COVID-19
Selection of peer-reviewed articles

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

UPDATE OF
25 MARCH 2021

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

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

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**Additionnal links:**
Rapid Evidence Reviews Group: https://isaric.tghn.org/covid-19-rapid-evidence-reviews-group/
Bibliovid: https://bibliovid.org
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<td>Lancet 23MAR2021</td>
<td>Dynamics of SARS-CoV-2 neutralising antibody responses and duration of immunity: a longitudinal study</td>
<td>Wan N.C., et al. Singapore gotopaper</td>
<td>Immunology</td>
<td>Aim: to investigate the peak levels and dynamics of neutralising antibody waning and IgG avidity maturation over time, and correlate this with clinical parameters, cytokines, and T-cell responses. Methods: longitudinal study of patients who had recovered from COVID-19 up to day 180 post-symptom onset by monitoring changes in neutralising antibody levels using a previously validated surrogate virus neutralisation test. Findings: Five distinctive patterns of neutralising antibody dynamics were identified as follows: - Negative: individuals who did not, at our intervals of sampling, develop neutralising antibodies at the 30% inhibition level (19 [12%] of 164 patient). - Rapid waning: individuals who had varying levels of neutralising antibodies from around 20 days after symptom onset, but seroreverted in less than 180 days (44 [27%] of 164 patients). - Slow waning: Individuals who remained neutralising antibody-positive at 180 days post-symptom onset (52 [29%] of 164 patients). - Persistent: although with varying peak neutralising antibody levels, these individuals had minimal neutralising antibody decay (52 [32%] of 164 patients). - Delayed response, a small group that showed an unexpected increase of neutralising antibodies during late convalescence (at 90 or 180 days after symptom onset; three [2%] of 164 patients). Persistence of neutralising antibodies was associated with disease severity and sustained level of pro-inflammatory cytokines, chemokines, and growth factors. By contrast, T-cell responses were similar among the different neutralising antibody dynamics groups. Neutralising antibody response dynamics in patients who have recovered from COVID-19 vary greatly, and prediction of immune longevity can only be accurately determined at the individual level.</td>
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<td>JAMA Netw Open 22MAR2021</td>
<td>Association of Age With SARS-CoV-2 Antibody Response</td>
<td>Yang H.S., et al. USA gotopaper</td>
<td>Immunology</td>
<td>Aim: To investigate the association of age with the quantity and quality of SARS-CoV-2 antibody responses. Methods: Cross-sectional study evaluating 31,426 SARS-CoV-2 antibody tests from pediatric and adult patients. Data were collected from a New York City hospital from April 9 to August 31, 2020. Findings: Among 31,426 antibody test results, the seroprevalence in the pediatric (197 [16.5%; 95% CI, 14.4%-18.7%]) and adult (5630 [18.6%; 95% CI, 18.2%-19.1%]) patient populations was similar. The SARS-CoV-2 IgG level showed a negative correlation with age in the pediatric population (r = -0.45, P &lt; .001) and a moderate but positive correlation with age in adults (r = 0.24, P &lt; .001). Patients aged 19 to 30 years exhibited the lowest IgG levels (eg, aged 25-30 years vs 1-10 years: 99 [44-180] relative fluorescence units [RFU] vs 443 [188-851] RFU). Children exhibited higher median (IQR) IgG levels, TAb levels, and SNAb activity compared with adolescents (eg, IgG levels: 473 RFU vs 191 RFU; P &lt; .001) and young adults (eg, IgG levels: 473 RFU vs 85 RFU; P &lt; .001). Children had higher antibody binding avidity compared with young adults, but the difference was not significant. This study suggests that SARS-CoV-2 viral specific antibody response profiles are distinct in different age groups. Age-targeted strategies for disease screening and management as well as vaccine development may be warranted.</td>
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| Nature Commun. 22MAR2021 | SARS-CoV-2 infection induces sustained humoral immune responses in convalescent patients following symptomatic COVID-19 | Wu J., et al. China [gotopaper](#) | Immunology | Aim: to quantify immunoglobulin M (IgM) and G (IgG) antibodies recognizing the SARS-CoV-2 receptor-binding domain (RBD) of the spike (S) or the nucleocapsid (N) protein, and neutralizing antibodies during a period of 6 months from disease onset in 349 symptomatic COVID-19 patients.  
> The positivity rate and magnitude of IgM-S and IgG-N responses increase rapidly.  
> High levels of IgM-S/N and IgG-S/N at 2-3 weeks after disease onset are associated with virus control and IgG-S titers correlate closely with the capacity to neutralize SARS-CoV-2.  
> Although specific IgM-S/N become undetectable 12 weeks after disease onset in most patients, IgG-S/N titers have an intermediate contraction phase, but stabilize at relatively high levels over the 6 month observation period.  
> At late time points, the positivity rates for binding and neutralizing SARS-CoV-2-specific antibodies are still >70%.  
These data indicate sustained humoral immunity in recovered patients who had symptomatic COVID-19, suggesting prolonged immunity. |
| Cell 20MAR2021 | SARS-CoV-2 variants B.1.351 and P.1 escape from neutralizing antibodies | Hoffmann M., et al. Germany [gotopaper](#) | Viral variants | Aim: to test sensitivity of SARS-CoV-2 variants B.1.1.7 (UK), B.1.351 (South Africa) and P.1 (Brazil) to cell entry inhibitors and antibodies, by using pseudoparticles.  
> B.1.1.7, B.1.351 and P.1 do not show augmented host cell entry.  
> Entry of all variants into human cells is susceptible to blockade by the entry inhibitors soluble ACE2, Camostat, EK-1 and EK-1-C4.  
> Entry of the B.1.351 and P.1 variant is partially (Casirivimab) or fully (Bamlanivimab) resistant to antibodies used for COVID-19 treatment.  
> Entry of these variants was less efficiently inhibited by plasma from convalescent COVID-19 patients and sera from BNT162b2 vaccinated individuals.  
These results suggest that SARS-CoV-2 may escape neutralizing antibody responses. |
Methods  
Longitudinal cross-sectional study, population-stratified, cluster random sampling method (100 communities from the 13 districts of Wuhan). Household systematically selected. A venous blood sample taken for immunological testing (pan-immunoglobulins, IgM, IgA, and IgG antibodies against SARS-CoV-2 nucleocapsid protein and neutralising antibodies).  
Findings  
> 9542 individuals from 3556 families had sampled for analyses.  
> 532 participants were positive for pan-immunoglobulins against SARS-CoV-2 (baseline seroprevalence of 6.92%)  
> 437 of 532 (82.1%) participants who were positive for pan-immunoglobulins were asymptomatic.  
> 69 (13.0%) of 532 individuals were positive for IgM antibodies, 84 (15.8%) were positive for IgA antibodies, 532 (100%) were positive for IgG antibodies, and 212 (39.8%) were positive for neutralising antibodies at baseline.  
> On the basis of data from 335 individuals who attended all three follow-up visits and who were positive for pan-immunoglobulins, neutralising antibody levels did not significantly decrease over the study period  
> Neutralising antibody titres were lower in asymptomatic individuals than in confirmed cases and symptomatic individuals.  
> Although titres of IgG decreased over time, the proportion of individuals who had IgG antibodies did not decrease substantially  
Conclusion  
6.92% of a cross-sectional sample of the population of Wuhan developed antibodies against SARS-CoV-2, with 39.8% of this population seroconverting to have neutralising antibodies. |
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Findings:  
> In vitro efficacy of favorpiravir  
- Vero E6 cells: Infectious titer reductions (fold change in comparison with untreated cells) ≥ 2 with 125 µM of favorpiravir and between 11 and 342 with 500 µM.  
- Caco-2 cells (no CPE with SARS-CoV-2 BavPat1 strain) infectious titer reductions around 5 with 125 µM of favorpiravir and between 144 and 7721 with 500 µM.  
> In vivo efficacy of favorpiravir  
- Intranasally infection of Syrian hamsters with different inoculums, receiving favorpiravir at the day of infection up to 2 dpi. Doses of favorpiravir: 18.75, 37.5, and 75 mg/day. Effect of favorpiravir in reducing infectious titer is dose dependent, in particular when low virus inocula were used to infect animal. Significant differences in virus replication in clarified lung homogenates between treated and untreated animals  
- Antiviral effect of favorpiravir correlates with incorporation of a large number of mutations into viral genomes and decrease of viral infectivity.  
- Antiviral efficacy is achieved with plasma drug exposure comparable with those previously found during human clinical trials (the highest dose of favorpiravir tested is associated with signs of toxicity in animals).  
Pharmacokinetic and tolerance studies are required to determine whether similar effects can be safely achieved in humans.  
Conclusion:  
High doses of favorpiravir are associated with antiviral activity against SARS-CoV-2 infection in a hamster model. The better antiviral efficacy was observed using a preventive strategy, suggesting that favorpiravir could be more appropriate for a prophylactic use. |
COVID-19 patients: NAT+, hospitalised and recovered, samples taken 48–86 days after disease onset;  
Asymptomatic patients: NAT+, with no signs of symptoms  
Close contacts: NAT-, no SARS-CoV-2 specific antibodies, in contact with patients between 5 days before disease onset and hospitalisation.  
> Virus-specific CD4+ and CD8+ T-cell memory was observed in recovered COVID-19 patients (in 94.44% and 88.33% of patients, respectively) and close contacts (in 57.97% and 14.49%, respectively).  
> The size and quality of the memory T-cell pool of COVID-19 patients are larger and better than those of close contacts.  
> However, the proliferation capacity, size and quality of T-cell responses in close contacts are readily distinguishable from healthy donors, suggesting close contacts are able to gain T-cell immunity against SARS-CoV-2 despite lacking a detectable infection.  
> Asymptomatic and symptomatic COVID-19 patients contain similar levels and qualities of SARS-CoV-2-specific T-cells.  
> CD4+ T memory and CD8+ T memory may have contracted to a stable plateau 48-86 days after symptom onset.  
> Virus-specific memory CD4+ T cell pool correlated with the titers of IgG against the S RBD region and the N protein, whereas no apparent correlation between CD8+ T cells and IgG titers was observed.  
This study demonstrates the versatility and potential of memory T cells from COVID-19 patients and close contacts, which may be important for host protection. |
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| **JAMA Netw Open 19MAR2021** | **Association of Vitamin D Levels, Race/Ethnicity, and Clinical Characteristics With COVID-19 Test Results** | Meltzer DO., et al. USA gotopaper | Public Health / Epidemiology | **Aim:** To examine whether COVID-19 test results are associated with differences in vitamin D levels of 30 ng/mL or greater, including for White individuals and for Black individuals.  
**Methods:** Single-center retrospective cohort study of 4638 individuals with a measured vitamin D level in the year before undergoing COVID-19 testing. The study was conducted at an academic medical center in Chicago, Illinois. Participants included individuals with data on vitamin D level within 365 days before COVID-19 testing.  
> Main outcome : positive result for COVID-19 in PCR testing.  
**Findings:**  
> Lower vitamin D levels were more common in Black individuals (<20 ng/mL: 829 of 2288 Black individuals [36%]) than White individuals (<20 ng/mL: 315 of 1999 White individuals [16%]).  
> The risk of having positive results in Black individuals was 2.64-fold greater with a vitamin D level of 30 to 39.9 ng/mL than a level of 40 ng/mL or greater and decreased by 5% per 1-ng/mL increase in level among individuals with a level of 30 ng/mL or greater.  
> There were no statistically significant associations of vitamin D levels with COVID-19 positivity rates in White individuals.  
> Randomized clinical trials to determine whether increasing vitamin D levels to greater than 30 to 40 ng/mL affect COVID-19 risk are warranted, especially in Black individuals. |
| **BMJ 18MAR2021** | **Association between living with children and outcomes from covid-19: OpenSAFELY cohort study of 12 million adults in England** | Forbes H., et al. UK gotopaper | Public Health / Epidemiology | To investigate whether risk of infection with SARS-CoV-2 and outcomes of covid-19 differed between adults living with and without children during the first two waves of the UK pandemic  
> Population based cohort study: two cohorts of adults (≥18 yrs) registered at a general practice (1 Feb - 1 Sept 2020)  
> Adjusted hazard ratios (HR) for SARS-CoV-2 infection, covid-19 related admission to hospital or intensive care, or death from covid-19, by presence of children in the household.  
**Findings:**  
> Among 9 334 392 adults aged ≤65 yrs, during wave 1, living with children was not associated with materially increased risks of recorded SARS-CoV-2 infection, covid-19 related hospital or intensive care admission, or death from covid-19.  
> In wave 2, among adults aged ≤65 yrs, living with children of any age was associated with an increased risk of recorded SARS-CoV-2 infection (HR 1.06 (95% CI 1.05 to 1.08) for living with children aged 0-11 years; 1.22 (1.20 to 1.24) for living with children aged 12-18 years) and covid-19 related hospital admission (1.18 (1.06 to 1.31) for living with children aged 0-11; 1.26 (1.12 to 1.40) for living with children aged 12-18).  
Living with children aged 0-11:  
> was associated with reduced risk of death from both covid-19 and non-covid-19 causes in both waves; living with children of any age was also associated with lower risk of dying from non-covid-19 causes.  
> For adults ≤65 yrs during wave 2, was associated with an increased absolute risk of having SARS-CoV-2 infection recorded of 40-60 per 10 000 people, from 810 to between 850 and 870, and an increase in hospital admissions of 1-5 per 10 000 people, from 160 to between 161 and 165.  
Living with children aged 12-18 years was associated with an increase of 160-190 per 10 000 in the number of SARS-CoV-2 infections and an increase of 2-6 per 10 000 in the number of hospital admissions.  
In contrast to wave 1, evidence existed of increased risk of reported SARS-CoV-2 infection and covid-19 outcomes among adults living with children during wave 2. However, this did not translate into a materially increased risk of covid-19 mortality, and absolute increases in risk were small. |
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<td>Lancet 17MAR2021</td>
<td>Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study</td>
<td>Hansen CH., et al. Denmark gotopaper</td>
<td>Public Health / Epidemiology</td>
<td>Using national PCR-test data from 2020 (4 million individuals (69% of the population) underwent 10.6 million tests), we estimated protection towards repeated infection with SARS-CoV-2.</td>
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**Methods**

