominantly to S1 and of the IgG1 sub-class, indicative of early class switching. Taken together, these data demonstrate that productive Tfh responses are elicited following SARS-CoV-2 infection in healthy adult rhesus macaques.

Tan AT, Linster M, Tan CW, et al. **Early induction of functional SARS-CoV-2 specific T cells associates with rapid viral clearance and mild disease in COVID-19 patients.** Cell Rep January 21, 2021. Full-text: <https://doi.org/10.1016/j.celrep.2021.108728>

This longitudinal immunological analysis in a small cohort from onset till outcome suggests that early induction of IFN- $\gamma$  secreting SARS-CoV-2 specific T cells is present in patients who have mild disease and accelerated viral clearance. Detection of functional SARS-CoV-2 specific T cells may be of prognostic value.

## Vaccine

CDC COVID-19 Response Team; Food and Drug Administration. **Allergic Reactions Including Anaphylaxis After Receipt of the First Dose of Moderna COVID-19 Vaccine — United States, December 21, 2020–January 10, 2021.** MMWR Morb Mortal Wkly Rep. ePub: 22 January 2021. Full-text: [http://dx.doi.org/10.15585/mmwr.mm7004e1external icon](http://dx.doi.org/10.15585/mmwr.mm7004e1external%20icon).

Two in a Million: from December 21, 2020 to January 10, 2021, CDC detected 10 cases of anaphylaxis after administration of a reported 4,041,396 first doses of

the Moderna COVID-19 vaccine (2.5 cases per million doses administered). No anaphylaxis-related deaths were reported. Nine events occurred in persons with a documented history of allergies or allergic reactions, five of whom had a previous history of anaphylaxis. The median interval from vaccine receipt to symptom onset was 7.5 minutes. Nine patients had onset within 15 minutes, and one had onset after 30 minutes.

## Diagnostics

Li Y, Lai D, Lei Q, et al. **Systematic evaluation of IgG responses to SARS-CoV-2 spike protein-derived peptides for monitoring COVID-19 patients.** Cell Mol Immunol (2021). Full-text: <https://doi.org/10.1038/s41423-020-00612-5>

Yang Li and colleagues from Shanghai identified and verified eight peptides derived from the S protein that may be of high diagnostic value. These peptides might be used in different circumstances alone or in combination as candidates to generate immunoassays for monitoring COVID-19. In comparison to the current protein-based immunoassays, peptide-based assays could be highly affordable and accessible.

## Clinical

Oran DP, Topol EJ. **The Proportion of SARS-CoV-2 Infections That Are Asymptomatic: A Systematic Review.** Ann Intern Med. 2021 Jan 22. PubMed: <https://pubmed.gov/33481642>. Full-text: <https://doi.org/10.7326/M20-6976>

How many are asymptomatic? After screening all observational, descriptive studies and reports of mass screening for SARS-CoV-2 that were either cross-sectional or longitudinal in design published through 17 November 2020 (n = 61), Daniel P. Oran and Eric J. Topol say, “at least one third”.

Pellegrini D, Kawakami R, Guagliumi G, et al. **Microthrombi As A Major Cause of Cardiac Injury in COVID-19: A Pathologic Study.** Circulation. 2021 Jan 22. PubMed: <https://pubmed.gov/33480806>. Full-text: <https://doi.org/10.1161/CIRCULATIONAHA.120.051828>

Of 40 hearts from deceased COVID-19 patients from Bergamo, 14 (35%) had evidence of myocyte necrosis, predominantly of the left ventricle. Notably, 9/14 (64%) had microthrombi in myocardial capillaries, arterioles, and small muscular arteries. Microthrombi were different in composition as compared to intramyocardial thromboemboli from COVID-19 negative subjects and to coronary thrombi retrieved from COVID-19 positive and negative STEMI pa-



tients. Tailored anti-thrombotic strategies may be useful to counteract the cardiac effects of COVID-19 infection.

Leidman E, Duca LM, Omura JD, Proia K, Stephens JW, Sauber-Schatz EK. **COVID-19 Trends Among Persons Aged 0–24 Years — United States, March 1–December 12, 2020.** MMWR Morb Mortal Wkly Rep 2021;70:88–94. Full-text: <http://dx.doi.org/10.15585/mmwr.mm7003e1>

Trends in children and adolescents paralleled trends in adults. Among children, adolescents, and young adults with available data for outcomes, 30,229 (2,5%) were hospitalized, 1973 (0,8%) required ICU admission, and 654 (0,023%) died. You think that this morbidity/mortality is low? Before considering herd immunity, take these numbers and calculate the affected populations in your country.

### Collateral Effects

Verma AM, Patel A, Subramanian S, et al. **From intravenous to subcutaneous infliximab in patients with inflammatory bowel disease: a pandemic-driven initiative.** Lancet Gastroenterology Correspondence| Volume 6, ISSUE 2, P88–89, February 01, 2021. Full-text: [https://doi.org/10.1016/S2468-1253\(20\)30392-7](https://doi.org/10.1016/S2468-1253(20)30392-7)

Facing the clinical imperative to minimise patient exposure to hospital facilities to mitigate against the risk of nosocomial acquisition of COVID-19, the authors switched their patients with inflammatory bowel diseases (IBD) from intravenous to subcutaneous infliximab. Experiences are encouraging: in 31 IBD patients, this strategy appeared safe and enabled patients requiring infliximab to have home treatment self-administered at their convenience on the day of dose instead of having to attend a scheduled appointment at the hospital for an infusion.

### Spanish

If you read Spanish, read Laborde A. **Moderna confirma que su vacuna contra la covid es efectiva contra las variantes británica y sudafricana.** El País 2021, published 25 January. Full-text: <https://elpais.com/sociedad/2021-01-25/moderna-confirma-que-su-vacuna-contra-la-covid-es-efectiva-contra-las-variantes-britanica-y-sudafricana.html>

La farmacéutica trabaja en una nueva versión de la vacuna para responder mejor a la cepa de Sudáfrica.

Vizoso S. **Rogelia murió por covid y a los 10 días resucitó.** El País 2021, published 25 January. Full-text: <https://elpais.com/sociedad/2021-01-25/rogelia-murio-por-covid-y-a-los-10-dias-resucito.html>

La confusión de un geriátrico provoca que una familia de Lugo entierre a otra mujer pensando que era su pariente.

## Portuguese

If you read portuguese, read Serafim S. **Treze princípios para motivar as pessoas a cumprirem as restrições da covid-19.** Público, published 25 January. Full-text: <https://www.publico.pt/2021/01/25/ciencia/noticia/treze-principios-motivar-pessoas-cumprirem-restricoes-covid19-1947503>

Estas orientações podem ser usadas por políticos ou outras pessoas que precisem de comunicar restrições na sua cidade ou empresa. São um contributo para uma comunicação eficaz neste momento de crise.

## French

If you read French, read Hecketsweiler C. **La deuxième vague de Covid-19 vue de l'hôpital Bichat : « Les malades comme moi, ils meurent ou ils sortent vivants ? »** Le Monde, published 25 January. Full-text: [https://www.lemonde.fr/planete/article/2021/01/25/la-deuxieme-vague-de-covid-19-vue-de-l-hopital-bichat-les-malades-comme-moi-ils-meurent-ou-ils-sortent-vivants\\_6067549\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/25/la-deuxieme-vague-de-covid-19-vue-de-l-hopital-bichat-les-malades-comme-moi-ils-meurent-ou-ils-sortent-vivants_6067549_3244.html)

Dans l'établissement parisien, après une période d'accalmie, le nombre d'hospitalisations en réanimation est reparti à la hausse, et les lits pourraient bientôt être comptés.

## 27 January

### Virology

Starr TN, Greaney AJ, Addetia A. **Prospective mapping of viral mutations that escape antibodies used to treat COVID-19.** Science 25 Jan 2021:eabf9302. Full-text: <https://doi.org/10.1126/science.abf9302>

Incredible work, mapping how all mutations to SARS-CoV-2's receptor-binding domain (RBD) affect binding by the antibodies from Regeneron and Lilly. There was not only a single amino acid mutation that fully escapes the

REGN-COV2 cocktail but also mutations that were selected in a persistently infected patient treated with REGN-COV2, as well those already present in circulating SARS-CoV-2 strains. According to Tyler Starr and colleagues, it is “concerning that so many escape mutations impose little cost on RBD folding or receptor affinity, and that some are already present at low levels among circulating viruses”.

Johnson BA, Xie X, Bailey AL et al. **Loss of furin cleavage site attenuates SARS-CoV-2 pathogenesis.** *Nature* January 25, 2021. Full-text: <https://doi.org/10.1038/s41586-021-03237-4>

SARS-CoV-2 has a furin cleavage site (PRRAR) in its spike protein that is absent in other CoVs. It has been postulated to be key to disease causing capability. To explore this, Bryan Johnson and colleagues from Texas generated a mutant SARS-CoV-2 deleting the furin cleavage site ( $\Delta$ PRRA). SARS-CoV-2  $\Delta$ PRRA replicates had faster kinetics, improved fitness in Vero E6 cells, and reduced spike protein processing as compared to parental SARS-CoV-2. However, the  $\Delta$ PRRA mutant had reduced replication in a human respiratory cell line and was attenuated in both hamster and K18-hACE2 transgenic mouse models of SARS-CoV-2 pathogenesis. Importantly, COVID-19 patient sera and RBD mAbs had lower neutralization values against the  $\Delta$ PRRA mutant versus parental SARS-CoV-2.

Claro IM, da Silva Sales FC, Ramundo MS, Candido DS, Silva CAM, de Jesus JG, et al. **Local transmission of SARS-CoV-2 lineage B.1.1.7, Brazil, December 2020.** *Emerg Infect Dis.* January 25, 2021. Full-text: <https://doi.org/10.3201/eid2703.210038>

In December 2020, research surveillance detected the new SARS-CoV-2 variant B.1.1.7 in São Paulo, Brazil. Rapid genomic sequencing and phylogenetic analysis revealed two distinct introductions of the lineage. One patient reported no international travel. According to the authors, “there may be more infections with this lineage in Brazil than reported”. It would be surprising if not.

## Diagnosis

Bal A, Destras G, Gaymard A. **Two-step strategy for the identification of SARS-CoV-2 variant of concern 202012/01 and other variants with spike deletion H69–V70, France, August to December 2020.** *Eurosurveillance* Volume 26, Issue 3, 21/Jan/2021. <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.3.2100008>

A technical paper, reporting a two-step strategy that enables the timely detection of VOC 202012/01, as well as other variants carrying  $\Delta$ H69/ $\Delta$ V70. This strategy allowed the first detection of the VOC 202012/01 in France.

## Clinical

Kooistra EJ, de Nooijer AH, Claassen WJ et al. **A higher BMI is not associated with a different immune response and disease course in critically ill COVID-19 patients.** *Int J Obes* (2021). <https://doi.org/10.1038/s41366-021-00747-z>

In 67 COVID-19 patients from Nijmegen, Netherlands requiring mechanical ventilation in the ICU, a higher BMI was not related to a different immunological response, unfavorable respiratory mechanics, or impaired outcome. The concentrations and kinetics of clinical inflammatory parameters and respiratory mechanics were similar in both groups.

Lowe KE, Zein J, Hatipoğlu U, et al. **Association of Smoking and Cumulative Pack-Year Exposure With COVID-19 Outcomes in the Cleveland Clinic COVID-19 Registry.** *JAMA Intern Med.* Published online January 25, 2021. Full-text: <https://doi.org/10.1001/jamainternmed.2020.8360>

Time to quit! Among 7102 patients from Cleveland, 6020 (84,8%) were never smokers, 172 (2,4%) were current smokers, and 910 (12,8%) were former smokers. There was a dose-response association between pack-years and adverse COVID-19 outcomes. Patients who smoked more than 30 pack-years had a 2,25 times higher odds of hospitalization (95% CI: 1,76-2,88) and were 1,89 times more likely to die following a COVID-19 diagnosis (95% CI: 1,29-1,76) when compared with never smokers.

## Collateral

Leitner MC, Richlan F. **Analysis System for Emotional Behavior in Football (ASEB-F): matches of FC Red Bull Salzburg without supporters during the COVID-19 pandemic.** *Humanit Soc Sci Commun* 8, 14 (2021). Full-text: <https://doi.org/10.1057/s41599-020-00699-1>

Less aggression! This study (our “alternative” paper of the day) has evaluated the effect of missing crowds in football on the emotions and behavior of players, staff and officials. These data from Austria show that in “ghost games” overall, “emotional situations” declined by 20%. More data on this topic (other leagues, other sports) are eagerly awaited!

Chen CY, Chen IH, O'Brien KS et al. **Psychological distress and internet-related behaviors between schoolchildren with and without overweight during the COVID-19 outbreak.** *Int J Obes* (2021). Full-text: <https://doi.org/10.1038/s41366-021-00741-5>

Online survey among 1357 schoolchildren (mean age = 10,7 years), showing that overweight kids had significantly higher levels of COVID-19 infection fear, stress, depression, perceived weight stigma, and problematic social media use than those not overweight.

Partridge E, McCleery E, Cheema R, et al. **Evaluation of Seasonal Respiratory Virus Activity Before and After the Statewide COVID-19 Shelter-in-Place Order in Northern California.** *JAMA Netw Open* January 2021; 4(1):e2035281. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.35281>

Using interrupted time series analysis of testing for viral respiratory pathogens, this study found that statistically significant lower rates of common community respiratory viruses appeared to be associated with a shelter-in-place order during the coronavirus pandemic. Decreases were most pronounced for influenza (93%) and for rhinovirus or enterovirus (81%). Lower rates of post-exposure viral activity were seen for respiratory syncytial virus, parainfluenzavirus, coronaviruses, and adenoviruses, however, these associations were not statistically significant.

## Treatment

White KM, Rosales, Yildiz S. **Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A.** Science 25 Jan 2021:eabf4058. Full-text: <https://doi.org/10.1126/science.abf4058>

SARS-CoV-2 viral proteins interact with the eukaryotic translation machinery and inhibitors of translation have potent antiviral effects. Plitidepsin has been clinically developed for the treatment of multiple myeloma with a well-established safety profile and pharmacokinetics. Kris White and colleagues report that the drug possesses antiviral activity 27,5-fold more potent than remdesivir against SARS-CoV-2 *in vitro*, with limited toxicity in cell culture. There was *in vivo* efficacy in two mouse models of SARS-CoV-2 infection with a reduction of viral replication in the lungs by two orders of magnitude using prophylactic treatment.

## French

If you read French, read **Covid-19 : le variant anglais représente près d'un cas positif sur dix en Ile-de-France.** Le Monde, published 26 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/26/covid-19-une-pme-sur-deux-craint-de-ne-pas-pouvoir-supporter-un-troisieme-confinement\\_6067608\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/26/covid-19-une-pme-sur-deux-craint-de-ne-pas-pouvoir-supporter-un-troisieme-confinement_6067608_3244.html)

Selon l'AP-HP, ce variant du SARS-CoV-2 représente 9,4 % de 1 080 cas dépistés en Ile-de-France entre les 11 et 21 janvier. Il y a trois semaines, une « enquête flash » avait constaté un taux de 2,5 % au niveau national.

Ducourtieux C. **Le Covid-19 a fait plus de 100 000 morts au Royaume-Uni : pourquoi un tel bilan ?** Le Monde, published 26 January. Full-text : [https://www.lemonde.fr/international/article/2021/01/26/le-covid-19-a-fait-plus-de-100-000-morts-au-royaume-uni-pourquoi-un-tel-bilan\\_6067682\\_3210.html](https://www.lemonde.fr/international/article/2021/01/26/le-covid-19-a-fait-plus-de-100-000-morts-au-royaume-uni-pourquoi-un-tel-bilan_6067682_3210.html)

Le pays est le plus endeuillé d'Europe et, proportionnellement à sa population, l'un des plus affectés dans le monde, devant les Etats-Unis ou le Mexique.

## 28 January

### Vaccine

Brouwer JM, Brinkkemper M, Maisonnasse P, et al. **Two-component spike nanoparticle vaccine protects macaques from SARS-CoV-2 infection.** Cell 2021, published 25 January. Full-text: [https://www.cell.com/cell/fulltext/S0092-8674\(21\)00078-7](https://www.cell.com/cell/fulltext/S0092-8674(21)00078-7)

Rogier Sanders, Philip Brouwer and colleagues present a two-component protein-based nanoparticle vaccine that displays twenty copies of pre-fusion SARS-CoV-2 S protein, capable of inducing potent neutralizing antibody responses in 400 in mice, rabbits and cynomolgus macaques. The vaccine-induced immunity protected macaques against a high dose challenge, resulting in strongly reduced viral infection and replication in upper and lower airways.

Muik A, Wallisch AK, Sanger B, et al. **Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine-elicited human sera.** bioRxiv 2021, posted 19 January. Full-text: <https://doi.org/10.1101/2021.01.18.426984>

Good news from the variants vaccine front. Ugur Sahin, Alexander Muik and colleagues report that after analyzing immune sera from individuals vaccinated with the Pfizer-BioNTech vaccine (Comirnaty™), it seems unlikely that the (“UK”) B.1.1.7 variant will escape vaccine-mediated protection. The authors investigated SARS-CoV-2-S pseudoviruses bearing either the Wuhan reference strain or the B.1.1.7 lineage spike protein with the sera of 16 participants in a previously reported trial with the mRNA-based COVID-19 vaccine Comirnaty™. The immune sera had equivalent neutralizing titers to both variants.

Wu K, Werner AP, Moliva JI, et al. **mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants.** bioRxiv 2021, published 25 January. Full-text: <https://doi.org/10.1101/2021.01.25.427948>

Good news from another variants vaccine front. Kai Wu et al. demonstrate that people aged 18-55 years who received two 100 µg doses of the mRNA-1273 vaccine, “maintained activity against all circulating strain variants tested to date”, and only the B.1.351 variant showed reduced neutralizing titers. Viral escape was not detected from any sample and neutralizing titers remained above those previously found to be protective in NHP challenge studies. (Editor’s Note: *All circulating strain variants?* The paper doesn’t seem to

mention the P.1 variant from Brazil.) See also the Moderna press release at <https://investors.modernatx.com/news-releases/news-release-details/moderna-covid-19-vaccine-retains-neutralizing-activity-against>

Cele S, Gazy I, Jackson L, et al. **Escape of SARS-CoV-2 501Y.V2 variants from neutralization by convalescent plasma.** medRxiv 2021, published 26 January. Full-text: <https://doi.org/10.1101/2021.01.26.21250224>

Bad news from the variants antibody front. Mutations in the B.1.351 variant (alias 501Y.V2) may cause the virus to lose much of its sensitivity to antibodies. That is the result of a pre-print paper by Tulio de Oliveira, Alex Sigal, Sandile Cele and colleagues. After examining the neutralizing effect of convalescent plasma collected from six adults hospitalized with COVID-19, the authors observed that neutralization of the B.1.351 variant was strongly attenuated, with IC50 6 to 200-fold higher relative to the first wave virus. Reduced protection against re-infection? Let's live on and see!

Wang Z, Schmidt F, Weisblum Y, et al. **mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants.** bioRxiv 2021, published 19 January. Full-text: <https://doi.org/10.1101/2021.01.15.426911>

And, finally, good news again: Michel Nussenzweig and colleagues tested samples from 14 and 6 people who had received the Moderna and the Pfizer-BioNTech vaccine, respectively. They saw a slight decrease in antibody activity against engineered viruses with three key mutations of the B.1.351 variant first discovered in South Africa.

## Epidemiology

Borges V, Sousa C, Menezes L, et al. **Tracking SARS-CoV-2 VOC 202012/01 (lineage B.1.1.7) dissemination in Portugal: insights from nationwide RT-PCR Spike gene drop out data.** Virological.org 2021, published 19 January. Full-text: <https://virological.org/t/tracking-sars-cov-2-voc-202012-01-lineage-b-1-1-7-dissemination-in-portugal-insights-from-nationwide-rt-pcr-spike-gene-drop-out-data/600>

Portugal is facing a highly dynamic epidemic situation. Here, João P Gomes, Vítor Borges and colleagues show that the B.1.1.7 variant represented 5,8% of all positive cases detected since week 49 of 2020 and 13,3% by the end of week 2, 2021. The authors anticipate that B.1.1.7 might reach up to 60% of positive cases by early February 2021. Robust public health measures on the horizon.



## Immunology

Combes AJ, Courau T, Kuhn NF, et al. **Global absence and targeting of protective immune states in severe COVID-19.** Nature 2021, published 25 January. Full-text: <https://doi.org/10.1038/s41586-021-03234-7>

Examining the serum from severe patients, Alexis Combes et al. demonstrate that these patients uniquely produce antibodies that functionally block the production of the mild disease-associated ISG-expressing cells, by engaging conserved signaling circuits that dampen cellular responses to interferons.

## Clinical

Tinelli G, Minelli F, Sica, Tshomba Y. **Complete aortic thrombosis in SARS-CoV-2 infection.** Eur Heart J 2021, published 26 January. Full-text: <https://doi.org/10.1093/eurheartj/ehab011>

A 74-year-old man with a history of diabetes mellitus, coronary artery disease, and previous myocardial infarction presents to the emergency department with cardiogenic shock. Three-dimensional computed tomographic (CT) angiography revealed a complete thrombotic occlusion of the aorta. SARS-CoV-2 infection was confirmed by RT-PCR. The patient died immediately after the CT scan.

Velasquez-Manoff M. **What If You Never Get Better From Covid-19?** The New York Times 2021, published 21 January. Full-text: <https://www.nytimes.com/2021/01/21/magazine/covid-aftereffects.html>

Some patients could be living with the after-effects of COVID-19 for years to come. Recent research into another persistent, mysterious disease might help us understand how to treat them.

## Spanish

If you read Spanish, read Perelman C. **Una mirada a las vacunas contra COVID-19: la mejor estrategia para acabar con la pandemia.** Academia de Ciencias de Morelos, published 24 January. Full-text: <http://www.acmor.org/articulo/una-mirada-las-vacunas-contra-covid-19-la-mejor-estrategia-para-acabar-con-la-pandemia>

## French

If you read French, read Larousserie D, Herzberg N, BouSSION M. **Ce que l'on sait de l'efficacité des vaccins et des anticorps sur les variants du Covid-19.** Le Monde 2021, published 22 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/22/ce-que-l-on-sait-des-effets-des-variants-du-covid-19-sur-les-personnes-vaccinees-ou-deja-immunisees\\_6067198\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/22/ce-que-l-on-sait-des-effets-des-variants-du-covid-19-sur-les-personnes-vaccinees-ou-deja-immunisees_6067198_3244.html)

Plusieurs études semblent indiquer que certains variants commencent à échapper aux anticorps formés contre le virus d'origine.

## German

If you read German, read **Sprechen kann genauso gefährlich sein wie Husten.** Der Spiegel 2021, published 20 January. Full-text: <https://www.spiegel.de/wissenschaft/medizin/corona-sprechen-kann-genauso-gefaehrlich-sein-wie-husten-wegen-der-aerosole-a-639c3daa-d167-430c-9e0e-8197bbd4a199>

In Innenräumen ist die Corona-Gefahr deutlich erhöht, so viel ist klar. Eine Studie legt nun nahe, dass nicht nur Singen oder Husten viele gefährliche Aerosole produzieren – das Gleiche gilt auch für einfaches Sprechen.

## 29 January

### Vaccine

Wang P, Lihong L, Iketani S, et al. **Increased Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 to Antibody Neutralization.** bioRxiv 2021, posted 26 January. Full-text: <https://doi.org/10.1101/2021.01.25.428137>

E484K is the bad boy on the block. David Ho, Pengfai Wang and colleagues at Columbia University produced retroviruses with spike proteins incorporating each of B1351's mutations separately, as well as all at once. E484K accounted for much of the effect. The serum of 12 people vaccinated with Moderna's vaccine and 10 people vaccinated with the Pfizer-BioNTech vaccine was six to nine times less potent against B.1.351. Serum from 20 previously infected people was 11 to 33 times less potent.

Kupferschmidt 20210126. **Vaccine 2.0: Moderna and other companies plan tweaks that would protect against new coronavirus mutations.** Science 2021, published 26 January. Full-text: <https://www.sciencemag.org/news/2021/01/vaccine-20-moderna-and-other-companies-plan-tweaks-would-protect-against-new>

Antibodies triggered by the vaccine may be a little less potent against the new variant B.1.351, first described in South Africa, vs the one the vaccine was developed for. So, researchers were perhaps relieved to hear the company will start development of booster shots tailored to B.1.351 and other variants.

Brunning A. **How are RNA vaccines made?** Periodic Graphics 2021, published 3 January. Link: <https://cen.acs.org/pharmaceuticals/vaccines/Periodic-Graphics-RNA-vaccines-made/99/i1>

RNA vaccines produced by Pfizer-BioNTech and Moderna have become the first COVID-19 vaccines. How are these vaccines made?

## Epidemiology

Sabino EC, Buss LF, Carvalho MPS, et al. **Resurgence of COVID-19 in Manaus, Brazil, despite high seroprevalence.** Lancet 2021, published 27 January. Full-text: [https://doi.org/10.1016/S0140-6736\(21\)00183-5](https://doi.org/10.1016/S0140-6736(21)00183-5)

This is not a retraction of the [pre-print paper](#) posted on 21 September or of the 8 December [Science article](#) below. But in view of the dramatic second wave of the COVID-19 pandemic in Manaus (if you read Spanish, read [111](#), [222](#), [333](#), [444](#), [555](#), [666](#), [777](#)), it is difficult to believe that there has ever been a “75% attack rate of SARS-CoV-2 in the Brazilian Amazon”. [Buss LF, Prete Jr A, Abraham CMM, et al. **Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic.** Science 2020, published 8 December. Full-text: <https://doi.org/10.1126/science.abe9728>]. The future will tell.

Loppreite M, Panzarasa P, Puliga M, et al. **Early warnings of COVID-19 outbreaks across Europe from social media.** Sci Rep 11, 2147 (2021). <https://doi.org/10.1038/s41598-021-81333-1>

The authors analyzed data from Twitter to uncover early-warning signals of the coming COVID-19 pandemic in Europe. Whistleblowing came primarily from the geographical regions that eventually turned out to be the key breeding grounds for infections. So, start setting up an integrated digital surveillance system in which social media will geo-localize chains of contagion.

## Virology

Calisher CH, Childs JE, Field HE, Holmes KV, Schountz T. **Bats: important reservoir hosts of emerging viruses.** Clin Microbiol Rev. 2006 Jul;19(3):531-45. PubMed: <https://pubmed.gov/16847084>. Full-text: <https://doi.org/10.1128/CMR.00017-06>

Bats – more than 1000 species, 25% of all recognized species of mammals; living in HUGE communities (ideal for viral spread); flying dozens of kilometers while searching for food. Bats – fast reactors for viral evolution? Never forget this 2006 primer for emerging infectious diseases.

## Immunology

Takahashi T, Iwasaki A. **Sex differences in immune responses.** Science. 2021 Jan 22;371(6527):347-348. PubMed: <https://pubmed.gov/33479140>. Full-text: <https://doi.org/10.1126/science.abe7199>

Evidence increasingly indicates that male sex is a risk factor for more severe disease and death from COVID-19. Sex differences beyond sex organs are present across species and extend to physiological systems, including the immune system. Male sex in animals is more often associated with lower immune responses and higher susceptibility and/or vulnerability to infections. This is also generally the case in humans: male patients have higher viral loads for hepatitis B virus (HBV) and HIV.

## Pathogenesis

Johnson BA, Xie X, Bailey AL, et al. **Loss of furin cleavage site attenuates SARS-CoV-2 pathogenesis.** Nature (2021). Full-text: <https://doi.org/10.1038/s41586-021-03237-4>

The authors generated a mutant SARS-CoV-2 deleting the furin cleavage site ( $\Delta$ PRRA). SARS-CoV-2  $\Delta$ PRRA replicates had faster kinetics, improved fitness in Vero E6 cells, and reduced spike protein processing as compared to parental SARS-CoV-2. However, the  $\Delta$ PRRA mutant had reduced replication in a human respiratory cell line and was attenuated in both hamster and K18-hACE2 transgenic mouse models of SARS-CoV-2 pathogenesis. The findings illustrate the critical role of the furin cleavage site in SARS-CoV-2 infection and pathogenesis. In its absence, the mutant  $\Delta$ PRRA virus is attenuated in its ability to replicate in certain cell types and cause disease *in vivo*.

## Spanish

If you read Spanish, read Linde P. **El nuevo debate sobre las mascarillas: ¿deben imponerse las más seguras?** El País 2021, published 28 January. Full-text: <https://elpais.com/sociedad/2021-01-27/el-nuevo-debate-sobre-las-mascarillas-deben-imponerse-las-mas-seguras.html>

Alemania y Francia comienzan a exigir protecciones médicas en lugares cerrados y Feijóo lo sugiere en España. La escasez de producción y el precio son los principales obstáculos.

## French

If you read French, read Rof G. **Covid-19 : dans les hôpitaux, une troisième vague paraît inéluctable.** Le Monde 2021, published 28 January. Full-text: [https://www.lemonde.fr/planete/article/2021/01/28/dans-les-hopitaux-une-troisieme-vague-parait-ineluctable\\_6067860\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/28/dans-les-hopitaux-une-troisieme-vague-parait-ineluctable_6067860_3244.html)

De plus en plus de malades en réanimation, reprise de la déprogrammation, nouveaux transferts de patients... Les signaux d'alerte se multiplient partout en France malgré le couvre-feu généralisé.

Mandard S, Rérolle R, Schittly R, et al. **« Marre du Covid-19 » : de confinements en couvre-feux, le récit d'une France qui en a « ras le bol »** – Le Monde 2021, published 27 January. Full-text: [https://www.lemonde.fr/planete/article/2021/01/27/face-au-covid-19-le-grand-abattement-des-francais\\_6067716\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/27/face-au-covid-19-le-grand-abattement-des-francais_6067716_3244.html)

Il y a ceux qui, face à l'épidémie, luttent pour garder le moral et ceux qui n'y arrivent plus. Ceux qui se sont installés dans le fatalisme et ceux qui s'impatientent.

## 30 January

### Immunology

#### Paper of the Day

Thomson E, Rosen LE, Shepherd JG, et al. **Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity.** Cell 2021, published 28 January. Full-text: <https://doi.org/10.1016/j.cell.2021.01.037>

Over the past months, the receptor-binding motif (RBM) mutation N439K has emerged independently in multiple SARS-CoV-2 lineages. N439K increases spike affinity for hACE2. Gyorgy Snell, Emma Thomson and colleagues show that 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.

Liu Z, VanBlargan LA, Bloyet LM, et al. **Identification of SARS-CoV-2 spike mutations that attenuate monoclonal and serum antibody neutralization.** *Cell Host Microbe* 2021, published 27 January. Full-text: <https://doi.org/10.1016/j.chom.2021.01.014>

Hard time ahead for anti-clonals. Sean Whelan, Zhuoming Liu and colleagues show that the mutation S477N confers resistance to neutralization by multiple monoclonal antibodies. Also E484K, the bad boy on the block (see yesterday's presentation of the Wang paper ([Increased Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 to Antibody Neutralization](#))) is less sensitive to neutralization by convalescent human sera.

Hope JL, Bradley LM. **Lessons in antiviral immunity.** *Science*. 2021 Jan 29;371(6528):464-465. PubMed: <https://pubmed.gov/33510014>. Full-text: <https://doi.org/10.1126/science.abf6446>

The COVID-19 pandemic is revealing widely varying immune responses and diverse clinical outcomes in SARS-CoV-2 infection, raising questions about how antiviral responses are orchestrated, factors that influence the longevity of immunological memory, and approaches that mediate robust protection from viral infections.

## Virology

Martin MA, VanInsberghe D, Koelle K. **Insights from SARS-CoV-2 sequences.** *Science*. 2021 Jan 29;371(6528):466-467. PubMed: <https://pubmed.gov/33510015>. Full-text: <https://doi.org/10.1126/science.abf3995>

In many ways, the SARS-CoV-2 pandemic offers a distinct opportunity for the field of phylodynamics. Methods development over the past 10 to 15 years, the widespread availability of sequencing technologies, open data sharing, and the tireless efforts of clinicians and scientists who collect these data mean that more can be learned from viral genomes than ever before.

## Transmission

da Silva Francisco R, Benittes F, Lamarca AP, et al. **Pervasive transmission of E484K and emergence of VUI-NP13L with evidence of SARS-CoV-2 co-infection events by two different lineages in Rio Grande do Sul, Brazil.** medRxiv 2021, posted 26 January. Full-text: <https://doi.org/10.1101/2021.01.21.21249764>

Fernando Rosado Spilki, Ronaldo da Silva Francisco and colleagues report two co-infection events caused by the simultaneous occurrence of B.1.1.28 (E484K) and other lineages. Both patients had typical mild to moderate flu-like symptoms with favorable outcomes after disease, no required hospitalization and spontaneous recovery. The possibility of co-infection by E484K adds a new factor to the complex interaction between immune response systems and SARS-CoV-2 Spike mutations.

## Clinical

Bellan M, Soddu D, Balbo PE, et al. **Respiratory and Psychophysical Sequelae Among Patients With COVID-19 Four Months After Hospital Discharge.** JAMA Netw Open. 2021 Jan 4;4(1):e2036142. PubMed: <https://pubmed.gov/33502487>. Full-text: <https://doi.org/10.1001/jamanetworkopen.2020.36142>

A consecutive series of 238 patients aged 18 years and older (or their caregivers) who had received a confirmed diagnosis of SARS-CoV-2 infection severe enough to require hospital admission from March 1 to June 29, 2020. (Out of 767 patients, 494 (64,4%) refused to participate, and 35 (4,6%) died during follow-up.) After 4 months, 128/238 patients (53,8%) had functional impairment. Post-traumatic stress symptoms were reported in a total of 41 patients (17,2%).

Daher A, Balfan, P, Aetou M et al. **Clinical course of COVID-19 patients needing supplemental oxygen outside the intensive care unit.** Sci Rep 11, 2256 (2021). <https://doi.org/10.1038/s41598-021-81444-9>

Patients with COVID-19 requiring oxygen therapy need long-term inpatient care with a median of 12 days in hospital including 8 days on supplemental oxygen, which should be taken into account when planning treatment capacity. The authors explain this result by the prolonged inflammatory course of the disease.

## Education

Rubin EJ, Baden LR, Morrissey S. **A Covid-19 Conversation with Anthony Fauci.** Audio interview (43 minutes). N Engl J Med 2021; 384: e22. Access: <https://doi.org/10.1056/NEJMe2101618>

The editors are joined by Dr. Anthony Fauci, U.S. Chief Medical Advisor, NIAID, to discuss COVID-19 testing, therapeutics, and vaccines.

## French

If you read French, read Audureau W, Maad A. **Ce que nous apprend la campagne de vaccination massive en Israël.** Le Monde 2021, published 29 January. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2021/01/29/ce-que-nous-apprend-la-campagne-de-vaccination-massive-en-israel\\_6068120\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2021/01/29/ce-que-nous-apprend-la-campagne-de-vaccination-massive-en-israel_6068120_4355770.html)

Alors qu'un tiers des Israéliens sont déjà vaccinés, les premières études évoquent une baisse des infections après deux doses.

Saliba F, Delcas M, Montoya A, et al. **En Amérique latine, la course chaotique aux vaccins contre le Covid-19.** Le Monde 2021, published 29 January. Full-text : [https://www.lemonde.fr/international/article/2021/01/29/en-amerique-latine-la-course-chaotique-aux-vaccins-contre-le-covid-19\\_6068097\\_3210.html](https://www.lemonde.fr/international/article/2021/01/29/en-amerique-latine-la-course-chaotique-aux-vaccins-contre-le-covid-19_6068097_3210.html)

L'achat de produits pharmaceutiques reste un défi majeur pour des pays durement touchés par l'épidémie. D'autant plus que les Etats riches ont préempté une quantité astronomique de doses.

Herzberg N. **Le variant sud-africain affaiblit un premier vaccin contre le Covid-19, celui de Novavax.** Le Monde 2021, published 29 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/29/covid-19-le-variant-sud-africain-affaiblit-un-premier-vaccin\\_6068052\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/29/covid-19-le-variant-sud-africain-affaiblit-un-premier-vaccin_6068052_3244.html)

Les études conduites sur le candidat de la firme américaine confirment que le mutant présent dans près de 30 pays peut diminuer l'efficacité vaccinale.



## Portuguese

If you read Portuguese, read Serafim TS. **Variante do Reino Unido tem potencial de maior letalidade, como disse a ministra da Saúde?** Público 2021, published 29 January. Full-text: <https://www.publico.pt/2021/01/29/ciencia/noticia/variante-reino-unido-potencial-maior-letalidade-ministra-saude-1948543>

A ministra da Saúde afirmou no Parlamento, nesta quinta-feira, que a variante do Reino Unido tem começado agora a ser descrita como tendo um potencial de maior letalidade. É mesmo assim?

## 31 January

### Immunology

#### Paper of the Day

Rappazzo CG, Tse LV, Kaku CI, et al. **Broad and potent activity against SARS-like viruses by an engineered human monoclonal antibody.** Science. 2021 Jan 25:eabf4830. PubMed: <https://pubmed.gov/33495307>. Full-text: <https://doi.org/10.1126/science.abf4830>

Although SARS-CoV and SARS-CoV-2 share 76% amino acid identity in their S proteins, only a limited number of cross-neutralizing antibodies have been described to date. Here, Laura Walker, Garrett Rappazzo and colleagues describe broadly neutralizing antibodies (bnAbs) as an attractive opportunity for therapeutic drug engineering to prevent or mitigate future outbreaks of SARS-related CoVs. They demonstrate that bnAbs can provide broad protection *in vivo*.

### Transmission

Atherstone C, Siegel M, Schmitt-Matzen E, et al. **SARS-CoV-2 Transmission Associated with High School Wrestling Tournaments — Florida, December 2020–January 2021.** MMWR Morb Mortal Wkly Rep 2021;70:141–143. DOI: <http://dx.doi.org/10.15585/mmwr.mm7004e4>

December 2020? Too soon for news about SARS-CoV-2 to have spread through Florida, USA. A total of 130 wrestlers, coaches, and referees attended the tournaments. The results: 54 (41,5%) of the 130 tournament attendees received testing, and 38 cases of SARS-CoV-2 infection were identified. The minimum attack rate was 30,2%.

## Prevention

Mack CD, Wasserman EB, Perrine CG, et al. **Implementation and Evolution of Mitigation Measures, Testing, and Contact Tracing in the National Football League, August 9–November 21, 2020.** MMWR Morb Mortal Wkly Rep 2021;70:130–135. DOI: <http://dx.doi.org/10.15585/mmwr.mm7004e2>

Prevention works. This CDC paper is broadly applicable throughout society to limit the spread of the virus, including in settings such as long-term care facilities, schools, and high-density environments.

Lewis D. **COVID-19 rarely spreads through surfaces. So why are we still deep cleaning?** Nature 2021, published 29 January. Full-text: <https://www.nature.com/articles/d41586-021-00251-4>

The coronavirus behind the pandemic can linger on doorknobs and other surfaces, but these aren't a major source of infection.

## Vaccine

Muik A, Wallisch AK, Sanger B, et al. **Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine-elicited human sera.** Science 2021, published 29 January. Full-text: <https://doi.org/10.1126/science.abg6105>

The authors tested SARS-CoV-2-S pseudoviruses bearing either the Wuhan reference strain or the B.1.1.7 lineage spike protein with sera of 40 participants who were vaccinated in a previously reported trial with the Pfizer-BioNTech mRNA-based vaccine Comirnaty. The immune sera had slightly reduced but overall largely preserved neutralizing titers against the B.1.1.7 lineage pseudovirus. These data indicate that the B.1.1.7 lineage will not escape BNT162b2-mediated protection.

Richmond P, Hatchuel L, Dong M, et al. **Safety and immunogenicity of S-Trimer (SCB-2019), a protein subunit vaccine candidate for COVID-19 in healthy adults: a phase 1, randomised, double-blind, placebo-controlled trial.** Lancet 2021, published 29 January. Full-text: [https://doi.org/10.1016/S0140-6736\(21\)00241-5](https://doi.org/10.1016/S0140-6736(21)00241-5)

Ralf Clemens, Peter Richmond and colleagues show that the Clover Biopharmaceuticals SCB-2019 vaccine (comprising S-Trimer protein formulated with either AS03 [GSK] or CpG/Alum adjuvants), elicited robust humoral and cellular immune responses against SARS-CoV-2, with high viral neutralizing activ-

ity. See also comment by Blakney AK, McKay PF. **Next-generation COVID-19 vaccines: here come the proteins.** Lancet 2021, published 29 January. Full-text: [https://doi.org/10.1016/S0140-6736\(21\)00258-0](https://doi.org/10.1016/S0140-6736(21)00258-0)

Callaway E, Mallapaty S. **Novavax offers first evidence that COVID vaccines protect people against variants.** Nature 2021, published 29 January. Full-text: <https://www.nature.com/articles/d41586-021-00268-9>

Novavax's experimental shot is highly effective against the variant identified in Britain – but saw a worrying drop in efficacy against a lineage detected in South Africa.

## Diagnostics

Scholkmann F, Restin T, Ferrari M, Quaresima V. **The Role of Methemoglobin and Carboxyhemoglobin in COVID-19: A Review.** J Clin Med. 2020 Dec 25;10(1):50. PubMed: <https://pubmed.gov/33375707>. Full-text: <https://doi.org/10.3390/jcm10010050>

MetHb and COHb can be elevated in COVID-19 patients and should be checked routinely in order to provide adequate medical treatment, as well as to avoid misinterpretation of fingertip pulse oximetry readings, which can be inaccurate and unreliable in case of elevated MetHb and COHb levels in the blood.

## Spanish

If you read Spanish, read Limón R. **Las otras secuelas de la covid.** El País 2021, published 30 January. Full-text: <https://elpais.com/ciencia/2021-01-29/las-otras-secuelas-de-la-covid.html>

El impacto de la pandemia en la vida cotidiana convierte las rutinas previas en lujos, privilegios y objetos de deseo. La infección genera miedos y altera modelos sociales, laborales y hasta de relaciones sexuales.