> Analysis of infection rates during the second surge of the COVID-19 epidemic (Sept 1 - Dec 31, 2020), by comparing infection rates between individuals with positive and negative PCR tests during the first surge (March - May, 2020)
> Alternative cohort analysis, comparing infection rates throughout the year between those with and without a previous confirmed infection at least 3 months earlier, irrespective of date.

**Findings**

> During the first surge (before June, 2020), 533381 people were tested, of whom 11727 (2.20%) were PCR positive, and 525339 were eligible for follow-up in the second surge, of whom 11068 (2.11%) had tested positive during the first surge.
> Among eligible PCR-positive individuals from the first surge of the epidemic, 72 (0.65% [95% CI 0.51–0.82]) tested positive again during the second surge compared with 16819 (3.27% [3.22–3.32]) of 514271 who tested negative during the first surge.
> Protection against repeat infection was 80.5% (95% CI 75.4–84.5).
> In the alternative cohort analysis, among those aged ≥65, observed protection against repeated infection was 47.1% (95% CI 24.7–62.8).
> No difference in estimated protection against repeated infection by sex (male 78.4% [72.1–83.2] vs female 79.1% [73.9–83.3]) or evidence of waning protection over time (3–6 months of follow-up 79.3% [74.4–83.3] vs ≥7 months of follow-up 77.7% [70.9–82.9]).

These findings could inform decisions on groups to vaccinate and advocate for vaccination of previously infected individuals, as natural protection, especially among older people, cannot be relied on.
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| JAMA 17MAR2021   | Four-Month Clinical Status of a Cohort of Patients After Hospitalization for COVID-19 | COMEBAC Study Group France | Public Health / Epidemiology - Long Covid | **Aim:** to describe the consequences at 4 months in patients hospitalized for COVID-19.  
**Findings**  
> 478 were evaluated by telephone (mean age, 61 years [SD, 16 years]; 201 men, 277 women).  
> 244 patients (51%) declared at least 1 symptom that did not exist before COVID-19: fatigue in 31%, cognitive symptoms in 21%, and new-onset dyspnea in 16%. There was further evaluation in 177 patients (37%), including 97 of 142 former ICU patients.  
> The median 20-item Multidimensional Fatigue Inventory score ($n = 130$) was 4.5 (interquartile range IR, 3.0-5.0) for reduced motivation and 3.7 (IR, 3.0-4.5) for mental fatigue (possible range, 1 [best] to 5 [worst]).  
> The median 36-item Short-Form Health Survey score ($n = 145$) was 25 (IR, 25.0-75.0) for the subscale “role limited owing to physical problems” (possible range, 0 [best] to 100 [worst]).  
> Computed tomographic lung-scan abnormalities were found in 108 of 171 patients (63%), mainly subtle ground-glass opacities. Fibrotic lesions were observed in 19 of 49 survivors (39%) with acute respiratory distress syndrome.  
> Among 94 former ICU patients, anxiety, depression, and posttraumatic symptoms were observed in 23%, 18%, and 7%, respectively.  
> The left ventricular ejection fraction was less than 50% in 8 of 83 ICU patients (10%). New-onset chronic kidney disease was observed in 2 ICU patients.  
> Serology was positive in 172 of 177 outpatients (97%).  
**Four months after hospitalization for COVID-19,** a cohort of patients frequently reported symptoms not previously present, and lung-scan abnormalities were common among those who were tested. |
| Nature 16MAR2021 | Clofazimine broadly inhibits coronaviruses including SARS-CoV-2 | Yuan S., et al. China | Therapeutics | Clofazimine is an anti-leprosy drug with a favourable safety profile  
**In vitro & in vivo studies**  
> We show that clofazimine possesses pan-coronaviral inhibitory activity, and can antagonize SARS-CoV-2 and MERS-CoV replication in multiple in vitro systems.  
> The FDA-approved molecule was found to inhibit viral spike-mediated cell fusion and viral helicase activity.  
> In a hamster model of SARS-CoV-2 pathogenesis, prophylactic or therapeutic administration of clofazimine significantly reduced viral load in the lung and faecal viral shedding, and also mitigated inflammation associated with viral infection.  
> Combinatorial application of clofazimine and remdesivir exhibited antiviral synergy in vitro and in vivo, and restricted upper respiratory tract viral shedding.  
Since clofazimine is orally bioavailable and has a comparatively low manufacturing cost, it is an attractive clinical candidate for outpatient treatment and remdesivir-based combinatorial therapy for hospitalized COVID-19 patients, particularly in developing countries. Taken together, our data provide evidence that clofazimine may have a role in the control of the current pandemic SARS-CoV-2, and, possibly most importantly, emerging CoVs of the future. |
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| NEJM 16MAR2021   | Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant | Madhi S.A., et al. [International gotopaper](#) | Vaccines - Variants | Efficacy of ChAdOx1 against emerging SARS-CoV-2 variants of concern, including the B.1.351 (S01Y.V2) variant first identified in South Africa. **Methods:**  
> Multicenter, double-blind, randomized, controlled trial in HIV- in South Africa.  
> Participants age: 18 to 65 years of age  
> Two doses of vaccine containing 5×10^{10} viral particles or placebo (0.9% sodium chloride solution) 21 to 35 days apart.  
> Serum samples obtained from 25 participants after the second dose were tested by pseudovirus and live-virus neutralization assays against the original D614G virus and the B.1.351 variant.  
*Primary end points:* safety and efficacy of the vaccine against laboratory-confirmed symptomatic coronavirus 2019 illness (Covid-19) more than 14 days after the second dose.  
*Findings:*  
> 2026 HIV-negative adults enrolled (median age, 30 years);  
> 1010 and 1011 participants received at least one dose of placebo or vaccine, respectively.  
> Both the pseudovirus and the live-virus neutralization assays showed greater resistance to the B.1.351 variant in serum samples obtained from vaccine recipients than in samples from placebo recipients.  
> In the primary end-point analysis, mild-to-moderate Covid-19 developed in 23 of 717 placebo recipients (3.2%) and in 19 of 750 vaccine recipients (2.5%), for an efficacy of 21.9% (95% confidence interval [CI], −49.9 to 59.8).  
> Among the 42 participants with Covid-19, 39 cases (92.9%) were caused by the B.1.351 variant; vaccine efficacy against this variant, analyzed as a secondary end point, was 10.4% (95% CI, −76.8 to 54.8).  
> The incidence of serious adverse events was balanced between the vaccine and placebo groups.  
**Conclusion:**  
A two-dose regimen of the ChAdOx1 nCoV-19 vaccine did not show protection against mild-to-moderate Covid-19 due to the B.1.351 variant. |
| Cell Rep. 16MAR2021 | Virological and immunological features of SARS-CoV-2-infected children who develop neutralizing antibodies | Cotugno N., et al. [Italy gotopaper](#) | Immunology | Aim: to define the humoral and cellular responses in SARS-CoV-2-infected children.  
**Methods:** Analysis of anti-SARS-CoV-2 antibodies and their neutralizing activity (PRNT) in 66 COVID-19-infected children at 7 (±2) days after symptom onset. Analysis of Ag-specific T and B cells defined as CD4+CD40L+ and SARS-CoV-2 Spike (S1+S2)-positive switched B cells.  
**Findings:**  
> Individuals with specific humoral responses presented faster virus clearance and lower viral load associated with a reduced in vitro infectivity.  
> The frequencies of SARS-CoV-2-specific CD4+CD40L+ T cells and Spike-specific B cells were associated with the anti-SARS-CoV-2 antibodies and the magnitude of neutralizing activity.  
> The plasma proteome confirmed the association between cellular and humoral SARS-CoV-2 immunity, and PRNT+ patients show higher viral signal transduction molecules (SLAMF1, CD244, CLEC4G).  
**Cellular and humoral anti-SARS-CoV-2 responses in children, which may drive future vaccination trial end points and quarantine measures policies.** |
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> Retrospective cohort study of one multi-hospital health system included 150,325 patients tested for COVID-19 infection via PCR from March 12, 2020 to August 30, 2020  
> Testing performed up to February 24, 2021 in these patients was included for analysis  
> Main outcome = reinfection (defined as infection ≥ 90 days after initial testing)  

Findings  
> Protection offered from prior infection was 81.8% (95% confidence interval 76.6 to 85.8), and against symptomatic infection was 84.5% (95% confidence interval 77.9 to 89.1)  
> Prior infection in patients with COVID-19 was highly protective against reinfection and symptomatic disease.  
> This protection increased over time, suggesting that viral shedding or ongoing immune response may persist beyond 90 days and may not represent true reinfection.  
> As vaccine supply is limited, patients with known history of COVID-19 could delay early vaccination to allow for the most vulnerable to access the vaccine and slow transmission.  

Patients with confirmed history of infection with SARS-CoV-2 are less likely to be retested or reinfected more than 90 days after their initial infection than those with initial negative tests. Protectiveness of prior infection against subsequent infection is high. |
| Nature 15MAR2021 | Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7 | Davies N.G., et al. UK [gotopaper](link) | Variants | Aim: to determine if variant B.1.1.7 leads to changes in disease severity by analysing a dataset linking 2,245,263 positive SARS-CoV-2 community tests and 17,452 COVID-19 deaths in England (1 Sept 2020 - 14 Feb 2021).  
> For 1,146,534 (51%) of these tests, the presence or absence of B.1.1.7 can be identified because of mutations in this lineage preventing PCR amplification of the spike gene target (S gene target failure, SGTF).  
> Based on 4,945 deaths with known SGTF status, we estimate that the hazard of death associated with SGTF is 55% (95% CI 39–72%) higher after adjustment for age, sex, ethnicity, deprivation, care home residence, local authority of residence and test date.  
> These data correspond to the absolute risk of death for a 55–69-year-old male increasing from 0.6% to 0.9% (95% CI 0.8–1.0%) within 28 days after a positive test in the community.  
> Correcting for misclassification of SGTF and missingness in SGTF status, we estimate a 61% (42–82%) higher hazard of death associated with B.1.1.7.  

This analysis suggests that B.1.1.7 is not only more transmissible than preexisting SARS-CoV-2 variants, but may also cause more severe illness. |
> Report and evaluate the control strategy implemented during a large SARS-CoV-2 epidemic in June–July 2020 in French Guiana that relied on curfews, targeted lockdowns, and other measures.  
> To describe how mathematical modelling was used during this crisis to support policy making and planning.  