## French

If you read French, read Herzberg N. **Covid-19 : Johnson & Johnson annonce le succès de son vaccin à une dose.** Le Monde 2021, published 29 January. Full-text : [https://www.lemonde.fr/planete/article/2021/01/29/covid-19-johnson-amp-johnson-annonce-le-succes-de-son-vaccin-a-une-dose\\_6068150\\_3244.html](https://www.lemonde.fr/planete/article/2021/01/29/covid-19-johnson-amp-johnson-annonce-le-succes-de-son-vaccin-a-une-dose_6068150_3244.html)

Le produit du groupe américain affiche une bonne protection contre les formes sévères et résiste au variant sud-africain, selon des résultats d'essais cliniques qui n'ont pas encore été détaillés ni analysés par des tiers.

## Portugues

If you read Portugues, read **Um guia para as vacinas da covid-19**. Público 2020, published 27 December. Full-text: <https://www.publico.pt/2020/12/27/infografia/guia-vacinas-covid19-548>

A campanha de vacinação em massa contra o coronavírus SARS-CoV-2, que provoca a covid-19, começou em várias partes do mundo. O PÚBLICO preparou um guia sobre que é uma vacina, como funcionam estas armas da medicina e as várias estratégias que se estão a usar.

## 1 February

No Top 10 papers today because we were busy finishing a new chapter. Can you imagine what it will be about? If you are familiar with the topic, you will immediately recognize some of the illustrations in the following preview of the 35 pages. Rendez-vous tomorrow evening.

## 2 February

### Variants

*With viruses, some mutations emerge while others recede. Rarely does one or more mutations confer a “selective advantage” to a new variant, for example enhanced transmissibility. Such variants can then become the new dominant virus.*

### Introduction

Over the last two months, several new SARS-CoV-2 variants have been described that are more transmissible, may escape both natural and vaccine-induced immunity and could impact COVID-19 morbidity and mortality. It is too early to assert that these variants will create a new pandemic within the pandemic, however, in countries like England, South Africa, Brazil, Ireland, Portugal and Israel, they may have modified the dynamic of the latest outbreaks for the worse. More transmissible SARS-CoV-2 variants will replace

older variants – [everywhere!](#) Countries where the prevalence of these new variants is still low should anticipate rapid spread within the next weeks and months and plan ahead accordingly, ie closing/restricting borders, etc.

The current *trio infernale*:

- B117 (first described in England; [Rambaut 2020](#))
- B1351 (first described in South Africa; [Tegally 2020](#))
- P1 (first described in Brazil; [Faria 2021](#))

>>> [More](#)

## 3 February

### Vaccines

#### Paper of the Day

Logunov DY, Dolzhenkova IV, Shcheblyakov DV et al. **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.** *Lancet* 2021, published 2 February. Full-text: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00234-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00234-8/fulltext)

A new entry in the COVID-19 Vaccine Club (CVC): Denis Logunov and colleagues report on the interim clinical efficacy results of the Russian Sputnik V vaccine (rAd26 and rAd5). From 21 days after the first dose of vaccine, 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). The vaccine will help to diversify the world SARS-CoV-2 vaccine pipeline. Welcome to the CVC, Sputnik V!

See also Jones I, Roy P. **Sputnik V COVID-19 vaccine candidate appears safe and effective.** *Lancet* 2021, published 2 February. Full-text: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00191-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00191-4/fulltext)

Krammer F, Srivastava K, PARIS team, Simon V. **Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine.** medRxiv 2021, posted 1 February. Full-text: <https://doi.org/10.1101/2021.01.29.21250653>

Individuals with pre-existing immunity against SARS-CoV-2 need only one dose of vaccine. Consequence: we could spare the second for other people. This is the result of a study by [Florian Krammer](#) and colleagues who provide evidence that the antibody response to the first vaccine dose in individuals with pre-existing immunity is equal to or even exceeds the titers found in naive individuals after the second dose. They also show that the reactogenicity is significantly higher in individuals who were previously infected with SARS-CoV-2. See also Willyard C. **Had Covid? You May Need Only One Dose of Vaccine, Study Suggests.** The New York Times 2021, published 1 February. Full-text: <https://www.nytimes.com/2021/02/01/health/have-you-had-covid-19-coronavirus.html>

Vogel AB, Kanevsky I, Che Y, et al. **Immunogenic BNT162b vaccines protect rhesus macaques from SARS-CoV-2.** Nature. 2021 Feb 1. PubMed: <https://pubmed.gov/33524990>. Full-text: <https://doi.org/10.1038/s41586-021-03275-y>

The people from BioNTech talk about the beginnings of the vaccine developed now in cooperation with Pfizer. This *Nature* paper reports the first antigen-specific immune responses in... mice and rhesus macaques.

## Epidemiology

Public Health England 20210115. **Investigation of novel SARS-COV-2 variant: Variant of Concern 202012/01 – Technical briefing 5.** UK Government 2021, updated 2 February; accessed 2 February 2021. Full-text: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/957504/Variant\\_of\\_Concern\\_VOC\\_202012\\_01\\_Technical\\_Briefing\\_5\\_England.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/957504/Variant_of_Concern_VOC_202012_01_Technical_Briefing_5_England.pdf)

The key messages:

- The spike protein mutation E484K has been detected in 11 B117 sequences (page 17). Preliminary information suggests more than one acquisition event.
- Estimated attack rates for cases with SGTF are 25 - 40% higher than estimated attack rates for cases with S gene detection results and no SGTF for most regions and age groups, excepting groups with few records such as the 80+ age group (page 17).

## Transmission

Vibholm LK, Nielsen SSF, Pahus MH, et al. **SARS-CoV-2 persistence is associated with antigen-specific CD8 T-cell responses.** *Ebiomedicine* 2021, published 1 February. Full-text: <https://doi.org/10.1016/j.ebiom.2021.103230>

No SARS-CoV-2 transmission from individuals that remain SARS-CoV-2 PCR positive by pharyngeal swab weeks after recovery. The authors enrolled 203 post-symptomatic participants with a previous RT-PCR-verified SARS-CoV-2 infection. At time point 1, a median of 23 days (range 15–44) after recovery, 26 individuals (12,8%) were PCR positive. At time point 2, 90 days (median, range 85–105) after recovery, 5 (5,3%) were positive. The persistent PCR positive group however, had SARS-CoV-2-specific CD8 T cell responses of significantly increased breadth and magnitude. Contact tracing among persistent PCR positive individuals revealed zero new COVID-19 diagnoses among 757 close contacts. *Persistent PCR positive individuals are not contagious at the post-symptomatic stage of the infection.*

## Virology

Tegally H, Wilkinson E, Lessels RJ, et al. **Sixteen novel lineages of SARS-CoV-2 in South Africa.** *Nat Med* 2021, published 2 February. Full-text: <https://doi.org/10.1038/s41591-021-01255-3>

SARS-CoV-2 lineages from pre-variant times. **Tulio de Oliveira, Houriiyah Tegally** and colleagues analyzed 1,365 near whole genomes and report the identification of 16 new lineages isolated between March and August 2020. Most lineages had unique mutations that had not been identified elsewhere. The authors show that genomic surveillance can be implemented on a large scale in Africa to identify new lineages and inform measures to control the spread of SARS-CoV-2.

## Diagnostics

Vogels CBF, Breban M, Alpert T, et al. **PCR assay to enhance global surveillance for SARS-CoV-2 variants of concern.** *medRxiv* 2021, posted 1 February. Full-text: <https://doi.org/10.1101/2021.01.28.21250486>

**Nathan Grubaugh, Chantal Vogels** and colleagues identified a deletion in the ORF1a gene (ORF1a  $\Delta$ 3675-3677) in the new “**trio infernale**” variants B117, B1351, and P1, which has not yet been widely detected in other SARS-CoV-2 lineages. Using ORF1a  $\Delta$ 3675-3677 as the primary target and spike  $\Delta$ 69-70 to differentiate, they designed and validated an open source PCR assay to detect

the new variants. The authors assure that their assay can be rapidly deployed in laboratories around the world to enhance surveillance for any local emergence of B117, B1351, P1.

## Press

Wei-Haas M. **Why some coronavirus variants are more contagious—and how we can stop them.** National Geographic 2021, published 27 January. Full-text: <https://www.nationalgeographic.com/science/2021/01/why-some-coronavirus-variants-are-more-contagious/>

In the United Kingdom, variant B.1.1.7 likely drove the region's record-setting spike of COVID-19 cases in January. The variant is now circulating in more than 60 countries, including the United States—and projections suggest it will become the most common virus variety in the US by mid-March.

## Portuguese

If you read Portuguese, read Amaro S, do Carmo I. **Notícias do túnel.** Público 2021, published 29 January. Full-text: <https://www.publico.pt/2021/01/29/sociedade/noticia/noticias-tunel-1947979>

A médica Isabel do Carmo esteve internada dez dias com covid-19 no Hospital de Santa Maria, em Lisboa. Este é o seu testemunho, que é também um alerta e um gesto de reconhecimento.

## 4 February

### Transmission

#### Paper of the Day

Marks M, Millat-Martinez P, Ouchi D, et al. **Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study.** Lancet Infect Dis 2021, published 2 February. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30985-3](https://doi.org/10.1016/S1473-3099(20)30985-3)

*A ground-breaking study!* Oriol Mitjà, Michael Marks and colleagues found that increasing viral load values in nasopharyngeal swabs of patients with COVID-19 were associated with a greater risk of transmission, measured by SARS-CoV-2 PCR positivity among contacts, and with a higher risk of transmission in a household environment compared with other indoor situations. Read also the comment by Cornelissen L. **Understanding the drivers of transmis-**



**sion of SARS-CoV-2.** Lancet Infect Dis 2021, published 2 February. Full-text: [https://doi.org/10.1016/S1473-3099\(21\)00005-0](https://doi.org/10.1016/S1473-3099(21)00005-0)

## Epidemiology

Kissane E, Madrigal A. **It's Time: The COVID Tracking Project Will Soon Come to an End.** The COVID Tracking Project 2021, published 1 February. Full-text: <https://covidtracking.com/analysis-updates/covid-tracking-project-end-march-7>

After a year of collecting, analyzing, and interpreting COVID-19 data for the United States, we're ending our data compilation work in early March. When should *COVID Reference* shut down its activity?

## Prevention

Krammer F. **Pandemic Vaccines: How Are We Going to Be Better Prepared Next Time?** Med (N Y). 2020 Dec 18;1(1):28-32. PubMed: <https://pubmed.gov/33521752>. Full-text: <https://doi.org/10.1016/j.medj.2020.11.004>

We did good, but in the future, we can do better. Discover Florian Krammer's 3-month timeline for developing vaccines against the next pandemic.

## Immunology

Sokal A, Chappert P, Barba-Spaeth G, et al. **Maturation and persistence of the anti-SARS-CoV-2 memory B cell response.** Cell 2021, published 2 February. Full-text: <https://doi.org/10.1016/j.cell.2021.01.050>

Excellent news from France: Matthieu Mahévas, Aurélien Sokal and colleagues longitudinally profiled memory B cells and found remarkable stability of the overall spike-specific memory B cell population up to 6 months after infection. Antigen-driven activation persisted and matured up to 6 months after SARS-CoV-2 infection and may provide long-term protection.

Bolouri H, Speake C, Skibinski D, et al. **The COVID-19 immune landscape is dynamically and reversibly correlated with disease severity.** J Clin Invest 2021, published 1 February. Full-text: <https://www.jci.org/articles/view/143648>

After assessing the immune landscape in longitudinal whole-blood specimens from 59 patients presenting with acute COVID-19, the authors found that the

immune landscape in COVID-19 formed 3 dominant clusters, which correlate with disease severity. They identified coordinated immune alterations accompanying clinical improvement or decline that were also seen in patients who experienced an IL-6 pathway blockade.

Brodin P. **Immune determinants of COVID-19 disease presentation and severity.** Nat Med. 2021 Jan;27(1):28-33. PubMed: <https://pubmed.gov/33442016>. Full-text: <https://doi.org/10.1038/s41591-020-01202-8>

Petter Brodin discusses the current understanding of the immunological determinants of COVID-19 disease presentation and severity and relate this to known immune system differences between young people and old and between men and women, as well as other factors associated with different disease presentations and severity.

Dong J, Zost SJ, Greaney AJ, et al. **Genetic and structural basis for recognition of SARS-CoV-2 spike protein by a two-antibody cocktail.** bioRxiv 2021, posted 28 January. Full-text: <https://doi.org/10.1101/2021.01.27.428529>

James Crowe, Jesse Bloom, Jinhui Dong and colleagues determined the structures of two human monoclonal antibodies COV2-2196 and COV2-2130, which form the basis of the investigational antibody cocktail AZD7442, in complex with the receptor binding domain (RBD) of SARS-CoV-2.

## Vaccine

Saadat S, Rikhtegaran-Tehrani Z, Logue J, et al. **Single Dose Vaccination in Healthcare Workers Previously Infected with SARS-CoV-2.** medRxiv 2021, posted 1 February. Full-text: <https://doi.org/10.1101/2021.01.30.21250843>

The same direction: Healthcare workers (HCW) with prior COVID-19 showed clear secondary antibody responses to vaccination with IgG spike binding titers rapidly increasing by 7 days and peaking by days 10 and 14 post-vaccination. The authors' conclusion: in times of vaccine shortage 1) a single dose of vaccine for patients already having had laboratory-confirmed COVID-19; and 2) patients who have had laboratory-confirmed COVID-19 can be placed lower on the vaccination priority list.

## Treatment

RECOVERY Collaborative Group. **Azithromycin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial.** *Lancet* 2021, published 2 February. Full-text: [https://doi.org/10.1016/S0140-6736\(21\)00149-5](https://doi.org/10.1016/S0140-6736(21)00149-5)

In patients admitted to hospital with COVID-19, azithromycin did not improve survival or other pre-specified clinical outcomes. Azithromycin use in patients admitted to hospital with COVID-19 should be restricted to patients in whom there is a clear antimicrobial indication. Read also the comment by Berwanger O. **Azithromycin, RECOVERY, and the power of large, simple trials.** *Lancet* 2021, published 2 February. Full-text: [https://doi.org/10.1016/S0140-6736\(21\)00307-X](https://doi.org/10.1016/S0140-6736(21)00307-X)

## 5 February

### Transmission

#### Paper of the Day

Letizia AG, Ge Y, Vangeti S, et al. **SARS-CoV-2 seropositivity and subsequent infection risk in healthy young adults: a prospective cohort study.** medRxiv 2021, posted 29 January. Full-text: <https://doi.org/10.1101/2021.01.26.21250535>

High transmission rate in a US Marine camp despite a 2-week home quarantine plus another 2-week quarantine at the camp. Would you have placed a bet on a 48% transmission rate after another 6 weeks (1079 out of 2247 young recruits)? The authors caution that “the crowded living conditions, demanding regimen and requirement for personal contact during basic training despite the pandemic leads not only to an increased risk for respiratory epidemics, but also potentially to higher exposure levels. The close quarters and constant contact among recruits that are needed for team building allows a viral infection to rapidly proliferate within a unit. The physically and mentally demanding training environment may also suppress immunity. These conditions may contribute to the high infection rate we observed during the six-week study period. These factors are not typically present in the civilian community.”

The worst is yet to come, though. A total of 19 out of 189 (10.1%, 1.1 cases per person-year) **initially seropositive** participants had at least one positive SARS-CoV-2 PCR result during the six-week study period. In other words: in

crowded living conditions, the re-infection rate with SARS-CoV-2 can be quite high. Bad news for ‘herd immunologists’.

## Epidemiology

Monod M, Blenkinsop A, Xi X, et al. **Age groups that sustain resurging COVID-19 epidemics in the United States.** Science. 2021 Feb 2:eabe8372. PubMed: <https://pubmed.gov/33531384>. Full-text: <https://doi.org/10.1126/science.abe8372>

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 at least 65 / 100 COVID-19 infections originate from individuals aged 20-49 in the US.

## Virology

McCarthy KR, Rennick LJ, Nambulli S, et al. **Recurrent deletions in the SARS-CoV-2 spike glycoprotein drive antibody escape.** Science 2021, published 3 January. Full-text: <https://science.sciencemag.org/content/early/2021/02/02/science.abf6950>

Coronaviruses acquire substitutions (variants) more slowly than other RNA viruses, due to a proofreading polymerase. In the spike glycoprotein, we find recurrent deletions overcome this slow substitution rate. In this *adaptive evolution* class, Paul Duprex, Kevin McCarthy and colleagues explain that deletion variants transmit efficiently, and are present in novel lineages, including those of current global concern. Deletions frequently occupy recurrent deletion regions (RDRs), which map to defined antibody epitopes. Deletions in RDRs confer resistance to neutralizing antibodies.

## Immunology

Collier D, De Marco A, Ferreira I, et al. **SARS-CoV-2 B.1.1.7 escape from mRNA vaccine-elicited neutralizing antibodies.** medRxiv 2021, posted 2 February. Full-text: <https://doi.org/10.1101/2021.01.19.21249840>

Ravindra Gupta, Dami Collier and colleagues assess immune responses following vaccination with mRNA-based vaccine BNT162b2. They measured neutralising antibody responses following a single immunization using pseudoviruses expressing the wild type Spike protein or the 8 mutations found in the B117 Spike protein. The vaccine sera exhibited a broad range of neutralizing titers against the wild type pseudoviruses that were modestly reduced against

B117. Introduction of the E484K mutation led to a more substantial loss of neutralizing activity by vaccine-elicited antibodies over that conferred by the B117 mutations alone.

## Vaccines

Voysey M, Costa Clemens SA, Madhi SA, et al. **Single Dose Administration, And The Influence Of The Timing Of The Booster Dose On Immunogenicity and Efficacy Of ChAdOx1 nCoV-19 (AZD1222) Vaccine.** *Lancet Preprints* 2021, posted 1 February. Full-text: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3777268](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268)

Andrew Pollard, Sarah Gilbert, Merryn Voysey and colleagues present data from Phase III efficacy trials of ChAdOx1 nCoV-19 in the United Kingdom and Brazil, and Phase I/II clinical trials in the UK and South Africa. They report that vaccine efficacy after a single standard dose of vaccine from day 22 to day 90 post vaccination was 76% (59%, 86%), and that protection did not wane during this initial 3-month period. The authors conclude that vaccination programs aimed at vaccinating a large proportion of the population with a single dose, with a second dose given after a 3 month period is an effective strategy for reducing disease, and may be optimal for rollout of a pandemic vaccine when supplies are limited.

Wu Z, Hu Y, Xu M, et al. **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.** *Lancet Infect Dis* 2021, published 3 February. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30987-7](https://doi.org/10.1016/S1473-3099(20)30987-7)

Weidong Yin, Yuliang Zhao, Zhiwei Wu and colleagues report the results of Sinovac's CoronaVac safety and immunogenicity data in adults aged 60 years or older (previous publications: [Zhang Y 2020](#), [Gao 2020](#)). Reminder: CoronaVac™ is an inactivated virus vaccine. On 12 January, the government of São Paulo, Brazil, announced the overall effectiveness of the Sinovac vaccine to be **50,38%**. The data was obtained with tests carried out on 12,508 volunteers in the country, all health professionals. According to a report of *The New York Times* ([7 January](#)), Sinovac has sold more than 300 million doses, mostly to low- and middle-income countries, accounting for about half of the total production of Sinovac. See also [COVID Reference Vaccines](#).

Gerberding JL, Haynes BF. **Vaccine Innovations — Past and Future.** *N Engl J Med* 2021; 384:393-396. Full-text: Full-text: <https://doi.org/10.1056/NEJMp2029466>

A 4-page overview by Julie Gerberding and Barton Haynes. The authors anticipate that the future holds great promise for vaccine-mediated control of global pathogens but providing affordable access to effective vaccines for everyone who could benefit from them remains an important challenge. Difficulties facing vaccinologists now include

- predicting the type and timing of the next pandemic;
- developing vaccines to combat rapidly changing pathogens such as HIV-1, influenza, and multidrug-resistant bacteria;
- and establishing rapid-response strategies to control emerging and reemerging infectious diseases.

## Treatment

Blanchard EL, Vanover D, Bawage SS, et al. **Treatment of influenza and SARS-CoV-2 infections via mRNA-encoded Cas13a in rodents.** *Nat Biotechnol* 2021, published 3 February. Full-text: <https://doi.org/10.1038/s41587-021-00822-w>

Cas13 treatment for influenza and SARS-CoV-2? In this study, Philip Santangelo, Chiara Zurla, Emmeline L. Blanchard and colleagues used messenger RNA (mRNA)-encoded Cas13a for mitigating influenza virus A and SARS-CoV-2 infection in mice and hamsters, respectively. In mice, Cas13a degraded influenza RNA in lung tissue efficiently when delivered after infection, whereas in hamsters, Cas13a delivery reduced SARS-CoV-2 replication and reduced symptoms.

## 6 February

### Virology

#### Paper of the Day

Kemp SA, Collier DA, Datir RP, et al. **SARS-CoV-2 evolution during treatment of chronic infection.** *Nature* 2021, published 5 February. Full-text: <https://www.nature.com/articles/s41586-021-03291-y>

In immune-suppressed patients, convalescent plasma therapy may lead to the emergence of viral variants with evidence of reduced susceptibility to neu-

tralizing antibodies. Here, Ravinda Gupta, Steven Kemp and colleagues demonstrate that convalescent plasma therapy led to large, dynamic virus population shifts, with the emergence of a dominant viral strain bearing D796H in S2 and  $\Delta$ H69/ $\Delta$ V70 in the S1 N-terminal domain NTD of the Spike protein.

## Epidemiology

Quammen D. **How viruses shape our world** - COVID-19 is a reminder of their destructive power, but they're crucial to humans' development and survival. National Geographic 2021, published 14 January. Full-text: <https://www.nationalgeographic.com/magazine/2021/02/viruses-can-cause-great-harm-but-we-could-not-live-without-them-feature/>

“Although feared as agents of disease, viruses also work wonders, shaping evolution from the very beginning. About 8 percent of our DNA comes from viruses that infected our long-ago ancestors and patched viral genes into their genomes. Some of these genes now play crucial roles in the early stages of the developing embryo and the placenta that surrounds this 13-week-old fetus.”

Bruckner TA, Parker DM, Bartell SM, et al. **Estimated seroprevalence of SARS-CoV-2 antibodies among adults in Orange County, California**. Sci Rep 11, 3081 (2021). Full-text: <https://doi.org/10.1038/s41598-021-82662-x>

In Orange County, a densely populated and diverse county in southern California, the SARS-CoV-2 seroprevalence in July and August 2020 may have been approximately 12 percent, seven-fold greater than the reported cases.

## Transmission

Madera S, Crawford E, Langelier C, et al. **Nasopharyngeal SARS-CoV-2 viral loads in young children do not differ significantly from those in older children and adults**. Sci Rep 11, 3044 (2021). Full-text: <https://doi.org/10.1038/s41598-021-81934-w>

This study of 5544 children and adults did not demonstrate higher nasopharyngeal viral loads in children under five years of age.

## Immunology

Ren X, Wen W, Fan X, et al. **COVID-19 immune features revealed by a large-scale single cell transcriptome atlas**. Cell 2021, published 3 February. Full-text: [https://www.cell.com/cell/fulltext/S0092-8674\(21\)00148-3](https://www.cell.com/cell/fulltext/S0092-8674(21)00148-3)

Zemin Zhang, Xianwen Ren and colleagues applied single-cell RNA sequencing to 284 samples from 196 COVID-19 patients and controls and created a comprehensive immune landscape with 1,46 million cells. The authors found SARS-CoV-2 RNAs in diverse epithelial and immune cell types, accompanied by dramatic transcriptomic changes within viral positive cells. Systemic up-regulation of S100A8/A9, mainly by megakaryocytes and monocytes in the peripheral blood, might contribute to the cytokine storms observed in severe COVID-19.

## Vaccine

Rossmann H, Shilo S, Meir T, Gorfine M, Shalit U, Segal E. **Patterns of covid-19 pandemic dynamics following deployment of a broad national immunization program**. GitHub 2021, posted 3 February. Full-text: <http://bit.ly/36KhjOU>

SARS-CoV-2 vaccines work under real-world conditions. Eran Segal, Hagai Rossmann and colleagues show that there was a 41% drop in COVID-19 infections in people aged 60 or older from mid-January to early February. During the same period, there was also a 31% drop in hospitalizations (Rossmann 2021, Figure 11). In people aged 59 and younger who received the vaccine later, cases dropped by only 12% and hospitalizations by 5%.

## Diagnostics

Teo AKJ, Choudhury Y, Tan IB, et al. **Saliva is more sensitive than nasopharyngeal or nasal swabs for diagnosis of asymptomatic and mild COVID-19 infection**. Sci Rep 11, 3134 (2021). Full-text: <https://doi.org/10.1038/s41598-021-82787-z>

Li Yang Hsu, Alvin Kuo Jing Teo and colleagues recruited 200 subjects, of which 91 and 46 were tested twice and thrice respectively. In total, 62,0%, 44,5%, and 37,7% of saliva, nasopharyngeal (NP) swab and self-administered nasal (SN) swab samples were positive. The percentage of test-positive saliva was higher than NP and SN swabs. The authors conclude that saliva is an alternative sample for COVID-19 screening and diagnosis.



Du Z, Pandey A, Bai Y, et al. **Comparative cost-effectiveness of SARS-CoV-2 testing strategies in the USA: a modelling study.** *Lancet Public Health* 2021, published 4 February. Full-text: [https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667\(21\)00002-5/fulltext](https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(21)00002-5/fulltext)

In communities where the virus is spreading rapidly, weekly testing coupled with a 2-week isolation period after a positive test is advisable. Where non-pharmacological measures are substantially curtailing the spread of the virus, monthly testing with a 1-week isolation period after a positive test is expected to be the most optimal strategy, according to this paper.

## Clinical

Tesoriero JM, Swain CE, Pierce JL, et al. **COVID-19 Outcomes Among Persons Living With or Without Diagnosed HIV Infection in New York State.** *JAMA Netw Open.* 2021 Feb 1;4(2):e2037069. PubMed: <https://pubmed.gov/33533933>. Full-text: <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2775827>

Persons living with diagnosed HIV might experience poorer COVID-related outcomes relative to persons living without diagnosed HIV. In this study, previous HIV diagnosis was associated with higher rates of severe disease requiring hospitalization, and hospitalization risk increased with progression of HIV disease stage. Hospitalization risk increased with disease progression to HIV stage 2 (aRR, 1,29 [95% CI: 1,11-1,49]) and stage 3 (aRR, 1,69 [95% CI: 1,38-2,07]) relative to stage 1.

## Treatment

Hoertel N, Sánchez-Rico M, Vernet R, et al. **Association between antidepressant use and reduced risk of intubation or death in hospitalized patients with COVID-19: results from an observational study.** *Mol Psychiatry* (2021). Full-text: <https://doi.org/10.1038/s41380-021-01021-4>

Antidepressant use could be associated with lower risk of death or intubation in patients hospitalized for COVID-19. This is the result of an observational study which included 7230 adults hospitalized for COVID-19, 345 patients of whom (4.8%) received an antidepressant within 48 h of hospital admission. Nicolas Hoertel et al. report a reduced risk of intubation or death (HR, 0.56; 95% CI, 0.43–0.73,  $p < 0.001$ ). Next step: controlled randomized clinical trials.

## Education

Thompson B, Baker N, Maxmen A. **Coronapod: Variants – what you need to know.** Nature Podcast 2021, published 5 February. Link: <https://www.nature.com/articles/d41586-021-00320-8>

Around the world, concern is growing about the impact that new, faster-spreading variants of the SARS-CoV-2 virus could have on the pandemic. In this episode of Coronapod, the authors discuss what these variants are, and the best way to respond to them, in the face of increasing evidence that some can evade the immunity produced by vaccination or previous infection.

## Media

BBC Sound. **The Shapeshifting Virus.** BBC 2021, published 30 January. Audio, 52:59. Link: <https://www.bbc.co.uk/sounds/play/w3ct205h>

News that at least three new variants of SARS-CoV-2 have emerged in three separate continents have sent a chill throughout the scientific community. All viruses mutate but the speed and scale of the changes and the fact they occurred independently, is seen as a wake-up call.

## 7 February

### Vaccine

#### Paper of the Day

Aran D. **Estimating real-world COVID-19 vaccine effectiveness in Israel.** GitHub 2021, posted 4 February. Full-text: [https://github.com/dviraran/covid\\_analyses/blob/master/Aran\\_letter.pdf](https://github.com/dviraran/covid_analyses/blob/master/Aran_letter.pdf)

This unpublished non-peer reviewed study suggests that the Pfizer-BioNTech vaccine might be between 66%-83% effective at preventing infection in individuals 60 years and older, 76-85% in those younger than 60 years, and 87-96% effective in preventing severe cases.

Emary KRW, Golubchik T, Aley PK, et al. **Efficacy of ChAdOx1 nCoV-19 (AZD1222) Vaccine Against SARS-CoV-2 VOC 202012/01 (B.1.1.7).** Lancet Preprints 2021, posted 4 February. Full-text: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3779160](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3779160)

This unpublished non-peer reviewed study by Andrew Pollard, Katherine Emary and colleagues reports that among participants in Phase II/III ChA-

dOx1 studies who had been infected with B117, vaccine efficacy against symptomatic SARS-CoV-2 infection was similar for B117 and non-B117 lineages (74,6% [95% CI: 41,6-88,9] and 84% [95% CI: 70,7-91,4], respectively). Importantly, virus neutralization activity by vaccine-induced antibodies was 9-fold lower against B117 than against a canonical non-B117 lineage.

## Epidemiology

Kamps BS. **Variants – 6 February update.** COVID Reference 2021, published 6 February. Full-text: <https://covidreference.com/variants> | See also the Comparison document with new additions between 31 January and 6 February: [http://www.bsk1.com/CR\\_Variants\\_Update.html](http://www.bsk1.com/CR_Variants_Update.html)

In many countries, the more transmissible SARS-CoV-2 variants B117, B1351 and P1 are currently replacing previously dominating lineages. B117, B1351 and P1 are already dominant in England (B117), South Africa (B1351) and Amazonia (P1). They also account for 50% or more of new infections in Ireland, Portugal and Israel (B117). Over the coming weeks, B117 will spread through most countries in continental Europe and the US.

## Comorbidities

Haarhaus M, Santos C, Haase M, et al. **Risks prediction of COVID-19 incidence and mortality in a large multi-national haemodialysis cohort: Implications for management of the pandemic in outpatient haemodialysis settings.** Clin Kidney J 2021, published 5 February. Full-text: <https://doi.org/10.1093/ckj/sfab037>

Outcomes in 38.256 hemodialysis (HD) patients from a multi-national dialysis cohort between March 3<sup>rd</sup> and July 3<sup>rd</sup> 2020. During the observational period, 1259 patients (3,3%) acquired COVID-19. Of these, 62% were hospitalized or died. Mortality was 22% among COVID-19 patients.

Graphical abstract:

Sultanian P, Lundgren P, Strömsöe A, et al. **Cardiac arrest in COVID-19: characteristics and outcomes of in- and out-of-hospital cardiac arrest. A report from the Swedish Registry for Cardiopulmonary Resuscitation.** Eur Heart J. 2021 Feb 5:ehaa1067. PubMed: <https://pubmed.gov/33543259>. Full-text: <https://doi.org/10.1093/eurheartj/ehaa1067>

Pedram Sultanian and colleagues studied out-of-hospital cardiac arrest (OHCA) and in-hospital cardiac arrest (IHCA) of all patients reported to the

Swedish Registry for Cardiopulmonary Resuscitation from 1 January to 20 July 2020. During the pandemic phase, COVID-19 was involved in at least 10% of all OHCA and 16% of IHCA, and, among COVID-19 cases, 30-day mortality was increased 3,4-fold in OHCA and 2,3-fold in IHCA.

Graphical abstract:

## Pediatrics

Ouldali N, Toubiana J, Antona D, et al. **Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children.** JAMA. 2021 Feb 1. PubMed: <https://pubmed.gov/33523115>. Full-text: <https://doi.org/10.1001/jama.2021.0694>

Among children with multi-system inflammatory syndrome in children (MIS-C), treatment with intravenous immunoglobulins (IVIG) and methylprednisolone vs IVIG alone might be associated with a more favorable fever course. This is the suggestion of a retrospective cohort study of 111 children with suspected MIS-C. **François Angoulvant**, Naïm Ouldali and colleagues report that 3 of 34 children (9%) in the IVIG and methylprednisolone group and 37 of 72 (51%) in the IVIG alone group did not respond to treatment. The combination therapy would also be associated with less severe acute complications, including acute left ventricular dysfunction and hemodynamic support requirement.

## Collateral Effects

Abbott A. **COVID's mental-health toll: how scientists are tracking a surge in depression.** Nature 2021, published 3 February. Full-text: <https://www.nature.com/articles/d41586-021-00175-z>

Researchers are using huge data sets to link changes in mental health to coronavirus response measures.

## 8 February

### Variants

#### Paper of the Day

Washington NL, Gangavarapu K, Zeller M, et al. **Genomic epidemiology identifies emergence and rapid transmission of SARS-CoV-2 B.1.1.7 in the United States.** medRxiv 2021, posted 7 February. Full-text: <https://www.medrxiv.org/content/10.1101/2021.02.06.21251159v1>

Kristian Andersen, Nicole L. Washington, Karthik Gangavarapu and colleagues from Helix and the Scripps Research Institute, La Jolla, sequenced 212 B117 genomes collected in the U.S. from December 2020 to January 2021. They found a doubling rate of a little over a week and an increased transmission rate of 35-45%. The authors show that the U.S. is on a similar trajectory as other countries where B117 rapidly became the dominant SARS-CoV-2 variant and warn that immediate and decisive action to minimize COVID-19 morbidity and mortality. Authorities in Germany, France, Italy, Spain and other countries should listen too.

### Vaccine

#### News from Oxford

University of Oxford 20210207. **ChAdOx1 nCov-19 provides minimal protection against mild-moderate COVID-19 infection from B.1.351 coronavirus variant in young South African adults.** University of Oxford 2021, published 7 February. Full-text: <https://www.ox.ac.uk/news/2021-02-07-chadox1-ncov-19-provides-minimal-protection-against-mild-moderate-covid-19-infection>

In an analysis, submitted as a pre-print prior to peer-review publication, a two-dose regimen of the ChAdOx1 nCoV-19 vaccine provides minimal protection against mild-to-moderate COVID-19 infection from the B1351 coronavirus variant first identified in South Africa.

### Epidemiology

Mohanam M, Malani A, Krishnan K, Acharya A. **Prevalence of SARS-CoV-2 in Karnataka, India.** JAMA. 2021 Feb 4. PubMed: <https://pubmed.gov/33538774>. Full-text: <https://doi.org/10.1001/jama.2021.0332>

The adjusted seroprevalence of SARS-CoV-2 across **Karnataka**, India, was 46,7%, suggesting approximately 31,5 million residents were infected, far greater than the 327.076 cases reported by August 29, 2020.

Gaudart J, Landier J, Huiart L, et al. **Factors associated with the spatial heterogeneity of the first wave of COVID-19 in France: a nationwide geo-epidemiological study.** Lancet Public Health 2021, published 5 February. Full-text: [https://doi.org/10.1016/S2468-2667\(21\)00006-2](https://doi.org/10.1016/S2468-2667(21)00006-2)

From March 19 to May 11, 2020, hospitals in metropolitan France notified a total of 100.988 COVID-19 cases, including 16.597 people who were admitted to intensive care and 17.062 deaths. Mortality and case fatality rates were higher in regions with older populations. Jean Gaudart et al. found no association between climate and in-hospital COVID-19 incidence, or between economic indicators and in-hospital COVID-19 incidence or mortality rates.

Roederer T, Mollo B, Vincent C, et al. **Seroprevalence and risk factors of exposure to COVID-19 in homeless people in Paris, France: a cross-sectional study.** Lancet Public Health 2021, published 5 February. Full-text: [https://doi.org/10.1016/S2468-2667\(21\)00001-3](https://doi.org/10.1016/S2468-2667(21)00001-3)

During the COVID-19 lockdown period from March 17 to May 11, 2020, French authorities in Paris and its suburbs relocated people experiencing recurrent homelessness to emergency shelters, hotels, and large venues. In this study by Thomas Roederer et al., more than half of surveyed individuals (426 of 818, 52%) tested positive by any serological test. Seroprevalence was highest among those living in workers' residences (88,7%), followed by emergency shelters (50,5%), and food distribution sites (27,8%). More than two thirds of COVID-19 seropositive individuals (68%) did not report any symptoms during the recall period. Living in crowded conditions was the strongest factor associated with exposure level. This study underscores the importance of providing safe, uncrowded accommodation, alongside adequate testing and public health information.

## Immunology

Koutsakos M, Rowntree LC, Hensen L, et al. **Integrated immune dynamics define correlates of COVID-19 severity and antibody responses.** Cell Rep Med 2021, published 4 February. Full-text: [https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791\(21\)00019-7](https://www.cell.com/cell-reports-medicine/fulltext/S2666-3791(21)00019-7)

Katherine Kedzierska, Marios Koutsakos and colleagues provide a comprehensive map of longitudinal immunological responses in COVID-19 patients. ICU patients with severe COVID-19 displayed higher levels of soluble IL-6, IL-6R, IL-18, and hyperactivation of innate, adaptive and myeloid compartments than patients with moderate disease.

## Treatment

Feld JJ, Kandel C, Biondi MJ, et al. **Peginterferon lambda for the treatment of outpatients with COVID-19: a phase 2, placebo-controlled randomised trial.** *Lancet Respir Dis* 2021, published 5 February. Full-text: [https://doi.org/10.1016/S2213-2600\(20\)30566-X](https://doi.org/10.1016/S2213-2600(20)30566-X)

Interferon lambda-1 is a type III interferon involved in innate antiviral responses with activity against respiratory pathogens. Here, Jordan Feld et al. randomly assigned (1:1) 30 patients to a single subcutaneous injection of peg-interferon lambda 180 µg or placebo within 7 days of symptom onset or first positive swab if asymptomatic. Of those with baseline viral load above 10<sup>6</sup> copies per mL, 15 (79%) of 19 patients in the peg-interferon lambda group had undetectable virus on day 7, compared with six (38%) of 16 in the placebo group (OR 6,25 [95% CI: 1,49–31,06]; p = 0,012).

## Collateral Effects

Dorward J, Khubone T, Gate K, et al. **The impact of the COVID-19 lockdown on HIV care in 65 South African primary care clinics: an interrupted time series analysis.** *Lancet HIV* 2021, published 4 February. Full-text: [https://doi.org/10.1016/S2352-3018\(20\)30359-3](https://doi.org/10.1016/S2352-3018(20)30359-3)

The study describes the impact of the 2020 national COVID-19 lockdown on HIV testing and treatment in *KwaZulu-Natal*, South Africa, where 1,7 million people are living with HIV. While antiretroviral therapy (ART) provision was generally maintained, HIV testing and ART initiations were heavily impacted.

## Spanish

If you read Spanish, read Gorospe P, Linde P, Catalán N, Sevillano EG. **Arquitectura de un supercontagio: cómo el virus se instaló dos semanas en un edificio de Bilbao.** *El País* 2021, published 7 February. Full-text: <https://elpais.com/sociedad/2021-02-06/arquitectura-de-un-supercontagio-como-el-virus-se-instalo-dos-semanas-en-un-edificio-de-bilbao.html>

Varios expertos creen que los dos ascensores de un bloque de viviendas del barrio de Santutxu aceleraron un brote letal con 33 infectados, cinco de los cuales fallecieron.

## French

If you read French, read Dagorn G. **Grippe, gastro ou bronchite : les mesures anti-Covid-19 ont éteint presque toutes les autres épidémies hivernales.** Le Monde 2021, published 7 February. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2021/02/07/grippe-gastro-bronchite-les-mesures-anti-covid-19-ont-permis-d-eviter-les-epidemies-saisonnieres\\_6069066\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2021/02/07/grippe-gastro-bronchite-les-mesures-anti-covid-19-ont-permis-d-eviter-les-epidemies-saisonnieres_6069066_4355770.html)

Lavage des mains, port du masque et distanciation physique ont considérablement réduit le niveau de circulation des virus saisonniers habituels.

Berthou E. « **Psychologiquement déstabilisante, la pandémie de Covid-19 a renforcé le complotisme** ». Le Monde 2021, published 7 February. Full-text :

[https://www.lemonde.fr/sciences/article/2021/02/06/psychologiquement-destabilisante-la-pandemie-a-renforce-le-complotisme\\_6069040\\_1650684.html](https://www.lemonde.fr/sciences/article/2021/02/06/psychologiquement-destabilisante-la-pandemie-a-renforce-le-complotisme_6069040_1650684.html)

Un cerveau intuitif, peu porté sur l'analyse, adhère à des croyances infondées qui font le lit des théories du complot. Thierry Ripoll, chercheur en psychologie cognitive, dissèque ce mécanisme dans « Pourquoi croit-on ? ».

Charrel M. **La pandémie de Covid-19 creuse le fossé en Europe, entre le Sud dépendant du tourisme et le Nord.** Le Monde 2021, published 7 February. Full-text : [https://www.lemonde.fr/economie/article/2021/02/07/la-pandemie-de-covid-19-creuse-l-ecart-economique-entre-le-sud-et-le-nord-de-l-europe\\_6069060\\_3234.html](https://www.lemonde.fr/economie/article/2021/02/07/la-pandemie-de-covid-19-creuse-l-ecart-economique-entre-le-sud-et-le-nord-de-l-europe_6069060_3234.html)

Tous les pays de la zone euro ne sont pas affectés de la même façon par la crise sanitaire. Les déséquilibres déjà existants entre l'Italie, le Portugal, l'Espagne ou la Grèce, et un Nord plus industriel, sont exacerbés.