Findings  
> The combination of these interventions coincided with a reduction in the basic reproduction number of SARS-CoV-2 from 1.7 to 1.1, which was sufficient to avoid hospital saturation.  
> We estimate that thanks to the young demographics, the risk of hospitalisation following infection was 0.3 times that of metropolitan France and that about 20% of the population was infected by July  
> Our model projections are consistent with a recent seroprevalence study. The study show-cases how mathematical modelling can be used to support healthcare planning in a context of high uncertainty. |
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| Clin Infect Dis. 12MAR2021 | Household SARS-CoV-2 transmission and children: a network prospective study | Soriano-Arandes A., Spain | Public Health / Epidemiology | Aim: describe the epidemiological and clinical characteristics of children with COVID-19 in Catalonia (Spain) and investigate the dynamics of household transmission. Prospective, observational, multicenter study performed during summer and school periods (1 July-31 October, 2020) on COVID-19 patients <16 years.  
> The study included 1040 COVID-19 patients <16 years. 47.2% were asymptomatic, 10.8% had comorbidities, and 2.6% required hospitalization. No deaths were reported.  
> Viral transmission was common among household members (62.3%).  
> More than 70% (756/1040) of pediatric cases were secondary to an adult, whereas 7.7% (80/1040) were index cases.  
> The Secondary Attack Rate (SAR) was significantly lower in households with COVID-19 pediatric index cases during the school period relative to summer (p=0.02), and when compared to adults (p=0.006).  
> No individual or environmental risk factors associated with the SAR were identified.  
Children are unlikely to cause household COVID-19 clusters or be major drivers of the pandemic even if attending school. |
Methods  
37 participants (median age 62 years; 35% female) measurement of neutralizing antibody responses following first and second immunisations using pseudoviruses expressing the wild-type Spike protein or the 8 amino acid mutations found in the B.1.1.7 spike protein.  
Findings  
> The GMT against wild type (WT) following the second dose of vaccine is substantially higher than after the first dose (318 vs 77). Correlation between total Spike IgG titres and serum neutralisation titres  
> Broad range of T cell responses (IFN-Gamma). No correlation with serum neutralization titers  
> Vaccine sera exhibited a broad range of neutralising titres against the wild-type pseudoviruses that were modestly reduced against B.1.1.7 variant. Reduction also evident in sera from some convalescent patients.  
> Decreased B.1.1.7 neutralisation also observed with monoclonal antibodies targeting the N-terminal domain (9 out of 10), the R8M (5 out of 31), but not in RBD neutralising mAbs binding outside the R8M.  
> Introduction of the E484K mutation in a B.1.1.7 background to reflect a newly emergent Variant of Concern (VOC 202102/02) led to a more substantial loss of neutralising activity by vaccine-elicited antibodies and mAbs (19 out of 31) over that conferred by the B.1.1.7 mutations alone.  
Conclusion:  
>Pseudovirus bearing S protein with the full set of mutations present in the B.1.1.7 variant result in small reduction in neutralisation by sera from BNT162B2 vaccines (more marked following the first dose than the second dose). This could be related to increased breadth/potency/concentration of antibodies following the boost dose.  
>E484K emergence on a B.1.1.7 background represents a threat to the vaccine BNT162b |
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Methods: > Randomized, double-blind, placebo-controlled phase 1 clinical trial of Ad26.COV2.S (NCT04436276). > Twenty-five participants; interim analysis at day 71. A single clinical site in Boston > 1 or 2 intramuscular injections with 5 × 10exp10 viral particles or 1 × 1exp011 viral particles of Ad26.COV2.S vaccine or placebo (day 1 and day 57).  
Main Outcomes and Measure: Humoral immune responses included binding and neutralizing antibody responses at multiple time points following immunization. Cellular immune responses included immunospot-based and intracellular cytokine staining assays to measure T-cell responses.  
Findings: > Binding and neutralizing antibodies emerged rapidly by day 8 after initial immunization in 90% and 25% of vaccine recipients, respectively. > By day 57, binding and neutralizing antibodies were detected in 100% of vaccine recipients after a single immunization. > On day 71, the geometric mean titers of spike-specific binding antibodies were 2432 to 5729 and the geometric mean titers of neutralizing antibodies were 242 to 449 in the vaccinated groups. > A variety of antibody subclasses, Fc receptor binding properties, and antiviral functions were induced. CD4+ and CD8+ T-cell responses were induced.  
Conclusion: Ad26.COV2.S induces rapid binding and neutralization antibody responses as well as cellular immune responses. |
| PNAS 09MAR2021  | A safe and highly efficacious measles virus-based vaccine expressing SARS-CoV-2 stabilized prefusion spike | Lu M., et al. USA gotopaper | Vaccines | Evaluation of a SARACoV 2 Measles virus (rMeV) vaccine efficacy in cotton rat, IFNAR−/−/mice, IFNAR−/−/hCD46 mice, and golden Syrian hamsters Recombinant attenuated vaccine candidates expressing various forms of the SARS-CoV-2 spike (S) protein and its receptor binding domain (RBD).  
Findings: > rMeV expressing stabilized prefusion S protein (rMeV-preS) was more potent in inducing SARS-CoV-2-specific neutralizing antibodies than rMeV expressing full-length S protein (rMeV-S), > rMeVs expressing different lengths of RBD (rMeV-RBD) were the least potent. > Animals immunized with rMeV-preS produced higher levels of neutralizing antibody than found in convalescent sera from COVID-19 patients and a strong Th1-biased T cell response. > rMeV-preS also provided complete protection of hamsters from challenge with SARS-CoV-2, preventing replication in lungs and nasal turbinate, body weight loss, cytokine storm, and lung pathology.  
Conclusion: rMeV-preS is a safe and highly efficacious vaccine candidate, supporting its further development as a SARS-CoV-2 vaccine. |
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| **BMJ 10MAR2021** | Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study | Challen R., et al. UK gotopaper | Public Health / Epidemiology | To establish whether there is any change in mortality from infection with a new variant of SARS-CoV-2, designated a variant of concern (VOC-202012/1) in December 2020, compared with circulating SARS-CoV-2 variants.  
Methods  
> Matched cohort study (participants were matched on age, sex, ethnicity, index of multiple deprivation, lower tier local authority region, and sample date of positive specimens, and differed only by detectability of the spike protein gene using the TaqPath assay)  
> Community based (pillar 2) covid-19 testing centres in the UK using the TaqPath assay (a proxy measure of VOC-202012/1 infection)  
> 54,906 matched pairs of participants who tested positive for SARS-CoV-2 in pillar 2 between 1 October 2020 and 29 January 2021, followed-up until 12 February 2021  
> Main outcome measure: Death within 28 days of the first positive SARS-CoV-2 test result.  
Findings  
> The mortality hazard ratio associated with infection with VOC-202012/1 compared with infection with previously circulating variants was 1.64 (95% confidence interval 1.32 to 2.04), corresponding to 64% increased risk of death, in patients who tested positive for covid-19 in the community.  
> In this comparatively low risk group, this represents an increase in deaths from 2.5 to 4.1 per 1000 detected cases.  
Increased risk of mortality is increased by infection with VOC-202012/01 is highly probable. If this finding applies to other populations, infection with VOC-202012/1 could cause substantial additional mortality compared with previously circulating variants. Healthcare capacity planning and national and international control policies are all impacted by this finding, which supports further coordinated and stringent measures to reduce deaths. |
> 4,182 incident cases of COVID-19 in which individuals self-reported their symptoms prospectively in the COVID Symptom Study app.  
> 558 (13.3%) participants reported symptoms lasting ≥28 days, 189 (4.5%) for ≥8 weeks and 95 (2.3%) for ≥12 weeks  
> Long COVID was characterized by symptoms of fatigue, headache, dyspnea and anosmia and was more likely with increasing age and body mass index and female sex  
> Experiencing more than five symptoms during the first week of illness was associated with long COVID (odds ratio = 3.53 (2.76–4.50)).  
> A simple model to distinguish between short COVID and long COVID at 7 days is presented, which could be used to identify individuals at risk of long COVID. |
> Shows marked hypermutation: 6 non-synonymous mutations in the spike protein by to 15/10/20, then 3 more by 30/11/20, plus deletion of 3 amino acids  
> Mutations N501Y, E484K and K417N are at key residues of the RBD – the two latter are key for neutralizing antibody binding  
> E484 and N501 pattern of nucleotide variation suggest evolution under positive selection  
> B.1.351 most likely evolved by mutation on circulating intermediate mutants  
> B.1.351 likely emerged in Nelson Madela Bay in early August and became dominant in Easter Cape, Western Cape and KwaZulu-Natal Provinces within weeks  
> It has a selective advantage, from increased transmissibility and/or immune escape |
BBV152 is a whole-virion inactivated SARS-CoV-2 vaccine (3 μg or 6 μg) formulated with a toll-like receptor 7/8 agonist molecule (IMDG) adsorbed to alum (Algel).

**Methods**

> Double-blind, randomised, multicentre, phase 2 clinical trial
> NCT04471519 to evaluate the immunogenicity and safety of BBV152 in healthy adults and adolescents (aged 12–65 years) at nine hospitals in India.
> Phase 1 trial data allowed to chose phase II formulations of BBV152: 3 μg and 6 μg with Algel-IMDG administered on day 0 and day 28.
> Participants with positive SARS-CoV-2 nucleic acid and serology tests were excluded.

**Primary outcome:** SARS-CoV-2 wild-type neutralising antibody titres and seroconversion rates at 4 weeks after the second dose

**Secondary outcome:** Cell-mediated responses (T-helper-1 profiling at 2 weeks after the second dose)

**Safety**: assessed in all participants who received at least one dose of the vaccine

**Findings**

> 380 participants enrolled and randomly assigned to the 3 μg with Algel-IMDG group (n=190) or 6 μg with Algel-IMDG group (n=190).
> GMTs; PRNT50 at day 56 were significantly higher in the 6 μg with Algel-IMDG group (197·0 [95% CI 155·6–249·4]) than the 3 μg with Algel-IMDG group (100·9 [74·1–137·4]; p=0·0041).
> Seroconversion based on PRNT50 at day 56 was reported in 171 (92·9% [95% CI 88·2–96·2]) of 184 participants in the 3 μg with Algel-IMDG group and 174 (98·3% [95·1–99·6]) of 177 participants in the 6 μg with Algel-IMDG group.
> GMTs (MNT50) at day 56 were 92·5 [95% CI 77·7–110·2] in the 3 μg with Algel-IMDG group and 160·1 [135·8–188·8] in the 6 μg with Algel-IMDG group.
> Seroconversion based on MNT50 at day 56 was reported in 162 (88·0% [95% CI 82·4–92·3]) of 184 participants in the 3 μg with Algel-IMDG group and 171 (96·6% [92·8–98·8]) of 177 participants in the 6 μg with Algel-IMDG group.
> The 3 μg with Algel-IMDG and 6 μg with Algel-IMDG formulations elicited T-cell responses that were biased to a Th1 phenotype at day 42.
> No significant difference in the proportion of participants who had a solicited local or systemic adverse reaction in the 3 μg with Algel-IMDG group (38 [20·0%; 95% CI 14·7–26·5] of 190) and the 6 μg with Algel-IMDG group (40 [21·1%; 15·5–27·5] of 190) was observed on days 0–7 and days 28–35; no serious adverse events were reported in the study.

**Conclusion**

BBV152 induced high neutralising antibody responses that remained elevated in all participants at 3 months after the second vaccination. The 6 μg with Algel-IMDG formulation has been selected for the phase 3 efficacy trial.

**Fields of expertise**

- Vaccines
- Public Health / Epidemiology

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**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**

**Authors and link**

Ella R., et al. India

[gotopaper](#)

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**Higher airborne pollen concentrations correlated with increased SARS-CoV-2 infection rates, as evidenced from 31 countries across the globe**

**Authors and link**

Damialis A., et al. Germany

[gotopaper](#)
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| **Nature 08MAR2021** | Antibody Resistance of SARS-CoV-2 Variants B.1.351 and B.1.1.7 | Wang P., et al. USA [gotopaper](#) | Virology | **Background:**
Authorized therapeutic or preventive interventions against COVID are directed toward the initial SARS-CoV-2 that emerged in 2019. The recent emergence of new SARS-CoV-2 variants B.1.1.7 in the UK11 and B.1.351 in South Africa is of concern because of their purported ease of transmission and extensive mutations in the spike protein.

**Findings:**
- **Monoclonal antibodies:** neutralizing activity of 12 RBD mAbs against authentic B.1.1.7 and B.1.351 viruses, as compared to the original SARS-CoV-2 strain (WT), in Vero E6 cells
  - > neutralization of B.1.1.7: only the activities of 910-3022 and S3095 are significantly impaired.
  - > neutralization of B.1.351: the activities of 910-30, 2-1520, LY-CoV555 (bamlanivimab)1,23, C12124, and REGN10933 (casirivimab)2-720,27, REGN10987 (imdevimab), C13524, and S309 retain their activities against B.1.351.
- Convalescent plasma from 20 patients more than one month after documented SARS-CoV-2 infection in the Spring of 2020
  - Most (16 of 20) plasma samples lost >2.5-fold neutralizing activity against B.1.351, while maintaining activity against B.1.1.7. Only plasma from 4 patients retain neutralizing activities similar to those against the WT.
- **Vaccinee Sera** obtained from 12 participants of a Phase 1 clinical trial of Moderna SARS-CoV-2 mRNA-1273 Vaccine conducted at the NIH.
  - Each vaccinee serum sample was assayed for neutralization against B.1.1.7, B.1.351, and WT viruses. No loss of neutralizing activity against B.1.1.7, whereas every sample lost activity against B.1.351.

| **Blood Advances 08MAR2021** | Heterogeneous NLRP3 inflammasome signature in circulating myeloid cells as a biomarker of COVID-19 severity | Courjon J., et al. France [gotopaper](#) | Immunology | The NLRP3 inflammasome can play a crucial role during innate immunity activation, but NLRP3 response during SARS-CoV-2 infection in patients is unknown.

**Aim:** Prospectively monitoring of caspase-1 activation levels in peripheral myeloid cells from healthy donors and patients with mild to critical COVID-19.

- The caspase-1 activation potential in response to NLRP3 inflammasome stimulation was opposed between nonclassical monocytes and CD66b+CD16dim granulocytes in severe and critical COVID-19 patients.
- CD66b+CD16dim granulocytes had decreased nigericin-triggered caspase-1 activation potential associated with an increased percentage of NLRP3 inflammasome impaired immature neutrophils and a loss of eosinophils in the blood.
- In patients who recovered from COVID-19, nigericin-triggered caspase-1 activation potential in CD66b+CD16dim cells was restored and the proportion of immature neutrophils was similar to control.

**NLRP3 inflammasome activation potential differs among myeloid cells. It could be used as a biomarker of COVID-19 patient evolution.**
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<tr>
<td>Nature Med. 04MAR2021</td>
<td>Resistance of SARS-CoV-2 variants to neutralization by monoclonal and serum-derived polyclonal antibodies</td>
<td>Chen R.E., et al. USA <a href="#">gotopaper</a></td>
<td>Virology</td>
<td>Background: Impact on antibody neutralization of a panel of authentic SARS-CoV-2 variants including a B.1.1.7 isolate, chimeric strains with South African or Brazilian spike genes and isogenic recombinant viral variants with designed mutations or deletions at positions 69-70, 417, 484, 501, 614 and/or 681 of the spike protein, using using monoclonal antibodies (mAbs), animal immune sera, human convalescent sera and human sera from recipients of the BNT162b2 mRNA vaccine</td>
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| JAMA 04MAR2021       | Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19A Randomized Clinical Trial | Lopez-Medina E., et al. Colombia/USA [gotopaper](#) | Therapeutics       | Aim: To determine whether ivermectin is an efficacious treatment for mild COVID-19. Double-blind, randomized trial conducted at a single site in Cali, Colombia, on adult patients with mild disease and symptoms for 7 days or fewer (enrolment July 15-November 30, followed up through December 21, 2020) Patients were randomized to receive ivermectin, 300 μg/kg of body weight per day for 5 days (n = 200) or placebo (n = 200). Primary outcome: time to resolution of symptoms within a 21-day follow-up period. Results: > 398 patients randomized in primary analysis population (median age, 37yo; 58% women) > Median time to resolution of symptoms was 10 days (IQR, 9-13) in the ivermectin group compared with 12 days (IQR, 9-13) in the placebo group (hazard ratio, 1.07 [95% CI, 0.87 to 1.32]; P = .53 by log-rank test). > By day 21, 82% in the ivermectin group and 79% in the placebo group had resolved symptoms. > The most common solicited adverse event was headache in 104 patients (52%) given ivermectin and 111 (56%) who received placebo. > The most common serious adverse event was multiorgan failure, occurring in 4 patients (2 in each group). Conclusion: Among adults with mild COVID-19, a 5-day course of ivermectin, compared with placebo, did not significantly improve the time to resolution of symptoms.
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| Blood 03MAR2021  | The SARS-CoV-2 receptor-binding domain preferentially recognizes blood group A | Wu S.C., et al. USA gotopaper | Virology | > The RBD of SARS-CoV-2 shares sequence similarity with an ancient lectin family known to bind blood group antigens  
   > Examined SARS-CoV-2 RBD binding with RBCs isolated from blood group A, B, or O individuals  

  **Methods**  
  > SARS-CoV receptor-binding domain (RBD) was cloned and purified  
  > SARS-CoV-2 RBD was incubated with HEK293T cells, HEK293 T cells expressing angiotensin-converting enzyme 2 (ACE2), or red blood cells (RBCs), followed by detection with anti-His antibody (Anti-His-Tag mAb-Alexa Fluor 647) and flowcytometric analysis  
  > Anti-A antibody was similarly used to detect the A antigen on blood group A RBCs  

  **Findings**  
  > SARS-CoV-2 RBD binds the blood group A expressed on respiratory epithelial cells, directly linking bloodgroup A and SARS-CoV-2  

However, because these results do not definitively demonstrate that blood group A directly contributes to SARS-CoV-2 infection, future studies are needed, including an examination of the overall affinity and residues within the RBD responsible for blood group A interactions.  