## 9 February

### Vaccine

#### Paper of the Day

Levine-Tiefenbrun M, Yelin I, Katz R, et al. **Decreased SARS-CoV-2 viral load following vaccination.** MedRxiv 2021, posted 8 February. Full-text: <https://www.medrxiv.org/content/10.1101/2021.02.06.21251283v1>

Roy Kishony, Matan Levine-Tiefenbrun and colleagues analyzed **positive** SARS-CoV-2 test results following the first shot of the Pfizer-BioNTech vaccine. They found that the viral load is reduced 4-fold for infections occurring 12-28 days after the first dose of vaccine. These reduced viral loads might hint to lower infectiousness, further contributing to vaccine impact on virus spread.

Xie X, Liu Y, Liu J, et al. **Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K and N501Y variants by BNT162b2 vaccine-elicited sera.** Nat Med 2021, published 8 February. Full-text: <https://www.nature.com/articles/s41591-021-01270-4>

In this *in vitro* study, the neutralization GMT of the serum panel against a virus with three mutations from the variant first detected in South Africa (E484K + N501Y + D614G) was slightly lower than the neutralization GMTs against a N501Y virus or a virus with three mutations from the UK variant ( $\Delta$ 69/70 + N501Y + D614G). The authors tested a panel of human sera from 20 participants in the Pfizer-BioNTech vaccine trial, drawn 2 or 4 weeks after immunization with two 30- $\mu$ g doses of Comirnaty spaced 3 weeks apart.

### Variants

Althaus C, et al. **Transmission of SARS-CoV-2 variants in Switzerland.** Institute of Social and Preventive Medicine (ISPM), University of Bern 2021, reported 5 February. Full-text: <https://ispmbern.github.io/covid-19/variants/>

For 5 February, the authors estimated the proportion of SARS-CoV-2 variants (501Y, B.1.1.7) to have reached 67% in Geneva and 35% in Zurich. They also estimated the increase in transmissibility slightly above 50%.

## Epidemiology

Davies N, Abbott S, Barnard C, et al. **Estimated transmissibility and severity of novel SARS-CoV-2 Variant of Concern 202012/01 in England.** CMMID Repository 2021, updated 6 February. Full-text: <https://cmmid.github.io/topics/covid19/uk-novel-variant.html?s=09>

The authors estimate that B117 is 43–82% (range of 95% credible intervals 38–106%) more transmissible than pre-existing variants of SARS-CoV-2. We find that without stringent control measures, COVID-19 hospitalizations and deaths are projected to reach higher levels in 2021 than were observed in 2020. Control measures of a similar stringency to the national lockdown implemented in England in November 2020 would be unlikely to reduce the effective reproduction number  $R_t$  to less than 1, unless primary schools, secondary schools, and universities are also closed.

## Virology

Ozono S, Zhang Y, Ode H, et al. **SARS-CoV-2 D614G spike mutation increases entry efficiency with enhanced ACE2-binding affinity.** Nat Commun 12, 848 (2021). Full-text: <https://www.nature.com/articles/s41467-021-21118-2>

The D614G mutation increases cell entry by acquiring higher affinity to ACE2. The mutation does not affect neutralization by antisera against prototypic viruses.

## Immunology

Hoagland DA, Møller R, Uhl SA. **Leveraging the antiviral type-I interferon system as a first line defense against SARS-CoV-2 pathogenicity.** Immunity 2021, published 29 January. Full-text: [https://www.cell.com/immunity/fulltext/S1074-7613\(21\)00040-6](https://www.cell.com/immunity/fulltext/S1074-7613(21)00040-6)

A longitudinal hamster cohort revealed a wave of inflammation including a Type-I interferon (IFN-I) response that was evident in all tissues regardless of viral presence but was insufficient to prevent disease progression. Bolstering the antiviral response with intranasal administration of recombinant IFN-I reduced viral disease, prevented transmission, and lowered inflammation *in vivo*. The authors conclude that intranasal IFN-I might be an effective means of early treatment.

Valenzuela Nieto G, Jara R, Watterson D, et al. **Potent neutralization of clinical isolates of SARS-CoV-2 D614 and G614 variants by a monomeric, sub-nanomolar affinity nanobody.** *Sci Rep* 11, 3318 (2021). Full-text: <https://www.nature.com/articles/s41598-021-82833-w>

The authors describe a novel simple method for the selection of nanobodies from *E. coli* bacterial display libraries, resulting in the selection of 30 nanobodies. They demonstrate that the nanobody W25 can recognize full-length Spike and RBD protein by ELISA and therefore predict that it might be suitable as a diagnostic reagent.

## Long COVID

Raven K. **Long-COVID – the nightmare that won’t end – a researcher’s first hand perspective.** Peacock Lab 2021, published 6 February. Full-text: <https://professorsharonpeacock.co.uk/long-covid-the-nightmare-that-wont-end-a-first-hand-perspective>

“I’ve given an account of my own experience with long COVID, which I hope will help to raise awareness of this debilitating illness, but it’s estimated there could be 300.000 other sufferers in the UK (3), with more joining those ranks every day. Some features are shared with others, others differ. But I think for all of us recognition, help, and research are key. And we need them desperately.”

## 10 February

### Virology

#### Paper of the Day

Greaney AJ, Loes AN, Crawford KHD, et al. **Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies.** *Cell* 2021, 8 February. Full-text: [https://www.cell.com/cell-host-microbe/fulltext/S1931-3128\(21\)00082-2](https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00082-2)

Five weeks after the [pre-print paper](#), now the publication in *Cell Host Microbe*. Jesse Bloom, Allison Greaney and colleagues comprehensively map how all mutations to the spike’s receptor-binding domain (RBD) reduce binding by antibodies in convalescent plasma. One major finding is that serum antibody binding is predominantly affected by mutations at just a few dominant epitopes in the RBD. The most important site is E484, where neutraliza-

tion by some sera is reduced > 10-fold by several mutations. The authors' approach doesn't just consist in reactively characterizing mutations they observe in new lineages; rather, they prospectively map effects of all mutations so we can watch out for the next ones. Their bet for the future? The 443-450 loop in RBD, for example G446.

## Epidemiology

Zeller M, Gangavarapu K, Anderson C, et al. **Emergence of an early SARS-CoV-2 epidemic in the United States.** medRxiv 2021, posted 8 February. Full-text: <https://www.medrxiv.org/content/10.1101/2021.02.05.21251235v1>

Superspreading during large-scale events plays a key role in the COVID-19 pandemic. The city of New Orleans, US, experienced one of the earliest and fastest accelerating outbreaks, coinciding with the annual Mardi Gras festival, which went ahead without precautions. Here, Kristian G. Andersen, Mark Zeller and colleagues sequence SARS-CoV-2 genomes during the first wave of the COVID-19 epidemic in Louisiana. They show that the Mardi Gras festival (25 Feb 2020 and the weeks leading up to it) dramatically accelerated transmission, eventually leading to secondary localized COVID-19 epidemics throughout the Southern US.

Staub K, Jüni P, Urner M, et al. **Public Health Interventions, Epidemic Growth, and Regional Variation of the 1918 Influenza Pandemic Outbreak in a Swiss Canton and Its Greater Regions.** Ann Intern Med. 2021 Feb 9. PubMed: <https://pubmed.gov/33556268>. Full-text: <https://doi.org/10.7326/M20-6231>

Strikingly similar patterns were found in the management of the COVID-19 outbreak in Switzerland, with a considerably higher amplitude and prolonged duration of the second wave and much higher associated rates of hospitalization and mortality. During the second wave in autumn, cantonal authorities reacted hesitantly and initially delegated the responsibility to enact public health measures to the municipalities. This hesitant attitude was largely due to concerns about the economic effect of public health interventions experienced during the first wave and the associated political pressure. Read also the comment by Mooney G. **The Dangers of Ignoring History Lessons During a Pandemic.** Ann Intern Med. 2021 Feb 9. PubMed: <https://pubmed.gov/33556270>. Full-text: <https://doi.org/10.7326/M21-0449>

## Vaccine

Petter E, Mor O, Zuckermann N, et al. **Initial real world evidence for lower viral load of individuals who have been vaccinated by BNT162b2.** GitHub 2021, posted 7 February. Full-text: <http://bit.ly/3aPIeTS>

Vaccination with Pfizer-BioNTech's Comirnaty could reduce the viral load by 1.6x to 20x in individuals who are positive for SARS-CoV-2. This estimate might improve after more individuals receive the second dose. Yaniv Erlich, Ella Petter and colleagues conclude that their findings indicate vaccination is not only important for an individual's protection but can also reduce transmission.

Stamatatos L, Czartoski J, Wan YH, et al. **Antibodies elicited by SARS-CoV-2 infection and boosted by vaccination neutralize an emerging variant and SARS-CoV-1.** MedRxiv 2021, posted 8 February. Full-text: <https://www.medrxiv.org/content/10.1101/2021.02.05.21251182v1>

[Andrew McGuire](#), Leonidas Stamatatos and colleagues found that a single shot of the Pfizer or Moderna mRNA vaccines boosts the neutralizing antibody response in people who were previously infected. Importantly, these antibodies also had neutralizing activity against the B1351 variant first detected in South Africa. The authors point to the importance of vaccination of both uninfected and of previously infected subjects. Read also Burton DR, Topo EJ. **Toward superhuman SARS-CoV-2 immunity?** Nat Med 27, 5–6 (2021). Full-text: <https://doi.org/10.1038/s41591-020-01180-x>

Burton DR, Topol EJ. **Variant-proof vaccines — invest now for the next pandemic.** Nature 2021, published 8 February. Full-text: <https://www.nature.com/articles/d41586-021-00340-4>

The rapid development and delivery of highly effective COVID-19 vaccines less than a year after the emergence of the disease is a huge success story. This was possible, in part, because of certain properties of the coronavirus SARS-CoV-2 that favor vaccine design — in particular, the spike protein on the viral surface. However, the next pathogen to emerge might be less accommodating. [Eric Topol](#) and Dennis Burton underline the importance of rational vaccine design based on broadly neutralizing antibodies.

Gadoth A, Halbrook M, Martin-Blais R, et al. **Cross-sectional Assessment of COVID-19 Vaccine Acceptance Among Health Care Workers in Los Angeles.** Ann Intern Med. 2021 Feb 9. PubMed: <https://pubmed.gov/33556267>. Full-text: <https://doi.org/10.7326/M20-7580>

In the context of a highly publicized coronavirus vaccine rollout, initial uptake by health care workers (HCWs) is critical for safety, health system functioning, and public opinion. In this survey, participants overwhelmingly acknowledged the importance and utility of general vaccination to a public health practice; however, they were widely hesitant about partaking in COVID-19 vaccination in either a trial or post-marketing settings and expressed uncertainties about the regulatory approval and protective capabilities of novel SARS-CoV-2 vaccines.

## Diagnostics

Guglielmi G. **Rapid coronavirus tests: a guide for the perplexed.** Nature 2021, published 9 February. Full-text: <https://www.nature.com/articles/d41586-021-00332-4>

Rapid tests, which typically mix nasal or throat swabs with liquid on a paper strip and return results within half an hour, are thought of as tests of infectiousness, not of infection. They can detect only high viral loads, so they will miss many people with lower levels of the SARS-CoV-2 virus. But the hope is that they will help to curb the pandemic by quickly identifying the most contagious people, who might otherwise unknowingly pass on the virus.

## French

If you read French, read Herzberg N. **Covid-19 : le chemin de croix du vaccin d'AstraZeneca.** Le Monde 2021, published 9 February. Full-text: [https://www.lemonde.fr/planete/article/2021/02/09/covid-19-le-chemin-de-croix-du-vaccin-d-astrazeneca\\_6069270\\_3244.html](https://www.lemonde.fr/planete/article/2021/02/09/covid-19-le-chemin-de-croix-du-vaccin-d-astrazeneca_6069270_3244.html)

Erreur de dosage lors des essais, manque de données sur les plus de 65 ans... L'arrêt de la campagne en Afrique du Sud constitue le dernier d'une série de revers pour ce vaccin très attendu.

Sénécat A. **Covid-19 : faut-il libérer les brevets des vaccins pour en produire plus ?** Le Monde 2021, published 9 February. Full-text: [https://www.lemonde.fr/les-decodeurs/article/2021/02/09/covid-19-faut-il-liberer-les-brevets-des-vaccins-pour-en-produire-plus\\_6069314\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2021/02/09/covid-19-faut-il-liberer-les-brevets-des-vaccins-pour-en-produire-plus_6069314_4355770.html)

Face à l'urgence sanitaire, l'idée de s'affranchir des contraintes de la propriété intellectuelle fait son chemin, mais se heurte à plusieurs obstacles.

## German

If you read German, read Berndt C, Endt C, Müller-Hansen S. **Die unsichtbare Welle**. Süddeutsche Zeitung 2021, published 5 February. Full-text: <https://www.sueddeutsche.de/wissen/coronavirus-mutante-b117-daten-1.5197700>

Die Infektionszahlen in Deutschland gehen zurück. Doch erste Daten zur Verbreitung der Variante B117 deuten darauf hin, dass es damit bald vorbei sein könnte. RKI-Chef Wieler rechnet mit einer weiteren Ausbreitung. Eine Analyse mit Grafiken.

## Beyond Corona

Milman O. **'Invisible killer': fossil fuels caused 8.7m deaths globally in 2018, research finds**. The Guardian 2021, published 9 February. Full-text: <https://www.theguardian.com/environment/2021/feb/09/fossil-fuels-pollution-deaths-research>

Air pollution caused by the burning of fossil fuels such as coal and oil was responsible for 8,7M deaths globally in 2018, a staggering one in five of all people who died that year, new research has found.

## 11 February

### Immunology

#### Paper of the Day

Anderson EM, Goodwin EC, Verma A, et al. **Seasonal human coronavirus antibodies are boosted upon SARS-CoV-2 infection but not associated with protection**. Cell 2021, published 9 February. Full-text: [https://www.cell.com/cell/fulltext/S0092-8674\(21\)00160-4](https://www.cell.com/cell/fulltext/S0092-8674(21)00160-4)

The authors show that ~20% of humans possess non-neutralizing antibodies against SARS-CoV-2 prior to the COVID-19 pandemic. They measured antibodies in a unique cohort: individuals who had donated samples prior to the pandemic and who subsequently became infected with SARS-CoV-2. These antibodies were not associated with protection against SARS-CoV-2 infections or hospitalizations, but they were boosted upon SARS-CoV-2 infection.

Tan AT, Linster M, Tan CW, et al. **Early induction of functional SARS-CoV-2-specific T cells associates with rapid viral clearance and mild disease in COVID-19 patients.** Cell Rep. 2021 Jan 21:108728. PubMed: <https://pubmed.gov/33516277>. Full-text: <https://doi.org/10.1016/j.celrep.2021.108728>

Peak viral load is correlated with disease severity – and there is a positive relation between early detection of IFN- $\gamma$ -secreting SARS-CoV-2-specific T cells and early control of infection. These are the key messages of a study that longitudinally tracked both viral loads and virus-specific T cells. Early antibody responses alone did not distinguish control of virus or disease severity.

## Epidemiology

Grubaugh ND, Hodcroft EB, Fauber JR, Phelan AL, Cevik M. **Public health actions to control new SARS-CoV-2 variants.** Cell 2021, published 29 January. Full-text: [https://www.cell.com/cell/fulltext/S0092-8674\(21\)00087-8](https://www.cell.com/cell/fulltext/S0092-8674(21)00087-8)

The emergence of more transmissible variants will exacerbate the pandemic and reduce the efficacy of some vaccines. Nathan D. Grubaugh and colleagues provide public health guidance for increased surveillance and measures to reduce community transmission. Much of this article uses the B117 variant as an example, but similar principles can be applied to other SARS-CoV-2 variants, including B1351 and P1.

Chen YH, Glymour M, Riley A, et al. **Excess mortality associated with the COVID-19 pandemic among Californians 18–65 years of age, by occupational sector and occupation: March through October 2020.** MedRxiv 2021, posted 22 January. Full-text: <https://www.medrxiv.org/content/10.1101/2021.01.21.21250266v1?s=09>

Risk ratios for mortality comparing pandemic time to non-pandemic time were highest among cooks (RR=1.60), packaging and filling machine operators (RR=1.59), miscellaneous agricultural workers (RR=1.55), bakers (RR=1.50), and construction laborers (RR=1.49).



## Transmission

Lachassinne E, de Pontual L, Caseris M, et al. **SARS-CoV-2 transmission among children and staff in daycare centres during a nationwide lockdown in France: a cross-sectional, multicentre, seroprevalence study.** *Lancet Child Adolesc Health*, published 8 February. Full-text: [https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(21\)00024-9/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00024-9/fulltext)

During a nationwide lockdown in France in June 2020, the authors enrolled 327 children (mean age 1,9 [SD 0,9] years; range 5 months to 4,4 years), 197 daycare center staff (mean age 40 [12] years), and 164 adults in a comparator group. 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. Intra-family transmission seemed more plausible than transmission within daycare centers.

Liu H, He S, Shen L, Hong J. **Simulation-based study of COVID-19 outbreak associated with air-conditioning in a restaurant featured.** *Physics of Fluids* 33, 023301 (2021). Full-text: <https://doi.org/10.1063/5.0040188>

COVID-19 is transmitted via droplets and virus-carrying aerosols. Here, Han Liu et al. conducted a systematic computational fluid dynamics (CFD)-based investigation of indoor airflow and the associated aerosol transport in a restaurant setting. They provide a spatial map of the airborne infection risk in the restaurant under different air conditioning and thermal settings.

## Prevention

Reddy S. **Double Face Masks? N95? Protect Yourself Against New Covid-19 Variants With These Mask Upgrades.** *WSJ* 2021, published 4 February. Full-text: <https://www.wsj.com/articles/double-face-masks-n95-protect-yourself-against-new-covid-19-variants-with-these-mask-upgrades-11612473349>

As new, more-contagious coronavirus variants circulate, doctors say it's important to improve the effectiveness of your mask practices—such as by “double masking”, to wear two at once. Numerous studies have found that masks help protect the wearers as well as those around them from the virus that causes COVID-19.

Tan IB, Tan C, Hsu LY, et al. **Prevalence and Outcomes of SARS-CoV-2 Infection Among Migrant Workers in Singapore.** JAMA. 2021 Feb 9;325(6):584-585. PubMed: <https://pubmed.gov/33560312>. Full-text: <https://doi.org/10.1001/jama.2020.24071>

Singapore 2020: 200.000 migrant workers exposed to SARS-CoV-2, 111.000 confirmed infections, 20 ICU patients, 1 death. How did they achieve that? Mass testing and isolation.

## Severe COVID

Liu L, Xie J, Wu W, et al. **A simple nomogram for predicting failure of non-invasive respiratory strategies in adults with COVID-19: a retrospective multicentre study.** Lancet Digital Health 2021, published 8 February. Full-text: [https://www.thelancet.com/journals/landig/article/PIIS2589-7500\(20\)30316-2/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30316-2/fulltext)

The authors developed and validated a nomogram and online calculator for the early prediction of non-invasive respiratory strategies (NIRS) failure in patients with COVID-19. These patients might benefit from early triage and more intensive monitoring. The nomogram, based on age, number of comorbidities, ROX index, Glasgow coma scale score, and use of vasopressors on day 1 of NIRS, had a discriminatory ability (C-statistic) of 0,84 (95% CI: 0,81–0,87) in predicting NIRS failure. Patients in whom NIRS fails have a high risk of death.

## Comorbidities

Williams R. **Coronavirus Brain Breach.** Biomedical Picture of the Day, posted 8 January. Link: <http://www.bpod.mrc.ac.uk/archive/2021/2/8>

This image shows the virus responsible for COVID-19, SARS-CoV-2 (red), in the act of infecting and killing human brain cells, with dead cells shown in green. The cells aren't those of a patient's brain of course, which would be impossible... | Continue reading at <http://www.bpod.mrc.ac.uk/archive/2021/2/8>.

## 12 February

### Society

#### Paper of the Day

Woolhandler S, Himmelstein DU, Ahmed S, et al. **Public policy and health in the Trump era.** *Lancet* 2021, published 10 February. Full-text: [https://doi.org/10.1016/S0140-6736\(20\)32545-9](https://doi.org/10.1016/S0140-6736(20)32545-9)

A lesson of leadership failure.

### Epidemiology

Carrat F, Figoni J, Henny J, et al. **Evidence of early circulation of SARS-CoV-2 in France: findings from the population-based “CONSTANCES” cohort.** *Eur J Epidemiol* (2021). Full-text: <https://doi.org/10.1007/s10654-020-00716-2>

Using serum samples routinely collected in 9144 adults from a French general population-based cohort, Fabrice Carrat et al. identified 13 participants with a positive anti-SARS-CoV-2 IgG test between November 2019 and January 2020. The results were 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 of risk of potential SARS-CoV-2 exposure. This report suggests early circulation of SARS-CoV-2 in Europe.

### Prevention

Brooks JT, Beezhold DH, Noti JD, et al. **Maximizing Fit for Cloth and Medical Procedure Masks to Improve Performance and Reduce SARS-CoV-2 Transmission and Exposure, 2021.** *MMWR Morb Mortal Wkly Rep.* ePub: 10 February 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7007e1>

From half-mask to double mask – the US is trying to make up ground on the disastrous first-year management of the COVID-19 pandemic. The CDC (finally, back!) conducted experiments to assess two ways of improving the fit of medical procedure masks: fitting a cloth mask over a medical procedure mask (double masking), and knotting the ear loops of a medical procedure mask and then tucking in and flattening the extra material close to the face. Each modification substantially improved source control and reduced wearer exposure. See also [Glenza J. CDC study recommends double masking to reduce Covid-19 exposure.](#) *The Guardian* 2021, published 10 February. Full-text: <https://www.theguardian.com/world/2021/feb/10/mask-guidance-cdc-two-masks-close-fitting>.

Graphical abstract:

## Immunology

Liu C, Martins AJ, Lau WW, et al. **Time-resolved Systems Immunology Reveals a Late Juncture Linked to Fatal COVID-19.** Cell 2021, published 10 February. Full-text: [https://www.cell.com/cell/fulltext/S0092-8674\(21\)00168-9](https://www.cell.com/cell/fulltext/S0092-8674(21)00168-9)

John Tsang, Can Liu and colleagues assessed the cell surface protein phenotype, transcriptome, and T cell clonality of peripheral immune cells of COVID-19 patients over time. They revealed a network of cell type specific signatures linked to disease severity, dissected timing effects, and uncovered a late period during which the host immune response undergoes a striking divergence in patients with distinct disease severity and outcomes. The ‘disease severity network’ pointed to attenuated inflammation and an “exhaustion”-like gene expression state in CD56<sup>dim</sup>CD16<sup>hi</sup> NK cells as a primary positive correlate of disease severity.

## Clinical

Zucman N, Uhel F, Descamps D, Roux D, Ricard JD. **Severe reinfection with South African SARS-CoV-2 variant 501Y.V2: A case report.** Clin Infect Dis 2021, published 10 February. Full-text: <https://doi.org/10.1093/cid/ciab129>

Noémie Zucman, Fabrice Uhel and colleagues report a case of severe SARS-CoV-2 reinfection with South African variant 501Y.V2, four months after recovering from a first episode of COVID-19. During the first episode, in September 2020, the 58-year-old man with a history of asthma had mild fever and dyspnea; symptoms resolved within a few days. In January 2021, 129 days after onset of the first infection, he presented to hospital for recurrent dyspnea and fever. Sequencing revealed the B1351 variant. Seven days later, the patient developed a severe acute respiratory distress syndrome requiring intubation and mechanical ventilation.

## Treatment

Ramakrishnan S, Nicolau DV, Langford B, et al. **Inhaled budesonide in the treatment of early COVID-19 illness: a randomised controlled trial.** medRxiv 2021, posted 8 February. Full-text: <https://doi.org/10.1101/2021.02.04.21251134>

Early administration of inhaled **budesonide** might reduce the likelihood of needing urgent medical care and reduced time to recovery following early

COVID-19 infection. This is the result of a randomized, open label trial of inhaled budesonide, compared to usual care, in adults within 7 days of the onset of mild COVID-19 symptoms. The primary endpoint (COVID-19-related urgent care visit, emergency department assessment or hospitalization) occurred in 10 of 69 participants in the usual care arm and in 1 of 70 participants in the budesonide arms ( $p = 0,004$ ). Clinical recovery was 1 day shorter in the budesonide arm compared to the usual care arm (median of 7 days versus 8 days respectively,  $p = 0,007$ ). Importantly, fewer participants randomized to budesonide had persistent symptoms at day 14 and day 28 compared to participants receiving usual care. Background of the study: multiple hospital cohorts have shown that patients with chronic respiratory disease are significantly under-represented. The authors hypothesize that the widespread use of inhaled glucocorticoids is responsible for this finding.

### Severe COVID

Huang Z, Ning B, Yang HS, et al. **Sensitive tracking of circulating viral RNA through all stages of SARS-CoV-2 infection.** J Clin Invest 2021, published 9 February. Full-text: <https://www.jci.org/articles/view/146031>

Sensitive detection of SARS-CoV-2 RNA in blood by CRISPR-augmented RT-PCR permits accurate COVID-19 diagnosis, and can detect COVID-19 cases with transient or negative nasal swab RT-qPCR results. Tony Hu, Zhen Huang and colleagues suggest that this approach could improve COVID-19 diagnosis and the evaluation of SARS-CoV-2 infection clearance, and predict severity of infection.

Sablerolles RSG, Lafeber M, van Kempen JAL, et al. **Association between Clinical Frailty Scale score and hospital mortality in adult patients with COVID-19 (COMET): an international, multicentre, retrospective, observational cohort study.** Lancet Healthy Longevity 2021, published 9 February. Full-text: [https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568\(21\)00006-4/fulltext](https://www.thelancet.com/journals/lanhl/article/PIIS2666-7568(21)00006-4/fulltext)

In some places, the scarcity of resources has necessitated triage of critical care for COVID-19 patients. In patients aged 65 years and older, triage decisions are regularly based on degree of frailty, measured by the Clinical Frailty Scale (CFS). Here, Roos Sablerolles et al. show that among patients younger than 65 years, frail patients had an increased incidence of admission to intensive care, whereas mildly frail patients had no significant difference in incidence compared to fit patients. Likewise, an increased hospital mortality risk was only observed in frail patients. However, the authors caution that treat-

ment decisions based on the CFS in patients younger than 65 years should be made with caution.

## Pediatrics

Brookman S, Cook J, Zucherman M, Broughton S, Harman K, Gupta A. **Effect of the new SARS-CoV-2 variant B.1.1.7 on children and young people.** Lancet Child Adolesc Health 2021, published 10 February. Full-text: [https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(21\)00030-4/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(21)00030-4/fulltext)

In children and young people, infection with B117 does not result in an appreciably different clinical course to the original strain. This is the result of a study that compared 20 children and young people admitted to King's College Hospital, London, between March 1, and May 31, 2020, and 60 children and young people admitted between Nov 1, 2020, and Jan 19, 2021. Atul Gupta, Sarah Brookman and colleagues conclude that severe acute respiratory COVID-19 remains an uncommon occurrence in children and young people.

## French

If you read French, read Foucart S. **Pandémie de Covid-19 : le virus circulait sans doute en France dès novembre 2019.** Le Monde 21, published 10 February. Full-text : [https://www.lemonde.fr/planete/article/2021/02/10/le-sars-cov-2-circulait-sans-doute-en-france-des-novembre-2019\\_6069431\\_3244.html](https://www.lemonde.fr/planete/article/2021/02/10/le-sars-cov-2-circulait-sans-doute-en-france-des-novembre-2019_6069431_3244.html)

Les résultats des travaux de chercheurs français mettent à mal l'hypothèse d'un départ de l'épidémie sur le marché chinois de Wuhan au début du mois de décembre 2019.

**Le point sur l'épidémie de Covid-19 en France : le variant britannique représente un quart des infections.** Le Monde 21, published 11 February. Full-text : [https://www.lemonde.fr/planete/article/2021/02/11/le-variant-britannique-du-sars-cov-2-represente-un-quart-des-infections-en-france\\_6069646\\_3244.html](https://www.lemonde.fr/planete/article/2021/02/11/le-variant-britannique-du-sars-cov-2-represente-un-quart-des-infections-en-france_6069646_3244.html)

Le ministre de la santé, Olivier Véran, a reconnu que la situation en Moselle est « inquiétante », car les variants sud-africain et brésilien sont « très présents ».

## 13 February

### Treatment

#### Paper of the Day

Horby PW, Campbell M, Staplin N, et al. for the RECOVERY Collaborative Group, and others. **Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): preliminary results of a randomised, controlled, open-label, platform trial.** medRxiv 2021, posted 11 February. Full-text: <https://www.medrxiv.org/content/10.1101/2021.02.11.21249258v1>

In COVID patients with low oxygen and inflammation, tocilizumab saves lives, keeps you off a ventilator, and gets you out of hospital quicker. This is another result of the great RECOVERY trial. After randomizing more than 4000 patients (oxygen saturation < 92% on air or requiring oxygen therapy; and evidence of systemic inflammation [C-reactive protein  $\geq$  75 mg/L]), treatment with tocilizumab reduced mortality (29% vs 33%), increased the chances of successful hospital discharge, and reduced the chances of requiring invasive mechanical ventilation (33% vs 38%). These benefits were on top of those previously reported for dexamethasone. Clinical guidelines need an update.

See also **Tocilizumab reduces deaths in patients hospitalised with COVID-19,** 11 February 2021. Link: <https://www.recoverytrial.net/news/tocilizumab-reduces-deaths-in-patients-hospitalised-with-covid-19>

### Vaccines

#### (Another) Paper of the Day

Madhi A, Baillie VL, Cutland CL, et al. **Safety and efficacy of the ChAdOx1 nCoV-19 (AZD1222) Covid-19 vaccine against the B.1.351 variant in South Africa.** medRxiv 2021, posted 12 February. Full-text: <https://www.medrxiv.org/content/10.1101/2021.02.10.21251247v1>

Shabir Madhi et al. report a ChAdOx1-nCoV19 (AstraZeneca) trial in HIV-uninfected people in South Africa. 23/717 (3.2%) placebo and 19/750 (2.5%) vaccine recipients developed mild-moderate Covid-19. Of the primary endpoint cases, 39/42 (92.9%) were the B.1.351 variant – against which vaccine efficacy was 10.4%. The authors conclude that a two-dose regimen of ChAdOx1-nCoV19 did not show protection against mild-moderate Covid-19 due to B.1.351 variant.

## Variants

Zhang W, Davis BD, Chen SS, Sincuir Martinez JM, Plummer JT, Vail E. **Emergence of a Novel SARS-CoV-2 Variant in Southern California.** JAMA. 2021 Feb 11. PubMed: <https://pubmed.gov/33571356>. Full-text: <https://doi.org/10.1001/jama.2021.1612>

In California, the proportion of SARS-CoV-2 cases associated with the CAL.20C variant rose from 3,8% to 25% between mid-November and late December. By then, it accounted for 24% of samples in one study, and 36,4% (66/181) of samples in a local Los Angeles cohort. The emerging predominance of this strain is temporally related to the time of onset of the current spike in SARS-CoV-2 infections in Southern California. CAL.20C is defined by mutations in the S protein (L452R, S13I, W152C) and in the ORF1a (I4205V) and ORF1b protein (D1183Y).

## Transmission

Edwards DA, Ausiello D, Salzman J, et al. **Exhaled aerosol increases with COVID-19 infection, age, and obesity.** PNAS 2021, published 23 February. Full-text: <https://www.pnas.org/content/118/8/e2021830118>

David Edwards et al. report studies of exhaled aerosol suggesting that a critical factor in SARS-CoV-2 superspreading events is the propensity of certain individuals to exhale large numbers of small respiratory droplets. Their findings indicate that 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 infection and body mass index multiplied by age (i.e., BMI-years).

## Immunology

Wang Z, Schmidt F, Weisblum Y, et al. **mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants.** Nature 2021, published 10 February. Full-text: <https://www.nature.com/articles/s41586-021-03324-6>

Michel Nussenzweig and colleagues tested samples from 14 and 6 people who had received the Moderna or the Pfizer-BioNTech vaccine, respectively. Activity against SARS-CoV-2 variants encoding E484K or N501Y or the K417N:E484K:N501Y combination was reduced by a small but significant margin.



Skelly DT, Harding AC, Gilbert Jaramillo J, et al. **Vaccine-induced immunity provides more robust heterotypic immunity than natural infection to emerging SARS-CoV-2 variants of concern.** Research Square 2021, posted 9 February, accessed 12 February. Full-text: <https://www.researchsquare.com/article/rs-226857/v1?s=09>

When testing antibody and T cell responses against B117, B1351 and a reference isolate (VIC001) representing the original circulating lineage B, Skelly et al. identified a reduction in antibody neutralization against the variants which was most evident in B1351. However, the majority of the T cell response was directed against epitopes conserved across all three strains. The reduction in antibody neutralization was less marked in post-boost vaccine-induced rather than in naturally-induced immune responses.

### Severe COVID

Chamberlain SR, Grant JE, Trender W. **Post-traumatic stress disorder symptoms in COVID-19 survivors: online population survey.** BJPsych Open 2021, published 9 February. Full-text: <https://www.cambridge.org/core/journals/bjpsych-open/article/posttraumatic-stress-disorder-symptoms-in-covid19-survivors-online-population-survey/66F00143472B15757736AE5E3E42E52C>

Samuel R. Chamberlain et al. examined post-traumatic stress disorder (PTSD) symptoms in 13,049 survivors of suspected or confirmed COVID-19, from the UK general population. Up to a third of COVID-19 patients who required ventilator support experienced extensive PTSD symptoms. Intrusive images were the most prominent elevated symptom.

### Beyond Corona

Sapoznik E, Chang BJ, Huh J, et al. **A versatile oblique plane microscope for large-scale and high-resolution imaging of subcellular dynamics.** Elife. 2020 Nov 12;9:e57681. PubMed: <https://pubmed.gov/33179596>. Full-text: <https://doi.org/10.7554/eLife.57681>

Using an oblique plane microscope (OPM), the authors image biological phenomena such as cell migration through confined spaces within a microfluidic device, subcellular photoactivation of Rac1, and large field of view imaging of neurons, developing embryos, and centimeter-scale tissue sections.

## 14 February

### Clinical

#### Paper of the Day

Davies NG, Jarvis CI, CMMID COVID-19 Working Group, et al. **Increased hazard of death in community-tested cases of SARS-CoV-2 Variant of Concern 202012/01.** medRxiv 2021, posted 11 February. Full-text: <https://doi.org/10.1101/2021.02.01.21250959>

Another analysis suggesting that B117 may cause more severe illness. Nicholas Davies et al. analyzed a large database of SARS-CoV-2 community test results and COVID-19 deaths, representing 52% of all SARS-CoV-2 community tests in England from 1 September 2020 to 5 February 2021. The result: among B117 cases, the hazard of death may be more than 50% higher. For a male aged 55–69, the absolute risk of death would increase from 0,6% to 0,9% over the 28 days following a positive test in the community.

### Epidemiology

Jahn K, Dreifuss D, Topolsky I, et al. **Detection of SARS-CoV-2 variants in Switzerland by genomic analysis of wastewater samples.** medRxiv 2021, posted 9 February. Full-text: <https://doi.org/10.1101/2021.01.08.21249379>

Katharina Jahn et al. found evidence for the presence of several mutations that define B117 and B1351 in a sample from a Swiss ski resort from 9-21 December, two weeks before its first verification in a patient sample from Switzerland. The authors conclude that sequencing SARS-CoV-2 in community wastewater samples may help detect and monitor the circulation of diverse lineages.

Ward H, Atchison C, Whitaker M, et al. **SARS-CoV-2 antibody prevalence in England following the first peak of the pandemic.** Nat Commun 12, 905 (2021). Full-text: <https://doi.org/10.1038/s41467-021-21237-w>

According to this study by Paul Elliott, Helen Ward and colleagues, an estimated 3,4 million people had developed antibodies to SARS-CoV-2 by mid-July 2020. Prevalence was two- to three-fold higher among health and care workers compared with non-essential workers, and in people of Black or South Asian than white ethnicity. The authors conclude that higher hospitalization and mortality from COVID-19 in minority ethnic groups may reflect higher rates of infection rather than differential experience of disease or care.

## Virology

Nanographics. **High resolution renderings of SARS-CoV-2 Cryo-ET.** Nanographics 2021, link: <https://nanographics.at/projects/coronavirus-3d/>

This is the first 3D image of SARS-CoV-2 made from a single scan of frozen virus particles. The authors used cryo-electron tomography scans and added colors to distinguish different parts of the virus. They release the image under Creative Commons Attribution license, so that everyone can use them freely in their work.

## Variants

Fontanet A, Autran B, Lina B, et al. **SARS-CoV-2 variants and ending the COVID-19 pandemic.** Lancet 2021, published 11 February. Full-text: [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00370-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00370-6/fulltext)

Arnaud Fontanet from the Pasteur Institute in Paris outlines the priorities to address in an environment with new SARS-CoV-2 variants:

1. Continue to suppress and push to eliminate SARS-CoV-2 while rolling out COVID-19 vaccines
2. Improve surveillance of SARS-CoV-2 variants through global sequencing and sharing of variant-specific PCR primers
3. Create a central repository of samples of sera and cells from individuals with past infection or past immunization with available COVID-19 vaccines for sero-neutralization and cellular immunity functional testing against newly discovered variants
4. Produce COVID-19 vaccines reactively and adapt them to newly emerging lineages
5. Ensure global access, availability, and affordability of COVID-19 vaccines to ensure no countries are left behind

## Immunology

Saelens X, Schepens B. **Single-domain antibodies make a difference.** Science. 2021 Feb 12;371(6530):681-682. PubMed: <https://pubmed.gov/33574203>. Full-text: <https://doi.org/10.1126/science.abg2294>

Xavier Saelens and Bert Schepens comment on a paper we presented on **18 January**. [Koenig PA, Das H, Liu H, et al. **Structure-guided multivalent nanobodies block SARS-CoV-2 infection and suppress mutational escape**

(<https://doi.org/10.1126/science.abe6230>): the authors “describe four SARS-CoV-2-neutralizing single-domain antibodies, or VHHs, and combinations thereof that can disable spike function. This extends the growing list of reports on SARS-CoV-2 spike-specific single-domain antibodies that have been proposed as potential therapeutics for COVID-19 patients.”

Munitz A, Edry-Botzer L, Itan M, et al. **Rapid seroconversion and persistent functional IgG antibodies in severe COVID-19 patients correlates with an IL-12p70 and IL-33 signature.** *Sci Rep* 11, 3461 (2021). Full-text: <https://doi.org/10.1038/s41598-021-83019-0>

Ariel Munitz et al. describe a rapid, quantitative, accurate, and robust serological method to detect seroconversion upon SARS-CoV-2 infection and the neutralization potential of the detected antibodies. Their analysis of the cytokine profile in COVID-19 patients also revealed a unique correlation of an IL-12p70/IL33 and IgG seroconversion that correlated with disease severity.

## Vaccine

Krammer F, Srivastava K, the PARIS team, Simon V. **Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine.** *MedRxiv* 2021, posted 1 February. Full-text: <https://doi.org/10.1101/2021.01.29.21250653>

Should individuals who already had SARS-CoV-2 infection receive one or two shots of the currently authorized mRNA vaccines? Florian Krammer et al. remind us that the antibody response to the first vaccine dose in individuals with pre-existing immunity is equal to or even exceeds the titers found in naïve individuals after the second dose. They conclude that giving only one dose of vaccine would not negatively impact on antibody titers and free up many urgently needed vaccine doses.

Wahl A, Gralinski LE, Johnson CE, et al. **SARS-CoV-2 infection is effectively treated and prevented by EIDD-2801.** *Nature* (2021). Full-text: <https://doi.org/10.1038/s41586-021-03312-w>

Victor Garcia, Angela Wahl and colleagues show that therapeutic and prophylactic administration of EIDD-2801 (**Molnupiravir**, MKK-4482), an oral broad spectrum antiviral currently in Phase II-III clinical trials, dramatically inhibits SARS-CoV-2 replication *in vivo* and thus has significant potential for the prevention and treatment of COVID-19.

## 15 February

### Variants

#### Paper of the Day

NERVTAG 20210211. **Update note on B.1.1.7 severity.** New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) 2021, published 12 February. Full-text: <https://www.gov.uk/government/publications/nervtag-update-note-on-b117-severity-11-february-2021>

It is now likely that infection with B.1.1.7 is associated with an increased risk of hospitalization and death compared to infection with previously circulating viruses.

**Variants – 13 February update.** COVID Reference 2021, published 13 February. Full-text: <https://covidreference.com/variants> | See also the Comparison document with new content added between 7 and 13 February: [http://www.bsk1.com/CR\\_Variants\\_Update.html](http://www.bsk1.com/CR_Variants_Update.html)

In most of continental Europe and the US, Easter 2021 (4 April) may be recalled later as a *B.1.1.7 Easter*.

### Epidemiology

Hay JA, Kennedy-Shaffer L, Kanjilal S, et al. **Estimating epidemiologic dynamics from cross-sectional viral load distributions.** MedRxiv 2021, posted 13 February. Full-text: <https://doi.org/10.1101/2020.10.08.20204222>

Cycle threshold (Ct) values from even limited numbers of random samples might provide estimates of an epidemic's trajectory. Michael Mina, Marc Lipsitch, James Hay and colleagues applied their methods to Ct values from surveillance conducted during the SARS-CoV-2 pandemic in a variety of settings. A new approach for real-time estimates of epidemic trajectories for outbreak management and response?

Helix 202102. **The Helix® COVID-19 Surveillance Dashboard.** Helix 2021; website: <https://www.helix.com/pages/helix-covid-19-surveillance-dashboard>

The B.1.1.7 strain is doubling every 10 days in the US. Should it be the last obstacle to achieving containment of SARS-CoV-2 in the country? Wait a few weeks before eliminating effective mitigation measures such as mask mandates and bans on gatherings.