Whatever the possible contribution of ABO(H) antigens to infection and possible disease progression, the ability of the SARS-CoV-2 to directly interact with the blood group A antigen uniquely expressed on respiratory epithelial cells provides clear evidence of a direct association between SARS-CoV-2 and the ABO(H) genetic locus. |
| Lancet Respir Med. 04MAR2021 | Sarilumab in patients admitted to hospital with severe or critical COVID-19: a randomised, double-blind, placebo-controlled, phase 3 trial | Lescure FX., et al. International gotopaper | Therapeutics | Aim: to assess safety and efficacy of sarilumab, an interleukin-6 receptor inhibitor, in patients with severe (requiring supplemental oxygen by nasal cannula or face mask) or critical (requiring greater supplemental oxygen, mechanical ventilation, or extracorporeal support) COVID-19.  

   > 60-day, randomised, double-blind, placebo-controlled, multinational phase 3 trial. Patients were randomly assigned (2:2:1 with permuted blocks of five) to receive intravenous sarilumab 400 mg, sarilumab 200 mg, or placebo.  

   > Primary endpoint: time to clinical improvement of two or more points (seven point scale ranging from 1 [death] to 7 [discharged from hospital]) in the modified intention-to-treat population.  

   > Secondary endpoint: proportion of patients alive at day 29.  

  **Findings**  
  > 420 patients were randomly assigned and 416 received placebo (n=84 [20%]), sarilumab 200 mg (n=159 [38%]), or sarilumab 400 mg (n=173 [42%]).  

   > At day 29, no significant differences were seen in median time to an improvement of two or more points between placebo (12.0 days [95% CI 9.0 to 15.0]) and sarilumab 200 mg (10.0 days [9.0 to 12.0]); hazard ratio [HR] 1.03 [95% CI 0.97 to 1.09]; log-rank p=0.96) or sarilumab 400 mg [10.0 days [9.0 to 13.0]; HR 1.14 [95% CI 0.84 to 1.54]; log-rank p=0.34), or in proportions of patients alive (77 [92%] of 84 patients in the placebo group; 143 [90%] of 159 patients in the sarilumab 200 mg group; difference +17 [9.0 to 25.0]; p=0.03 vs placebo; and 159 [92%] of 173 patients in the sarilumab 400 mg group; difference 0.2 [9.0 to 7.4]; p=0.85 vs placebo).  

   > At day 29, there were non-significant survival differences between sarilumab 400 mg (88%) and placebo (79%; difference +9% [95% CI +7.7 to 25.5]; p=0.25) for patients who had critical disease.  

   > No unexpected safety signals were seen.  

   > The rates of treatment-emergent adverse events were 65% (55 of 84) in the placebo group, 65% (103 of 159) in the sarilumab 200 mg group, and 70% (121 of 173) in the sarilumab 400 mg group, and of those leading to death 11% (nine of 84) were in the placebo group, 11% (17 of 159) were in the sarilumab 200 mg group, and 10% (18 of 173) were in the sarilumab 400 mg group.  

   > This trial did not show efficacy of sarilumab in patients admitted to hospital with COVID-19 and receiving supplemental oxygen. |
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| Lancet 04MAR2021 | Azithromycin for community treatment of suspected COVID-19 in people at increased risk of an adverse clinical course in the UK (PRINCIPLE): a randomised, controlled, open-label, adaptive platform trial | PRINCIPLE Trial Collaborative Group UK gotopaper | Therapeutics | Aim: to assess the effectiveness of azithromycin to treat suspected COVID-19 among people in the community who had an increased risk of complications. 

Open-label, multi-arm, adaptive platform randomised trial, we randomly assigned people aged 65 years and older, or 50 years and older with at least one comorbidity, who had been unwell for 14 days or less with suspected COVID-19.

Treatments: usual care plus azithromycin 500 mg daily for three days, usual care plus other interventions, or usual care alone.

Coprimary endpoints within 28 days from randomisation: time to first self-reported recovery, and hospital admission or death related to COVID-19 |

Findings > 2120 participants were included in the Bayesian primary analysis, 500 participants in the azithromycin plus usual care group, 823 in the usual care alone group, and 797 in other intervention groups.

> 402/500 (80%) participants in the azithromycin plus usual care group and 631/823 (77%) in the usual care alone group reported feeling recovered within 28 days.

> We found little evidence of a meaningful benefit in the azithromycin plus usual care group in time to first reported recovery versus usual care alone (hazard ratio 1·08, 95% Bayesian credibility interval [BCI] 0·95 to 1·23), equating to an estimated benefit in median time to first recovery of 0·94 days (95% BCI −0·56 to 2·43).

> The probability that there was a clinically meaningful benefit of at least 1·5 days in time to recovery was 0·23. 16/500 (3%) participants in the azithromycin plus usual care group and 28/823 (3%) participants in the usual care alone group were hospitalised (absolute benefit in percentage 0·3%, 95% BCI −1·7 to 2·2).

> No deaths in either study group. Safety outcomes were similar in both groups.

These findings do not justify the routine use of azithromycin for reducing time to recovery or risk of hospitalisation for people with suspected COVID-19 in the community. |
| Antimicrob Agents Chemother 01MAR2021 | Human Safety, Tolerability, and Pharmacokinetics of Molnupiravir, a Novel Broad-Spectrum Oral Antiviral Agent with Activity Against SARS-CoV-2 | Painter W. P., et al. USA gotopaper | Therapeutics | > Molnupiravir, EIDD-2801/MK-4482, prodrug of the active antiviral ribonucleoside analog 14ß-d-N4-hydroxycytidine (NHC; EIDD-1931)

> Single and multiple doses of molnupiravir were evaluated in this first-in-human, phase 1, randomized, double-blind, placebo-controlled study in healthy volunteers, which included evaluation of the effect of food on pharmacokinetics.

Findings > EIDD-1931 appeared rapidly in plasma, with a median time of maximum observed concentration of 1.00 to 1.75 hours, and declined with a geometric half-life of approximately 1 hour, with a slower elimination phase apparent following multiple doses or higher single doses (7.1 hours at 24th highest dose tested). Mean maximum observed concentration and area under the concentration versus time curve increased in a dose-proportional manner, and there was no accumulation following multiple doses. When administered in a fed state, there was a decrease in the rate of absorption, but no decrease in overall exposure

> Molnupiravir was well tolerated. Fewer than half of subjects reported an adverse event, the incidence of adverse events was higher following administration of placebo, and 93.3% of adverse events were mild. One discontinued early due to rash. There were no serious adverse events and there were no clinically significant findings in clinical laboratory, vital signs, or electrocardiography.

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

**Methods:**
> Retrospective analysis of patients admitted with COVID-19 from February 1st through May 12th, 2020 with study period ending on June 11th, 2020.
> Antecedent of statin use
> Multivariable logistic regression model to predict the propensity of receiving statins, adjusting for baseline sociodemographic and clinical characteristics, and outpatient medications.
> The primary endpoint includes in-hospital mortality within 30 days.

**Findings:**
> 2626 patients enrolled, of whom 951 (36.2%) were antecedent statin users.
> Among 1296 patients (648 statin users, 648 non-statin users) identified with 1:1 propensity-score matching, statin use is significantly associated with lower odds of the primary endpoint in the propensity-matched cohort (OR 0.47, 95% CI 0.36–0.62, \( p < 0.001 \)).

**Conclusion:**
Antecedent statin use in patients hospitalized with COVID-19 is associated with lower inpatient mortality. |
| Nature 26FEB2021 | SARS-CoV-2 spike D614G change enhances replication and transmission | Zhou B., et al. International | Virology | **Aim:** to understand if the S-614G has represents a fitness advantage that improves replication and/or transmission in humans.

The S-614G variant:
> has enhanced binding to human host cell surface receptor ACE2
> has increased replication in primary human bronchial and nasal airway epithelial cultures and in a human ACE2 knock-in mouse model
> has markedly increased replication and transmissibility in hamster and ferret models of SARS-CoV-2 infection.

The S-614G substitution results in subtle increases in binding and replication in vitro, and it provides a real competitive advantage in vivo, particularly during the transmission bottle neck. |
| Clin Infect Dis. | Persistence of antibodies to SARS-CoV-2 in relation to symptoms in a nationwide prospective study | den Hartog G., et al. Netherlands | Immunology | Study change in Immunoglobulin (Ig) isotype seropositivity and IgG binding strength of SARS-CoV-2-specific serum antibodies up to 7 months following onset of symptoms in a nationwide sample

**Methods**
> prospective representative serological study were included based on IgG seroconversion to the Spike S1 protein of SARS-CoV-2 (\( N = 353 \)) with up to three consecutive serum samples per seroconverted participant (\( N = 738 \))

**Findings**
> While SARS-CoV-2-specific IgM and IgA antibodies declined rapidly after the first month post onset of disease, specific IgG was still present in 92% (95% confidence interval, CI, 89-95) of the participants after 7 months.
> The estimated 2-fold decrease of IgG antibodies was 158 days (95% CI 136-189).
> Concentrations sustained better in persons reporting significant symptoms compared to asymptomatic persons or those with mild upper respiratory complaints only.
> Similarly, avidity of IgG antibodies for symptomatic persons showed a steeper increase over time compared with persons with mild or no symptoms (\( p = 0.022 \)).

IgG antibodies sustain in 92% of the participants after 7 months post onset of symptoms whereas IgM and IgA antibodies wane. Concentrations are higher in symptomatic persons and avidity increases with time.

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

**Title**: BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting

**Authors**: Dagan N., et al.

**Field of expertise**: Vaccines

**Key facts**: Evaluation of the effectiveness of the BNT162b2 mRNA vaccine based on data from Israel’s largest health care organization.

**Findings**
- Each study group (vaccinated and control) included 596,618 persons.
- Estimated vaccine effectiveness for the study outcomes at days 14-20 after the first dose and at ≥7 days after the second dose was as follows:
  - for documented infection, 46% (95% confidence interval [CI], 40 to 51) and 92% (95% CI, 88 to 95);
  - for symptomatic Covid-19, 57% (95% CI, 50 to 63) and 94% (95% CI, 87 to 98);
  - for hospitalization, 74% (95% CI, 56 to 86) and 87% (95% CI, 55 to 100);
  - for severe disease, 62% (95% CI, 39 to 80) and 92% (95% CI, 75 to 100).
- Estimated effectiveness in preventing death from Covid-19 was 72% (95% CI, 19 to 100) for days 14-20 after the first dose.
- Estimated effectiveness in specific subpopulations assessed for documented infection and symptomatic Covid-19 was consistent across age groups, with potentially slightly lower effectiveness in persons with multiple coexisting conditions.

**BNT162b2 mRNA vaccine is effective for a wide range of Covid-19-related outcomes, a finding consistent with that of the randomized trial.**

### Clin Infect Dis. 24FEB2021

**Title**: Persistence of antibodies to SARS-CoV-2 in relation to symptoms in a nationwide prospective study

**Authors**: den Hartog G., et al.

**Field of expertise**: Public Health / Epidemiology

**Aim**: to study changes in Immunoglobulin (Ig) isotype seropositivity and IgG binding strength of SARS-CoV-2-specific serum antibodies up to 7 months following onset of symptoms in a nationwide sample.

**Methods**: prospective representative serological study in the Netherlands were included based on IgG seroconversion to the Spike S1 protein of SARS-CoV-2 (N=353), with up to three consecutive serum samples per seroconverted participant (N=738). IgM, IgA and IgG antibody concentrations to S1, and increase in IgG were determined.

**Findings**
- While SARS-CoV-2-specific IgM and IgA Abs declined rapidly after the first month post onset of disease, specific IgG was still present in 92% of the participants after 7 months.
- The estimated 2-fold decrease of IgG antibodies was 158 days.
- Concentrations sustained better in persons reporting significant symptoms compared to asymptomatic persons or those with mild upper respiratory complaints only.
- SARS-CoV-2-specific IgG antibodies persist and show increasing avidity over time, indicative of underlying immune maturation.

### Cell 23FEB2021

**Title**: Extremely potent human monoclonal antibodies from COVID-19 convalescent patients

**Authors**: Andreano E., et al.

**Field of expertise**: Therapeutics

**Findings**
- 453 neutralizing antibodies were identified by single cell sorting 4,277 SARS-CoV-2 spike protein specific memory B cells from 14 COVID-19 survivors.
- The most potent neutralizing antibodies recognized the spike protein receptor binding domain, followed in potency by antibodies recognizing the S1 domain, the spike protein trimer and the S2 subunit.
- Only 1.4% of the antibodies neutralized the authentic virus with a potency of 1-10 ng/mL.
- The most potent monoclonal antibody, engineered to reduce the risk of antibody dependent enhancement and prolong half-life, neutralized the authentic wild type virus and emerging variants containing D614G, E484K and N501Y substitutions.
- Prophylactic and therapeutic efficacy in the hamster model was observed at 0.25 and 4 mg/kg respectively in absence of Fc-functions.
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| Cell 23FEB2021   | No higher infectivity but immune escape of SARS-CoV-2 501Y.V2 variants | Li Q., et al. China gotopaper | Variants | > Experiments with 18 pseudotyped viruses showed that the 501Y.V2 variants do not confer increased infectivity in multiple cell types except for murine ACE2-overexpressing cells, where a substantial increase in infectivity was observed.  
> The susceptibility of the 501Y.V2 variants to 12 of 17 neutralizing monoclonal antibodies was substantially diminished.  
> Neutralization ability of the sera from convalescent patients and immunized mice was also reduced for these variants.  
> The neutralization resistance was mainly caused by E484K and N501Y mutations in the receptor-binding domain of Spike.  
> The neutralization resistance detected for the 501Y.V2 variants suggests the potential for compromised efficacy of monoclonal antibodies and vaccines. |
Methods: Neutralization of a B.1.351 viral isolate and compare it to 127 neutralization of Victoria, an early Wuhan related isolate. Neutralization assays were performed on a large panel of monoclonal Abs convalescent sera from early in the pandemic, sera from patients suffering from B.1.1.7 and finally from 130 recipients of the Oxford-AstraZeneca and Pfizer-BioNTech vaccines.  
Findings:  
> The receptor binding domain mutations provide tighter ACE2 binding and widespread escape from monoclonal Ab neutralization largely driven by E484K although K417N and N501Y act together against some important antibody classes.  
> In a number of cases it would appear that convalescent and some vaccine serum offers limited protection against this variant.  
> Neutralization of B.1.351 by sera from naturally infected or vaccinated individuals is significantly reduced, leading in some cases to a complete inability to neutralize B.1.351 virus. |
| Lancet Infect Dis. 23FEB2021 | Identification and validation of clinical phenotypes with prognostic implications in patients admitted to hospital with COVID-19: a multicentre cohort study | Gutiérrez-Gutiérrez B., et al. Spain gotopaper | Clinics | Aim: to determine whether clinical phenotypes of patients with COVID-19 can be derived from clinical data, to assess the reproducibility of these phenotypes and correlation with prognosis, and to derive and validate a simplified probabilistic model for phenotype assignment.  
Methods: data from two cohorts: the COVID-19@Spain cohort, a retrospective cohort including 4035 consecutive adult patients admitted to 127 hospitals in Spain, and the COVID-19@HULP cohort, including 2226 consecutive adult patients admitted to a teaching hospital in Madrid.  
The authors developed a simplified probabilistic model for phenotype assignment, including 16 variables.  
Findings:  
> Three distinct phenotypes were derived in the derivation cohort:  
A: Younger patients with, less frequently male, had mild viral symptoms, and had normal inflammatory parameters (516 [19%] patients).  
B: patients with obesity, lymphocytopenia, and moderately elevated inflammatory parameters (1955 [73%]).  
C: older patients with more comorbidities and even higher inflammatory parameters than phenotype B (116 [8%]).  
> 30-day mortality rates were 2.5% for A patients, 30.5% for B patients and 60.7% for C patients.  
> The predicted phenotypes in the internal validation cohort and external validation cohort showed similar mortality rates to the assigned phenotypes (internal validation cohort: 5.3% for phen A, 31.3% for phen B, and 59.5% for phen C; external validation cohort: 3.7% for phen A, 23.7% for phen B, and 51.4% for phenotype C). |
- Prespecified pooled analysis of trials of ChAdOx1 nCoV-19 (Single blinded: one phase 1/2, UK; one phase 2/3, UK; one phase 3, Brazil. Double-blinded: one phase 1/2, South Africa)
- Exploratory analyses of the impact on immunogenicity and efficacy of extending the interval between priming and booster doses.
- Immunogenicity and protection afforded by the first dose, before a booster dose has been offered.