Alpert T, Lasek-Nesselquist E, Brito AF, et al. **Early introductions and community transmission of SARS-CoV-2 variant B.1.1.7 in the United States.** medRxiv 2021, posted 12 February. Full-text: <https://doi.org/10.1101/2021.02.10.21251540>

Nathan D. Grubaugh, Tara Alpert and colleagues highlight the primary ports of entry for B.1.1.7 in the US. New York is likely one of the key hubs for introductions and domestic spread. The authors also provide evidence for increased community transmission in several states.

## Immunology

Tarke A, Sidney J, Kidd CK, et al. **Comprehensive analysis of T cell immunodominance and immunoprevalence of SARS-CoV-2 epitopes in COVID-19 cases.** Cell Rep Med. 2021 Jan 26:100204. PubMed: <https://pubmed.gov/33521695>. Full-text: <https://doi.org/10.1016/j.xcrm.2021.100204>

Alessandro Sette, Alison Tarke and colleagues show a broad T cell repertoire, suggesting that viral escape of T cell immunity is unlikely. CD4 immunodominant regions correlate with HLA binding and not with high common cold coronavirus homology. RBD is poorly recognized by CD4s. Epitope pools can be used to optimize detection of T cell responses.

Batra M, Tian R, Zhang C, et al. **Role of IgG against N-protein of SARS-CoV2 in COVID19 clinical outcomes.** Sci Rep 11, 3455 (2021). <https://doi.org/10.1038/s41598-021-83108-0>

Mehri Mirsaedi, Mayank Batra and colleagues at the University of Miami studied 400 RT-PCR confirmed SARS-CoV-2 patients to determine independent factors associated with poor outcomes. Their findings suggest that titers of IgG targeting the N protein of SARS-CoV-2 at admission might be a prognostic factor for the clinical course of disease.

Wu KJ. **The Body Is Far From Helpless Against Coronavirus Variants.** The Atlantic 2021, published 12 February. Full-text: <https://www.theatlantic.com/science/archive/2021/02/antibody-evolution/618004>

The mission of the human immune system is threefold. 1. Memorize the features of dangerous microbes that breach the body's barriers. 2. Launch an

attack to bring them to heel. 3. Then squirrel away intel to quash future assaults.

## Vaccine

Shimabukuro TT, Cole M, Su JR. **Reports of Anaphylaxis After Receipt of mRNA COVID-19 Vaccines in the US-December 14, 2020-January 18, 2021.** JAMA. 2021 Feb 12. PubMed: <https://pubmed.gov/33576785>. Full-text: <https://doi.org/10.1001/jama.2021.1967>

During December 14, 2020 through January 18, 2021, a total of 9 943 247 doses of the Pfizer-BioNTech vaccine and 7 581 429 doses of the Moderna vaccine were reported administered in the US. CDC identified 66 case reports that met Brighton Collaboration case definition criteria for anaphylaxis (levels 1, 2 or 3): 47 following Pfizer-BioNTech vaccine, for a reporting rate of 4.7 cases/million doses administered, and 19 following Moderna vaccine, for a reporting rate of 2.5 cases/million doses administered.

McKie R. **Life savers: the amazing story of the Oxford/AstraZeneca Covid vaccine.** The Guardian 2021, published 14 February. Full-text: <https://www.theguardian.com/world/2021/feb/14/life-savers-story-oxford-astrazeneca-coronavirus-vaccine-scientists>

A year ago, Sarah Gilbert and Andrew Pollard began work on the response to a new virus. Now, as their vaccine is being given to millions, they tell of their incredible 12 months.

## Clinical

Rentsch CT, Beckman JA, Tomlinson L, et al. **Early initiation of prophylactic anticoagulation for prevention of coronavirus disease 2019 mortality in patients admitted to hospital in the United States: cohort study.** BMJ. 2021 Feb 11;372:n311. PubMed: <https://pubmed.gov/33574135>. Full-text: <https://doi.org/10.1136/bmj.n311>

Early initiation of prophylactic anti-coagulation compared with no anti-coagulation among patients admitted to hospital with COVID-19 was associated with a decreased risk of 30-day mortality and no increased risk of serious bleeding events. This is the result of a study of 4297 patients admitted to hospital with COVID-19, 3627 (84,4%) received prophylactic anti-coagulation within 24 hours of admission. More than 99% (n = 3600) of treated patients received subcutaneous heparin or enoxaparin. The cumulative incidence of

mortality at 30 days was 14,3% (95% CI: 13,1% to 15,5%) among those who received prophylactic anti-coagulation and 18,7% (15,1% to 22,9%) among those who did not.

## Society

Barlow P, van Schalkwyk MCI, McKee M, Labonté R, Stuckler D. **COVID-19 and the collapse of global trade: building an effective public health response.** Lancet Planetary Health 2021, published 10 February. Full-text: [https://www.thelancet.com/journals/lanplh/article/PIIS2542-5196\(20\)30291-6/fulltext](https://www.thelancet.com/journals/lanplh/article/PIIS2542-5196(20)30291-6/fulltext)

The pandemic affects international trade through reductions in both supply and demand. Pepita Barlow et al. describe the implications for health. Problems include reduced access to medical supplies, budgetary shortfalls, and a general decline in economic activity—leading, in many cases, to recessions, threats to social safety nets, and to increased precariousness of income, employment, and food security. The authors map a pathway for post-pandemic recovery after the collapse of trade and the global economy.

## Spanish

If you read Spanish, read Domínguez N. **La endiablada búsqueda de una cura para la covid.** El País 2021, published 12 February. Full-text: <https://elpais.com/ciencia/2021-02-12/la-endiablada-busqueda-de-una-cura-para-la-covid.html>

Varios fármacos experimentales en las últimas fases de prueba muestran resultados prometedores para evitar la infección y salvar la vida a los enfermos más graves.

## French

If you read French, read Gozlan M. **Amour et sexualité à l'heure de la Covid-19.** Le Monde 2021, published 14 February. Full-text: <https://www.lemonde.fr/blog/realitesbiomedicales/2021/02/14/amour-et-sexualite-a-lheure-de-la-covid-19/>

La pandémie de Covid-19 a eu des répercussions sur la sexualité dans le monde entier dans la mesure où elle a modifié et compliqué les relations amoureuses entre individus, que ceux-ci soient confinés ensemble ou séparément, qu'ils soient en couple ou célibataires.



## 16 February

### Diagnostics

#### Paper of the Day

Kevadiya BD, Machhi J, Herskovitz J, et al. **Diagnostics for SARS-CoV-2 infections.** Nat Mater, 2021, published 15 February. Full-text: <https://www.nature.com/articles/s41563-020-00906-z>

Comprehensive review on SARS-CoV-2 diagnostic testing. A must-read.

### Epidemiology

Shallcross L, Burke D, Abbott O. **Factors associated with SARS-CoV-2 infection and outbreaks in long-term care facilities in England: a national cross-sectional survey.** Lancet Health Longevity 2021, published 11 February. Full-text: [https://doi.org/10.1016/S2666-7568\(20\)30065-9](https://doi.org/10.1016/S2666-7568(20)30065-9)

Laura Shallcross et al. found that half of long-term care facilities (LTCFs) in England had no cases of SARS-CoV-2 infection in the first wave of the pandemic. Reduced transmission from staff is associated with (there is a lesson here!)

1. adequate sick pay,
2. minimal use of agency staff,
3. an increased staff-to-bed ratio, and
4. staff cohorting with either infected or uninfected residents.

Increased transmission from residents is associated with an increased number of new admissions to the facility and poor compliance with isolation procedures.

### Virology

Laue M, Kauter A, Hoffmann T, et al. **Morphometry of SARS-CoV and SARS-CoV-2 particles in ultrathin plastic sections of infected Vero cell cultures.** Sci Rep 11, 3515 (2021). <https://doi.org/10.1038/s41598-021-82852-7>

Profile of the criminal. Particle size: about 100 nm without spikes; maximal spike length: 23 nm; number of spikes per virus: 25.

## Transmission

Avadhanula V, Nicholson EG, Ferlic-Stark L, et al. **Viral load of SARS-CoV-2 in adults during the first and second wave of COVID-19 pandemic in Houston, TX: the potential of the super-spreader.** J Infect Dis 2021, published 15 February. Full-text: <https://doi.org/10.1093/infdis/jiab097>

Pedro Piedra, Vasanthi Avadhanula and colleagues describe the first two waves of the SARS-CoV-2 pandemic in Houston, US. They observed an increase in the weekly median viral load that predated the onset of each wave by approximately two weeks. A small group of individuals with extremely high and high viral load represented 7,1% and 20,8%, respectively, of the RT-PCR positives in this study. The authors believe that these individuals' characteristics could be consistent with the super-spreader phenomenon. Greater awareness of the social dynamics of these individuals would be needed to understand the spread of SARS-CoV-2.

## Prevention

Lyon RF. **The COVID-19 Response Has Uncovered and Increased Our Vulnerability to Biological Warfare.** Military Medicine 2021, published 15 February. Full-text: <https://doi.org/10.1093/milmed/usab061>

The public health crisis after the emergence of SARS-CoV-2 has highlighted nations' bioweapon vulnerabilities and the potential for disastrous effects on national security.

## Vaccine

Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KRW, Pollard AJ. **What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2.** Lancet Infect Dis. 2021 Feb;21(2):e26-e35. PubMed: <https://pubmed.gov/33125914>. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30773-8](https://doi.org/10.1016/S1473-3099(20)30773-8)

The most important efficacy endpoint – protection against severe disease and death – is difficult to assess in Phase III clinical trials. In this review, Andrew Pollard, Susan Hodgson and colleagues explore the challenges in assessing the efficacy of candidate SARS-CoV-2 vaccines, discuss the caveats needed to interpret reported efficacy endpoints, and provide insight into answering the seemingly simple question, “Does this COVID-19 vaccine work?”. A must-read.

Rosenbaum L. **Escaping Catch-22 — Overcoming Covid Vaccine Hesitancy.** N Engl J Med 2021. Full-text: <https://doi.org/10.1056/NEJMms2101220>

Though many people initially believed a vaccine was the magic bullet that would save us from a devastating pandemic and return our lives to normalcy, we now find ourselves contemplating simultaneously how to ethically allocate a limited number of vaccine doses to the many people who want them and how to increase vaccine uptake among those who don't.

## Clinical

Pilz S, Chakeri A, Ioannidis JPA, et al. **SARS-CoV-2 re-infection risk in Austria.** Eur J Clin Invest 2021, published 15 February. Full-text: <https://onlinelibrary.wiley.com/doi/pdf/10.1111/eci.13520>

In Austria, people with a previous SARS-CoV-2 infection during the first pandemic wave had a 91 percent lower risk of re-infection during the second wave. Stefan Pilz et al. recorded 40 tentative re-infections in 14,840 COVID-19 survivors of the first wave (0.27%) and 253,581 infections in 8,885,640 individuals of the remaining general population (2.85%) translating into an odds ratio (95% confidence interval) of 0.09 (0.07 to 0.13).

## Treatment

Thomas S, Patel D, Bittel B, et al. **Effect of High-Dose Zinc and Ascorbic Acid Supplementation vs Usual Care on Symptom Length and Reduction Among Ambulatory Patients With SARS-CoV-2 Infection: The COVID A to Z Randomized Clinical Trial.** JAMA Netw Open. 2021 Feb 1;4(2):e210369. PubMed: <https://pubmed.gov/33576820>. Full-text: <https://doi.org/10.1001/jamanetworkopen.2021.0369>

Commonly available oral supplements, such as zinc and ascorbic acid (ie, vitamin C), have been proposed to reduce the duration and severity of viral infections by boosting the immune response. In this randomized clinical trial (n = 214) of ambulatory patients diagnosed with SARS-CoV-2 infection, treatment with high-dose zinc gluconate, ascorbic acid, or a combination of the 2 supplements did not significantly decrease the duration of symptoms compared with standard of care. See also the comment by Michos ED, Cainzos-Achirica M. **Supplements for the Treatment of Mild COVID-19-Challenging Health Beliefs With Science From A to Z.** JAMA Netw Open. 2021 Feb 1;4(2):e210431. PubMed: <https://pubmed.gov/33576814>. Full-text: <https://doi.org/10.1001/jamanetworkopen.2021.0431>

## 17 February

### Immunology

#### Paper of the Day

Schultze JL, Aschenbrenner AC. **COVID-19 and the human innate immune system.** Cell 2021, published 16 February. Full-text: [https://www.cell.com/cell/fulltext/S0092-8674\(21\)00218-X](https://www.cell.com/cell/fulltext/S0092-8674(21)00218-X)

Variability in innate immune system components is probably a main contributor to the heterogeneous disease courses observed for COVID-19. Here, Joachim Schultze and Anna Aschenbrenner of the German Center for Neurodegenerative Diseases in Bonn, Germany, link the clinical observations with experimental findings that have been made during the first year of the pandemic. They provide a conceptual framework for the interaction of the human innate immune system with SARS-CoV-2.

### Epidemiology

Phillips N. **The coronavirus is here to stay — here's what that means.** Nature 2021, published 16 February. Full-text: <https://www.nature.com/articles/d41586-021-00396-2>

A Nature survey shows many scientists expect the virus that causes COVID-19 to become endemic, but it could pose less danger over time.

### Transmission

Marr L, Miller S, Prather K, et al. **FAQs on Protecting Yourself from COVID-19 Aerosol Transmission.** Cloud 2021, Version 1.87, 9 December. Full-text: <https://tinyurl.com/FAQ-aerosols>

Excellent summary of aerosol protection.

Dattner I, Goldberg Y, Katriel G, et al. **The role of children in the spread of COVID-19: Using household data from Bnei Brak, Israel, to estimate the relative susceptibility and infectivity of children.** PLoS Comput Biol. 2021 Feb 11;17(2):e1008559. PubMed: <https://pubmed.gov/33571188>. Full-text: <https://doi.org/10.1371/journal.pcbi.1008559>

The fact that the fraction of children among confirmed cases has been found to be low in many countries can be accounted for by two (non-exclusive) hypotheses: (1) Children display milder symptoms than adults when infected, so are less likely to be tested in a typical testing policy triggered by symptoms,

(2) Children are less susceptible to infection than adults. The answer by Dattner and all? *Both!*

## Immunology

Sherina N, Piralla A, Du L, et al. **Persistence of SARS-CoV-2 specific B- and T-cell responses in convalescent COVID-19 patients 6-8 months after the infection.** *Med* 2021, published 10 February. Full-text: [https://www.cell.com/med/fulltext/S2666-6340\(21\)00038-6](https://www.cell.com/med/fulltext/S2666-6340(21)00038-6)

Qiang Pan-Hammarström, Natalia Sherina and colleagues show that specific memory B and T cells develop in > 95% of COVID-19 patients and that memory B and T cell responses were maintained at least 6-8 months after infection. Levels of specific IgM/IgA antibodies declined after 1 month while levels of specific IgG antibodies and plasma neutralizing activities remained relatively stable up to 6 months after diagnosis. Anti-SARS-CoV-2 IgG antibodies were still present, though at a significantly lower level, in 80% of the samples collected at 6-8 months after symptom onset. The authors analyzed 119 samples from 88 convalescent donors who experienced mild to critical disease.

Gentili M, Hacohen N. **Some antibodies can dampen antiviral defences in people with severe COVID.** *Nature* 2021, published 16 February. Full-text: <https://www.nature.com/articles/d41586-021-00352-0>

Defects in the immune defenses induced by the protein interferon are associated with some severe cases of COVID-19. An analysis of patient blood samples sheds light on how antibodies might contribute to these defects. Nir Hacohen and Matteo Gentili comment on a study we presented on [January 28](#): Combes AJ, Courau T, Kuhn NF, et al. **Global absence and targeting of protective immune states in severe COVID-19.** *Nature* 2021, published 25 January. Full-text: <https://doi.org/10.1038/s41586-021-03234-7>

## Vaccine

Chua L, McPheeb R, Huang W, et al. **A preliminary report of a randomized controlled phase 2 trial of the safety and immunogenicity of mRNA-1273 SARS-CoV-2 vaccine.** *Vaccine* 2021, published 9 February. Full-text: <https://www.sciencedirect.com/science/article/pii/S0264410X21001535?via%3Dihub>

Half-doses (50 µg) of Moderna's mRNA-1273 vaccine might be as good as full doses (100 µg) at eliciting robust immune responses.

## Clinical

Islam N, Lewington S, Kharbanda RK, et al. **Sixty-day consequences of COVID-19 in patients discharged from hospital: an electronic health records study.** Eur J Public Health 2021, published 15 February. Full-text: <https://doi.org/10.1093/eurpub/ckab009>

Among patients discharged following admission for community-acquired COVID-19, there is a high rate of major adverse events, with about 30% of patients re-admitted or dead within 60 days. Nazrul Islam and colleagues followed COVID-19 patients discharged between 15 March and 14 July 2020 from hospitals in Oxfordshire, UK. Rates of re-admission or death were twice as high among those  $\geq 65$  years as those  $< 65$  years [standardized rate ratio: 2,21 (95% CI: 1,45–3,56)] and among women than men [2,25 (1,05–4,18)].

## Severe COVID

Schwab P, Mehrjou A, Parbhoo S, et al. **Real-time prediction of COVID-19 related mortality using electronic health records.** Nat Commun 12, 1058 (2021). Full-text: <https://www.nature.com/articles/s41467-020-20816-7>

Patrick Schwab et al. present the COVID-19 early warning system (CovEWS), a real-time early warning system for predicting mortality of COVID-19 positive patients, using routinely collected clinical measurements and laboratory results from electronic health records (EHRs). CovEWS predicted mortality from 78,8% (95% CI: 76,0, 84,7%) to 69,4% (95% CI: 57,6, 75,2%) specificity at sensitivities greater than 95% between, respectively, 1 and 192 h prior to mortality events.

## Spanish

If you read Spanish, read Ansele M. **Las nuevas variantes del virus se enfrentan a los más de 100 millones de personas que ya han pasado la covid.** El País 2021, published 16 February. Full-text: <https://elpais.com/ciencia/2021-02-15/las-nuevas-variantes-del-virus-se-enfrentan-a-los-mas-de-100-millones-de-personas-que-ya-han-pasado-la-covid.html>

La comunidad científica investiga si algunas mutaciones del coronavirus facilitan las reinfecciones.

## French

If you read French, read Inserm. **La souche historique du SARS-CoV-2 décroît alors que progression du variant britannique s'intensifie.** INSERM 2021, published 15 February. Full-text : <https://presse.inserm.fr/la-souche-historique-du-sars-cov-2-decroit-alors-que-progression-du-variant-britannique-sintensifie/42204/>

Face à l'apparition des variants du SARS-COV2, les cartes de progression de l'épidémie de Covid 19 ont été rebattues. D'après les derniers scénarios élaborés par les chercheurs de l'Inserm sous la direction de Vittoria Colizza, le variant « britannique » pourrait devenir dominant en France la dernière semaine de février ou la première semaine de mars, avec de grandes disparités régionales. Pour le moment, le déploiement prévu de la vaccination aurait un impact limité sur ces trajectoires mais le renforcement des « mesures barrières » pourrait permettre de gagner du temps.

## 18 February

### Treatment

#### Paper of the Day

de Vries RD, Schmitz KS, Bovier Full-text:, et al. **Intranasal fusion inhibitory lipopeptide prevents direct-contact SARS-CoV-2 transmission in ferrets.** Science 2021, published 17 February. Full-text: <https://doi.org/10.1126/science.abf4896>

Matteo Porotto, Rory de Vries and colleagues propose a highly stable SARS-CoV-2 specific lipopeptide as a candidate antiviral for pre-exposure and early post-exposure prophylaxis for SARS-CoV-2 transmission in humans. Daily intranasal administration to ferrets completely prevented SARS-CoV-2 direct-contact transmission during 24-hour co-housing with infected animals, under stringent conditions that resulted in infection of 100% of untreated animals. The intranasal [SARSHRC-PEG4]2-chol peptide presented in this study is the first successful prophylaxis that prevents SARS-CoV-2 transmission in a relevant animal model, providing complete protection during a 24-hour period of intense direct contact.

### Epidemiology

Emanuel EJ, Bright R, Gounder C. **A Dismal Spring Awaits Unless We Slow the Spread of Covid-19.** The New York Times 2021, published 17 February.

Full-text: <https://www.nytimes.com/2021/02/17/opinion/covid-19-precautions.html>

How soon life returns to normal depends on what we do now.

## Variants

Hodcroft EB, Domman DB, Snyder DJ, et al. **Emergence in late 2020 of multiple lineages of SARS-CoV-2 Spike protein variants affecting amino acid position 677.** medRxiv 2021, posted 14 January. Full-text: <https://doi.org/10.1101/2021.02.12.21251658>

Emma Hodcroft et al. describe 7 newly identified coronavirus variants in the US with a mutation in spike position 677 (also named after birds, Mockingbird to Yellowhammer). The authors promise to keep an eye on S:677 polymorphisms for effects on proteolytic processing, cell tropism, and transmissibility.

Hoffmann M, Arora P, Groß R, et al. **SARS-CoV-2 variants B.1.351 and B.1.1.248: Escape from therapeutic antibodies and antibodies induced by infection and vaccination.** medRxiv 2021, posted 11 February. Full-text: <https://doi.org/10.1101/2021.02.11.430787>

Stefan Pöhlmann, Markus Hoffmann and colleagues show that B1351 (first detected in South Africa) and P1 (alias B11248, first detected in Brazil) were partially (casirivimab, in REGN-COV2, Regeneron) or fully (bamlanivimab, Lilly) resistant to monoclonal antibodies and was less efficiently inhibited by serum/plasma from convalescent individuals or those vaccinated with the Pfizer-BioNTech vaccine.

## Vaccines

Collier D, Ferreira I, Datir R, et al. **Age-related heterogeneity in Neutralising antibody responses to SARS-CoV-2 following BNT162b2 vaccination.** MedRxiv 2021, posted 16 February. Full-text: <https://doi.org/10.1101/2021.02.03.21251054>

Ravindra Gupta, Dami Collier and colleagues present a study of the immune response to the Pfizer/BioNTech vaccine in people aged 80 or older compared to younger people. Three weeks after the first dose a lower proportion of participants over 80 years old achieved an adequate neutralization titer of > 1:20 for 50% neutralization as compared to those under 80 (8/17 versus 19/24, p = 0,03); however, T cell responses were not different in those above or below 80



years. Following the second dose, 50% neutralizing antibody titers were above 1:20 in all individuals and there was no longer a difference by age.

Rommel A. **COVID vaccines and safety: what the research says.** Nature 2021, published 16 February. Full-text: <https://www.nature.com/articles/d41586-021-00290-x>

It is clear that coronavirus vaccines are safe and effective, but as more are rolled out, researchers are learning about the extent and nature of side effects.

## Clinical

Purdy A, Ido F, Sterner S, et al. **Myocarditis in COVID-19 presenting with cardiogenic shock: a case series.** European Heart Journal - Case Reports, Volume 5, Issue 2, 16 February 2021. Full-text: <https://academic.oup.com/ehjcr/article/5/2/ytab028/6138217>

Adam Purdy and colleagues describe two cases of COVID-19 induced myocarditis presenting with cardiogenic shock. These cases highlight the importance of recognizing late presentation viral myocarditis secondary to COVID-19 infection, even in patients without underlying cardiac disease.

Lecler A, Cotton F, Lersy F, Kremer S, Héran F; SFNR's COVID Study Group. **Ocular MRI Findings in Patients with Severe COVID-19: A Retrospective Multicenter Observational Study.** Radiology. 2021 Feb 16:204394. PubMed: <https://pubmed.gov/33591889>. Full-text: <https://doi.org/10.1148/radiol.2021204394>

Augustin Lecler et al. report a series of patients with severe COVID-19 presenting with abnormal MRI findings of the ocular globe, showing that 7% of patients with severe COVID-19 presented with one or several nodules of the posterior pole of the globe.

## Severe COVID

Zeberg H, Pääbo S. **A genomic region associated with protection against severe COVID-19 is inherited from Neandertals.** PNAS 2021, published 2 March. Full-text: <https://www.pnas.org/content/118/9/e2026309118>

Svante Pääbo and Hugo Zeberg show that a haplotype on chromosome 12, which is associated with a ~22% reduction in relative risk of becoming se-

verely ill with COVID-19 when infected by SARS-CoV-2, is inherited from the Neanderthals. A great thanks to them!

## Pediatrics

Blatz AM, Oboite M, Chiotos K, et al. **Cutaneous findings in SARS-CoV-2-associated Multisystem Inflammatory Disease in Children (MIS-C)**. Open Forum Infectious Diseases, published 16 February. Full-text: <https://doi.org/10.1093/ofid/ofab074>

The differential diagnosis of pediatric rash in times of COVID.

## German

If you read German, read Hecking C. **Adiós Corona-Tristesse**. Der Spiegel, 17 February. Full-text: <https://www.spiegel.de/reise/europa/la-gomera-deutsche-im-corona-exil-adios-corona-tristesse-a-663cccf-1fcf-4372-a8e6-0b279836d7a4>

Badewetter, offene Restaurants, Glasfaser-Internet: Hunderte Deutsche verbringen den Shutdown-Winter auf La Gomera. Hier können sie entspannen. Denn die Kanareninsel ist fast virusfrei – zumindest offiziell.

## 19 February

### Variants

#### Paper of the Day

Garcia-Beltran WF, Lam EC, St. Denis K, et al. **Circulating SARS-CoV-2 variants escape neutralization by vaccine-induced humoral immunity**. medRxiv 2021, posted 18 February. Full-text: <https://doi.org/10.1101/2021.02.14.21251704>

While many strains, such as B.1.1.7, B.1.1.298, or B.1.429, continue to be potently neutralized despite the presence of individual receptor-binding domain (RBD) mutations, other circulating SARS-CoV-2 variants escape vaccine-induced humoral immunity. The P.2 variant, which contains an E484K mutation within the RBD region, was capable of significantly reducing the neutralization potency of fully vaccinated individuals. Similarly, the P.1 strain, which has three RBD mutations, more effectively escaped neutralization. Finally, B.1.351 variants exhibited remarkable resistance to neutralization, largely due to three mutations in RBD but with a measurable contribution from non-RBD mutations. The magnitude of the effect is such that B.1.351 strains escape

neutralizing vaccine responses like SARS-CoV-1 (SARS 2002/2003) and bat-derived WIV1-CoV, suggesting that a relatively small number of mutations can mediate potent escape from vaccine responses. Alejandro Balazs, Wilfredo F. Garcia-Beltran and colleagues emphasize the need to develop broadly protective interventions against the evolving pandemic.

Resende PC, Delatorre D, Gräf T, et al. **Evolutionary Dynamics and Dissemination Pattern of the SARS-CoV-2 Lineage B.1.1.33 During the Early Pandemic Phase in Brazil.** *Front. Microbiol* 2021, 17 February. Full-text: <https://www.frontiersin.org/articles/10.3389/fmicb.2020.615280/>

Paula Cristina Resende et al. investigated the origin of the major and most widely disseminated SARS-CoV-2 Brazilian lineage B.1.1.33 that evolved from an ancestral clade, here designated B.1.1.33-like. The B.1.1.33-like lineage may have been introduced from Europe or may have arisen in Brazil in early February 2020 and a few weeks later gave origin to the lineage B.1.1.33.

## Virology

Kistler KE, Bedford T. **Evidence for adaptive evolution in the receptor-binding domain of seasonal coronaviruses OC43 and 229e.** *Elife*. 2021 Jan 19;10:e64509. PubMed: <https://pubmed.gov/33463525>. Full-text: <https://doi.org/10.7554/eLife.64509>

Kathryn Kistler and Trevor Bedford provide evidence that at least two of the *seasonal* coronaviruses, OC43 and 229E, are undergoing adaptive evolution in regions of the viral spike protein that are exposed to human humoral immunity. This suggests that reinfection may be due, in part, to positively selected genetic changes in these viruses that enable them to escape recognition by the immune system.

## Transmission

Kissler S, Fauver JR, Mack C, et al. **Densely sampled viral trajectories suggest longer duration of acute infection with B.1.1.7 variant relative to non-B.1.1.7 SARS-CoV-2.** *dash.harvard.edu* 2021, accessed 17 February. Full-text: <https://dash.harvard.edu/handle/1/37366884>

B.1.1.7 may cause longer infections with similar peak viral concentration compared to non-B.1.1.7 variants. This extended duration may contribute to B.1.1.7 SARS CoV-2's increased transmissibility. Yonatan Grad, Stephen Kissler and colleagues assessed longitudinal PCR tests performed in a cohort

of 65 individuals infected with SARS-CoV-2 undergoing daily surveillance testing, including seven infected with B.1.1.7.

	<b>B.1.1.7</b>	<b>non-B.1.1.7</b>
Mean duration of the <b>proliferation</b> phase	5,3 days (2,7, 7,8) (90% credible interval)	2,0 days (0,7, 3,3)
Mean duration of the <b>clearance</b> phase	8,0 days (6,1, 9,9)	6,2 days (5,1, 7,1)
Mean overall duration of infection ( <b>proliferation + clearance</b> phase)	13,3 days (10,1, 16,5)	8,2 days (6,5, 9,7)
Peak viral concentration	19,0 Ct (15,8, 22,0)	20,2 Ct (19,0, 21,4)
log <sub>10</sub> RNA copies/ml	8,5 (7,6, 9,4)	8,2 (7,8, 8,5)

Tan ZP, Silwal L, Bhatt SP, et al. **Experimental characterization of speech aerosol dispersion dynamics**. Sci Rep 11, 3953 (2021). Full-text: <https://www.nature.com/articles/s41598-021-83298-7>

Relative to sneezing and coughing, non-symptomatic aerosol-producing activities such as speaking are highly understudied. Here, Vrishank Raghav, Zu Puayen Tan and colleagues of Auburn University, US, delve into the details of *jet phases* and *puff phases*. One of their conclusions: speaking may represent a higher transmission risk than coughs and sneezes. Sneezing and coughing are singular events with a plume-front that passes by quickly, whereas speaking is a prolonged activity continuously producing plumes of aerosols.

Shriner SA, Ellis JW, Root JJ, Roug A, Stopak SR, Wiscomb GW, et al. **SARS-CoV-2 exposure in escaped mink, Utah, USA**. Emerg Infect Dis. 2021 Mar. Full-text: <https://doi.org/10.3201/eid2703.204444>

Free-range mink, presumed domestic escapees, exhibited high antibody titers, suggesting a potential SARS-CoV-2 transmission pathway to native wildlife. Interactions or shared resources between escaped mink and wild mink or other wildlife species represent potential transmission pathways for spillover of SARS-CoV-2 into wildlife and could lead to health consequences or establishment of new reservoirs in susceptible wildlife

Illingworth C, Hamilton W, Warne B, et al. **Superspreaders drive the largest outbreaks of hospital onset COVID-19 infection.** OSF Preprints 2021, posted 15 February. Full-text: <https://osf.io/wmkn3/>

Chris Illingworth et al. provides a detailed retrospective analysis of nosocomial SARS-CoV-2 transmission. Their data were consistent with a pattern of superspreading, where 20% of individuals caused 80% of transmission events.

## Prevention

Arnold C. **Covid-19: How the lessons of HIV can help end the pandemic.** BMJ 2021, published 16 February. Full-text: <https://doi.org/10.1136/bmj.n216>

Harm reduction, which proved its worth in HIV/AIDS, can help stem the COVID-19 pandemic by helping people change their behavior. Carrie Arnold explains how.

## Immunology

Neeland MR, Bannister S, Clifford V, et al. **Innate cell profiles during the acute and convalescent phase of SARS-CoV-2 infection in children.** Nat Commun 12, 1084 (2021). Full-text: <https://www.nature.com/articles/s41467-021-21414-x>

Melanie Neeland et al. provide a comprehensive characterization of innate cells responding during the acute and convalescent phase of mild pediatric COVID-19. The authors report acute and convalescent innate immune responses in 48 children and 70 adults infected with, or exposed to, SARS-CoV-2. The authors found that infection in children is characterized by increased activation of neutrophils and low circulating proportions of all monocyte subsets, dendritic cells and natural killer cells, in contrast to SARS-CoV-2-infected adults who showed reductions in the non-classical monocyte fraction only.

## Vaccine

Kupferschmidt K. **Unprotected African health workers die as rich countries buy up COVID-19 vaccines.** Science 2021, published 17 February. Full-text: <https://www.sciencemag.org/news/2021/02/unprotected-african-health-workers-die-rich-countries-buy-covid-19-vaccines>

While we are discussing how soon we can immunize everyone in the EU or the US, health workers continue to die in countries with zero doses administered so far.

## 20 February

### Treatment

#### Paper of the Day

Murai IH, Fernandes AL, Sales LP, et al. **Effect of a Single High Dose of Vitamin D3 on Hospital Length of Stay in Patients With Moderate to Severe COVID-19: A Randomized Clinical Trial.** JAMA. 2021 Feb 17. PubMed: <https://pubmed.gov/33595634>. Full-text: <https://doi.org/10.1001/jama.2020.26848>

The end of all speculations and hopes on immunomodulatory and anti-inflammatory properties of 25-hydroxyvitamin D? In this multicenter placebo-controlled trial from Brazil including 240 hospitalized patients with COVID-19 who were moderately to severely ill, vitamin D had no effect. A single high dose of vitamin D3, compared with placebo, did not significantly reduce hospital length of stay.

Leaf DE, Ginde AA. **Vitamin D3 to Treat COVID-19: Different Disease, Same Answer.** JAMA. 2021 Feb 17. PubMed: <https://pubmed.gov/33595641>. Full-text: <https://doi.org/10.1001/jama.2020.26850>

Comment: according to Adit Ginde and David Leaf, several limitations should be considered. The main issue: the study was underpowered. And as always, further studies should determine whether vitamin D3 supplementation could be useful in other settings, dosages and patient populations. It is important to remain open-minded.

### Epidemiology

Mwananyanda L, Gill CJ, MacLeod W, et al. **Covid-19 deaths in Africa: prospective systematic postmortem surveillance study.** BMJ. 2021 Feb 17;372:n334. PubMed: <https://pubmed.gov/33597166>. Full-text: <https://doi.org/10.1136/bmj.n334>

Do we vastly underestimate the impact of COVID-19 in Africa? Maybe. In this study of all deceased people of all ages at a University Hospital in Lusaka, Zambia, 70/364 (19,2%) were PCR positive. Most deaths in people with COVID-

19 (51/70; 73%) occurred in the community; none had been tested for SARS-CoV-2 before death.

## Variants

Liu Y, Liu J, Xia H, et al. **Neutralizing Activity of BNT162b2-Elicited Serum - Preliminary Report.** N Engl J Med. 2021 Feb 17. PubMed: <https://pubmed.gov/33596352>. Full-text: <https://doi.org/10.1056/NEJMc2102017>

Some more *in vitro* data on vaccine efficacy in SARS-CoV-2 variants. The authors produced different recombinant viruses, among them one with all the mutations found in the S gene in the B.1.351 lineage. After a single shot of BNT162b2 from Pfizer/BioNTech, neutralization of the B.1.351-spike virus was weaker by approximately two thirds. However, according to Yang Liu and colleagues, it remains unclear what this reduction means in terms of protection.

Wu K, Werner AP, Koch M, et al. **Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine - Preliminary Report.** N Engl J Med. 2021 Feb 17. PubMed: <https://pubmed.gov/33596346>. Full-text: <https://doi.org/10.1056/NEJMc2102179>

Same with Moderna's vaccine. *In vitro* reductions by a factor of 2,7-6,4 in titers of neutralizing antibodies against the partial or full panel of mutations. Again, protection against B.1.351 remains to be determined.

Twitter: Some more *in vitro* data on vaccine efficacy in SARS-CoV-2 variants (in particular B.1.351), after BNT162b2 from Pfizer/BioNTech <https://doi.org/10.1056/NEJMc2102017> and Moderna <https://doi.org/10.1056/NEJMc2102179>

## Vaccines

Amit S, Regev-Yochay G, Afek A, et al. **Early rate reductions of SARS-CoV-2 infection and COVID-19 in BNT162b2 vaccine recipients.** Lancet February 18, 2021. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00448-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00448-7/fulltext)

Good news from Israel, showing substantial early reductions in SARS-CoV-2 infection and symptomatic COVID-19 rates following first mRNA vaccine dose administration. Using a retrospective cohort of 9109 vaccine-eligible HCWs, Sharon Amit and colleagues estimate adjusted rate reductions of SARS-CoV-2

infections of 30% and 75% for days 1–14 and days 15–28 after the first dose, respectively.

Olliaro P. **What does 95% COVID-19 vaccine efficacy really mean?** *Lancet Inf Dis* February 17, 2021. Full-text: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00075-X/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00075-X/fulltext)

Important note of caution: using simple mathematics, Piero Olliaro explains that 94–95% efficacy does not mean that 95% of people are protected from disease with the vaccine. This distinction is all the more important as we do not know whether and how it could vary if the vaccines were deployed on populations with different exposures, transmission levels, and attack rates.

## Clinical

Pifarré i Arolas H, Acosta E, López-Casasnovas G. et al. **Years of life lost to COVID-19 in 81 countries.** *Sci Rep* February 18, 2021. Full-text: <https://www.nature.com/articles/s41598-021-83040-3>

Some numbers: The total years life lost (YLL) as of January 06, 2021 is 20.507.518. In heavily affected countries this is between 2 and 9 times the median YLL of seasonal influenza or between a quarter and a half of heart disease. Three quarters of the YLL are borne by people dying before age 75. Men have lost 45% more years of life than women.

Lee JT, Hesse EM, Paulin HN, et al. **Clinical and Laboratory Findings in Patients with Potential SARS-CoV-2 Reinfection, May–July 2020.** *Clin Infect Dis.* 2021 Feb 18:ciab148. PubMed: <https://pubmed.gov/33598716>. Full-text: <https://doi.org/10.1093/cid/ciab148>

Reinfection within 90 days of the initial infection seems to be unlikely. Investigating 73 patients with potential SARS-CoV-2 reinfection in the US in May–July 2020, the authors ruled out reinfection in almost all cases.

Reuken PA, Stallmach A, Pletz MW et al. **Severe clinical relapse in an immunocompromised host with persistent SARS-CoV-2 infection.** *Leukemia* February 19, 2021. <https://www.nature.com/articles/s41375-021-01175-8>

Another case of a female patient with a rituximab-treated B cell lymphoma with severe relapse 4 months after moderate COVID-19. These days, hemato-



logic therapies should be selected with caution, particularly those containing anti-CD20 antibodies.

## 21 February

### Vaccines

#### Paper of the Day

Voysey M, Costa Clemens SA, Madhi SA. **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.** *Lancet* February 19, 2021. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00432-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00432-3/fulltext)

In the case of the ChAdOx1 nCoV-19 (AZD1222) vaccine, it may be better to wait with the second shot. This pre-specified pooled analysis of AstraZeneca's vaccine trials suggests that a 3-month dose interval might have advantages over a program with a shorter dosing interval. 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% at  $\geq 12$  weeks) than in those with a short interval (vaccine efficacy 55% at  $< 6$  weeks).

### Epidemiology

Tian L, Li X, Qi F et al. **Harnessing peak transmission around symptom onset for non-pharmaceutical intervention and containment of the COVID-19 pandemic.** *Nat Commun* February 19, 2021. <https://www.nature.com/articles/s41467-021-21385-z>

Epidemiological modeling study, focusing on transmission around symptom onset by both pre-symptomatic and symptomatic viral carriers.

### Immunology

Sette A, Crotty S. **Adaptive immunity to SARS-CoV-2 and COVID-19.** *Cell*. 2021 Feb 18;184(4):861-880. PubMed: <https://pubmed.gov/33497610> . Full-text: <https://doi.org/10.1016/j.cell.2021.01.007>

CD4+ T cells, CD8+ T cells, and neutralizing antibodies all contribute to control of SARS-CoV-2 in both non-hospitalized and hospitalized cases of COVID-19. In this brilliant review of the adaptive immune response to SARS-CoV-2, Alessandro Sette and Shane Crotty discuss the specific functions and kinetics of

these adaptive immune responses, as well as their interplay with innate immunity and implications for COVID-19 vaccines and immune memory against re-infection.

Lee HK, Knabl L, Pipperger L, et al. **Immune transcriptomes of highly exposed SARS-CoV-2 asymptomatic seropositive versus seronegative individuals from the Ischgl community.** *Sci Rep* 11, 4243 (2021). <https://www.nature.com/articles/s41598-021-83110-6>

The ski resort of Ischgl, Austria experienced a superspreading event in early March 2020. In April, a seroprevalence of approximately 42% was found in the Ischgl population (n = 1867), with approximately 17% of these being asymptomatic. This comparative investigation of immune cell transcriptomes from 43 asymptomatic seropositive and 52 highly exposed seronegative individuals 4 – 6 weeks following the superspreading event showed no statistically significant differences. These results demonstrate that development of an antibody response to COVID-19 following viral exposure and seroconversion in asymptomatic cases is not necessarily associated with sustained alterations in the immune system transcriptome.

Rha MS, Jeong HW, Ko JH, et al. **PD-1-Expressing SARS-CoV-2-Specific CD8<sup>+</sup> T Cells Are Not Exhausted, but Functional in Patients with COVID-19.** *Immunity*. 2021 Jan 12;54(1):44-52.e3. PubMed: <https://pubmed.gov/33338412>. Full-text: <https://doi.org/10.1016/j.immuni.2020.12.002>

More about SARS-CoV-2-specific CD8<sup>+</sup> T cells. The highlights: 1) SARS-CoV-2-specific CD8<sup>+</sup> T cells are effector memory cells in convalescent individuals; 2) CCR7+CD45RA<sup>+</sup> cells are increased among SARS-CoV-2-specific cells in the late phase; 3) SARS-CoV-2-specific CD8<sup>+</sup> T cells have fewer IFN- $\gamma$ <sup>+</sup> cells than flu-specific cells; 4) PD-1-expressing SARS-CoV-2-specific CD8<sup>+</sup> T cells are not exhausted but functional.

Wheatley AK, Juno JA, Wang JJ, et al. **Evolution of immune responses to SARS-CoV-2 in mild-moderate COVID-19.** *Nat Commun* 12, 1162 (2021). <https://www.nature.com/articles/s41467-021-21444-5>

This longitudinal cohort of 64 participants who recovered from COVID-19 suggests that SARS-CoV-2 vaccines might require greater immunogenicity and durability than natural infection to drive long term protection. Both neutralizing and binding antibody responses decay after recovery from COVID-

19, assessed by both polyclonal assays and at the level of single antibody clonotypes with a mass spectrometry-based assay.

Supasa P, Daming Z, Dejnirattisai W, et al. **Reduced neutralization of SARS-CoV-2 B.1.1.7 variant by convalescent and vaccine sera.** Cell 2021, published 18 February. Full-text: [https://www.cell.com/cell/fulltext/S0092-8674\(21\)00222-1](https://www.cell.com/cell/fulltext/S0092-8674(21)00222-1)

Gavin Screaton, Piyada Supasa and colleagues mapped the impact of the N501Y mutation by structure/function analysis of a large panel of well-characterised monoclonal antibodies. B.1.1.7 was harder to neutralize but widespread escape from monoclonal antibodies or antibody responses generated by natural infection or vaccination was not observed (Supasa 2021).

## Clinical

Jeffery-Smith A, Iyanger N, Williams SV, et al. **Antibodies to SARS-CoV-2 protect against re-infection during outbreaks in care homes, September and October 2020.** Euro Surveill. 2021 Feb;26(5):2100092. PubMed: <https://pubmed.gov/33541486>. Full-text: <https://doi.org/10.2807/1560-7917.ES.2021.26.5.2100092>

Prior infection with SARS-CoV-2 as determined by antibody or RT-PCR positivity was highly protective at 4 months. Only one re-infection occurred in a seropositive staff member, whose antibodies were boosted following re-infection.

Rha MS, Jeong HW, Ko JH, et al. **PD-1-Expressing SARS-CoV-2-Specific CD8<sup>+</sup> T Cells Are Not Exhausted, but Functional in Patients with COVID-19.** Immunity. 2021 Jan 12;54(1):44-52.e3. PubMed: <https://pubmed.gov/33338412>. Full-text: <https://doi.org/10.1016/j.immuni.2020.12.002>

More about SARS-CoV-2-specific CD8<sup>+</sup> T cells. The highlights: 1) SARS-CoV-2-specific CD8<sup>+</sup> T cells are effector memory cells in convalescent individuals; 2) CCR7+CD45RA<sup>+</sup> cells are increased among SARS-CoV-2-specific cells in the late phase; 3) SARS-CoV-2-specific CD8<sup>+</sup> T cells have fewer IFN- $\gamma$ <sup>+</sup> cells than flu-specific cells; 4) PD-1-expressing SARS-CoV-2-specific CD8<sup>+</sup> T cells are not exhausted but functional.

## Treatment

Qiao J, Li YS, Zeng R. **SARS-CoV-2 Mpro inhibitors with antiviral activity in a transgenic mouse model.** Science 18 Feb 2021: eabf1611. <https://science.sciencemag.org/content/early/2021/02/17/science.abf1611.full>

The authors designed and synthesized 32 new bicycloproline-containing protease inhibitors derived from either boceprevir or telaprevir, two (older) approved drugs for hepatitis C. Two compounds (MI-09 and MI-30) showed excellent antiviral activity in cell-based assays and displayed good pharmacokinetic properties and safety in rats.

Raman AS, Barge VB, Darivenula AK, et al. **A Phase II Safety and Efficacy Study on Prognosis of Moderate Pneumonia in COVID-19 patients with Regular Intravenous Immunoglobulin Therapy.** J Infect Dis. 2021 Feb 15;jiab098. PubMed: <https://pubmed.gov/33585890> . Full-text: <https://doi.org/10.1093/infdis/jiab098>

Immunoglobulins for COVID-19? In this open-label, multicenter, randomized study on COVID-19 patients with moderate pneumonia in India, 100 patients were randomized 1:1 either to receive IVIG + standard of care (SOC) or SOC only. Duration of hospital stay was significantly shorter in the IVIG group compared to that of SOC alone (7,7 vs. 17,5 days). Duration for normalization of body temperature, oxygen saturation and mechanical ventilation were significantly shorter in IVIG compared to SOC. Percentages of patients on mechanical ventilation were not significantly different (24% vs 38%). Median time to RT-PCR negativity was significantly shorter with IVIG than SOC (7 vs 18 days).

## Beyond Corona

Killock D. **Unleashing the immune system against cancer.** Nature 2020, published 10 December. Full-text: <https://www.nature.com/articles/d42859-020-00076-7>

2010 witnessed a second landmark in the development of immune-checkpoint inhibitors (ICIs) when ipilimumab became the first agent shown to prolong overall survival (OS) in patients with advanced-stage melanoma.

## French

If you read French, read Stromboni C. **Sous la pression du variant anglais, Dunkerque voit flamber l'épidémie de Covid-19.** Le Monde 2021, published 20 February. Full-text : [https://www.lemonde.fr/planete/article/2021/02/20/sous-la-pression-du-variant-anglais-dunkerque-voit-flamber-l-epidemie-de-covid-19\\_6070631\\_3244.html](https://www.lemonde.fr/planete/article/2021/02/20/sous-la-pression-du-variant-anglais-dunkerque-voit-flamber-l-epidemie-de-covid-19_6070631_3244.html)

Le taux d'incidence est trois fois plus élevé que la moyenne nationale, et la part du variant « B.1.1.7 » estimée à 72 % des cas. L'hôpital voit affluer de nombreux patients, souvent plus jeunes.

Dagorn G. **Covid-19 : comment le variant B.1.1.7, apparu en Angleterre, menace de relancer l'épidémie en France.** Le Monde 2021, published 19 February. Full-text : [https://www.lemonde.fr/les-decodeurs/article/2021/02/19/comment-le-variant-britannique-menace-de-destabiliser-l-epidemie-en-france\\_6070563\\_4355770.html](https://www.lemonde.fr/les-decodeurs/article/2021/02/19/comment-le-variant-britannique-menace-de-destabiliser-l-epidemie-en-france_6070563_4355770.html)

En deux mois, ce variant a précipité l'Angleterre dans une nouvelle phase de l'épidémie, et pourrait provoquer une troisième vague tout aussi brutale en France.

## 22 February

### Epidemiology

#### Paper of the Day

Nelson EJ, McKune SL, Ryan KA, et al. **SARS-CoV-2 Positivity on or After 9 Days Among Quarantined Student Contacts of Confirmed Cases.** JAMA February 19, 2021. doi:10.1001/jama.2021.2392 <https://jamanetwork.com/journals/jama/fullarticle/2776857>

Testing at day 9 instead of 14 days of strict quarantine in students: this study found no evidence that an earlier return to school with a negative test result was linked with subsequent symptomatic illness. Among 799 student contacts of confirmed COVID-19 cases with a negative test result on days 9 to 14, only 1 student became symptomatic after returning to school and had a positive SARS-CoV-2 test result on day 14 after an initial negative test result on day 9. The virus from this student was genetically distinct from the virus isolated from the confirmed COVID-19 case to which the student had been exposed.

Brecht I, Peckeu L, Laga M, et al. **Reducing contacts to stop SARS-CoV-2 transmission during the second pandemic wave in Brussels, Belgium, August to November 2020.** Euro Surveill February 17, 2021;26(7):pii=2100065. <https://doi.org/10.2807/1560-7917.ES.2021.26.7.2100065>

This study shows how stringent physical distancing measures (a limit to three close contacts per person, a curfew, closure of bars and recommended teleworking) that were introduced 1 month after a persistent increase in Rt, sufficiently controlled transmission in Belgium, even with high case numbers and without closing schools or full lockdown (remember, this was prior to the occurrence of B.1.1.7).

## Virology

Cao W, Dong C, Kim S, et al. **Biomechanical Characterization of SARS-CoV-2 Spike RBD and Human ACE2 Protein-Protein Interaction.** Cell February 17, 2021. Full-text: [https://www.cell.com/biophysj/fulltext/S0006-3495\(21\)00141-7](https://www.cell.com/biophysj/fulltext/S0006-3495(21)00141-7)

Using spectroscopy, the authors studied the interaction between the receptor-binding domain (RBD) at viral surface spike (S) protein of different coronaviruses and the angiotensin-converting enzyme 2 (ACE2) receptor expressed on many human cell types. The dissociate rate for RBD-CoV2-ACE2 and RBD-CoV1-ACE2 bonds or interactions were significantly different, possibly explaining the greater infectivity of SARS-CoV-2 vs SARS-CoV-1.

## Vaccine

Gee J, Marquez P, Su J, et al. **First Month of COVID-19 Vaccine Safety Monitoring — United States, December 14, 2020–January 13, 2021.** MMWR Morb Mortal Wkly Rep. ePub: 19 February 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7008e3>

From December 14, 2020 to January 13, 2021, a total of 13,794,904 COVID-19 vaccine doses were administered in the US. Anaphylaxis rates were comparable with those reported after receipt of other vaccines. No unexpected patterns of reactions or other safety concerns have been identified during early monitoring.

## Transmission

Kristiansen MF, Heimustovu BH, á Borg S, Mohr TH, Gislason H, Møller LF, et al. **Epidemiology and clinical course of first wave coronavirus disease cases, Faroe Islands.** *Emerg Infect Dis.* 2021 Mar [date cited]. <https://doi.org/10.3201/eid2703.202589>

The Faroe Islands are a unique place to investigate the effects of COVID-19. Because of large scale testing in the country, few unrecorded cases are expected. Mapping the transmission chains of COVID-19 on the islands reveals that most cases infected few or no secondary contacts, whereas 3 super-spreading cases set off long, aggressive chains that led to most of the identified secondary locally transmitted cases.

## Clinical

Elezkurtaj S, Greuel S, Ihlow J, et al. **Causes of death and comorbidities in hospitalized patients with COVID-19.** *Sci Rep* 11, February 19, 2021. <https://www.nature.com/articles/s41598-021-82862-5>

They die from COVID-19. In 26 decedents who had clinically presented with severe COVID-19, Sefer Elezkurtaj from the Charité in Berlin, Germany, found that septic shock and multi-organ failure was the most common immediate cause of death, often due to suppurative pulmonary infection. The majority of patients died of COVID-19 with only contributory implications of pre-existing health conditions.

Bajaj R, Sinclair HC, Patel K. **Delayed-onset myocarditis following COVID-19.** *Lancet Resp Med* February 19, 2021. DOI:[https://doi.org/10.1016/S2213-2600\(21\)00085-0](https://doi.org/10.1016/S2213-2600(21)00085-0). Full text: [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00085-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00085-0/fulltext)

Nine patients with acute cardiac decompensation, negative RT-PCR for SARS-CoV-2, markedly increased serum troponin, and substantially raised inflammatory markers: Retesh Bajaj and colleagues from London suggest that this series describes cardiogenic shock due to a multisystem inflammatory syndrome in adults (MIS-A) after COVID-19.

## Co-morbidities

Brix TH, Hegedüs L, Hallas J, et al. **Risk and course of SARS-CoV-2 infection in patients treated for hypothyroidism and hyperthyroidism.** *Lancet Diabetes and Endocrinology* February 19, 2021. [https://www.thelancet.com/journals/landia/article/PIIS2213-8587\(21\)00028-0/fulltext](https://www.thelancet.com/journals/landia/article/PIIS2213-8587(21)00028-0/fulltext)

This large case-control study from Denmark indicates that patients treated for hypothyroidism or hyperthyroidism do not have an increased risk of contracting SARS-CoV-2 infection. The results also suggest that treatment for thyroid dysfunction, when controlling for relevant confounding, does not influence the prognosis of SARS-CoV-2 infection.

Mitchel KM, Dimitrov D, Silhol R, et al. **The potential effect of COVID-19-related disruptions on HIV incidence and HIV-related mortality among men who have sex with men in the USA: a modelling study.** *Lancet HIV* February 19, 2021. [https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018\(21\)00022-9/fulltext](https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(21)00022-9/fulltext)

What is the impact of COVID-19 on the HIV pandemic? This deterministic, compartmental HIV transmission model for MSM in Baltimore, US, used available data on COVID-19-related disruptions to HIV services to predict effects of reductions in sexual partners, condom use, HIV testing, viral suppression, PrEP and ART use. Results: it depends. A 25% reduction in sexual partnerships is estimated to offset the effect of the combined service disruptions on new HIV infections.

## Treatment

Mathews KS, Soh H, Shaefi S, et al. **Prone Positioning and Survival in Mechanically Ventilated Patients With Coronavirus Disease 2019-Related Respiratory Failure.** *Crit Care Med.* 2021 Feb 17. PubMed: <https://pubmed.gov/33595960> . Full-text: [https://journals.lww.com/ccmjournals/Abstract/9000/Prone\\_Positioning\\_and\\_Survival\\_in\\_Mechanically.95335.aspx](https://journals.lww.com/ccmjournals/Abstract/9000/Prone_Positioning_and_Survival_in_Mechanically.95335.aspx)

Pro-proning: among 2338 eligible patients in this multicenter cohort study, 702 (30.0%) were proned within the first 2 days of ICU admission. After inverse probability weighting, baseline and severity of illness characteristics were “well-balanced” between proned and non-proned patients. Patients



proned within the first 2 days of ICU admission had a lower adjusted risk of death compared with non-proned patients (HR: 0.84; 95% CI: 0.73–0.97).

## 23 February

### Transmission

#### Paper of the Day

Wang Z, Galea ER, Grandison A, et al. **Inflight Transmission of COVID-19 Based on Experimental Aerosol Dispersion Data.** *Journal of Travel Medicine*, February 19, 2021. taab023, <https://doi.org/10.1093/jtm/taab023>

No nuts on planes. This elegant analysis demonstrated that while there is a significant reduction in aerosol concentration due to the nature of the cabin ventilation and filtration system, this does not necessarily mean that there is a low probability or risk of in-flight infection. Main results: 1. The economy cabin exhibits the highest probability of infection. 2. Average risk (without masks) for a 2-hour flight in a B777–200 aircraft ranges from 0.1% to 2.5% and for a 12-hour flight from 0.8% to 10.8%, respectively. 3. If all passengers wear face masks throughout the 12-hour flight, the average infection probability can be reduced by approximately 73%/32% for high/low efficiency masks. 4. If face masks are worn by all passengers except during a one-hour meal service, the average infection probability is increased by 59%/8% compared to the situation where the mask is not removed. Bottom line: Don't remove your KN95 mask. No nuts, no meals. And better forget your frequent flyer status as long as you are unvaccinated (actually, forget it anyway, we'll get warm here up north and Zoom works fine).

Bender JK, Brandl M, Höhle M, Buchholz U, Zeitlmann N. **Analysis of asymptomatic and presymptomatic transmission in SARS-CoV-2 outbreak, Germany, 2020.** *Emerg Infect Dis* February 18, 2021 Apr [date cited]. [https://wwwnc.cdc.gov/eid/article/27/4/20-4576\\_article](https://wwwnc.cdc.gov/eid/article/27/4/20-4576_article)

Jennifer K. Bender and colleagues determined secondary attack rates (SAR) among close contacts of 46 symptomatic and 7 asymptomatic patients from Southern Germany. Little to no transmission occurred from asymptomatic case-patients. Pre-symptomatic transmission was more frequent than symptomatic transmission.

## Virology

Kim MC, Cui C, Shin KR, et al. **Duration of Culturable SARS-CoV-2 in Hospitalized Patients with Covid-19.** N Engl J Med. 2021 Feb 18;384(7):671-673. PubMed: <https://pubmed.gov/33503337> . Full-text: <https://doi.org/10.1056/NEJMc2027040>

How long can we find culturable virus? Not beyond day 12. Min-Chul Kim and colleagues from Seoul, Korea, cultured SARS-CoV-2 in serial respiratory samples obtained from 21 hospitalized patients with COVID-19 to assess the duration of shedding of viable virus. The latest positive viral culture was 12 days after symptom onset (in one patient). Viral culture was positive only in samples with a cycle-threshold value of 28.4 or less.

## Diagnostics

Harrithøj LH, Gybel-Brask M, Afzal S, et al. **Comparison of sixteen serological SARS-CoV-2 immunoassays in sixteen clinical laboratories.** J Clin Microbiol. 2021 Feb 11;JCM.02596-20. PubMed: <https://pubmed.gov/33574119>. Full-text: <https://doi.org/10.1128/JCM.02596-20>

This comparative study of 15 commercial and one in-house laboratory serological SARS-CoV-2 assays pinpoints differences in accuracy; most total-Ab and IgG assays (not all), including assays with potential for high-throughput production in automated laboratories, reached pre-defined criteria for acceptable performance. Diagnostic accuracy was higher in the group of the SARS-CoV-2 total Ab assays compared to the group of the SARS-CoV-2 IgG assays.

Al Suwaidi H, Senok A, Varghese R, et al. **Saliva for molecular detection of SARS-CoV-2 in school-aged children.** Clin Microb Infection, February 19, 2021. [https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(21\)00084-7/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00084-7/fulltext)

Use saliva in children! For this COVID-19 screening study in Dubai, United Arab Emirates, each child provided paired nasopharyngeal (NP) swab and saliva. Main results: detection in NP swab (16.7%; 81/485) and saliva (15.9%; 77/485) did not differ. Cycle threshold values were significantly higher in NP swab/saliva pairs with discordant findings compared to those with both specimens positive.

## Clinical

Schinkel M, Appelman B, Butler J, et al. **Association of clinical sub-phenotypes and clinical deterioration in COVID-19: further cluster analyses.** *Intensive Care Med* (2021). February 18, 2021. <https://doi.org/10.1007/s00134-021-06363-9>

Among patients admitted to ten teaching hospitals across the Netherlands, three sub-phenotypes were identified.

- Sub-phenotype 1 (n = 592) mainly included females (75%, median age 63), characterized by a high prevalence of gastro-intestinal complaints (84%) and sputum production (63%). Co-morbidities and medication usage were scarce. The composite outcome of ICU admittance/death rates was relatively low (25%).
- Sub-phenotype 2 (n = 876) included more males (80%, median age 63 years) with few co-morbidities and the lowest medication usage of all three groups. Patients presented with less symptoms than those in sub-phenotype 1, but ICU admittance/death rates were higher (31%).
- Sub-phenotype 3 (n = 551) mostly consisted of older males (80%, median age 76) with multiple co-morbidities, mainly diabetes (62%), hypertension (88%) and other cardiovascular diseases (72%), and consequent medication usage. Patients reported less symptoms such as dyspnea (67%), headache (9%) and myalgia (12%). ICU admission and/or 21-day mortality occurred in 43%.

The authors believe the main value of these sub-phenotypes lies not with their ability to discriminate between clinical outcomes, but in their potential to understand disease heterogeneity and find more homogeneous patient subgroups that may respond more similarly to certain treatments.

## Collateral damage

Fong MW, Leung NHL, Cowling BJ, Wu P. **Upper respiratory infections in schools and childcare centers reopening after COVID-19 dismissals, Hong Kong.** *Emerg Infect Dis*, February 17, 2021 (May date cited). [https://wwwnc.cdc.gov/eid/article/27/5/21-0277\\_article](https://wwwnc.cdc.gov/eid/article/27/5/21-0277_article)

A large number of outbreaks of acute upper respiratory tract infections (URTIs), likely rhinovirus infections, were identified in October–November 2020 in reopened primary schools, secondary schools, kindergartens, childcare centers, and nursery schools in Hong Kong; these outbreaks led to further territory-wide school dismissals for younger children. Increased susceptibility to rhinoviruses during prolonged school closures and dismissals for coro-

navirus disease and varying effectiveness of nonpharmaceutical interventions may have heightened transmission of cold-causing viruses when school attendance resumed.

## Co-morbidities

Quartuccio L, Treppo E, Binutti M, Del Frate G, De Vita S. **Timing of Rituximab and immunoglobulin level influence the risk of death for COVID-19 in ANCA-associated vasculitis.** *Rheumatology (Oxford)*. 2021 Feb 20:keab175. PubMed: <https://pubmed.gov/33609106> . Full-text: <https://doi.org/10.1093/rheumatology/keab175>

SARS-CoV-2 infections in two patients with polyangiitis who had been treated with rituximab. One died, one was asymptomatic. As timing of rituximab and IgG levels were quite different between the two cases, the authors speculate that this conditioned the final outcome greatly.

## Severe COVID-19

Shah P, Smith H, Olarewaju A, et al. **Is Cardiopulmonary Resuscitation Futile in Coronavirus Disease 2019 Patients Experiencing In-Hospital Cardiac Arrest?** *Critical Care Medicine: February 2021 - Volume 49 - Issue 2 - p 201-208.* Full-text: <https://doi.org/10.1097/CCM.0000000000004736>

Well, probably yes. Out of 1094 COVID-19 patients who were admitted to three hospitals in Georgia, 63 patients suffered from in-hospital cardiac arrest with attempted resuscitation and were included in this study. Although return of spontaneous circulation was achieved in 29% of patients, it was brief in all of them. The in-hospital mortality was 100%.

## Treatment

Ma S, Xu C, Liu S, et al. **Efficacy and safety of systematic corticosteroids among severe COVID-19 patients: a systematic review and meta-analysis of randomized controlled trials.** *Sig Transduct Target Ther* 6, 83 (2021). <https://doi.org/10.1038/s41392-021-00521-7>

In this meta-analysis including 7 RCTs and 6250 severe COVID-19 patients, corticosteroid treatment was related to a reduction of all-cause mortality and disease progression, but not with an increase in serious adverse events. Of note, survival benefit was absent if RECOVERY trial was excluded. More robust supporting data are required.

## 24 February

### Immunology

#### Paper of the Day

Tang J, Ravichandran S, Lee Y, et al. **Antibody affinity maturation and plasma IgA associate with clinical outcome in hospitalized COVID-19 patients.** *Nat Commun* 12, 1221 (February 22, 2021). Full-text: <https://www.nature.com/articles/s41467-021-21463-2>

A comprehensive longitudinal antibody analysis on 25 SARS-CoV-2 PCR-confirmed hospitalized COVID-19 patients. In more severe COVID-19 patients, even though they could generate high binding and neutralizing antibody titers, there was a block to antibody affinity maturation that may be linked to deficiency in CD4 cells, and especially T follicular helper cell subsets, which are required for entry into the germinal center. Sustained high levels of pro-inflammatory cytokines (IL-6 and IL-8), high serum IgA, and blunted affinity maturation against the pre-fusion spike protein were predictive of the worst outcome for hospitalized patients. An elevated inflammatory response may be augmented by low-affinity antibodies that are not efficient in controlling SARS-CoV-2 replication.

### Epidemiology

Zimmerman FJ, Anderson NW. **Association of the Timing of School Closings and Behavioral Changes With the Evolution of the Coronavirus Disease 2019 Pandemic in the US.** *JAMA Pediatr* February 22, 2021. <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2776608>

This cross-sectional study used US COVID-19 data (March to May 2020) and anonymized cell phone as well as internet data. The main findings: voluntary behavioral changes, such as reductions in time spent at work, had an association with COVID-19 incidence and mortality that was 3 times stronger than that of school closures. According to Nathaniel W. Anderson and Frederick J. Zimmerman, their findings suggest that less harmful ways of preventing SARS-CoV-2 transmission are available than mandatory school closures (note: this is based on data prior to the occurrence of more transmittable variants).

Gold JA, Gettings JR, Kimball A, et al. **Clusters of SARS-CoV-2 Infection Among Elementary School Educators and Students in One School District – Georgia, December 2020–January 2021.** *MMWR Morb Mortal Wkly Rep.*

ePub: 22 February 2021. Full-text:  
<http://dx.doi.org/10.15585/mmwr.mm7008e4>

Vaccinate and test the teachers! This investigation in a Georgia school district from December 1, 2020 to January 22, 2021, identified nine clusters of COVID-19 cases involving 13 educators and 32 students at six elementary schools. Consistent with findings from international studies, the report found that initial infections among educators played a substantial role in in-school SARS-CoV-2 transmission and subsequent chains of infection to other educators, students, and households, highlighting the importance of preventing infections among educators in particular.

## Virology

Bullock HA, Goldsmith CS, Zaki SR, Martines RB, Miller SE. **Difficulties in differentiating coronaviruses from subcellular structures in human tissues by electron microscopy.** Emerg Infect Dis, February 18, 2021 Apr [date cited]. [https://wwwnc.cdc.gov/eid/article/27/4/20-4337\\_article](https://wwwnc.cdc.gov/eid/article/27/4/20-4337_article)

In attempts to attribute pathology directly to tissue damage caused by SARS-CoV-2, investigators have inaccurately reported subcellular structures, including coated vesicles, multivesicular bodies, and vesiculating rough endoplasmic reticulum, as coronavirus particles. Hannah A. Bullock from Atlanta and colleagues describe some morphologic features of coronavirus that distinguish it from subcellular structures.

## Clinical

Dai CL, Kornilov SA, Roper RT, et al. **Characteristics and Factors Associated with COVID-19 Infection, Hospitalization, and Mortality Across Race and Ethnicity.** Clin Infect Dis. 2021 Feb 20:ciab154. PubMed: <https://pubmed.gov/33608710>. Full-text: <https://doi.org/10.1093/cid/ciab154>

This retrospective cohort study examining 629,953 patients tested for SARS-CoV-2 in a large US health system, Hispanics who tested positive at a higher rate required excess hospitalization and mechanical ventilation and had higher odds of in-hospital mortality despite younger age.

## Long COVID-19

Klein H, Asseo K, Karni N, et al. **Onset, duration and unresolved symptoms, including smell and taste changes, in mild COVID-19 infections.** A cohort study in Israeli patients. *Clin Microbiol Infect.* 2021 Feb 16:S1198-743X(21)00083-5. PubMed: <https://pubmed.gov/33607252>. Full-text: <https://doi.org/10.1016/j.cmi.2021.02.008>

Of 103 patients with mild COVID-19, 46% had at least one unresolved symptom at six months, most commonly fatigue (22%), smell and taste changes (15% and 8%, respectively), and breathing difficulties (8%).

Logue JK, Franko NM, McCulloch D, et al. **Sequelae in Adults at 6 Months After COVID-19 Infection.** *JAMA Netw Open*, February 19, 2021;4(2):e210830. Full-text: <https://doi.org/10.1001/jamanetworkopen.2021.0830>

A longitudinal prospective cohort of adults with COVID-19 (11 asymptomatic, 150 outpatients with mild disease, 16 with severe illness) was compared with a concurrent cohort of healthy patients. Between 3 and 9 months after onset of illness, the most common persistent symptoms were fatigue (14%) and loss of sense of smell or taste (14%). Notably, 14 participants, including 9 non-hospitalized individuals, reported negative impacts on activity of daily living after infection. With > 60 million cases worldwide, even a small incidence of long-term debility could have enormous health and economic consequences.

Zhou M, Wong CK, Un KC, et al. **Cardiovascular sequelae in uncomplicated COVID-19 survivors.** *PLoS One.* 2021 Feb 11;16(2):e0246732. PubMed: <https://pubmed.gov/33571321>. Full-text: <https://doi.org/10.1371/journal.pone.0246732>

Cardiac abnormality is common (but mostly self-limiting) among COVID survivors with mild disease: a systematic cardiac screening was performed among 97 consecutive COVID-19 survivors (mean age 46 years, all with non-severe disease), including treadmill exercise test and cardiac magnetic resonance imaging (CMR). Median duration from discharge to screening was 11 days. Cardiac abnormalities were detected in 42.3% including sinus bradycardia (29.9%), newly detected T-wave abnormality (8.2%) and elevated troponin level (6.2%). For COVID-19 survivors with persistent elevation of troponin levels after discharge or newly detected T wave abnormalities, echocardiography and CMR did not reveal any evidence of infarct, myocarditis, or left ventricular systolic dysfunction.

## Collateral damage

Ghafil C, Matsushima K, Henry R, et al. **Trends in Trauma Admissions During the COVID-19 Pandemic in Los Angeles County, California.** JAMA Netw Open. February 22, 2021;4(2):e211320. Full-text: <https://doi.org/10.1001/jamanetworkopen.2021.1320>

Less accidents (for a few weeks) but more gunshots? In this retrospective cohort study of 6777 trauma admissions in Los Angeles County from January 1 to June 7, 2020, overall volume transiently decreased but quickly returned to baseline. Mechanisms of injury were significantly different, with a steady increase in admissions for “penetrating” injuries (in other words: mainly gunshots).

## Treatment

Hunt BJ, De Paula EV, McLintock C, Dumantepe M. **Prophylactic anticoagulation for patients in hospital with covid-19.** BMJ. 2021 Feb 19;372:n487. PubMed: <https://pubmed.gov/33608304>. Full-text: <https://doi.org/10.1136/bmj.n487>

The risk of hospital-associated venous thromboembolism for medical inpatients is greatest in the first 90 days post-discharge, and many units are using unlicensed extended thromboprophylaxis with LMWH or direct acting oral anticoagulants for patients discharged after COVID-19. Recent retrospective data showing low rates of hospital-associated venous thromboembolism post-discharge are reassuring, but according to this editorial, randomized trials formally evaluating the need for extended thromboprophylaxis are now required.

## 25 February

### Variants

#### Paper of the Day

Zhou D, Dejnirattisai W, Supasa P, et al. **Evidence of escape of SARS-CoV-2 variant B.1.351 from natural and vaccine induced sera.** Cell February 23, 2021. Full-text: <https://www.cell.com/action/showPdf?pii=S0092-8674%2821%2900226-9>

The new variants have multiple changes in the immunodominant spike protein which facilitates viral cell entry via the ACE receptor. Mutations in the receptor recognition site on the spike are of great concern due to their poten-



tial for immune escape. Daming Zhou and colleagues from Oxford, UK describe a structure-function analysis of B.1.351 using a large cohort of convalescent and vaccinee serum samples. The receptor binding domain mutations provide tighter ACE2 binding and widespread escape from monoclonal antibody neutralization largely driven by E484K although K417N and N501Y act together against some important antibody classes. The neutralization titer for B.1.351 reduced 8 to 9-fold for both the Pfizer and AstraZeneca vaccinees. E484K, K417N and N501Y caused widespread escape from monoclonal antibodies. However, let's keep in mind that even if antibody responses to the new variants are not able to prevent infection, they may moderate severity. Moreover, T cell responses to spike may not be disrupted by the mutational changes described here.

Li Q, Nie J, Wu J. **No higher infectivity but immune escape of SARS-CoV-2 501Y.V2 variants.** Cell February 23, 2021. <https://www.cell.com/action/showPdf?pii=S0092-8674%2821%2900231-2>

More experiments on B.1.351 (also known as 501Y.V2). These variants DO NOT confer increased infectivity in multiple cell types except for murine (not human!) ACE2-overexpressing cells, where a substantial increase in infectivity was observed. As seen in the other paper, the susceptibility of the variants to neutralizing monoclonal antibodies was substantially diminished, and the neutralization ability of the sera from convalescent patients and immunized mice was also reduced. The neutralization resistance was mainly caused by E484K and N501Y mutations in the receptor-binding domain of Spike.

Vasques Nonaka CK, Franco MM, Gräf T, et al. **Genomic evidence of SARS-CoV-2 reinfection involving E484K spike mutation, Brazil.** Emerg Infect Dis. February 19, 2021. [https://wwwnc.cdc.gov/eid/article/27/5/21-0191\\_article](https://wwwnc.cdc.gov/eid/article/27/5/21-0191_article)

A case of reinfection from distinct virus lineages in Brazil harboring the E484K mutation, a variant associated with escape from neutralizing antibodies (see above). Both episodes were considered to be mild.

## Transmission

Spinelli MA, Gliden DV, Gennatas ED. **Importance of non-pharmaceutical interventions in lowering the viral inoculum to reduce susceptibility to infection by SARS-CoV-2 and potentially disease severity.** Lancet Inf Dis February 22, 2021. Full-text: [https://doi.org/10.1016/S1473-3099\(20\)30982-8](https://doi.org/10.1016/S1473-3099(20)30982-8)

Matthew Spinelli and colleagues argue that even as safe and effective vaccines are being rolled out, non-pharmaceutical interventions (including social distancing, mask wearing, and improved ventilation) will continue to play an essential role in suppressing SARS-CoV-2 transmission until equitable and widespread vaccine administration has been completed. In this personal viewpoint, they review the influence of the viral inoculum on disease susceptibility for several human pathogens and the preliminary data available for SARS-CoV-2.

## Diagnostics

Toh ZQ, Higgings RA, Anderson J, et al. **The use of dried blood spots for the serological evaluation of SARS-CoV-2 antibodies.** *Journal of Public Health*, fdab011, 22 February 2021. <https://doi.org/10.1093/pubmed/fdab011>

Zheng Quan Toh and colleagues from Melbourne compared the SARS-CoV-2 IgG antibody response in paired serum and eluates from dried blood spot specimens. The IgG seropositivity rate was similar between serum and DBS specimens (18.9%, 18/95 versus 16.8%, 16/95), respectively. DBS would facilitate serosurveillance efforts particularly in hard-to-reach populations.

## Clinical

Markewitz R, Torge A, Wandinger KP. et al. **Clinical correlates of anti-SARS-CoV-2 antibody profiles in Spanish COVID-19 patients from a high incidence region.** *Sci Rep* 11, 4363 (2021). <https://doi.org/10.1038/s41598-021-83969-5>

No prognostic value of SARS-CoV-2 antibodies (assessed by the EUROIMMUN assay) in this cohort. Serum samples from 347 Spanish patients from a high-incidence region were collected at one point in time (ranging from 0 to 33 days since onset of symptoms). Neither the presence, nor the levels of antibodies served as prognostic markers. The presence and level of antibodies was not associated with age, sex, duration of hospitalization, treatment in the ICU or death. A subgroup of patients (IgG 4%) did not develop antibodies at the time of sample collection. Compared to the patients that did, no differences were found.

Zhao Y, Cunningham MH, Mediavilla JR, et al. **Diagnosis, clinical characteristics, and outcomes of COVID-19 patients from a large healthcare system in northern New Jersey.** *Sci Rep* 11, 4389 (2021). <https://doi.org/10.1038/s41598-021-83959-7>

In this large cohort of 722 patients from New Jersey, viral load, as indicated by the cycle of threshold (Ct) values from the RT-PCR test, was significantly higher in the oldest patient group ( $\geq 80$ ), and inversely correlated with survival.

dos Santos LA, Germano de Góis Filho P, Fantini Silva AM, et al. **Recurrent COVID-19 including evidence of reinfection and enhanced severity in thirty Brazilian healthcare workers.** *J Infection*, February 12, 2021. DOI:<https://doi.org/10.1016/j.jinf.2021.01.020>

In 33 patients with recurrent COVID-19 and a positive PCR, recurrence was associated with working as a healthcare professional, blood-group A, and low IgG response to infection. All had recovered from first episode symptoms, returned to work and later suffered recurrent symptoms. Of note, recurrent episodes tended to be more severe, with one fatal infection.

## Treatment

Cross RW, Prasad AN, Borisevich V. **Use of convalescent serum reduces severity of COVID-19 in nonhuman primates.** *Cell Rep* February 23, 2021. Full-text: <https://doi.org/10.1016/j.celrep.2021.108837>

Several human clinical trials on the passive transfer of convalescent plasma have yielded mixed results. In this animal experiment on 10 African green monkeys, sera with high SARS-CoV-2 neutralizing antibody titers showed the greatest benefit. Data suggested passive transfer as a therapy in humans in early stages of disease.

Xie C, Chen Y, Luo D, et al. **Therapeutic potential of C1632 by inhibition of SARS-CoV-2 replication and viral-induced inflammation through upregulating let-7.** *Sig Transduct Target Ther* 6, 84 (2021). <https://doi.org/10.1038/s41392-021-00497-4>

MicroRNAs (miRNAs) are small, non-coding RNAs that play regulatory roles in gene expression by targeting their mRNA. The authors report that let-7, an miRNA that is ubiquitously expressed in human cells, blocks SARS-CoV-2 replication by targeting S and M protein. In addition, let-7 suppresses the expression of multiple inflammatory factors. C1632, a small molecule serving as a let-7 stimulator, is capable of upregulating the expression of let-7, thus possibly reducing viral replication and secretion of inflammatory cytokines.

## 26 February

### Vaccines

#### Paper of the Day

Dagan N, Barda N, Kepten E, et al. **BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting.** NEJM February 24, 2021. <https://www.nejm.org/doi/full/10.1056/NEJMoa2101765>

No doubt, paper of the day! Encouraging real-life data from Israel: Estimated vaccine effectiveness (> 1 M people vaccinated) during the follow-up period starting 7 days after the second dose was 92% for documented infection, 94% for symptomatic COVID-19, 87% for hospitalization, and 92% for severe COVID-19. Estimated effectiveness days 14 through 20 (after one dose) and days 21 through 27 (gradual shifting between the first and second vaccine doses) was 46% and 60% for documented infection, 57% and 66% for symptomatic COVID-19, 74% and 78% for hospitalization, 62% and 80% for severe COVID-19, and 72% and 84% for COVID-19–related death, respectively.

Kyriakidis NC, López-Cortés A, González EV, et al. **SARS-CoV-2 vaccines strategies: a comprehensive review of phase 3 candidates.** npj Vaccines 6, 28 (2021). <https://www.nature.com/articles/s41541-021-00292-w>

Comprehensive is right. A fantastic review discusses different strategies used for vaccine development and provides an overview of the current leading vaccine candidates against SARS-CoV-2.

### Epidemiology

Lendacki FR, Teran RA, Gretsch S, Fricchione MJ, Kerins JL. **COVID-19 Outbreak Among Attendees of an Exercise Facility — Chicago, Illinois, August–September 2020.** MMWR Morb Mortal Wkly Rep. ePub: 24 February 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7009e2>

Have you recently met your personal trainer from the local gym? Did he tell you how he disagrees with the lockdown and the closing of the gym, after all they had worked so hard to develop wonderful hygiene management concepts? That all classes would be held at ≤ 25% capacity (i.e., 10–15 persons)? That mask use, temperature checks, symptom screenings would be required on entry (ok, patrons were allowed to remove masks during exercise) and that patrons would

bring their own mats and weights and would be stationed  $\geq 6$  ft apart? Then show him this report. During August 24–September 1, 2020, an exercise facility at Chicago did exactly this. The results: 55 COVID-19 cases were identified among 81 attendees of indoor high-intensity classes. Twenty-two (40%) persons with COVID-19 attended on or after the day symptoms began. Most attendees (76%) wore masks infrequently, including persons with (84%) and without COVID-19 (60%).

Harvey RA, Rassen JA, Kabelac CA, et al. **Association of SARS-CoV-2 Seropositive Antibody Test With Risk of Future Infection.** *JAMA Intern Med* February 24, 2021. Full-text: <https://doi.org/10.1001/jamainternmed.2021.0366>

Seropositivity is associated with protection from infection. In this cohort study of more than 3.2 million US patients with a SARS-CoV-2 antibody test, 0.3% of those indexed with positive test results had evidence of a positive nucleic acid amplification test beyond 90 days after index, compared with 3.0% indexed with negative antibody test results. During the follow-up periods, the ratio (95% CI) of positive PCR results among individuals who had a positive antibody test at index vs those with a negative antibody test at index was 2.85 (95% CI: 2.73-2.97, consistent with prolonged RNA shedding!) 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.

Katz MH. **How to Advise Persons Who Are Antibody Positive for SARS-CoV-2 About Future Infection Risk.** *JAMA Intern Med* February 24, 2021. <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2776809>

In his comment, Mitchell H. Katz still believes that vaccination against SARS-CoV-2 is recommended regardless of antibody status (as nobody knows how long antibody protection due to natural infection will last).

Davido B, Mascitti H, Fortier-Beaulieu M, et al. **Blue toes' following vaccination with the BNT162b2 mRNA COVID-19 vaccine.** *Journal of Travel Medicine*, 23 February 2021, taab024, <https://doi.org/10.1093/jtm/taab024>

COVID toes-like syndrome linked to COVID-19 vaccine: This interesting case report describes a young Caucasian female (aged 41) who presented with chil-

blain-like skin changes on her toes that appeared 4 days after the first injection with the Pfizer-BioNTech-162b2 vaccine.

## Epidemiology

Groves LM, Usagawa L, Elm J, et al. **Community Transmission of SARS-CoV-2 at Three Fitness Facilities — Hawaii, June–July 2020**. *MMWR Morb Mortal Wkly Rep.* ePub: 24 February 2021. DOI: <http://dx.doi.org/10.15585/mmwr.mm7009e1>

Twenty-one COVID-19 cases were linked to an index case in a fitness instructor, who, along with a patient who was also an instructor, taught classes < 1 day, 1 to < 2 days, and ≥ 2 days before symptom onset; aggregate attack rates were 95% (20 of 21), 13% (one of eight), and 0% (zero of 33). Of note, use of masks was not required in the fitness facilities.

## Clinical

Folgueira MD, Luczkowiak J, Lasala F, et al. **Prolonged SARS-CoV-2 cell culture replication in respiratory samples from patients with severe COVID-19**. *Clin Microbiology Inf* February 22, 2021. Full-text: <https://doi.org/10.1016/j.cmi.2021.02.014>

See title. This study from Madrid found a completely different pattern of SARS-CoV-2 viability in upper respiratory tract samples from mild cases, in which viral replication occurs for a short period (10 days), compared with hospitalized patients with severe COVID-19, in whom viable virus can frequently be demonstrated during prolonged periods of up to 4 weeks, both in their upper and lower respiratory tract samples, even in the presence of high levels of neutralizing activity.

Blain H, Gamon L, Tuaille E, et al. **Atypical symptoms, SARS-CoV-2 test results, and immunization rates in 456 residents from eight nursing homes facing a COVID-19 outbreak**. *Age and Ageing*, February 23, 2021, afab050, <https://doi.org/10.1093/ageing/afab050>

A retrospective longitudinal study in eight NHs with at least ten rRT-PCR-positive residents. Among 456 residents, 161 residents had a positive rRT-PCR (35%),

17% of whom were asymptomatic before testing. Temperature > 37.8°C, oxygen saturation < 90%, unexplained anorexia, behavioral change, exhaustion, malaise, and falls before testing were independent predictors of a further positive rRT-PCR. Hubert Blain and colleagues from France conclude that NH residents with unusual fatigue, behavioral change, anorexia, malaise or falls should be tested by rRT-PCR for an early identification of the first SARS-CoV-2 cases.

Gutiérrez-Gutiérrez B, del Toro MD, Borobia AM, et al. **Identification and validation of clinical phenotypes with prognostic implications in patients admitted to hospital with COVID-19: a multicentre cohort study.** *The Lancet Infectious Diseases* February 23, 2021. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00019-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00019-0/fulltext)

Patients admitted to hospital with COVID-19 can be classified into three phenotypes that correlate with mortality. Using two large cohorts with more than 3500 patients from Spain, the authors developed and validated a simplified tool for the probabilistic assignment of patients into phenotypes, including a total of 16 variables. Patients with phenotype A were younger, were less frequently male, had mild viral symptoms, and had normal inflammatory parameters. Patients with phenotype B included more patients with obesity, lymphocytopenia, and moderately elevated inflammatory parameters. Patients with phenotype C included older patients with more co-morbidities and even higher inflammatory parameters than phenotype B. These results might help to better classify patients for clinical management. However, whether the model and derived calculator might be helpful in clinical practice is unknown. Moreover, the pathophysiological mechanisms of the phenotypes must be investigated.

### Severe COVID-19

Yao Y, Ye F, Li K, et al. **Genome and epigenome editing identify CCR9 and SLC6A20 as target genes at the 3p21.31 locus associated with severe COVID-19.** *Sig Transduct Target Ther* February 22, 2021, 6, 85. <https://www.nature.com/articles/s41392-021-00519-1>

Recently, genome-wide association studies (GWASs) have identified chromosome 3p21.31 (sentinel variant: rs11385942) to be associated with severe

COVID-19. By utilizing CRISPR/Cas9-mediated genomic deletion, the authors identified *CCR9* and *SLC6A20* as potential target genes of the 3p21.31 *locus*.

Feldstein LR, Tenforde MW, Friedman KW, et al. **Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19.** JAMA Network February 24, 2021. JAMA February 24, 2021. <https://jamanetwork.com/journals/jama/fullarticle/2777026>

Incredibly large case series of 1116 patients aged less than 21 years hospitalized between March 15 and October 31, 2020, at 66 US hospitals in 31 states. Comparing children and adolescents with MIS-C vs those with severe COVID-19, MIS-C was distinguished by certain demographic features and clinical presentations including being aged 6 to 12 years, being of non-Hispanic Black race, having severe cardiovascular or mucocutaneous involvement, and having more extreme inflammation.

## 27 February

### Treatment

#### Paper of the Day

Rubin EJ, Longo DL, Baden LR. **Interleukin-6 Receptor Inhibition in Covid-19 - Cooling the Inflammatory Soup.** N Engl J Med. 2021 Feb 25. PubMed: <https://pubmed.gov/33631064>. Full-text: <https://doi.org/10.1056/NEJMe2103108>

In their nice editorial, Eric Rubin, Dan Longo, and Lindsey Baden discuss how we can make sense of these disparate results between COVACTA and the REMAP-CAP data. Differences among the trials (enrolment criteria, timing of therapy, primary outcome, and background care, especially steroid use) may account for the discrepancy. In addition, inflammation may not be the same: patients with severe disease at initial presentation may have a different pathogenesis than those in whom inflammatory disease develops later, which suggests that the timing of treatment may be crucial in understanding responses. However, according to the authors, these points raise thorny issues. Is the value of interleukin-6 inhibition dependent on the timing of treatment, being beneficial only if proximate to an acute late inflammatory decompensation event? We rely on clinical trials to either endorse or reject possible in-



terventions. But what if the results of trials change as the underlying therapies improve, a particular problem with platform trials, which always need to include contemporaneous controls? For now, we are left with evidence of benefit from interleukin-6 inhibitors, but how to best use them remains unclear.

## Transmission

Marcus JE, Frankel DN, Pawlak MT, et al. **Risk Factors Associated With COVID-19 Transmission Among US Air Force Trainees in a Congregant Setting.** *JAMA Netw Open.* 2021 Feb 1;4(2):e210202. PubMed: <https://pubmed.gov/33630090>. Full-text: <https://doi.org/10.1001/jamanetworkopen.2021.0202>

Basic military training is the first step in the transition of a civilian to an enlisted member of the US Air Force. It brings together more than 39,000 trainees every year from around the US and represents an “ideal” setting to assess symptoms and lab values of a young, healthy population living in congregant-setting cohorts in a controlled environment. Among 10,613 US Air Force basic trainees in 263 cohorts, 403 trainees (3%) received a COVID-19 diagnosis in 129 cohorts (49%). Of these, 204 (51%) were symptomatic, and 199 (49%) were asymptomatic. Median cycle threshold values were lower in symptomatic trainees compared with asymptomatic trainees (21.2 vs 34.8). Cohorts with infection clusters were predominantly men, had more symptomatic trainees, and had more symptoms per patient compared with cohorts without clusters.

## Immunology

Zhou S, Butler-Laporte G, Nakanishi T, et al. **A Neanderthal OAS1 isoform protects individuals of European ancestry against COVID-19 susceptibility and severity.** *Nat Medicine* February 25, 2021. <https://www.nature.com/articles/s41591-021-01281-1>

OAS proteins are part of the innate immune response against RNA viruses. They are induced by interferons and activate latent RNase L, resulting in direct viral and endogenous RNA destruction, as demonstrated in *in vitro* studies. In this large-scale study of 931 proteins assessed for COVID-19 outcomes in > 14,000 cases and 1.2 million controls of European ancestry, Sirui Zhou and colleagues from Montreal, Canada provide evidence that increased OAS1 levels in the non-infectious state are strongly associated with reduced risks (22-46%) of severe COVID-19, hospitalization and susceptibility. Further analyses

suggested that a Neanderthal isoform of OAS1 in individuals of European ancestry affords this protection.

## Vaccines

Prendecki M, Clarke C, Brown J, et al. **Effect of previous SARS-CoV-2 infection on humoral and T-cell responses to single-dose BNT162b2 vaccine.** *Lancet* February 25, 2021. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00502-X/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00502-X/fulltext)

Early evidence for vaccine responses following previous natural infection. Maria Prendecki and colleagues looked at 72 HCWs from Imperial College Healthcare NHS Trust in London who were vaccinated, among them 21 (29%) participants with evidence of previous SARS-CoV-2 infection. Immune responses were analyzed 21-25 days after the first shot. In almost all individuals with previous SARS-CoV-2 infection, strong humoral and cellular responses to one dose of BNT162b2 vaccine, with evidence of high titers of virus neutralization were seen. In contrast, most infection-naïve individuals generated only weak T cell responses and low titers of neutralizing antibodies.

Manisty C, Otter AD, Treibel TA, et al. **Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals.** *Lancet* February 25, 2021. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00501-8/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00501-8/fulltext)

Same direction: in this nested case-control analysis of 51 participants of COVIDsortium (24 seropositive) seronegative individuals had anti-S titers after one dose of vaccine comparable to peak anti-S titers in individuals with a previous natural infection who had not yet been vaccinated. Among those with a previous SARS-CoV-2 infection, vaccination increased anti-S titers more than 140-fold from peak pre-vaccine levels. This increase appears to be at least one order of magnitude greater than reported after a conventional prime-boost vaccine strategy in previously uninfected individuals.

Ozonoff A, Nanishi E, Levy O. **Bell's palsy and SARS-CoV-2 vaccines.** *The Lancet Infectious Diseases*, February 24, 2021. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00076-1/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00076-1/fulltext)

Bell's palsy is a type of facial paralysis that results in a temporary inability to control the facial muscles on the affected side of the face. Al Ozonoff and col-

leagues say that observed incidence of Bell's palsy following mRNA vaccination is 3-7 times higher than would be expected in the general population. According to their comment, this signals a potential safety phenomenon and suggests inaccurate reporting to the public. However, it is also noted that Bell's palsy usually self-resolves and that the mRNA vaccines offer a substantial net benefit to public health.

## Co-morbidities

Kwan JY, Lin LT, Bell R, et al. **Elevation in viral entry genes and innate immunity compromise underlying increased infectivity and severity of COVID-19 in cancer patients.** *Sci Rep* 11, 4533 (2021). <https://doi.org/10.1038/s41598-021-83366-y>

What is the potential biological rationale behind the enhanced risk of COVID-19 among cancer patients? Jennifer Yin Yee Kwan from Toronto and colleagues suggest an increased expression of SARS-CoV-2 viral entry genes in the cancer state, particularly in respiratory, gastrointestinal, and genitourinary tract tissues. Elevation of ACE2, TMPRSS2, and CTSL in cancer vs. normal tissue was observed in many of the tissues examined. Moreover, it appeared that some entry genes have transient elevation with radiotherapy or chemotherapies.

## Treatment

REMAP-CAP Investigators, Gordon AC, Mouncey PR, et al. **Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19.** *N Engl J Med.* 2021 Feb 25. PubMed: <https://pubmed.gov/33631065>. Full-text: <https://doi.org/10.1056/NEJMoa2100433>

Two weeks ago, encouraging (but not peer-reviewed) results from the RECOVERY trial revitalized the strategy of blocking interleukin-6 in patients with severe COVID-19 (<https://www.recoverytrial.net/news/tocilizumab-reduces-deaths-in-patients-hospitalised-with-covid-19>). Now we are getting some more evidence, provided by REMAP-CAP. REMAP-CAP is an international, adaptive platform trial designed to determine effective treatment strategies for patients with severe pneumonia in both pandemic and non-pandemic settings. Patients eligible for the platform are assessed for eligibility to potentially undergo randomization to multiple interventions across multiple domains. Adult patients with COVID-19, within 24 hours after starting organ support in the ICU, were randomly assigned to receive tocilizumab (8 mg per kg of body weight), sarilumab (400 mg), or standard care (control). Both tocil-

izumab and sarilumab met the predefined criteria for efficacy. At that time, 353 patients had been assigned to tocilizumab, 48 to sarilumab, and 402 to control. The median number of organ support-free days was 10 in the tocilizumab group, 11 (0 to 16) in the sarilumab group, and 0 in the control group. An analysis of 90-day survival showed improved survival in the pooled interleukin-6 receptor antagonist groups, yielding a hazard ratio for the comparison with the control group of 1.61 (95% credible interval, 1.25 to 2.08).

Rosas IO, Bräu N, Waters M, et al. **Tocilizumab in Hospitalized Patients with Severe Covid-19 Pneumonia.** N Engl J Med. 2021 Feb 25. PubMed: <https://pubmed.gov/33631066>. Full-text: <https://doi.org/10.1056/NEJMoa2028700>

But can we trust these platform data? In COVACTA, a large randomized Phase III trial, 438 patients who were hospitalized with severe pneumonia were randomized 2:1 to receive TCZ or placebo, the use of TCZ did not result in significantly better clinical status or lower mortality (19.7% versus 19.4%) at 28 days.

## Pediatrics

Cheong RCT, Jephson C, Frauenfelder C, et al. **Otolaryngologic Manifestations in Pediatric Inflammatory Multisystem Syndrome Temporally Associated With COVID-19.** JAMA Otolaryngol Head Neck Surg. 2021 Feb 25. PubMed: <https://pubmed.gov/33630068>. Full-text: <https://doi.org/10.1001/jamaoto.2020.5698>

Single-center exploratory observational cohort study focusing on otolaryngologic manifestations of 50 children 18 years or younger presenting with PIMS-TS. Elevated rates of otolaryngology manifestations, such as dysphonia, dysphagia, and anosmia/hyposmia that persisted for longer than 6 weeks.

## 28 February

### Variants

#### Paper of the Day

WHO 20210223. **Weekly epidemiological update - 23 February 2021.** WHO 2021, published 23 February. Full-text: <https://www.who.int/publications/m/item/weekly-epidemiological-update--23-february-2021>

If you are interested in variants, read the *Special Focus: Update on SARS-CoV-2 Variants of Concern* on page 7 to 13 with an excellent table on the current information we have on B.1.1.7, B.1.351 and P.1.

Naveca F, Nascimento V, Souza V, et al. **COVID-19 epidemic in the Brazilian state of Amazonas was driven by long-term persistence of endemic SARS-CoV-2 lineages and the recent emergence of the new Variant of Concern P.1.** Research Square 2021, posted 25 February. Full-text: <https://doi.org/10.21203/rs.3.rs-275494/v1>

The second wave in the Northern Brazilian state of Amazonas coincides with the emergence of the P.1 variant in late November 2020. P.1 replaced the parental lineage in less than two months. The authors report that successive lineage replacements in Amazonas were driven by a complex combination of variable levels of social distancing measures and the emergence of a more transmissible VOC P.1 virus. They provide insights to understanding the mechanisms that underlie COVID-19 waves and the risk of disseminating P.1 in Brazil and potentially worldwide.

Faria NR, Mellan TA, Whittaker C, et al. **Genomics and epidemiology of a novel SARS-CoV-2 lineage in Manaus.** GitHub 2021, posted 27 February. Full-text: [https://github.com/CADDE-CENTRE/Novel-SARS-CoV-2-P1-Lineage-in-Brazil/blob/main/manuscript/FINAL\\_P1\\_MANUSCRIPT\\_25-02-2021\\_combined.pdf](https://github.com/CADDE-CENTRE/Novel-SARS-CoV-2-P1-Lineage-in-Brazil/blob/main/manuscript/FINAL_P1_MANUSCRIPT_25-02-2021_combined.pdf)

Using a combination of genomic and epidemiological data, Nuno Faria and colleagues characterize the emergence and characteristics of P.1 that acquired 17 mutations, including the trio in the spike protein (K417T, E484K and N501Y) associated with increased binding to the human ACE2 receptor. The authors show that P.1 emerged around early November 2020. They estimate that P.1 could be 1.4–2.2 times more transmissible and able to evade 25–61% of protective immunity elicited by previous infection with non-P.1 lineages. These data need to be confirmed by further studies.

## Epidemiology

**Global.health 2021.** Link: <https://global.health/>

This initiative by people from Oxford, Harvard, Northeastern, Boston Children's Hospital, Georgetown, University of Washington, and Johns Hopkins is meant to be an easy-to-use global data repository and visualization platform that collects anonymized information about individual cases from around the

world in one place. The goal: open access to real-time epidemiological anonymized data. See also Maxmen A. **Massive Google-funded COVID database will track variants and immunity.** Nature. 2021 Feb 24. PubMed: <https://pubmed.gov/33627862>. Full-text: <https://doi.org/10.1038/d41586-021-00490-5>

## Virology

FT 2021026. **The same covid-19 mutations are appearing in different places.** Financial Times 2021, published 26 February. Link: <https://www.economist.com/graphic-detail/2021/02/27/the-same-covid-19-mutations-are-appearing-in-different-places>

Excellent ancestry tree of SARS-CoV-2. The Financial Times argues that convergent evolution might make travel restrictions redundant.

## Transmission

Davis AC, Zee M, Clark AD, et al. **Computational Fluid Dynamics Modeling of Cough Transport in an Aircraft Cabin.** medRxiv 2021, posted 17 February. Full-text: <https://doi.org/10.1101/2021.02.15.431324>

Track particles released by coughing from a passenger seated in different seats on a Boeing 737 aircraft. The authors report that 80% of the particles were removed from the cabin in 1.3 to 2.6 minutes, depending on conditions, and 95% of the particles were removed in 2.3 to 4.5 minutes. We know from other reports that this is not sufficient to prevent SARS-CoV-2 transmission onboard aircraft. Remember the paper we presented on 23 February: Wang Z, Galea ER, Grandison A, et al. **Inflight Transmission of COVID-19 Based on Experimental Aerosol Dispersion Data.** Journal of Travel Medicine, February 19, 2021. taab023, <https://doi.org/10.1093/jtm/taab023>

## Vaccine

WHO 20210223. **Weekly epidemiological update - 23 February 2021.** WHO 2021, published 23 February. Full-text: <https://www.who.int/publications/m/item/weekly-epidemiological-update--23-february-2021>

Three pages about WHO's current COVID-19 vaccine policy recommendations (page 4 to 6): age requirements, pregnant women, breastfeeding mothers, people with compromised immune system, living with HIV, or previously infected with SARS-CoV-2, people with a history of severe allergic reaction.

FDA 20210226. **Vaccines and Related Biological Products Advisory Committee February 26, 2021 Meeting Announcement.** FDA 2021, published 26 February. Documents: <https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-february-26-2021-meeting-announcement#event-materials>

Find here the documents that will lead to the approval of vaccine #4 – the one-shot adenovirus vector vaccine by Johnson & Johnson. The best news of the day: the vaccine had only a slightly reduced overall efficacy rate in South Africa (64% vs 72% in the US). Most importantly, the J&J vaccine showed 86% and 82% efficacy against severe disease of COVID-19 in the US and South Africa, respectively.

## Diagnostics

Carreño JM, Mendu DR, Simon V, et al. **Longitudinal analysis of SARS-CoV-2 seroprevalence using multiple serology platforms.** medRxiv 2021, posted 26 February. Full-text: <https://doi.org/10.1101/2021.02.24.21252340>

Florian Krammer, Juan Manuel Carreño and colleagues look at longitudinal SARS-CoV-2 seroprevalence using multiple serology platforms. Good correlation was observed between the MS and Kantaro RBD ELISAs and between the MS and Kantaro spike ELISAs. By contrast, modest correlations were observed between the Abbott Architect and both RBD and spike-based assays.

## 1 March

### Virology

#### Paper of the Day

Zhou B, Thi Nhu Thao T, Hoffmann D, et al. **SARS-CoV-2 spike D614G change enhances replication and transmission.** Nature 26 February 2021. <https://www.nature.com/articles/s41586-021-03361-1>

Extensive study on the first update of SARS-CoV-2, namely the mutation at codon 614 (already partially dominant last spring in many countries). It is shown that the S-614G variant has enhanced binding to human host cell surface receptor ACE2, increased replication in primary human bronchial and nasal airway epithelial cultures as well as markedly increased replication and transmissibility in hamsters and ferrets. It will be interesting to see data on such *in vivo* competitive advantages with the new variants.

## Epidemiology

Mensah AA, Sinnathamby M, Zaidi A, et al. **SARS-CoV-2 infections in children following the full re-opening of schools and the impact of national lockdown: prospective, national observational cohort surveillance, July-December 2020, England.** *J Infection* February 24, 2021. <https://doi.org/10.1016/j.jinf.2021.02.022>

In England, childhood cases closely followed adult infection rates and national lockdown whilst keeping schools open was associated with large declines in SARS-CoV-2 infection rates, first in adults and then in school-aged children. There was a strong correlation in weekly infection rates between adults and all three educational cohorts during periods of both low and high community infection rates. Two messages from this paper: Schools are not the drivers but low community infection rates are required to allow schools to remain open safely.

Hyde Z. **Difference in SARS-CoV-2 attack rate between children and adults may reflect bias.** *Clinical Infectious Diseases* 26 February 2021, ciab183, <https://doi.org/10.1093/cid/ciab183>

In her brief review, Zoë Hyde from Perth, Australia argues that lower secondary attack rates in children compared to adults may reflect lower testing in children and reduced exposure, rather than a genuine difference in biological susceptibility. Additionally, children may shed infectious virus for a shorter period than adults and their antibody response may be less broad, with implications for both polymerase chain reaction and serological testing. After reviewing the data available so far, she thinks it likely that children are more susceptible to SARS-CoV-2 infection than first thought, and they probably play an important role in community transmission.

## Immunology

Pawlowski C, Puranik A, Bandi H. et al. **Exploratory analysis of immunization records highlights decreased SARS-CoV-2 rates in individuals with recent non-COVID-19 vaccinations.** *Sci Rep* 11, 4741 (2021). <https://doi.org/10.1038/s41598-021-83641-y>

Do existing vaccines afford protection against SARS-CoV-2 infection through trained immunity? By analyzing immunization records from 137,037 individuals, Colin Pawlowski and colleagues from Cambridge found that several vaccines such as polio, MMR, flu or hepatitis A/hepatitis B vaccines administered



in the past 1-5 years were associated with decreased SARS-CoV-2 infection rates, even after adjusting for geographic SARS-CoV-2 incidence and testing rates, demographics, co-morbidities, and number of other vaccinations. But can we believe this? Can we control for the “healthy user effect” (that persons who have recently had other vaccines may engage in general health-seeking behaviors which decrease their risk of SARS-CoV-2 infection)? The authors say yes. In a “negative control” experiment on patients who have recently taken cancer screens (who may also have lower rates due to the “healthy user effect”), their propensity score matching method was able to correct for confounding.

## Transmission

Metlay JP, Haas JS, Soltoff AE, Armstrong KA. **Household Transmission of SARS-CoV-2.** JAMA Netw Open. 2021 Feb 1;4(2):e210304. PubMed: <https://pubmed.gov/33635324>. Full-text: <https://doi.org/10.1001/jamanetworkopen.2021.0304>

In this large hospital and ambulatory care network based in Boston, US, 7262 index cases were linked to 17,917 additional at-risk individuals assigned to the same addresses. Overall household infection risk was 10.1%. Independent factors significantly associated with higher transmission risk included age greater than 18 years and multiple comorbid conditions (adjusted OR for individuals with hypertension, 1.93). In sensitivity analyses limiting the maximum size of the household to as small as 2 persons, the calculated transmission risk increased to only 13.8%.

Kraay ANM, Hayashi MAL, Berendes DM, Sobolik JS, Leon JS, Lopman BA. **Risk for fomite-mediated transmission of SARS-CoV-2 in child daycares, schools, nursing homes, and offices.** Emerg Infect Dis. February 24, 2021. [https://wwwnc.cdc.gov/eid/article/27/4/20-3631\\_article](https://wwwnc.cdc.gov/eid/article/27/4/20-3631_article)

SARS-CoV-2 can persist on surfaces, suggesting possible surface-mediated transmission of this pathogen. Using a transmission model to explore the potential for fomite transmission without other pathways, Alicia N.M. Kraay from Atlanta and colleagues found that fomites might be a substantial source of transmission risk, particularly in schools and child daycares. Combining surface cleaning and decontamination with mask wearing can help mitigate this risk.

## Clinical

van Westen-Lagerweij NA, Meijer E, Meeuwse EG, et al. **Are smokers protected against SARS-CoV-2 infection (COVID-19)? The origins of the myth.** npj Primary Care Respiratory Medicine February 26, 2021, volume 31, Article number: 10. <https://www.nature.com/articles/s41533-021-00223-1>

Do you believe that alcohol disinfects the stomach? Ok, then you don't need to read any further. For the rest of us, this commentary dispels a few myths (or, if you will, bullsh\*t studies) about smoking and COVID-19.

Struyf T, Deeks JJ, Dinnes J, et al. **Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19.** Cochrane Database Syst Rev. 2021 Feb 23;2:CD013665. PubMed: <https://pubmed.gov/33620086>. Full-text: <https://doi.org/10.1002/14651858.CD013665.pub2>

Are there signs and symptoms predicting COVID-19? This Cochrane review says no.

## Treatment

Janiaud P, Axfors C, Schmitt AM, et al. **Association of Convalescent Plasma Treatment With Clinical Outcomes in Patients With COVID-19: A Systematic Review and Meta-analysis.** JAMA. 2021 Feb 26. PubMed: <https://pubmed.gov/33635310>. Full-text: <https://doi.org/10.1001/jama.2021.2747>

This review of all RCTs published until January 29 showed that compared with placebo or standard of care, convalescent plasma was not significantly associated with a decrease in all-cause mortality or with any benefit for other clinical outcomes.

Gupta A, Madhavan MV, Poterucha TJ, et al. **Association between antecedent statin use and decreased mortality in hospitalized patients with COVID-19.** Nat Commun 12, 1325 (2021). <https://doi.org/10.1038/s41467-021-21553-1>

Better take your statins! Among 1296 patients (648 statin users, 648 non-statin users) identified with 1:1 propensity-score matching, statin use was significantly associated with lower odds of in-hospital mortality within 30 days in the propensity-matched cohort (OR 0.47, 95% CI: 0.36–0.62, p < 0.001). The potential benefits from statins extend beyond cholesterol-lowering prop-

erties, as there is a robust literature supporting the anti-inflammatory properties of statins, suggesting that these drugs can stabilize and restore endothelial function. Randomized clinical trials are ongoing (and needed).

Herrett E, Williamson E, Brack K, et al. **Statin treatment and muscle symptoms: series of randomised, placebo controlled n-of-1 trials.** *BMJ*. 2021 Feb 24;372:n135. PubMed: <https://pubmed.gov/33627334>. Full-text: <https://www.bmj.com/content/372/bmj.n135>

And for those patients who supposedly can't tolerate a statin, it's probably not the case. In this nice study among 151 participants who had recently stopped or were considering stopping treatment with statins because of muscle symptoms, no difference in muscle symptom scores was found between the statin and placebo periods. Withdrawals because of intolerable muscle symptoms were 18 participants (9%) during a statin period and 13 (7%) during a placebo period. Two thirds of those completing the trial reported restarting long-term treatment with statins.

## 2 March

### Immunology

#### Paper of the Day

Shen B, Tasdogan A, Ubellacker JM, et al. **A mechanosensitive peri-arteriolar niche for osteogenesis and lymphopoiesis.** *Nature*, February 24, 2021. <https://doi.org/10.1038/s41586-021-03298-5>

Exercise will boost your immune system! What we all “knew” already, can now be explained. A specialized type of bone cell progenitor has been identified in the bone marrow and shown to support the generation of lymphocytes in response to movement. Bo Shen and colleagues have identified a role for movement in stimulating communication between one type of stromal cell and immune progenitors in mice, ultimately helping the animals to fight infection. The discovery that mechanosensitive osteogenic progenitors have a role in fighting infections is exciting.

Balz K, Kaushik A, Chen M, et al. **Homologies between SARS-CoV-2 and allergen proteins may direct T cell-mediated heterologous immune responses.** *Sci Rep* February 25, 2021, 11, 4792. <https://doi.org/10.1038/s41598-021-84320-8>

Different systematic bioinformatic approaches were used to identify potentially cross-reactive allergen- and SARS-CoV-2-T cell epitopes. Numerous candidate epitope pairs were identified, highlighting an important role of MHC class I inhalant allergens. According to Kathrin Balz and colleagues, findings generate further hypotheses in how the adaptive immune system responds differentially with respect to the atopy status of the host. Their study warrants an immediate investigation of these predicted T cell epitopes to link their possible role in driving the immune response against SARS-CoV-2 and eventually shape the COVID-19 outcome.

## Epidemiology

Lim T, Delorey M, Bestul N, et al. **Changes in SARS CoV-2 Seroprevalence Over Time in Ten Sites in the United States, March - August, 2020.** Clin Infect Dis. 2021 Feb 26:ciab185. PubMed: <https://pubmed.gov/33639620>. Full-text: <https://doi.org/10.1093/cid/ciab185>

In a well-designed large-scale seroprevalence study, Travis Lim and colleagues tested 78,990 specimens from ten US sites that experienced different epidemic curves, over multiple time points between March and August 2020. During this period, less than 10% of the population had detectable antibodies to SARS-CoV-2 at all sites except New York (23.2%) and Florida (13.3%).

## Virology

Zhou D, Chan JF, Zhou B, et al. **Robust SARS-CoV-2 Infection in Nasal Turbinates after Treatment with Systemic Neutralizing Antibodies.** Cell Host Microbe February 24, 2021. Full-text: <https://www.sciencedirect.com/science/article/pii/S1931312821000986?via%3Dihub>

Viral infection in nasal turbinate may outcompete antibody treatment. Using a Syrian hamster model, the authors show that ZDY20, ZB8 and 2-15 (three of the most promising classes of RBD-specific human neutralizing Abs) prophylactic intraperitoneal or intranasal injection of individual HuNAb or DNA vaccination significantly reduced infection in the lungs but not in the nasal turbinates of hamsters intranasally challenged with SARS-CoV-2. Although post-challenge HuNAb therapy suppresses viral loads and lung damage, robust infection is observed in nasal turbinates treated within 1-3 days. This has significant implications for sub-protection, reinfection and vaccine.

## Vaccines

Rinott E, Youngster I, Lewis YE. **Reduction in COVID-19 Patients Requiring Mechanical Ventilation Following Implementation of a National COVID-19 Vaccination Program — Israel, December 2020–February 2021.** MMWR Morb Mortal Wkly Rep, 26 February 2021. DOI: [http://dx.doi.org/10.15585/mmwr.mm7009e3external icon](http://dx.doi.org/10.15585/mmwr.mm7009e3external%20icon).

Again, encouraging data from Israel. The percentage of COVID-19 patients aged  $\geq 70$  years requiring mechanical ventilation fluctuated during October–December 2020 but has considerably and consistently decreased after implementation of the vaccination campaign prioritizing older adults. The decline in the ratio of persons aged  $\geq 70$  years to those  $< 50$  years requiring mechanical ventilation began around the time of start of administration of the second dose of vaccine (January 10, 2021).

## Clinical

Cuevas AM, Clark JM, Potter JJ. **Increased TLR/MyD88 signaling in patients with obesity: is there a link to COVID-19 disease severity?** Int J Obes (Lond). 2021 Feb 26. PubMed: <https://pubmed.gov/33637950>. Full-text: <https://doi.org/10.1038/s41366-021-00768-8>

Why is obesity a risk factor for severe COVID-19? The authors review current knowledge and hypothesize that people with obesity, especially excess abdominal/visceral fat and associated metabolic complications, have over-expression of MyD88 in the adipose tissue and perhaps in other cells and tissues (like immune cells) that triggers an exaggerated inflammatory response of the immune system.

## Severe COVID-19

Deinhardt-Emmer S, Böttcher S, Häring C, et al. **SARS-CoV-2 causes severe epithelial inflammation and barrier dysfunction.** J Virol 2021 Feb 26;JVI.00110-21. PubMed: <https://pubmed.gov/33637603>. Full-text: <https://doi.org/10.1128/JVI.00110-21>

To elucidate the viral effects on the barrier integrity and immune reactions, Stefanie Deinhardt-Emmer and colleagues from Jena, Germany used monocell culture systems and a complex human chip model composed of epithelial, endothelial, and mononuclear cells. SARS-CoV-2 efficiently infected epithelial cells with high viral loads and inflammatory response, including interferon

expression. By contrast, the adjacent endothelial layer was not infected nor did it show productive viral replication or release of interferon. With prolonged infection, both cell types were damaged, and the barrier function was deteriorated, allowing the viral particles to have to carry too much.

Althaus K, Marini I, Zlamal J, et al. **Antibody-induced procoagulant platelets in severe COVID-19 infection.** Blood February 25, 2021, 137 (8): 1061–1071. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7791311/>

Severe COVID-19 is associated with antibody-mediated up-regulation of platelet apoptosis. In addition, Karina Althaus and colleagues from Tübingen, Germany found a correlation between platelet apoptosis markers and SOFA score, plasma levels of D-dimer, and the incidence of thromboembolic complications in severe COVID-19 patients. These data indicate that platelet apoptosis may contribute to sustained inflammation and increased thromboembolic risk in COVID-19 patients and could potentially present a potential therapeutic target.

## Treatment

Piepenbrink MS, Park JG, Oladunni FS, et al. **Therapeutic activity of an inhaled potent SARS-CoV-2 neutralizing human monoclonal antibody in hamsters.** Cell Reports February 24, 2021. DOI: <https://doi.org/10.1016/j.xcrm.2021.100218>

Antibodies delivered via inhalation for the prevention and treatment of SARS-CoV-2: Michael S. Piepenbrink from Birmingham, US shows that this works. Fully human monoclonal antibodies (hmAbs) potently neutralize SARS-CoV-2. The most potent hmAb, 1212C2 was derived from an IgM memory B cell, exhibited *in vivo* prophylactic and therapeutic activity against SARS-CoV-2 in hamsters when delivered intraperitoneally, achieving a meaningful reduction in upper and lower respiratory viral burden and lung pathology. Furthermore, liquid nebulized inhaled treatment of SARS-CoV-2 infected hamsters with as low as 0.6 mg/kg of inhaled dose, corresponding to approximately 0.03 mg/kg of lung-deposited dose, mediated a reduction in respiratory viral burden that is below the detection limit, and mitigated lung pathology. The therapeutic efficacy achieved at an exceedingly low-dose of inhaled 1212C2 supports the rationale for local lung delivery and achieving dose-sparing benefits as compared to the conventional parenteral route of administration.

Bugin K, Woodcock J. **Trends in COVID-19 therapeutic clinical trials.** Nature Reviews Drug Discovery, 25 February 2021. <https://www.nature.com/articles/d41573-021-00037-3>

Janet Woodcock and Kevin Bugin have comprehensively assessed the ongoing COVID-19 therapeutic clinical development efforts worldwide. Surveying the clinical trial landscape, their most important finding is that the vast majority of trials of therapeutics for COVID-19 are not designed to yield actionable information; low randomization rates and underpowered outcome data render matters of safety and efficacy generally uninterpretable.

Milic J, Novella A, Meschiari M, et al. **Darunavir/cobicistat is associated with negative outcomes in HIV-negative patients with severe COVID-19 pneumonia.** AIDS Res Hum Retroviruses. 2021 Feb 23. PubMed: <https://pubmed.gov/33619997>. Full-text: <https://doi.org/10.1089/AID.2020.0305>

The HIV protease inhibitor darunavir doesn't work in COVID. Didn't we know this already? In this retrospective study in HIV-negative patients with COVID-19 pneumonia admitted to a tertiary care hospital in Modena, Italy, patients on darunavir/c (c=cobicistat is a pharmacoenhancer) had higher rates of mortality (25% vs 10%,  $p < 0.0001$ ) and of mechanical ventilation and death (37% vs. 25%,  $p = 0.03$ ). Multiple serious interactions associated with darunavir/c were observed in the 19 patients who died. According to the authors, darunavir/c "should not be recommended as a treatment option for COVID-19 pneumonia outside clinical trials". The question is: why did the authors study this now?

## 3 March

### Vaccine

#### Paper of the Day

Saadat S, Tehrani ZR, Logue J, et al. **Binding and Neutralization Antibody Titers After a Single Vaccine Dose in Health Care Workers Previously Infected With SARS-CoV-2.** JAMA. March 1, 2021. doi:10.1001/jama.2021.3341. <https://jamanetwork.com/journals/jama/fullarticle/2777171?resultClick=1>

Health care workers with previous COVID-19, based on laboratory-confirmed serology testing, had higher antibody titer responses to a single dose of mRNA vaccine (Pfizer-BioNTech or Moderna, depending on personal preference and

availability) than those who were not previously infected. Although the groups were small and only 59 volunteers were enrolled (17 in the Ab-negative, 16 in the asymptomatic, and 26 in the symptomatic group), this data indicates that one shot is enough in people with prior infection. Of note, titers did not differ between asymptomatic and symptomatic disease.

## Virology

Tse H, Lung CD, Wong SC, et al. **Emergence of a Severe Acute Respiratory Syndrome Coronavirus 2 virus variant with novel genomic architecture in Hong Kong.** *Clinical Infectious Diseases* 02 March 2021, ciab198, <https://doi.org/10.1093/cid/ciab198>

SARS-CoV-2 lineages have emerged continuously, mostly through the genomic accumulation of substitutions. Herman Tse and colleagues highlight the considerable evolutionary potential of SARS-CoV-2. They report three infections caused by a variant with a novel genomic architecture resulting from deletion of an 882-nucleotide region spanning ORF6 to ORF8 together with duplication and transposition of a 57-nucleotide segment from the 5'-untranslated region (UTR). The tolerance of a major and unusual genomic arrangement led to the formation of ORF6x, which involved recruitment of typically non-coding sequences into the open reading frame. These events greatly increased the genetic diversity of SARS-CoV-2, thereby accelerating the evolution of new potentially advantageous genotypes and compensating for the relatively low mutation rates in coronaviruses. On a more immediate note, caution is warranted when using diagnostic assays targeting only accessory genes or proteins such as Orf8, given the risk of false-negative results.

## Clinical

Rodebaugh TL, Frumkin MR, Reiersen AM, et al. **Acute symptoms of mild to moderate COVID-19 are highly heterogeneous across individuals and over time.** *Open Forum Infectious Diseases* March 1, ofab090, <https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofab090/6154666>

Thomas L. Rodebaugh from St. Louis, US, and colleagues asked 162 participants with acute COVID-19 to respond to surveys up to 31 times for up to 17 days. Several statistical methods were used to characterize the temporal dynamics of these symptoms. Results: the course of symptoms during the initial weeks of



COVID-19 is highly heterogeneous and is neither predictable nor easily characterized using typical survey methods. However, the pattern of symptoms over time suggested a fluctuating course for many patients. Participants who showed clinical deterioration were more likely to present with higher reports of severity of cough and diarrhea.

Cavanaugh AM, Thoroughman D, Miranda H, Spicer K. **Suspected Recurrent SARS-CoV-2 Infections Among Residents of a Skilled Nursing Facility During a Second COVID-19 Outbreak — Kentucky, July–November 2020.** MMWR Morb Mortal Wkly Rep 2021;70:273–277. [https://www.cdc.gov/mmwr/volumes/70/wr/mm7008a3.htm?s\\_cid=mm7008a3\\_w#suggestedcitation](https://www.cdc.gov/mmwr/volumes/70/wr/mm7008a3.htm?s_cid=mm7008a3_w#suggestedcitation)

Five residents of a skilled nursing facility received positive PCR results in two separate COVID-19 outbreaks separated by 3 months. Residents received at least four negative test results between the two outbreaks, suggesting the possibility of reinfection. Severity of disease in the five residents during the second outbreak was worse than that during the first outbreak and included one death.

## Long COVID

Gacci M, Coppi M, Baldi E, et al. **Semen impairment and occurrence of SARS-CoV-2 virus in semen after recovery from COVID-19.** Human Reproduction March 1, 2021. Full-text: <https://academic.oup.com/humrep/advance-article/doi/10.1093/humrep/deab026/6125160>

Mauro Gacci from Florence, Italy, and colleagues performed a large prospective cross-sectional study on 43 sexually active men who were known to have recovered from SARS-CoV-2 (3-6 weeks after negative swab). One patient had a positive PCR in semen (21 days after the second negative swab). Of note, 11/43 were oligo-crypto-azoospermic and all azoospermic patients reported a previous unimpaired fertility status suggesting that semen impairment was due to COVID-19. However, a main limitation of the study is the lack of samples obtained prior to COVID-19.

## Severe COVID-19

Yang P, Zhao Y, Li J. et al. **Downregulated miR-451a as a feature of the plasma cfRNA landscape reveals regulatory networks of IL-6/IL-6R-associated cytokine storms in COVID-19 patients.** Cell Mol Immunol (2021). <https://doi.org/10.1038/s41423-021-00652-5>

Cell-free circulating RNAs (cfRNAs) in plasma carry information from pathologic sites, and they have been reported to play important roles in disease development. Compared with healthy donors, significantly higher mRNA expression of IL-6R was observed; miR-451a, a known negative regulator of IL-6R translation, was down-regulated, which may promote IL-6R expression at the protein level.

## Co-morbidities

Jee J, Stonestrom AJ, Devlin S, et al. **Oncologic immunomodulatory agents in patients with cancer and COVID-19.** Sci Rep March 1, 2021, 11, 4814 (2021). <https://doi.org/10.1038/s41598-021-84137-5>. <https://www.nature.com/articles/s41598-021-84137-5>

A large single-center, retrospective analysis of 820 cancer patients with COVID-19 treated with various immunomodulatory agents within 90 days prior to SARS-CoV-2 diagnosis, mainly anti-CD20 therapies (rituximab, ofatumumab, or obinutuzumab) and immunotherapy (PD-1, PDL-1, or CTLA-4 blockade). Of note, whereas cytotoxic chemotherapy itself was not a risk for worse outcomes, pre-COVID-19 neutropenia was associated with worse COVID-19. In assessing whether certain oncologic medications are associated with worse COVID-19 outcomes, considering cancer type, degree of effect (i.e. neutropenia or other bone marrow suppression) and other patient-specific factors is crucial.

## Treatment

Janiaud P, Axfors C, Ioannidis JP, et al. **Recruitment and Results Reporting of COVID-19 Randomized Clinical Trials Registered in the First 100 Days of the Pandemic.** JAMA Netw Open March 1, 2021;4(3):e210330. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776802>

All RCTs (n = 516) registered in ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform between January 1 and April 9, 2020, were included. Overall, 30% of COVID-19 RCTs initiated in the first 100 days of the pandemic did

not begin recruitment, and only 10% had results reported by mid-October, suggesting the possibility of substantial research waste.

Li S, Liu S, Jiang Z, et al. **Study on the promotion of lymphocytes in patients with COVID-19 by broad-spectrum chemokine receptor inhibitor vMIP-II and its Mechanism of signal transmission in vitro.** *Sig Transduct Target Ther* March2, 2012. 6, 104. <https://doi.org/10.1038/s41392-021-00516-4>

Viral macrophage inflammatory protein (vMIP) is a homologue of a chemokine derived from the recombinant natural human herpes virus 8 gene. It has been proved that vMIP can effectively inhibit the process of HIV infecting target cells through chemokine receptors. In this pilot study, 10 patients and 35 uninfected volunteers from Wuhan were treated with vMIP (given as injection). vMIP-II significantly improved the lymphocyte decrease of COVID-19. It was shown that vMIP-II inhibits multiple chemokine receptors and their related phosphorylation signaling pathways. In other words, this study shows that vMIP-II can reconstruct the cellular immune function lost in acute SARS-CoV-2 infection. The elucidation of the molecular mechanism of vMIP-II increasing CD8+ TCM provides a new strategy for the treatment of COVID-19.

## Pediatric

Takefuji Y, Besançon L, Steadson D, Flahault A, Ludvigsson JF. **Open Schools, Covid-19, and Child and Teacher Morbidity in Sweden.** *NEJM* March 1, 2021, DOI: [10.1056/NEJMc2101280](https://doi.org/10.1056/NEJMc2101280).  
[https://www.nejm.org/doi/full/10.1056/NEJMc2101280?query=featured\\_home](https://www.nejm.org/doi/full/10.1056/NEJMc2101280?query=featured_home)

Ludvigsson JF. **The first eight months of Sweden's COVID-19 strategy and the key actions and actors that were involved.** *Acta Paediatr* 2020;109:2459-2471. <https://doi.org/10.1111/apa.15582>

Controversial discussion about the Swedish approach. Sweden allowed COVID-19 to spread in the hope that the population would develop “herd immunity.” The younger the patients, the fewer deaths due to COVID-19 were reported by Ludvigsson et al. (Feb. 18 issue). The authors of the correspondence letters don't believe that this was a good idea.

## 4 March

### Vaccine

#### Paper of the Day

Oliver SE, Gargano JW, Scobie H, et al. **The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Janssen COVID-19 Vaccine — United States, February 2021.** *MMWR Morb Mortal Wkly Rep.* ePub: 2 March 2021. DOI: <https://www.cdc.gov/mmwr/volumes/70/wr/mm7009e4.htm>

The Janssen COVID-19 vaccine is a recombinant, replication-incompetent adenovirus serotype 26 (Ad26) vector vaccine, encoding the stabilized prefusion spike glycoprotein of SARS-CoV-2. On February 27, 2021, the FDA issued an Emergency Use Authorization (EUA). This is an interim recommendation for use in persons aged  $\geq 18$  years for the prevention of COVID-19, discussing the available data and the question who to vaccinate and when. Answer: everybody, ASAP. Of note, the Janssen vaccine seems to work in the B.1.351 lineage from South Africa as well in the P.2 lineage from Brazil.

### Epidemiology

Van Loon W, Hommes F, Theuring S, et al. **Renewed absence of SARS-CoV-2 infections in the day care context in Berlin, January 2021.** *Clinical Infectious Diseases* March 2. Full-text: <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab199/6155930>

The second round of a longitudinal study in 12 randomly selected kindergartens across Berlin including 156 children, 80 staff, and 488 household members of children and staff. According to the authors, repeated absence of SARS-CoV-2 infection four months apart, at weekly community incidences of 38 (first round in September) and 110/100,000, support the initial interpretation that kindergartens are not silent transmission reservoirs.

### Virology

Phuong HVM, Tung TS, Trang UTH, et al. **Novel mutation of SARS-CoV-2, Vietnam, July 2020.** *Emerg Infect Dis.* 2021 May [date cited]. <https://doi.org/10.3201/eid2705.210013>

Now that the whole world is sequencing the virus, we are likely to see many such studies. A cluster in Danang, Vietnam, began July 25, 2020, and resulted in 551 confirmed cases and 35 deaths. The authors analyzed 26 sequences from this cluster and identified a novel shared mutation in non-structural

protein 9, suggesting a single introduction into Vietnam. The single-nucleotide polymorphism, C835T, was not reported in any other sequences collected globally. However, it has no known associations with virulence or transmissibility.

## Variants

Plante JA, Mitchell BM, Plante KS, et al. **The Variant Gambit: COVID's Next Move.** *Cell Host Microbe* March 01, 2021. [https://www.cell.com/cell-host-microbe/fulltext/S1931-3128\(21\)00099-8](https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00099-8)

Nice review that outlines factors driving SARS-CoV-2 variant evolution, explores the potential impact of specific mutations and examines the risk of further mutations. Jessica A. Plante and colleagues from the World Reference Center for Emerging Viruses and Arboviruses consider also the experimental studies needed to understand the threat these variants pose.

## Transmission, Prevention

Lubrano R, Bliose S, Testa A, et al. **Assessment of Respiratory Function in Infants and Young Children Wearing Face Masks During the COVID-19 Pandemic.** *JAMA Netw Open* March 2, 2021. 4(3):e210414. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2776928>

Are surgical masks associated with episodes of oxygen desaturation or respiratory distress among children? This study from Italy says no. Among 47 children (22 aged 24 months or younger!) the use of facial masks was not associated with significant changes in Sao2 or Petco2.

Wilmes P, Zimmer J, Schulz J, et al. **SARS-CoV-2 transmission risk from asymptomatic carriers: Results from a mass screening programme in Luxembourg.** *Lancet Regional Health* February 27, 2021. DOI: <https://doi.org/10.1016/j.lanpe.2021.100056>

To accompany the lifting of COVID-19 lockdown measures, Luxembourg implemented a mass screening (MS) program. Based on a participation of 49% amongst the resident population and 22% amongst cross-border workers, the MS program allowed identification of 1099 cases corresponding to 26% of positive cases related to an early summer epidemic wave. Among the index cases, 567 (67%) reported symptoms at the time of being informed of their positive test result (these may have been pre-symptomatic at the time of the test), whereas 283 (33%) were asymptomatic. Asymptomatic individuals had signifi-

cant secondary attack rates, both in households and among close contacts, but these were lower compared to those for symptomatic cases.

## Clinical

Van den Hurk K, Merz EM, Prinsze FJ, et al. **Low awareness of past SARS-CoV-2 infection in healthy plasma donors.** Cell Reports Med February 25, 2021. <https://doi.org/10.1016/j.xcrm.2021.100222>

See title. They know nothing. Katja van den Hurk and colleagues asked individuals donating plasma across the Netherlands between May 11th and 18th 2020. Among 3676 with antibody and questionnaire data, 239 (6.5%) were positive for SARS-CoV-2 antibodies. Of those, 48% did not suspect COVID-19 despite the majority reporting symptoms. 11% of seropositive individuals reported no symptoms and 27% very mild symptoms at any time during the first peak of the epidemic. Anosmia/ageusia and fever were most strongly associated with seropositivity. Almost 13% of the individuals who tested negative for SARS-CoV-2 did suspect a SARS-CoV-2 infection, a large majority (84%) because of symptoms indicative of COVID-19.

Baldassarri M, Picchiotti N, Fava F, et al. **Shorter androgen receptor polyQ alleles protect against life-threatening COVID-19 disease in European males.** EBioMedicine. 2021 Feb 26;65:103246. PubMed: <https://pubmed.gov/33647767>. Full-text: <https://doi.org/10.1016/j.ebiom.2021.103246>

A genetic polymorphism predisposing some men to develop a more severe disease irrespective of age: in a cohort of 1178 men and women with COVID-19, Margherita Baldassarri from Siena, Italy, and colleagues used a supervised Machine Learning approach on a synthetic representation of genetic variability due to poly-amino acid repeats. Comparing the genotype of patients with extreme manifestations (severe vs. asymptomatic), they found an association between the poly-glutamine repeat number of the androgen receptor (AR) gene, serum testosterone concentrations, and COVID-19 outcome in male patients. Failure of the endocrine feedback to overcome AR signaling defects by increasing testosterone levels during the infection leads to the fact that polyQ  $\geq 23$  becomes dominant to testosterone levels for the clinical outcome.

Strålin K, Wahlström E, Walther S, et al. **Mortality trends among hospitalised COVID-19 patients in Sweden: A nationwide observational cohort study.** *Lancet Regional Health* February 26, 2021 DOI: <https://doi.org/10.1016/j.lanepe.2021.100054>

There was a gradual decline in mortality during the spring of 2020 in Swedish hospitalised COVID-19 patients. The results remained after adjustment for age, sex, co-morbidities, level of care dependency, country of birth, healthcare region, and SAPS3 (ICU treated patients). Read about the many explanations for this phenomenon. However, the bottom line is that in studies using mortality as an endpoint, the timing of inclusion may play a crucial role regarding outcome. The results of before-and-after studies on specific interventions should be interpreted with caution.

### Collateral damage (today: benefit)

Shepherd JP, Moore SC, Long A, et al. **Association Between COVID-19 Lockdown Measures and Emergency Department Visits for Violence-Related Injuries in Cardiff, Wales.** *JAMA* March 2, 2021. 2021; 325(9):885-887. <https://jamanetwork.com/journals/jama/article-abstract/2776868>

Less violence during lockdown. In Cardiff, Wales, the average weekly number of violent injury admissions dropped from 28.4 to 16.5 during lockdown. There was also a 92% reduction in weapon use. This may reflect closure of city center pubs and clubs where most violence takes place. Cheers.

## 5 March

### Variants

#### Paper of the Day

Davies NG, Abbott S, Barnard RS, et al. **Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England.** *Science* 03 Mar 2021: eabg3055. Full-text: <https://science.sciencemag.org/content/early/2021/03/03/science.abg3055>

Difficult months ahead: the B.1.1.7 variant emerged in southeast England in November 2020 and is rapidly spreading toward dominance. In this brilliant article, Nicholas Davies and colleagues from London estimate that this variant has a 43–90% (range of 95% credible intervals 38–130%) higher reproduction number than pre-existing variants. A fitted two-strain dynamic transmission model shows that B.1.1.7. will lead to large resurgences of COVID-19 cases. Without

stringent control measures, including limited closure of educational institutions and a greatly accelerated vaccine roll-out, COVID-19 hospitalizations and deaths across England in 2021 will exceed those in 2020.

## Virology

Murray CJ, Piot P. **The Potential Future of the COVID-19 Pandemic.** JAMA March 3, 2021. Full-text: <https://jamanetwork.com/journals/jama/fullarticle/2777343>

Will SARS-CoV-2 become a recurrent seasonal Infection? Peter Piot and Christopher Murray don't know, how could they? According to their nice viewpoint, there is too much uncertainty about the probability and frequency of emergence of new variants, the reduction in vaccine efficacy for each variant, the critical question of cross-variant immunity, and the consistency of safe human behavior. However, the prospect of persistent and seasonal COVID-19 is real.

## Immunology

Le Bert N, Clapham HE, Tan AT. **Highly functional virus-specific cellular immune response in asymptomatic SARS-CoV-2 infection.** J Exp Med March 1, 2021. 218 (5): e20202617. <https://doi.org/10.1084/jem.20202617>

Nina Le Bert and colleagues from Singapore studies T cells longitudinally in a cohort of asymptomatic (n = 85) and symptomatic (n = 75) COVID-19 patients after seroconversion. Important findings: asymptomatic SARS-CoV-2-infected individuals are not characterized by weak antiviral immunity; on the contrary, they mount a highly functional virus-specific cellular immune response.

## Vaccine

Kimberly G. Blumenthal KG, Freeman EE, Saff RR. **Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2.** NEJM, March 3, 2021. DOI: 10.1056/NEJMc2102131. <https://www.nejm.org/doi/full/10.1056/NEJMc2102131>

Case series of 12 delayed large but varying local reactions to the mRNA-1273 vaccine, with a median onset on day 8 after the first dose. After the second shot, 6 had no recurrence, 3 had similar and 3 had recurrent reactions that were of a lower grade than those after the initial dose.



Kadire SR, Wachter RM, Lurie N. **Delayed Second Dose versus Standard Regimen for Covid-19 Vaccination.** N Engl J Med March 4, 2021; 384:e28. DOI: 10.1056/NEJMclde2101987.

<https://www.nejm.org/doi/full/10.1056/NEJMclde2101987>

Nice case vignette on the question of whether we delay the second dose. Robert M. Wachter says yes, Nicole Lurie says no. No clear winner.

## Transmission

Shumsky RA, Debo L, Lebeaux RM, et al. **Retail store customer flow and COVID-19 transmission.** PNAS February 26, 2021.

<https://doi.org/10.1073/pnas.2019225118>

Nice modelling study on how customer flows in retail stores affect the rate of COVID-19 transmission. The model calculates the disease transmission rate in a retail environment and determines how the rate depends on the customer flow policy (one-way versus two-way), the travel speed distribution, and store size. Restricting customer flow to one-way movement is highly effective if direct exposure is the dominant mode of transmission. However, it is not effective if more indirect (“wake”) exposure dominates.

Schumm MA, Hadaya JE, Mody N, et al. **Filtering Facepiece Respirator (N95 Respirator) Reprocessing: A Systematic Review.** JAMA. March 3, 2021; doi: 10.1001/jama.2021.2531.

<https://jamanetwork.com/journals/jama/fullarticle/2777342?resultClick=1>

Max A. Schumm and colleagues have reviewed 42 studies (through January 31, 2021) that examined 65 types of masks. Ultraviolet germicidal irradiation, vaporized hydrogen peroxide, moist heat, and microwave-generated steam processing effectively sterilized N95 respirators and retained filtration performance. Ultraviolet irradiation and vaporized hydrogen peroxide damaged respirators the least.

## Collateral damage

Knudsen AK, Stene-Larsen K, Gustavson K, et al. **Prevalence of mental disorders, suicidal ideation and suicides in the general population before and during the COVID-19 pandemic in Norway: A population-based repeated cross-sectional analysis.** Lancet Regional Health February 27, 2021. Volume 4, 100071, May 01, 2021DOI: <https://doi.org/10.1016/j.lanepe.2021.100071>

Credible data from Norway: except for a decrease in mental disorders in the first pandemic period, the findings suggest stable levels of mental disorders, suicidal ideation and suicide deaths during the first six months of the COVID-19 pandemic compared to pre-pandemic levels.

## Treatment

Touafchia A, Bagheri H, Carrié D, et al. **Serious bradycardia and remdesivir for coronavirus 2019 (COVID-19): a new safety concerns.** Clin Microbiol Infection February 26, 2021. DOI: <https://doi.org/10.1016/j.cmi.2021.02.013>

Oops: this post-marketing study in a real-world setting suggests that the use of remdesivir is significantly associated with an increased risk of reporting bradycardia and serious bradycardia when compared with the use of hydroxychloroquine, lopinavir/ritonavir, tocilizumab or glucocorticoids.

Lamontagne F, Agoritsas T, Siemieniuk R, et al. **A living WHO guideline on drugs to prevent covid-19.** BMJ. 2021 Mar 1;372:n526. PubMed: <https://pubmed.gov/33649077>. Full-text: <https://doi.org/10.1136/bmj.n526>

This is the first version of a living (up-to-date, evolving and EBM) guideline, focusing on the evidence for hydroxychloroquine. 53 authors from 45 centers say on 12 pages, "Do not use it!"

## 6 March

### Variants

#### Paper of the Day

Shen X, Tang H, McDanal C, et al. **SARS-CoV-2 variant B.1.1.7 is susceptible to neutralizing antibodies elicited by ancestral Spike vaccines.** *Cell Host Microbe* March 03, 2021. [https://www.cell.com/cell-host-microbe/fulltext/S1931-3128\(21\)00102-5](https://www.cell.com/cell-host-microbe/fulltext/S1931-3128(21)00102-5)

*Good news.* Using a lentivirus-based pseudovirus assay, Xiaoying Shen and colleagues from Duke, Durham, US, show that B.1.1.7 is probably not a neutralization escape variant of concern for COVID-19 vaccines. Moreover, B.1.1.7 is unlikely to increase the risk of SARS-CoV-2 re-infection.

Wibmer CK, Ayres F, Hermanus T, et al. **SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma.** *Nature Medicine* 02 March 2021. <https://www.nature.com/articles/s41591-021-01285-x>

B.1.351 is a bigger problem. This study (for months available as a pre-print only, now as a beautiful paper in *Nature Medicine*) shows that this lineage completely escapes three classes of therapeutically relevant antibodies. The B.1.351 pseudovirus also exhibited substantial to complete escape from neutralization, but not binding, by convalescent plasma. The overwhelming majority of monoclonal antibodies already on the path to licensure target residues K417 or E484 and are therefore likely to be futile against this variant.

### Virology

Schroeder S, Pott F, Niemeyer D, et al. **Interferon antagonism by SARS-CoV-2: a functional study using reverse genetics.** *Lancet Microbe* March 04, 2021. [https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247\(21\)00027-6/fulltext](https://www.thelancet.com/journals/lanmic/article/PIIS2666-5247(21)00027-6/fulltext)

Do differences in receptor usage determine all the differences in disease presentation between SARS-CoV and SARS-CoV-2? This work by Christian Drosten and colleagues shows that SARS-CoV-2 suppresses cytokine induction and interferon signaling with lower efficiency than SARS-CoV, despite the shared genome architecture and expression of homologous viral proteins. Gene encoding protein 6 as a genetic marker of virulence varied between SARS-CoV and SARS-CoV-2, thus providing a target for genome-based surveillance of circulating strains of SARS-CoV-2. The authors recommend to monitor sequence evolution of SARS-CoV ORF6.

## Immunology

Bost P, De Sanctis F, Canè S et al. **Deciphering the state of immune silence in fatal COVID-19 patients.** Nat Commun March 4, 2021 12, 1428. <https://www.nature.com/articles/s41467-021-21702-6#citeas>

This study shows innate and adaptive immune dysfunction, including loss of immune suppression by blood myeloid cells and the replacement of lung memory CD8+ T cells by naive T cells, suggesting a state of “immune silence” that correlates with a severe clinical manifestation and fatal outcome.

## Diagnostics

Azzolini C, Donati S, Premi E, et al. **SARS-CoV-2 on Ocular Surfaces in a Cohort of Patients With COVID-19 From the Lombardy Region, Italy.** JAMA Ophthalmology March 4, 2021. <https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2777178>

SARS-CoV-2 was present on the ocular surface in 52 of 91 COVID-19 patients, showing a wide variability in the viral load. Some had positive conjunctival swabs while having a negative nasopharyngeal swab. However, the authors did not determine the infectivity of the viral material detected. Clinical relevance remains unclear.

Moshe M, Daunt A, Flower B, et al. **SARS-CoV-2 lateral flow assays for possible use in national covid-19 seroprevalence surveys (React 2): diagnostic accuracy study.** BMJ. 2021 Mar 2;372:n423. PubMed: <https://pubmed.gov/33653694> . Full-text: <https://doi.org/10.1136/bmj.n423>

In contrast to routine serology assays, the use of lateral flow immunoassays (LFIAs) does not require the support of central laboratories and offers a rapid and affordable method of testing. This study shows that LFIA sensitivity is variable on serum and finger prick testing, and often differs from that stated by the manufacturer. Specificity of all LFIAs was high. However, none showed sufficient sensitivity and specificity to be considered for routine clinical use. One further LFIA (Surescreen) was identified as suitable for use in seroprevalence studies because it showed comparable performance to the LFIA currently used in the React 2 seroprevalence studies (Fortress). However, the performance of Surescreen was not significantly better than Fortress.

## Clinical

Martinez MW, Tucker AM, Bloom J, et al. **Prevalence of Inflammatory Heart Disease Among Professional Athletes With Prior COVID-19 Infection Who Received Systematic Return-to-Play Cardiac Screening.** *JAMA Cardiol* March 4 2021; <https://jamanetwork.com/journals/jamacardiology/fullarticle/2777308>

"The virus challenged me and I defeated it." That's what Zlatan Ibrahimovic, famous Swedish soccer player who caught COVID-19 last September, posted on Instagram (you don't know him? Then please take 94 seconds: <https://www.youtube.com/watch?v=GcCVfNA7otY>).

"But you are not Zlatan. Do not challenge the virus. Use your head, respect the rules. Social distancing and masks, always. We will win."

Zlatan was right! But should we have been worried about him? Probably not. In this multicenter, retrospective cross-sectional study of RTP cardiac testing performed on 789 professional athletes with COVID-19 (58% symptomatic, 42% asymptomatic or pauci-symptomatic), imaging evidence of inflammatory heart disease (performed around 3 weeks after positive testing) that resulted in restriction from play was identified in 5 athletes (0.6%) only. No adverse cardiac events occurred in the athletes who underwent cardiac screening and resumed professional sport participation. Thus, with regard to mild COVID-19, there were many Zlatans. On the field, however, there is only one.

## Comorbidities

Bloom CI, Drake TM, Docherty AB, et al. **Risk of adverse outcomes in patients with underlying respiratory conditions admitted to hospital with COVID-19: a national, multicentre prospective cohort study using the ISARIC WHO Clinical Characterisation Protocol UK.** *Lancet Resp Med* March 04, 2021. [https://doi.org/10.1016/S2213-2600\(21\)00013-8](https://doi.org/10.1016/S2213-2600(21)00013-8)

Analyzing 75,463 patients from the UK, Chloe Bloom and colleagues show that patients with chronic pulmonary disease had a high level of mortality, with a prevalence of 40% for in-hospital death. Of patients with asthma, only those with severe asthma had increased mortality compared to those without an underlying respiratory condition. Patients with asthma (aged ≥ 50 years) had a lower mortality risk if they had used inhaled corticosteroids within 2 weeks of admission.

## Treatment

López-Medina E, López P, Hurtado IC, et al. **Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial.** JAMA March 4, 2021; doi: 10.1001/jama.2021.3071. <https://jamanetwork.com/journals/jama/fullarticle/2777389>

The next hydroxychloroquine? Because of some evidence of activity *in vitro*, ivermectin has attracted huge interest. Several countries have included ivermectin in their treatment guidelines, leading to a surge in the demand for the drug by the general population and even alleged distribution of veterinary formulations. In this RCT that included 476 patients from Cali, Colombia, the duration of symptoms was not significantly different for patients who received either a 5-day course of ivermectin or placebo (median time to resolution of symptoms, 10 vs 12 days; hazard ratio for resolution of symptoms, 1.07). This is consistent with PK models showing that ivermectin levels do not reach the IC50 even for a dose level 10-times higher than the approved dose.

### Graphic

Lescure FX, Honda H, Fowler RA, et al. Sarilumab in patients admitted to hospital with severe or critical COVID-19: a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Resp Med March 04, 2021. [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(21\)00099-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00099-0/fulltext)

This large placebo-controlled multinational Phase III trial evaluated two doses of sarilumab, an interleukin-6 receptor inhibitor, in 416 patients with severe or critical COVID-19. At day 29, no significant differences were seen between the arms. The authors bravely suggest several potential reasons for why sarilumab was not effective (IL-6 insufficient to quell the inflammatory phase of the disease, patient selection not based on inflammation markers, dosage too low, use of confounding concomitant steroids, etc). However, this strategy seems not be a game changer in this pandemic.

## French

If you read French, read HerzbergN, Aeberhardt C. **Covid-19 : comment la lutte contre les variants pourrait modifier les stratégies vaccinales.** Le Monde 2021, published 25 February. Full-text : [https://www.lemonde.fr/planete/article/2021/02/25/covid-19-la-lutte-contre-les-variants-s-organise\\_6071122\\_3244.html](https://www.lemonde.fr/planete/article/2021/02/25/covid-19-la-lutte-contre-les-variants-s-organise_6071122_3244.html)

L'apparition de nouvelles mutations du virus contraint les laboratoires à adapter leurs vaccins, les agences sanitaires à inventer de nouvelles procédures réglementaires, et les Etats à réexaminer leur stratégie vaccinale.

## 7 March

### Variants

#### Paper of the Day

De Souza WM, Amorm MR, Sesti-Costa R, et al. **Levels of SARS-CoV-2 Lineage P.1 Neutralization by Antibodies Elicited after Natural Infection and Vaccination.** Lancet Preprints 2021, posted 1 March. Full-text: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3793486](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3793486)

William de Souza and colleagues isolated two P.1-containing specimens from nasopharyngeal and bronchoalveolar lavage samples of patients in Manaus, Brazil. They found that the immune plasma of COVID-19 convalescent blood donors had 6-fold less neutralizing capacity against the P.1 than against the B lineage. Moreover, five months after booster immunization with the Chinese CoronaVac vaccine, plasma from vaccinated individuals failed to efficiently neutralize P.1 lineage isolates.

Faria NR, Mellan TA, Whittaker C, et al. **Genomics and epidemiology of a novel SARS-CoV-2 lineage in Manaus, Brazil.** MedRxiv 2021, posted 3 March. Full-text: <https://doi.org/10.1101/2021.02.26.21252554>

Using a combination of genomic and epidemiological data, Nuno Faria and colleagues characterize the emergence and characteristics of P.1 that acquired 17 mutations, including the trio in the spike protein (K417T, E484K and N501Y) associated with increased binding to the human ACE2 receptor. The authors show that P.1 emerged around early November 2020. They estimate that P.1 could be 1.4–2.2 times more transmissible and able to evade 25–61% of protective immunity elicited by previous infection with non-P.1 lineages.

Wang P, Wang M, Yu J, et al. **Increased Resistance of SARS-CoV-2 Variant P.1 to Antibody Neutralization.** bioRxiv 2021, posted 2 March. Full-text: <https://doi.org/10.1101/2021.03.01.433466>

David D. Ho, Pengfei Wang and colleagues report that P.1 is not only refractory to multiple neutralizing monoclonal antibodies, but also more resistant to

neutralization by convalescent plasma (6.5-fold) and vaccinee sera (2.2-2.8-fold).

Cele S, Gazy I, Jackson L, et al. **Escape of SARS-CoV-2 501Y.V2 from neutralization by convalescent plasma.** MedRxiv 2021, posted 27 February. Full-text: <https://doi.org/10.1101/2021.01.26.21250224>

We already knew that people previously infected with the non-B.1.351 variant don't neutralize B.1.351 very effectively. Now Alex Sigal, Tulio de Oliveira, Sandile Cele and colleagues show that people infected with B.1.351 can neutralize both B.1.351 and (to a slightly lesser extent) 'regular' non-B.1.351 viruses (Cele 2021). If these data are confirmed, a variant B.1.351-targeted booster vaccine could be a solution for countries where B.1.351 is the dominant strain.

Starr TN, Greaney AJ, Dingens AS, Bloom JD. **Complete map of SARS-CoV-2 RBD mutations that escape the monoclonal antibody LY-CoV555 and its cocktail with LY-CoV016.** bioRxiv 2021, posted 21 February. Full-text: <https://doi.org/10.1101/2021.02.17.431683>

Jesse Bloom, Tyler Starr and colleagues completely map all mutations to the SARS-CoV-2 spike receptor binding domain (RBD) that escape binding by LY-CoV555 (bamlanivimab, a monoclonal antibody manufactured by Lilly), and its cocktail combination with LY-CoV016. Individual mutations that escape binding are present in B.1.351 and P.1 (E484K escapes LY-CoV555, K417N/T escape LY-CoV016). Additionally, the L452R mutation in the B.1.429 lineage escapes LY-CoV555.

## Transmission

Dinklage F, Ehmann A, Erdmann E, et al. **Why Is the Risk of Coronavirus Transmission so High Indoors?** Die Zeit 2020, published 26 November. Full-text: <https://www.zeit.de/wissen/gesundheit/2020-11/coronavirus-aerosols-infection-risk-hotspot-interiors>

Whenever people gather in closed spaces, the infection risk climbs. This interactive tool shows how the coronavirus spreads. Find out how safe your environment is. See also the [German version](#).



## Immunology

Tarke A, Sidney J, Methot N, et al. **Negligible impact of SARS-CoV-2 variants on CD4+ and CD8+ T cell reactivity in COVID-19 exposed donors and vaccinees.** bioRxiv 2021, posted 1 March. Full-text: <https://doi.org/10.1101/2021.02.27.433180>

Good news from the T cell front. [Alessandro Sette](#), [Alba Grifoni](#), [Shane Crotty](#), [Alison Tarke](#) and colleagues did a comprehensive analysis of SARS-CoV-2-specific CD4+ and CD8+ T cell responses from COVID-19 convalescent subjects recognizing the ancestral strain, compared to variant lineages B.1.1.7, B.1.351, P.1, and CAL.20C as well as recipients of the Moderna (mRNA-1273) or the Pfizer/BioNTech (BNT162b2) COVID-19 vaccines. The comfortable result: CD4+ and CD8+ T cell responses in convalescent COVID-19 subjects or COVID-19 mRNA vaccinees are not substantially affected by mutations found in the SARS-CoV-2 variants.

## Vaccines

Vasileiou E, Simpson CR, Robertson C, et al. **Effectiveness of First Dose of COVID-19 Vaccines Against Hospital Admissions in Scotland: National Prospective Cohort Study of 5.4 Million People.** Lancet Preprints 2021, posted 19 February. Full-text: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3789264](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3789264)

A single dose of the Pfizer-BioNTech or AstraZeneca vaccine results in substantial reductions in the risk of COVID-19 related hospitalization. In a study from Scotland, the first vaccine dose protected well over 80% of vaccinees against COVID-19 related hospitalization at 28-34 days post-vaccination (Pfizer-BioNTech: 85%; AstraZeneca: 94%). Comparable results (81%) were seen in people aged  $\geq$  80 years ([Vasileiou 2021](#)).

Hall VJ, Foulkes S, Saei A, et al. **Effectiveness of BNT162b2 mRNA Vaccine Against Infection and COVID-19 Vaccine Coverage in Healthcare Workers in England, Multicentre Prospective Cohort Study (the SIREN Study) Victoria Jane Hall.** Lancet Preprints 2021, published 22 February. Full-text: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3790399](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3790399)

These data from the SIREN (Sarscov2 Immunity and REinfection Evaluation) study suggest that the Pfizer-BioNTech vaccine effectively prevents both symptomatic and asymptomatic infection in working age adults. (The SIREN study is a prospective cohort study among staff working in publicly funded hospitals.) The vaccine was 72% effective (95% CI 58-86) 21 days after first

dose and 86% effective (95% CI 76-97) seven days after two doses in the antibody negative cohort (Hall 2021).

## French

If you read French, read **Covid-19 : « A court terme, l'effet positif des vaccins risque de ne pas suffire pour compenser l'impact délétère des variants »**. Le Monde 2021, published 6 March. Full-text : [https://www.lemonde.fr/planete/article/2021/03/06/covid-19-a-court-terme-l-effet-positif-des-vaccins-risque-de-ne-pas-suffire-pour-compenser-l-impact-deleterere-des-variants\\_6072159\\_3244.html](https://www.lemonde.fr/planete/article/2021/03/06/covid-19-a-court-terme-l-effet-positif-des-vaccins-risque-de-ne-pas-suffire-pour-compenser-l-impact-deleterere-des-variants_6072159_3244.html)

Simon Cauchemez, modélisateur à l'Institut Pasteur, doute que les mesures actuelles permettent une amélioration à la mi-avril, comme espéré par le gouvernement.

Mandard S. **Covid-19 : les pics de pollution aux particules fines soupçonnés de jouer un rôle dans le rebond épidémique**. Le Monde 2021, published 6 March. Full-text : [https://www.lemonde.fr/planete/article/2021/03/06/covid-19-les-pics-de-pollution-aux-particules-fines-soupconnes-de-jouer-un-role-dans-le-rebond-epidémique\\_6072189\\_3244.html](https://www.lemonde.fr/planete/article/2021/03/06/covid-19-les-pics-de-pollution-aux-particules-fines-soupconnes-de-jouer-un-role-dans-le-rebond-epidémique_6072189_3244.html)

Pour l'épidémiologiste Antoine Flahault, les épisodes de pollution liés aux sables du Sahara pourraient expliquer la reprise des contaminations et des hospitalisations.

Editorial. **Covid-19 : changer le regard sur le vaccin**. Le Monde 2021, published 5 March. Full-text : [https://www.lemonde.fr/idees/article/2021/03/05/covid-19-changer-le-regard-sur-le-vaccin\\_6072064\\_3232.html](https://www.lemonde.fr/idees/article/2021/03/05/covid-19-changer-le-regard-sur-le-vaccin_6072064_3232.html)

Cinq semaines après avoir exclu le reconfinement général du pays que de nombreux médecins appelaient de leurs vœux, Emmanuel Macron peut se targuer de deux résultats. A ce jour, l'épidémie n'a pas connu de hausse exponentielle, comme certains modèles le laissaient craindre. Et aucun de ses opposants politiques ne lui fait grief d'avoir fait ce choix risqué. Compte tenu de la fragilité économique et psychologique du pays, il existe désormais un quasi-consensus pour rejeter cette solution radicale. La partie, cependant, est encore loin d'être gagnée.

## 8 March

### Variants

Firestone MJ, Lorentz AJ, Meyer S, et al. **First Identified Cases of SARS-CoV-2 Variant P.1 in the United States — Minnesota, January 2021.** MMWR Morb Mortal Wkly Rep. ePub: 3 March 2021. [https://www.cdc.gov/mmwr/volumes/70/wr/mm7010e1.htm?s\\_cid=mm7010e1\\_x](https://www.cdc.gov/mmwr/volumes/70/wr/mm7010e1.htm?s_cid=mm7010e1_x)

The arrival of P.1 in the US. Both guys had returned from southeastern Brazil. According to the authors, this “underscores the importance of community prevention strategies to slow transmission of SARS-CoV-2 including use of well-fitting masks, physical distancing, washing hands, quarantine, testing of persons who have had contact with a person with laboratory-confirmed COVID-19, isolating persons with symptoms of COVID-19 or with diagnosed COVID-19 and” (*drumroll, please*) “adhering to CDC recommendations to delay travel”. Maybe it's not the best idea to vacation in Brazil (or anywhere!) right now.

Ojelade M, Rodriguez A, Gonzalez D, et al. **Travel from the United Kingdom to the United States by a Symptomatic Patient Infected with the SARS-CoV-2 B.1.1.7 Variant — Texas, January 2021.** MMWR Morb Mortal Wkly Rep. ePub: 3 March 2021. [https://www.cdc.gov/mmwr/volumes/70/wr/mm7010e2.htm?s\\_cid=mm7010e2\\_w](https://www.cdc.gov/mmwr/volumes/70/wr/mm7010e2.htm?s_cid=mm7010e2_w)

Another jerk who traveled from UK to US after experiencing COVID-19-compatible symptoms, infected with the B.1.1.7 variant. “Persons should not travel if they are experiencing symptoms compatible with COVID-19 or if they have received a positive SARS-CoV-2 test result and have not met criteria to discontinue isolation, have had close contact with a person with suspected or confirmed COVID-19 and have not subsequently met criteria to end quarantine, or have a pending SARS-CoV-2 viral test result”. Questions?

Fujino T, Nomoto H, Kutsuna S, Ujiie M, Suzuki T, Sato R, et al. **Novel SARS-CoV-2 variant identified in travelers from Brazil to Japan.** Emerg Infect Dis. 2021 Apr [date cited]. <https://doi.org/10.3201/eid2704.210138>

A family of four, traveling in early January to Tokyo, Japan, from Amazonas state in Brazil via Istanbul, Turkey (by the way, wouldn't it have been shorter

heading west?). Souvenir: A new lineage, resembling P.1, but with some interesting new mutations. Cringe.

Maggi F, Novazzi F, Genoni A, Baj A, Spezia PG, Focosi D, et al. **Imported SARS-CoV-2 variant P.1 detected in traveler returning from Brazil to Italy.** Emerg Infect Dis. 2021 Apr [date cited]. <https://doi.org/10.3201/eid2704.210183>

A family of three, flying from São Paulo, Brazil, via Madrid, Spain, to Milan (Malpensa Airport) in Italy, in mid-January. In the luggage: P.1.

## Diagnostics

Ott IM, Strine MS, Watkins AE, Boot M, Kalinich CC, Harden CA, et al. **Stability of SARS-CoV-2 RNA in nonsupplemented saliva.** Emerg Infect Dis. 2021 Apr [date cited]. <https://doi.org/10.3201/eid2704.204199>

Use saliva and simple plastic tubes! For this (important) study, saliva from COVID-19 inpatients and at-risk healthcare workers was collected into sterile wide-mouth containers without preservatives (non-supplemented) to evaluate the temporal stability of SARS-CoV-2 RNA at different holding temperatures. Of note, SARS-CoV-2 RNA from saliva was consistently detected at similar levels regardless of the holding time and temperatures tested.

## Clinical

Nguyen NT, Chinn J, Nahmias J, et al. **Outcomes and Mortality Among Adults Hospitalized With COVID-19 at US Medical Centers.** JAMA Netw Open March 5, 2021;4(3):e210417. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777028>

The largest US cohort of hospitalized COVID-19 adults to date. Among 192,550 adults hospitalized with COVID-19, 55,593 (28.9%) were admitted to the ICU and 26,221 (13.6%) died during hospitalization. Not surprisingly, in-hospital mortality increased with age; 179 of 12,644 patients (1.4%) aged 18 to 29 years died, and 8277 of 31,135 patients (26.6%) 80 years or older died. Of the patients admitted to the ICU, 15,431 of 55,593 (27.8%) died. The median hospital length of stay among patients who were not admitted to the ICU was 6 days, with a median cost per admission of \$10,520. The median hospital length of stay for those admitted to the ICU was 15 days, with a median cost per admission of \$39,825. Of note, mortality declined over the course of the 6 month period, from 22.1% in March to 6.5% in August.

Karagiannidis C, Windisch W, McAuley DF, et al. **Major differences in ICU admissions during the first and second COVID-19 wave in Germany.** *Lancet Resp Med* March 05, 2021. [https://doi.org/10.1016/S2213-2600\(21\)00101-6](https://doi.org/10.1016/S2213-2600(21)00101-6)

According to Christian Karagiannidis and colleagues who analyzed the data from the federal German hospital payment institute, the data “clearly suggests a dramatic improvement in the management of patients with COVID-19”. Compared with the first wave, 50% fewer of all hospitalized patients were admitted to the ICU during the second wave of the pandemic. By contrast, the prognosis of ICU patients, those requiring mechanical ventilation and those not, remained steady.

### Co-morbidities

Attauabi M, Seidelin J, Burisch J; **Danish COVID-IBD Study Group.** **Association between 5-aminosalicylates in patients with IBD and risk of severe COVID-19: an artefactual result of research methodology?** *Gut*. 2021 Mar 3;gutjnl-2021-324397. PubMed: <https://pubmed.gov/33658323>. Full-text: <https://doi.org/10.1136/gutjnl-2021-324397>

Discussion whether mesalamine/sulfasalazine is associated with an increased risk of severe COVID-19 in people with inflammatory bowel disease (IBD). And how to adjust for any potential effect modifiers and confounders in order to determine the granular effect of IBD-related medications. No definitive answer yet.

Ungaro RC, Brenner EJ, Gearry RB, et al. **Effect of IBD medications on COVID-19 outcomes: results from an international registry.** *Gut*. 2020 Oct 20;gutjnl-2020-322539. PubMed: <https://pubmed.gov/33082265>. Full-text: <https://doi.org/10.1136/gutjnl-2020-322539>

### Treatment

PRINCIPLE Trial Collaborative Group. **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.** *Lancet* March 04, 2021. [https://doi.org/10.1016/S0140-6736\(21\)00461-X](https://doi.org/10.1016/S0140-6736(21)00461-X)

Azithromycin makes no sense. This UK-based, open-label, adaptive platform randomized trial of interventions against COVID-19 in people at increased risk of an adverse clinical course (PRINCIPLE) randomly assigned people aged 65 years and older, or 50 years and older, with at least one co-morbidity, who

had been unwell for 14 days or less with suspected COVID-19, to usual care plus azithromycin 500 mg daily for three days, usual care plus other interventions, or usual care alone. In total, 402 (80%) of 500 participants in the azithromycin group and 631 (77%) of 823 participants in the usual care alone group reported feeling recovered within 28 days.

## Pediatrics

LaRovere KL, Riggs BJ, Poussaint TY, et al. **Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome.** JAMA Neurol March 5, 2021. doi:10.1001/jamaneurol.2021.0504.

<https://jamanetwork.com/journals/jamaneurology/fullarticle/2777392?resultClick=1>

In this study of 1695 patients 21 years or under, hospitalized at 61 US hospitals for acute COVID-19 or multisystem inflammatory syndrome, 365 (22%) had neurologic involvement. Among those with neurologic involvement, 322 (88%) had transient symptoms and survived, and 43 (12%) developed life-threatening conditions clinically adjudicated to be associated with COVID-19, including severe encephalopathy (n = 15; 5 with splenial lesions), stroke (n = 12), CNS infection/demyelination (n = 8), Guillain-Barré syndrome/variants (n = 4), and acute fulminant cerebral edema (n = 4).

## Spanish

If you read Spanish, read Zafra M, Linde P, López JV. **Así puede pasar el aire (y el coronavirus) de unas viviendas a otras a través del baño.** El País 2021, published 7 March. Full-text: <https://elpais.com/sociedad/2021-03-06/asi-puede-pasar-el-aire-y-el-coronavirus-de-unas-viviendas-a-otras-a-traves-del-bano.html>

Los conductos de ventilación de los baños en edificios antiguos conectan los pisos y, en circunstancias muy concretas, se sospecha que pueden ser una vía de contagio de la covid.

## French

If you read French, read **Covid-19 : l'appel des ordres de santé à tous les soignants, « faites-vous vacciner », c'est un « devoir déontologique ».** Le Monde 2021, published 7 March. Full-text :

[https://www.lemonde.fr/planete/article/2021/03/07/faites-vous-vacciner-l-appel-des-ordres-de-sante-a-tous-les-soignants\\_6072226\\_3244.html](https://www.lemonde.fr/planete/article/2021/03/07/faites-vous-vacciner-l-appel-des-ordres-de-sante-a-tous-les-soignants_6072226_3244.html)

Ils sont fous, les Gaulois? Seul un tiers des soignants sont actuellement vaccinés en France. « Ce n'est pas tolérable », estime Alain Fischer, le coordinateur de la campagne de vaccination. Les soignants sont « les plus exposés au virus, tout en étant au contact des populations les plus fragiles », estiment les organisations signataires. Ils doivent se faire vacciner « parce que cela relève de leur devoir déontologique, protéger leurs patients en toutes circonstances, et parce qu'il est impératif qu'ils puissent eux-mêmes se protéger contre le virus, ainsi que leurs proches, et freiner la propagation de l'épidémie », poursuivent-elles. Soyons plus clair encore (*the CR Editors*): Si vous êtes incapables de vous faire vacciner, changez de métier.

## 9 March

### Immunology

#### Paper of the Day

Huang L, Shi Y, Gong B, et al. **Dynamic blood single-cell immune responses in patients with COVID-19**. *Sig Transduct Target Ther* March 6, 2021, 6, 110. <https://doi.org/10.1038/s41392-021-00526-2>

More details on pathogenesis, mainly the host immune process, imbalances and pathways. In this incredible work, Lulin Huang and colleagues obtained single-cell mRNA sequencing data of 341,420 (!) peripheral blood mononuclear cells and 185,430 clonotypic T cells and 28,802 clonotypic B cells from 25 samples of 16 patients with COVID-19 for dynamic studies.

Gao L, Zhou J, Yang S, et al. **The dichotomous and incomplete adaptive immunity in COVID-19 patients with different disease severity**. *Sig Transduct Target Ther* 6, 113 (2021). <https://doi.org/10.1038/s41392-021-00525-3>

Specific B-cell and T-cell responses in 74 symptomatic patients with various disease severity: B cell responses were only transiently induced in early infection phase in asymptomatic or mild patients. In keeping with this, sustained GC responses that give rise to long-term memory B cells and IgG-secreting plasma cells were almost absent in these patients. This may explain that asymptomatic patients often fail to generate long-term SARS-CoV-2-specific IgG response. In contrast to humoral immunity, the virus-specific TH1 and CD8+ T cell immune responses were rapidly induced and sustained in asymp-

tomatic or mild symptomatic patients as compared to patients with moderate or severe disease.

Casado JL, Häemmerle J, Vizcarra P, et al. **SARS CoV-2 infections in health care workers with pre-existing T cell response: a prospective cohort study.** March 02, 2021. <https://doi.org/10.1016/j.cmi.2021.02.020>

José L. Casado and colleagues from Madrid looked at pre-existing T-cell responses. Twenty of 38 HCWs included (53%) had a previous specific CD8+ T cell response that does not seem to reduce incident SARS-CoV-2 infections, but may contribute to asymptomatic or mild disease, rapid viral clearance and differences in seroconversion.

## Epidemiology

Guy GP Jr., Lee FC, Sunshine G, et al. **Association of State-Issued Mask Mandates and Allowing On-Premises Restaurant Dining with County-Level COVID-19 Case and Death Growth Rates — United States, March 1–December 31, 2020.** MMWR Morb Mortal Wkly Rep. ePub: 5 March 2021. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7010e3.htm>

Mask mandates were associated with statistically significant decreases in county-level daily COVID-19 case and death growth rates within 20 days of implementation. Allowing on-premises restaurant dining was associated with increases in county-level case and death growth rates within 41–80 days after reopening. It will be a while until we can finally go to the restaurant again (does anyone else know how to order a dish?)

## Virology

Liu Y, Hu G, Wang Y, et al. **Functional and genetic analysis of viral receptor ACE2 orthologs reveals a broad potential host range of SARS-CoV-2.** PNAS March 23, 2021 118 (12) e2025373118; <https://www.pnas.org/content/118/12/e2025373118>

SARS-CoV-2 has the potential to infect a broad range of mammalian hosts, including domestic animals, pets, livestock, and animals commonly found in zoos and aquaria.



## Variants

Alexandre G, Bosetti P, Feri A, et al. **Early assessment of diffusion and possible expansion of SARS-CoV-2 Lineage 20I/501Y.V1 (B.1.1.7, variant of concern 202012/01) in France, January to March 2021.** Euro Surveill. 2021;26(9):pii=2100133. <https://doi.org/10.2807/1560-7917.ES.2021.26.9.2100133>

Spread of B.1.1.7. in France, in January. The authors estimate the population-level effective reproduction number will be respectively 39% (95%: 33–45%) and 56% (95%: 50–62%) higher on 1 March and 1 April 2021 than what would be expected if only the classical lineages were circulating.

## Vaccine

Nawwar AA, Searle J, Singh R, Lyburn ID. **Oxford-AstraZeneca COVID-19 vaccination induced lymphadenopathy on [18F]Choline PET/CT-not only an FDG finding.** Eur J Nucl Med Mol Imaging. 2021 Mar 4:1-2. PubMed: <https://pubmed.gov/33661328>. Full-text: <https://doi.org/10.1007/s00259-021-05279-2>

Lymphadenopathy is seen in some people after vaccination. In this case report of a cancer patient who underwent PET/CT 3 days after vaccination, nodal uptake was reactive in the axilla. Nice pictures.

## Clinical

Wongvibulsin S, Garibaldi BT, Antar AAR, et al. **Development of Severe COVID-19 Adaptive Risk Predictor (SCARP), a Calculator to Predict Severe Disease or Death in Hospitalized Patients With COVID-19.** Ann Intern Med. 2021 Mar 2. PubMed: <https://pubmed.gov/33646849>. Full-text: <https://doi.org/10.7326/M20-6754>

Using longitudinal data from more than 3000 patients hospitalized with COVID-19, the authors have developed a novel tool that can provide dynamic risk predictions for progression from moderate disease to severe illness or death in patients with COVID-19 at any time within the first 14 days of their hospitalization - on the basis of readily available clinical information. Check this out: [https://rsconnect.biostat.jhsph.edu/covid\\_trajectory](https://rsconnect.biostat.jhsph.edu/covid_trajectory)

## Comorbidities

Ardestani A, Azizi Z. **Targeting glucose metabolism for treatment of COVID-19.** Sig Transduct Target Ther March 6, 2021, 6, 112. <https://doi.org/10.1038/s41392-021-00532-4>

Some thoughts on how dysregulated glucose metabolism in people with diabetes may explain the increased susceptibility to SARS-CoV-2 and why uncontrolled diabetes can lead to excessive adaptive immune reactions in patients with critical COVID-19 symptoms.

## Long COVID

Subbaraman N. **US health agency will invest \$1 billion to investigate ‘long COVID’.** Nature News 04 March 2021. <https://www.nature.com/articles/d41586-021-00586-y>

Nidhi Subbaraman reports that the US will spend big on research into ‘long COVID’ – the long-lasting health effects of a SARS-CoV-2 infection (see our recent review) for which experts have coined a new term: post-acute sequelae SARS-CoV-2 infection (PASC).

## Treatment

Vimaleswaran KS, Frouhi NG, Khunti K. **Vitamin D and covid-19.** BMJ 04 March 2021; 372 doi: <https://doi.org/10.1136/bmj.n544>

Is there a role of vitamin D in prevention and management of COVID-19? The authors of this editorial believe that “existing evidence supports a compelling case for further research”.

## French

If you read French, read **Les hôpitaux et cliniques d’Île-de-France vont déprogrammer 40 % de leurs activités.** Le Monde 2021, published 8 March. Full-text : [https://www.lemonde.fr/sante/article/2021/03/08/covid-19-les-hopitaux-et-cliniques-d-ile-de-france-vont-deprogrammer-40-de-leurs-activites\\_6072352\\_1651302.html](https://www.lemonde.fr/sante/article/2021/03/08/covid-19-les-hopitaux-et-cliniques-d-ile-de-france-vont-deprogrammer-40-de-leurs-activites_6072352_1651302.html)

L’agence régionale de santé d’Île-de-France a donné « l’ordre ferme » aux hôpitaux franciliens de déprogrammer 40 % de leurs activités, afin d’augmenter le nombre de lits de réanimation réservés aux personnes atteintes du Covid-19.

## 10 March

### Variants

#### Paper of the Day

Wang P, Nair MS, Liu L, et al. **Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7.** *Nature* March 8, 2021. <https://www.nature.com/articles/s41586-021-03398-2>

For younger readers: once upon a time, in the stone age (c. 1996), David Ho from the Aaron Diamond Center was deemed “man of the year” (Time Magazine), after explaining the dynamics of HIV replication to the world. Today he explains why B.1.351 is so worrisome. While B.1.1.7 is refractory to neutralization by many mAbs but not more resistant to convalescent plasma (CP) or vaccinee sera (VS), B.1.351 is not only refractory to neutralization by almost all mAbs but also by CP (9.4 fold) and VS (10.3-12.4 fold). SARS-CoV-2 “is traveling in a direction that could ultimately lead to escape from our current therapeutic and prophylactic interventions directed to the viral spike”.

### Epidemiology

Chen X, Chen Z, Azman AS, et al. **Serological evidence of human infection with SARS-CoV-2: a systematic review and meta-analysis.** *Lancet* March 08, 2021. [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(21\)00026-7/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00026-7/fulltext)

After reviewing 404 (!) studies, the authors conclude that antibody-mediated herd immunity is far from being reached in most settings. Of note, the pooled infection-to-case ratio was similar between the region of the Americas (6.9, 95% CI: 2.7–17.3) and the European region (8.4, 95% CI: 6.5–10.7), but higher in India (56.5, 95% CI: 28.5–112.0), the only country in the South-East Asia region with data.

Leung K, Wu JT, Leung GM. **Real-time tracking and prediction of COVID-19 infection using digital proxies of population mobility and mixing.** *Nat Commun* 12, 1501 (2021). <https://www.nature.com/articles/s41467-021-21776-2>

Big Brother is watching you. However, sometimes he can be helpful. Using digital transactions made on Octopus cards (which are ubiquitously used by the Hong Kong population), the authors describe a framework that integrates digital proxies of human mobility and physical mixing into conventional epi-

demic models. At the end of the day, real-time estimates of  $R_t$  (accurate now-cast and short-term forecast of the epidemic) was obtained in Hong Kong.

## Vaccine

Ella R, Reddy S, Jogdand H, et al. **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.** Lancet March 08, 2021. [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(21\)00070-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00070-0/fulltext)

Inactivated vaccines have the advantage of being easily stored and shipped. BBV152 (COVAXIN) is a whole-virion inactivated SARS-CoV-2 vaccine adjuvanted with Algel-IMDG. An imidazoquinoline molecule (IMDG), a TLR7/8 agonist, is added to augment cell-mediated responses. According to the Phase I/II data from India presented here, BBV152 has shown the potential to provide durable humoral and cell-mediated immune responses (even against variants of concern). The Algel-IMDG formulation was selected for the ongoing Phase III efficacy trial, which involves 25,800 volunteers. BBV152 has received emergency use authorisation in India.

Rapaka RR, Hammershaimb EA, Neuzil KM. **Are some COVID vaccines better than others? Interpreting and comparing estimates of efficacy in trials of COVID-19 vaccines.** Clinical Infectious Diseases 06 March 2021, ciab213, <https://doi.org/10.1093/cid/ciab213>

Do you have colleagues who still “prefer” the BioNTech vaccine? Give him this viewpoint to read. Rekha Rapaka and colleagues from Maryland discuss the caveats of cross-trial comparisons. And why it matters how point estimates of efficacy were determined, in what epidemiologic setting, and against what endpoints.

Blumenthal KG, Robinson LB, Camargo Jr CA, et al. **Acute Allergic Reactions to mRNA COVID-19 Vaccines.** JAMA March 8, 2021; <https://jamanetwork.com/journals/jama/fullarticle/2777417?resultClick=1>

Of 64,900 vaccine recipients in Massachusetts, anaphylaxis was confirmed in 16 (0.025%). Of note, 15/16 were female, 10 had a prior history of allergies and 5 had a history of anaphylaxis. Mean time to anaphylaxis onset was 17 minutes (range, 1-120). All recovered.

## Transmission

Paul LA, Daneman N, Brown KA, et al. **Characteristics associated with household transmission of SARS-CoV-2 in Ontario, Canada: A cohort study.** *Clinical Infectious Diseases* 05 March 2021, ciab186, <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab186/6159706>

Among 26,714 cases of COVID-19 residing in 21,226 households, longer testing delays ( $\geq 5$  days versus 0 days, OR = 3.02) and male gender (OR = 1.28) were associated with greater odds of household secondary transmission, as well as (not surprisingly) larger average family size and a higher proportion of households with multiple persons per room.

## Clinical

Kompaniyets L, Goodman AB, Belay B, et al. **Body Mass Index and Risk for COVID-19–Related Hospitalization, Intensive Care Unit Admission, Invasive Mechanical Ventilation, and Death — United States, March–December 2020.** *MMWR Morb Mortal Wkly Rep.* ePub: 8 March 2021. <https://www.cdc.gov/mmwr/volumes/70/wr/mm7010e4.htm>

Among 148,494 US adults with COVID-19, a non-linear “dose response” relationship was found between body mass index and COVID-19 severity, with lowest risks at BMIs near the threshold between healthy weight and overweight in most instances, then increasing with higher BMI. Overweight and obesity were risk factors for invasive mechanical ventilation. Obesity was a risk factor for hospitalization and death, particularly among adults aged < 65 years.

## Graphic

Lugon JC, Smit M, Salamun J, et al. **Novel outpatient management of mild to moderate COVID-19 spares hospital capacity and safeguards patient outcome: The Geneva PneumoCoV-Ambu study.** *PLOS One*, March 4, 2021. <https://doi.org/10.1371/journal.pone.0247774>

Calling patients every 48 hours for the first 10 days following diagnosis, with a standardized interview about self-reported symptoms or every 24 hours if patients presented a worsening clinical condition: this small study in relatively young patients shows that such an outpatient management of mild to moderate COVID-19-related pneumonia is possible. Costly and unnecessary hospitalizations were avoided and hospital capacity was spared.

## Treatment

Loffredo M, Lucero H, Chen DY, et al. **The in-vitro effect of famotidine on sars-cov-2 proteases and virus replication.** Sci Rep March 8, 2021, 11, 5433. <https://www.nature.com/articles/s41598-021-84782-w>

*In silico* studies have proposed one of the two SARS-CoV-2 proteases, 3CL<sup>pro</sup> or PL<sup>pro</sup>, as potential molecular targets of famotidine activity. Somewhat disappointing: Madeline Loffredo and colleagues show here that the drug neither binds with nor inhibits the functions of these proteases.

## 11 March

### Variants

#### Paper of the Day

Tegally H, Wilkinson E, Giovanetti M. et al. **Emergence of a SARS-CoV-2 variant of concern with mutations in spike glycoprotein.** Nature March 9, 2021. [https://www.nature.com/articles/s41586-021-03402-9\\_reference.pdf](https://www.nature.com/articles/s41586-021-03402-9_reference.pdf)

The future “reference” paper on the detection of B.1.351 (or 501Y.V2), characterized by eight lineage-defining mutations in the spike protein, including three at important residues in the receptor-binding domain (K417N, E484K and N501Y). This lineage was identified in South Africa after the first epidemic wave in a severely affected metropolitan area, and spread rapidly. The genomic data, showing the rapid expansion and displacement of other lineages in multiple regions, suggest that this lineage is associated with a selection advantage, most plausibly as a result of increased transmissibility or immune escape. Nevertheless, congrats to co-author Wolfgang Preiser!

### Epidemiology

Agrawal S, Orschler L, Lackner S. **Long-term monitoring of SARS-CoV-2 RNA in wastewater of the Frankfurt metropolitan area in Southern Germany.** Sci Rep 11, 5372 (2021). <https://www.nature.com/articles/s41598-021-84914-2>

After monitoring the time course of the SARS-CoV-2 RNA concentration in raw sewage in the Frankfurt metropolitan area for several months, Shelesh Agrawal and colleagues believe that wastewater-based epidemiology has the potential to serve as an early warning system for SARS-CoV-2 infections and as a monitoring system to identify global hotspots.

Brault V, Mallein B, Rupprecht JF, et al. **Group testing as a strategy for COVID-19 epidemiological monitoring and community surveillance.** PLOS Computational Biology, March 4, 2021. <https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1008726>

Group testing could provide the means for regular and massive screenings. In this paper, the authors do not address any diagnostic problems—e.g. how to use a minimal number of tests to obtain an individual diagnostic—but rather focus on population-scale application of pooling.

## Immunology

Grzelak L, Velay A, Madec Y, et al. **Sex differences in the evolution of neutralizing antibodies to SARS-CoV-2.** Journal of Infectious Diseases 07 March 2021, jiab127, <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiab127/6161322?searchresult=1>

More robust humoral responses in women than in men? In 308 healthcare workers with mild disease, anti-S and anti-N antibodies were detected in 99% and 59% of individuals at 3-6 months, respectively. Anti-S antibodies and NAbS declined faster in males than in females, independently of age and BMI, suggesting an association of sex with evolution of the humoral response.

## Vaccine

Saad-Roy CM, Morris SE, Metcalf JE, et al. **Epidemiological and evolutionary considerations of SARS-CoV-2 vaccine dosing regimes.** Science 09 Mar 2021: eabg8663. <https://science.sciencemag.org/content/early/2021/03/08/science.abg8663>

Delaying the second dose? Maybe easier said than done. Chadi Saad-Roy and colleagues urge caution. According to their models, a vaccine strategy with a very long inter-dose period could lead to marginal short-term benefits at the cost of a higher infection burden in the long term and substantially more potential for viral evolution and the development of new variants. However, current uncertainties surrounding the strength and duration of adaptive immunity in response to natural infection or vaccination lead to very broad range of possible outcomes of various dosing regimens.

Capetti AF, Stangalini CA, Borgonovo F, et al. **Impressive boosting of anti-S1/S2 IgG production in COVID-19-experienced patients after the first shot of the BNT162b2 mRNA COVID-19 Vaccine.** *Clinical Infectious Diseases* 06 March 2021, ciab214, <https://doi.org/10.1093/cid/ciab214>

But is one shot enough after infection? The next study, comparing COVID-19 naïve people versus asymptomatic/pauci-symptomatic (A/P) people versus symptomatic/hospitalized (S/H) COVID-19 patients. Titers (logarithmic scale!) before and after the first dose of the BNT162b2 vaccine.

## Virology

Baggen J, Persoons L, Vanstreels E, et al. **Genome-wide CRISPR screening identifies TMEM106B as a proviral host factor for SARS-CoV-2.** *Nat Genet* March 8, 2021. <https://www.nature.com/articles/s41588-021-00805-2.pdf>

Jim Baggen and colleagues from Belgium have identified two new host factors required for coronavirus infection. The lysosomal protein TMEM106B serves as an essential specific host factor for SARS-CoV-2 infection in multiple human cell lines. The phosphoinositide 3-kinase (PI3K) type 3 appears to be a common host factor for SARS-CoV-2 that could be targeted by small molecules.

## Diagnostics

Shrotri M, Harris RJ, Rodger A, Planche T, Sanderson F, Mahungu T, et al. **Persistence of SARS-CoV-2 N-antibody response in healthcare workers, London, UK.** *Emerg Infect Dis.* 2021 Apr [date cited]. [https://wwwnc.cdc.gov/eid/article/27/4/20-4554\\_article](https://wwwnc.cdc.gov/eid/article/27/4/20-4554_article)

Nucleocapsid (N) antibodies appear more stable than Spike (S) antibodies in the short term. N antibody titers were stable and sustained for < 12 weeks in 312 seropositive participants. This was consistent across demographic and clinical variables and contrasts with reports of short-term antibody waning.

Van Elslande J, Gruwier L, Godderis P. **Estimated half-life of SARS-CoV-2 anti-spike antibodies more than double the half-life of anti-nucleocapsid antibodies in healthcare workers.** *Clinical Infectious Diseases* 08 March 2021, ciab219, <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab219/6162856?searchresult=1>



Oops, the opposite? See title. We would like to attend a Zoom meeting between Madhumita Shrotri and Jan Van Elslande. Different time periods, methods, participants? The debate goes on.

Noh JY, Kwak JE, Yang JS, et al. **Longitudinal assessment of anti-SARS-CoV-2 immune responses for six months based on the clinical severity of COVID-19.** Journal of Infectious Diseases 04 March 2021, jia124, <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jia124/6158870?searchresult=1>

Ji Yun Noh and colleagues from Seoul have investigated the longitudinal profile of anti-SARS-CoV-2 antibodies in patients who recovered from COVID-19. Neutralizing antibodies were detected in 86.9% until six months after diagnosis of SARS-CoV-2 infection. Patients with pneumonia had significantly higher titers (and stronger T cell immunity) than patients without.

## 12 March

### Vaccine

#### Paper of the Day

Stephenson KE, Le Gars M, Sadoff J, et al. **Immunogenicity of the Ad26.COV2.S Vaccine for COVID-19.** JAMA March 11, 2021. <https://jamanetwork.com/journals/jama/fullarticle/2777598>

The COVID-19 vaccine from Janssen (Johnson & Johnson) is the fourth vaccine recommended in the EU for preventing COVID-19. Ad26.COV2.S is a recombinant, replication-incompetent Ad26 vector encoding the full length and stabilized SARS-CoV-2 S protein derived from the first Wuhan strain. This phase I study (in 25 recipients from Boston) shows that a single immunization induced rapid binding and neutralization antibody responses as well as cellular immune responses, including induction of RBD-specific binding antibodies in 90% of vaccine recipients by day 8.

Vijayasingham L, Bischof E, Wolfe J. **Sex-disaggregated data in COVID-19 vaccine trials.** Lancet March 05, 2021. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00384-6/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00384-6/fulltext)

Lavanya Vijayasingham and colleagues argue that sex factors, including sex-disaggregated analysis and reporting, are still neglected in COVID-19 trial data reporting.

## Epidemiology

Richard Q, Alizon S, Choisy M, et al. **Age-structured non-pharmaceutical interventions for optimal control of COVID-19 epidemic.** PLOS Computational Biology March 4, 2021. <https://doi.org/10.1371/journal.pcbi.1008776>

Complex models, trying to elucidate that countries with contrasted population age-structures and social or physical contacts may need different NPIs.

Bokharaie VS. **A study on the effects of containment policies and vaccination on the spread of SARS-CoV-2.** PLOS March 4, 2021. <https://doi.org/10.1371/journal.pone.0247439>

Same direction. A method to predict the spread of the SARS-CoV-2 in a population with a known age-structure, and then, to quantify the effects of various containment policies, including those policies that affect each age-group differently.

Mulenga LB, Hines JZ, Fwoloshi S, et al. **Prevalence of SARS-CoV-2 in six districts in Zambia in July, 2020: a cross-sectional cluster sample survey.** Lancet Global Health March 09, 2021. [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(21\)00053-X/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(21)00053-X/fulltext)

Almost 1 in 100 diagnosed: According to this first large cross-sectional cluster-sample survey of households in Africa (performed in July), the number of laboratory-confirmed cases reported in official statistics in Zambia underestimated SARS-CoV-2 infections by a factor of 92.

## Virology

Lythgoe KA, Hall M, Ferretti L, et al. **SARS-CoV-2 within-host diversity and transmission.** Science 09 Mar 2021: eabg0821 Full-text: <https://doi.org/10.1126/science.abg0821>

Katrina A. Lythgoe and colleagues deep-sequenced 1313 clinical samples from the UK. Interestingly, most samples harbored few intrahost variants, and estimated transmission bottleneck sizes were very small, with maximum likelihood estimates between 1 and 8 among household transmission pairs, mean-

ing that if mutations do arise they will be prone to loss at the point of transmission. The results suggest that transmission-enhancing and/or immune-escape variants are likely to arise infrequently, but could spread rapidly if successfully transmitted.

## Clinical

Poletti P, Tirani M, Cereda D, et al. **Association of Age With Likelihood of Developing Symptoms and Critical Disease Among Close Contacts Exposed to Patients With Confirmed SARS-CoV-2 Infection in Italy.** JAMA Netw Open March 10, 2021;4(3):e211085. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777314>

Of 5484 quarantined case contacts who were monitored daily for symptoms for at least 2 weeks, 2824 (51.5%) tested positive. The proportion of infected persons who developed symptoms ranged from 18.1% (95% CI, 13.9%-22.9%) among participants younger than 20 years to 64.6% (95% CI, 56.6%-72.0%) for those aged 80 years or older.

## Long COVID

Weng J, Li Y, Li J, et al. **Gastrointestinal sequelae 90 days after discharge for COVID-19.** Lancet Gastroenterology Hepatology March 9, 2021. [https://www.thelancet.com/journals/langas/article/PIIS2468-1253\(21\)00076-5/fulltext](https://www.thelancet.com/journals/langas/article/PIIS2468-1253(21)00076-5/fulltext)

In this retrospective study from Hubei and Guangdong provinces, 52 (44%) of 117 patients reported gastrointestinal symptoms after discharge at a 90 day telephone interview: loss of appetite (24%), nausea (18%), acid reflux (18%), and diarrhoea (15%). Of note, severe illness during hospitalisation was not associated with post-discharge gastrointestinal sequelae.

## Collateral damage (and benefits)

Maselli-Schoueri JH, Werneck de Carvalho LE, Affonso Fonseca FL, et al. **Hospital Admissions Associated With Noncommunicable Diseases During the COVID-19 Outbreak in Brazil.** JAMA Netw Open March 8, 2021; 4(3):e210799. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777139>

Reduction in hospital admissions for NCDs from January to June 2020 compared with the corresponding period in each of the 3 previous years in São Paulo, Brazil. Decrease was 68% for musculoskeletal diseases, 44% for metabolic diseases, 38% for CVDs, and 35% for neoplasms.

## Treatment

Ozaki K, Reinhard CT. **The future lifespan of Earth's oxygenated atmosphere.** *Nat. Geosci.* 14, 138–142 (2021). <https://doi.org/10.1038/s41561-021-00693-5>

We'd prefer to present other papers in this section. However, there is some good news: we'll get some more weeks to find a potent treatment for SARS-CoV-2. Using a combined biogeochemistry and climate model to examine the likely timescale of oxygen-rich atmospheric conditions on Earth, these authors estimate that the mean future lifespan of Earth's atmosphere, with oxygen levels more than 1% of the present atmospheric level, is  $1.08 \pm 0.14$  billion years.

## 13 March

### Variants

#### Paper of the Day

Collier DA, De Marco A, Ferreira IA, et al. **Sensitivity of SARS-CoV-2 B.1.1.7 to mRNA vaccine-elicited antibodies.** *Nature* March 11, 2021. <https://www.nature.com/articles/s41586-021-03412-7>

A pseudovirus bearing S protein with the full set of mutations present in the B.1.1.7 variant did result in a small reduction in neutralization by sera from vaccinees that was more marked following the first dose vs the second dose. Worryingly, Dami A. Collier and colleagues measured further reduction in neutralization titers by vaccine sera when E484K was present alongside the B.1.1.7 S mutations. They conclude that “E484K emergence on a B.1.1.7 background represents a threat to the vaccine BNT162b”.

Borges V, Sousa C, Menezes L, et al. **Tracking SARS-CoV-2 lineage B.1.1.7 dissemination: insights from nationwide spike gene target failure (SGTF) and spike gene late detection (SGTL) data, Portugal, week 49 2020 to week 3 2021.** *Eurosurveillance* Mar 11, 2021, Article Volume 26, Issue 10. <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.10.2100130>

Dissemination of the B.1.1.7 lineage in Portugal. Both SGTF and SGTL (a proxy for monitoring trends of B.1.1.7) samples had significantly lower median Ct

values of N and ORF1ab gene targets (ca 3.5 and 1.8 Ct units, respectively) compared with samples where the S gene was unbiasedly detected.

## Epidemiology

Sartorius B, Lawson AB, Pullan RL. **Modelling and predicting the spatio-temporal spread of COVID-19, associated deaths and impact of key risk factors in England.** Sci Rep 11, March 8, 2021, 5378. <https://doi.org/10.1038/s41598-021-83780-2>

This high resolution spatial-temporal model highlights differences in epidemic dynamics across small areas in England, emphasizing the importance of monitoring at a granular sub-national scale. A geographically staggered approach combined with enhanced community surveillance will be increasingly important.

Boffetta P, Violante F, Durando P, et al. **Determinants of SARS-CoV-2 infection in Italian healthcare workers: a multicenter study.** Sci Rep March 11, 2021, 5788. <https://www.nature.com/articles/s41598-021-85215-4.pdf>

The prevalence of infection ranged from 3% to 22%, and was correlated with that of the respective areas within Italy. Of note, there was a lack of a clear pattern in risk according to job categories.

## Vaccine

Krammer F, Srivastava K, Alshammary H, et al. **Antibody Responses in Seropositive Persons after a Single Dose of SARS-CoV-2 mRNA Vaccine.** March 10, 2021. <https://www.nejm.org/doi/full/10.1056/NEJMc2101667>

In 110 vaccinees, the antibody titers of those with pre-existing infection were 10 to 45 times higher than those of vaccinees without pre-existing immunity at the same time points after the first mRNA vaccine dose. The problem with all these studies: until we know whether this translates into similar protection, the one-shot strategy will not gain widespread acceptance. When we do know one day, this will largely not matter (there will be enough vaccine available) and will only be interesting for cost reasons.

Steinberg J, Thomas A, Iravavi A. **18Fluorodeoxyglucose PET/CT findings in a systemic inflammatory response syndrome after COVID-19 vaccine.** *Lancet* March 08, 2021. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00464-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00464-5/fulltext)

Julie Steinberg and colleagues from St. Louis describe an interesting case of a (self-resolving) systemic inflammatory response syndrome in a 65-year-old woman, starting one day after Moderna's mRNA vaccine. PET/CT showed uptake in the fat stranding posterior to the right deltoid, moderately increased uptake within multiple right axillary lymph nodes and diffusely increased splenic uptake.

Fernández-Prada M, Rivero-Calle I, Calvache-González A, Martín-Torres F. **Acute onset supraclavicular lymphadenopathy coinciding with intramuscular mRNA vaccination against COVID-19 may be related to vaccine injection technique, Spain, January and February 2021.** *Euro Surveill.* 2021;26(10):pii=2100193. <https://doi.org/10.2807/1560-7917.ES.2021.26.10.2100193>

María Fernández-Prada and colleagues report on 20 female HCWs with acute onset of a single supraclavicular lymphadenopathy coinciding with the ipsilateral intramuscular administration of an mRNA vaccine. Of note, 17 reported that the injection point had been unusually high. All lymphadenopathies had inflammatory symptoms (pain, swelling), were rounded and mobile, and all but one appeared in the first 24 h to 9 days after vaccine administration. All improved clinically, and 15 completely resolved between 5 and 16 days from onset.

## Transmission

Klompas M, Baker MA, Griesbach D, et al. **Transmission of SARS-CoV-2 from asymptomatic and presymptomatic individuals in healthcare settings despite medical masks and eye protection.** *Clinical Infectious Diseases*, 11 March 2021. ciab218, <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab218/6168040?searchresult=1>

Three instances of SARS-CoV-2 transmission in Boston, despite medical masks and eye protection, including one transmission despite both parties being masked. Whole genome sequencing confirmed perfect homology between source and exposed persons' viruses in all cases. These findings teach the importance of not relying upon medical masks and eye protection alone.

Pan X, Li X, Kong P, et al. **Assessment of Use and Fit of Face Masks Among Individuals in Public During the COVID-19 Pandemic in China.** JAMA Netw Open March 11, 2021, 4(3):e212574. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2777405?resultClick=1>

“Wear a mask.” If it were only that simple, even in China! For this study, during July and August 2020, 6003 (!) people wearing masks were assessed at public places, such as markets, train stations, airports, hospitals, and schools in Beijing, Yunnan, Shanxi, and Jiangsu. Face mask airtightness was commonly suboptimal, mostly secondary to gaps at the upper face mask edge. Sealing the upper face mask edge with an adhesive tape was associated with significantly improving the airtightness of commonly used face masks.

## Long COVID-19

Sudre CH, Murray B, Varsavsky T, et al. **Attributes and predictors of long COVID.** Nat Med March 10, 2021. <https://www.nature.com/articles/s41591-021-01292-y>

Is it possible to predict long COVID-19? Among 4182 people who self-reported their symptoms prospectively in the COVID Symptom Study app, a total of 558 (13.3%) reported symptoms lasting  $\geq 28$  days, 189 (4.5%) for  $\geq 8$  weeks and 95 (2.3%) for  $\geq 12$  weeks. Experiencing more than five symptoms during the first week of illness was associated with long COVID in all sexes and age groups (odds ratio = 3.5). Main caveat: the population was limited by being confined to app contributors (disproportionately female patients). May not be generalizable.

## 14 March

### Immunology

#### Paper of the Day

Amanat F, Thapa M, Lei T, et al. **The plasmablast response to SARS-CoV-2 mRNA vaccination is dominated by non-neutralizing antibodies that target both the NTD and the RBD.** medRxiv 2021, posted 9 March. Full-text: <https://doi.org/10.1101/2021.03.07.21253098>

Florian Krammer, Fatima Amanat and colleagues studied the plasmablast response to SARS-CoV-2 mRNA-based vaccination. The authors demonstrate

that the antibody responses to SARS-CoV-2 mRNA vaccination comprise a large proportion of non-neutralizing antibodies and are co-dominated by NTD and RBD antibodies. The NTD portion of the spike represents, therefore, an important vaccine target. Since all viral variants of concern are heavily mutated in this region, these observations warrant further attention to optimize SARS-CoV-2 vaccines. Finally, broadly cross-reactive mAbs to  $\beta$ -coronavirus spike proteins are induced after vaccination and suggest a potential development path for a pan- $\beta$ -coronavirus vaccine.

Ellebedy A, Turner J, O'halloran J, et al. **SARS-CoV-2 mRNA vaccines induce a robust germinal centre reaction in humans.** Research Square 2021, posted 9 March. Full-text: <https://doi.org/10.21203/rs.3.rs-310773/v1>

Did you feel that your arm is on “fire” after getting your SARS-CoV-2 mRNA vaccine? Did you get some fine needle aspirates of your draining axillary lymph nodes? You could have investigated the dynamics of antibody secreting plasmablasts (PBs) and germinal center (GC) B cells induced by these vaccines in SARS-CoV-2 naïve and antigen-experienced humans. Ellebedy et al did just that. They demonstrated that SARS-CoV-2 mRNA-based vaccination of humans induces a robust and persistent GC B cell response that engages pre-existing as well as new B cell clones. High-affinity, broad, and durable humoral immunity on the horizon?

Muecksch F, Weisblum Y, Barnes CO, et al. **Development of potency, breadth and resilience to viral escape mutations in SARS-CoV-2 neutralizing antibodies.** bioRxiv 2021, posted 8 March. Full-text: <https://doi.org/10.1101/2021.03.07.434227>

Might affinity maturation generate antibodies that are resilient to viral evolution? Paul Bieniasz, Frauke Muecksch and colleagues think so. After analyzing six independent antibody lineages, they found that for certain ones, maturation enabled neutralization of circulating SARS-CoV-2 variants of concern and heterologous sarbecoviruses. The authors conclude that increasing antibody diversity through prolonged or repeated antigen exposure may improve protection against diversifying SARS-CoV-2 populations, and perhaps against other pandemic threat coronaviruses.



## Epidemiology

CMMID 202103. **European COVID-19 Forecast hub**. London School of Hygiene & Tropical Medicine and ECDC 2021. Website: <https://covid19forecasthub.eu>

The *European COVID-19 Forecast hub* aims to collate and meaningfully combine short-term forecasts of COVID-19 from across Europe in order to 1) improve situational awareness and 2) quantify the current trajectory of COVID-19 everywhere whilst acknowledging uncertainty.

Graphic

Mallapaty S. **The search for animals harbouring coronavirus — and why it matters**. *Nature* 2021, published 2 March. Full-text: <https://www.nature.com/articles/d41586-021-00531-z>

Monitoring pets, livestock and wildlife to see where SARS-CoV-2 could hide, and whether it might resurge.

Graphic

## Transmission

Hensley MK, Bain WG, Jacobs J, et al. **Intractable Coronavirus Disease 2019 (COVID-19) and Prolonged Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Replication in a Chimeric Antigen Receptor-Modified T-Cell Therapy Recipient: A Case Study**. *Clin Infect Dis* 2021. Full-text: <https://doi.org/10.1093/cid/ciab072>

Prolonged transmission from immunosuppressed patients is possible. A chimeric antigen receptor-modified T cell therapy recipient developed severe coronavirus disease 2019, intractable RNAemia, and viral replication lasting > 2 months. Deep sequencing revealed multiple sequence variants consistent with intra-host viral evolution.

## Virology

Braun KM, Moreno GK, Halfmann PJ, et al. **Transmission of SARS-CoV-2 in domestic cats imposes a narrow bottleneck**. *PLOS Pathogens* 2021, published 26 February. Full-text: <https://doi.org/10.1371/journal.ppat.1009373>

How is genetic variation generated and selected within and between individual hosts? Using domestic cats as a model, Thomas Friedrich, Katarina Braun and colleagues show that within-host SARS-CoV-2 genetic variation is pre-

dominantly influenced by genetic drift and purifying selection. In particular, they identified a notable variant at amino acid position 655 in spike (H655Y), which was previously shown to confer escape from human monoclonal antibodies. This variant arises rapidly and persists at intermediate frequencies in index cats.

## Variants

Grint DJ, Wing K, Williamson E, et al. **Case fatality risk of the SARS-CoV-2 variant of concern B.1.1.7 in England.** MedRxiv 2021, posted 8 March. Full-text: <https://doi.org/10.1101/2021.03.04.21252528>

The authors draw data from a research platform that covers 40% of England's population registered with a general practitioner. B.1.1.7 status was known for 184,786 people. The B.1.1.7 group was younger with a lower proportion of older cases (80+: 0.9% VOC vs. 1.6% non-B.1.1.7 cases), with fewer co-morbidities (2+ co-morbidities: 2.9% vs. 3.8%). After controlling for co-morbidities, age, week, region & other sociodemographics, the authors found an increased risk of death for B.1.1.7 compared with non-B.1.1.7 cases (HR: 1.67; 95% CI: 1.34 - 2.09; P < 0.0001).

Tablizo FA, Kim KM, Lapid CM, et al. **Genome sequencing and analysis of an emergent SARS-CoV-2 variant characterized by multiple spike protein mutations detected from the Central Visayas Region of the Philippines.** medRxiv 2021, posted 6 March. Full-text: <https://doi.org/10.1101/2021.03.03.21252812>

The authors describe the emergence of a new SARS-CoV-2 lineage, mainly from the [Central Visayas region](#) of the Philippines: 13 lineage-defining mutations, including the co-occurrence of the E484K, N501Y, and P681H mutations at the spike protein region, as well as three additional radical amino acid replacements towards the C-terminal end of the said protein. A three amino acid deletion at positions 141 to 143 (LGV141\_143del) in the spike protein is reminiscent of a region preceding the 144Y deletion found in the B.1.1.7 variant. See also the 'P.3' proposition by Andrew Rambaut: <https://github.com/cov-lineages/pango-designation/issues/27>.

## Vaccines

Shah A, Gribben C, Bishop J, et al. **Effect of vaccination on transmission of COVID-19: an observational study in healthcare workers and their households.** GitHub preprint, posted 12 March. Full-text:

[https://github.com/ChronicDiseaseEpi/hcw/blob/master/vaccine\\_manuscript.pdf](https://github.com/ChronicDiseaseEpi/hcw/blob/master/vaccine_manuscript.pdf)

Household members of vaccinated healthcare workers have a lower risk for being infected with SARS-CoV-2 (rate per 100 person-years 9.40 versus 5.93; HR 0.70, 95% CI: 0.63 to 0.78). This is the result of a Scottish cohort comprised of 194,362 household members (mean age 31.1 ± 20.9 years) and 144,525 healthcare workers (mean age 44.4 ± 11.4 years). As household members of healthcare workers can also be infected by other people, this 30% risk reduction is probably an underestimate of the effect vaccination will have on transmission of SARS-CoV-2.

Fischer R, van Doremalen N, Adney D, et al. **ChAdOx1 nCoV-19 (AZD1222) protects against SARS-CoV-2 B.1.351 and B.1.1.7.** bioRxiv 2021, posted 11 March. Full-text: <https://doi.org/10.1101/2021.03.11.435000>

Thinking of maybe not getting the vaccine because of the new variants? Think again! Here, Robert Fischer, Neeltje van Doremalen and colleagues show a lack of disease in Syrian hamsters vaccinated with the AstraZeneca vaccine when infected with B.1.1.7 or B.1.351 (first detected in the UK and South Africa, respectively). The authors observed a 9.5-fold reduction of virus-neutralizing antibody titer in vaccinated hamster sera against B.1.351 compared to B.1.1.7. Vaccinated hamsters challenged with B.1.1.7 or B.1.351 did not lose weight compared to control animals. Interesting data from a pre-print paper that need to be confirmed in clinical vaccine practice.

Public Health England 20210222. **PHE monitoring of the early impact and effectiveness of COVID-19 vaccination in England.** UK Government 2021, 22 February; accessed 5 March 2021. Full-text: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/963532/COVID-19\\_vaccine\\_effectiveness\\_surveillance\\_report\\_February\\_2021\\_FINAL.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/963532/COVID-19_vaccine_effectiveness_surveillance_report_February_2021_FINAL.pdf)

Public Health England reports on 11,860 confirmed cases of COVID in those aged over 80 years. The Pfizer-BioNTech vaccine effectiveness was 57% (95% CI: 48-63%) from 28 days after the first dose of vaccination. In 8119 individuals aged over 80 years with a confirmed PCR positive test and followed for at least 21 days, the case fatality ratio was lower in cases vaccinated at least 14 days before onset than in unvaccinated cases. This would indicate that within vaccinated individuals who do become symptomatic the vaccine confers additional protection against death.

Ghebreyesus TA. A **'me first' approach to vaccination won't defeat Covid.** The Guardian 2021, published 5 March. Full-text: <https://www.theguardian.com/commentisfree/2021/mar/05/vaccination-covid-vaccines-rich-nations>

Of the 225m vaccines administered so far, most have been in a handful of rich nations. This has to change, for all our sakes, says Tedros Adhanom Ghebreyesus, director general of WHO. The normal rules of business that protect the profits of vaccine manufacturers will have to be set aside if that is what it takes to ensure everybody is immunized against SARS-CoV-2. See also Boseley S. A **'me first' approach to vaccination won't defeat Covid.** The Guardian 2021, published 5 March. Full-text: <https://www.theguardian.com/world/2021/mar/05/covid-vaccines-who-chief-backs-patent-waiver-to-boost-production>

Boseley S, Brooks L. **UK will diverge from EU and US on approving tweaked Covid vaccines.** The Guardian 2021, published 4 March. Full-text: <https://www.theguardian.com/society/2021/mar/04/vaccines-tweaked-for-covid-variants-will-be-fast-tracked-safely-says-uk-regulator>

The UK will adopt a different standard from Europe and the US when it considers approval for coronavirus vaccines that have been tweaked to deal with variants, the UK regulator has said.

## Clinical

Wohlfahrt J, Fonager J, Albertsen M, et al. **Increased Risk of Hospitalisation Associated with Infection with SARS-CoV-2 Lineage B.1.1.7 in Denmark.** Lancet Preprints 2021, posted 2 March. Full-text: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3792894](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3792894)

Infection with B.1.1.7 was associated with an increased risk of hospitalization compared with other lineages (adjusted odds ratio: 1.64).

## Notes

## Notes