**FINDINGS**

> 24,422 participants across the four studies (Apr 23-Dec 6, 2020), 17,178 included in the primary analysis (8,597 receiving ChAdOx1 nCoV-19, 8,581 receiving control vaccine). 332 NAAT-positive infections met the primary endpoint of symptomatic infection >14 days after the second dose.

> Overall vaccine efficacy >14 days after the second dose was 66·7% (95% CI 57·4–74·0), with 84/8,597 (1·0%) cases in the ChAdOx1 nCoV-19 group and 248/8,581 (2·9%) in the control group.

> There were no hospital admissions for COVID-19 in the ChAdOx1 nCoV-19 group after the initial 21-day exclusion period, and 15 in the control group.

> 108/12,282 (0·9%) participants in the ChAdOx1 nCoV-19 group and 127/11,962 (1·1%) in the control group had serious adverse events. There were 7 deaths considered unrelated to vaccination (2 in the ChAdOx1 nCoV-19 group and 5 in the control group), including one COVID-19-related death in one participant in the control group.

> Exploratory analyses showed that vaccine efficacy after a single standard dose from day 22 to day 90 after vaccination was 76·0% (59·3–85·9). Modelling analysis indicated that protection did not wane during this initial 3-month period.

> Antibody levels were maintained during this period with minimal waning by day 90 (geometric mean ratio [GMR] 0·66 [95% CI 0·59–0·74]).

> In the participants who received two standard doses, after the second dose, efficacy was higher in those with a longer prime-boost interval (vaccine efficacy 81·3% [95% CI 60·3–91·2] at ≥12 weeks) than in those with a short interval (vaccine efficacy 55·1% [33·0–69·9] at <6 weeks).

> Immunogenicity: binding antibody responses >2-fold higher after an interval of ≥12 or more weeks compared with an interval of <6 weeks in those who were aged 18–55 years (GMR 2·32 [2·01–2·68]).

The results of this primary analysis of two doses of ChAdOx1 nCoV-19 were consistent with those seen in the interim analysis of the trials and confirm that the vaccine is efficacious, with results varying by dose interval. A 3-month dose interval might have advantages over a programme with a short dose interval.
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Methods: retrospective cohort of 9109 vaccine-eligible HCWs, comparing vaccinated versus unvaccinated.  
Findings:  
> there were 170 SARS-CoV-2 infections among HCWs in the period between Dec 19, 2020, and Jan 24, 2021, of which 99 (58%) HCWs reported symptoms. Of the 170 HCWs who became infected, 89 (52%) were unvaccinated, 78 (46%) tested positive after the first dose, and 3 (2%) tested positive after the second dose.  
> Among the 125 infections that could be traced, 87 (70%) were community acquired and there were no nosocomial clusters.  
> Compared with a SARS-CoV-2 infection rate of 7·4 per 10 000 person-days in unvaccinated HCWs, infection rates were 5·5 per 10 000 person-days and 3·0 per 10 000 person-days on days 1–14 and 15–28 after the first dose of the vaccine, respectively.  
> Adjusted rate reductions of SARS-CoV-2 infections were 30% (95% CI 2–50) and 75% (72–84) for days 1–14 and days 15–28 after the first dose, respectively.  
> Data show substantial early reductions in SARS-CoV-2 infection and symptomatic COVID-19 rates following first vaccine dose administration. |
Methods: Cases reported were screened for laboratory and clinical findings of potential reinfection followed by requests for medical records and laboratory specimens.  
Findings:  
> Among 73 potential reinfection patients with available records, 30 patients had recurrent COVID-19 symptoms explained by alternative diagnoses with concurrent SARS-CoV-2 positive RT-PCR.  
> 24 patients remained asymptomatic after recovery but had recurrent or persistent RT-PCR.  
> 19 patients had recurrent COVID-19 symptoms with concurrent SARS-CoV-2 positive RT-PCR but no alternative diagnoses. These 19 patients had symptom recurrence a median of 57 days after initial symptom onset.  
> Six of these patients had paired specimens available for further testing, but none had laboratory findings confirming reinfections.  
> No confirmation of SARS-CoV-2 reinfection within 90 days of the initial infection based on the clinical and laboratory characteristics of cases in this investigation. |
| Cell 18FEB2021 | Reduced neutralization of SARS-CoV-2 B.1.1.7 variant by convalescent and vaccine sera | Supasa P., et al. UK | Variants | Analysis of the ability of B.1.1.7 to evade antibody responses elicited by natural SARS-CoV-2 infection or vaccination, by mapping the impact of N501Y by structure/function analysis of a large panel of well-characterised monoclonal antibodies.  
> B.1.1.7 is harder to neutralize than parental virus, compromising neutralization by some members of a major class of public antibodies through light chain contacts with residue 501.  
> Original strain convalescent and vaccine sera show reduced B.1.1.7 neutralization  
> N501Y enhances RBD: ACE2 binding affinity 7-fold  
> N501Y compromises neutralisation by many antibodies with public V-region IGHV3-53  
> Widespread escape from monoclonal antibodies or antibody responses generated by natural infection or vaccination was not observed. |
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| Nature Commun. 18FEB2021 | Interleukin-3 is a predictive marker for severity and outcome during SARS-CoV-2 infections | Bénard A., et al. Germany gotopaper | Clinics | **Aim:** To identify IL-3 as an independent prognostic marker for the outcome during SARS-CoV-2 infections  
**Methods:** prospective multicentric study. In total, 105 (32 non-severe; 32 severe; 41 recovered) patients positive for SARS-CoV-2 PCR from oral swabs, oral fluid, or BALF were enrolled. Blood samples were collected at the onset of symptoms (±24 h), and 1, 2, 3, 4, 5, 6, or 7 days later; or after recovery from SARS-CoV-2 infection (time of recovery = 16 days ± 2 days).  
- A mouse model of pulmonary HSV-1 infection was used to characterize the IL-3 mechanism  
**Findings:**  
>Patients with severe COVID-19 exhibit reduced circulating plasmacytoid dendritic cells (pDCs) and low plasma IFNα and IFNα levels when compared to non-severe COVID-19 patients.  
>As compared with neutralization of USA-WA1/2020, neutralization of Δ242-244+D614G virus was similar and ∼90% reductions by a factor of 2.7 (K417N, E484K, and N501Y). In serum samples obtained 1 week after the participants received the second dose of vaccine, we detected reductions by a factor of 2.7 in titters of neutralizing antibodies against the partial panel of mutations and by a factor of 6.4 against the full panel of mutations.  
> The binding of IL-3 to the CD123 receptor agonists, may therefore have the potential as novel therapeutic agents in SARS-CoV-2 infected patients. |
> All the 20 serum samples neutralized USA-WA1/2020 (pseudovirus wild-type) and all mutant viruses at titers of ≥ 1:40 or greater.  
> As compared with neutralization of USA-WA1/2020, neutralization of Δ242-244+D614G virus was similar and neutralization of the B.1.351-spike virus was weaker by approximately two thirds.  
> Results suggest that virus with mutant residues in the receptor-binding domain (RBD) region of the B.1.1.7 lineage caused by the B.1.351 variant had no significant effect on neutralization.  
> A decrease in titters of neutralizing antibodies against the B.1.351 variant and a subset of its mutations affecting the RBD was observed.  
> In serum samples obtained 1 week after the participants received the second dose of vaccine, we detected reductions by a factor of 2.7 in titters of neutralizing antibodies against the partial panel of mutations and by a factor of 6.4 against the full panel of mutations.  
> Levels of neutralization against the other tested variants that were similar to those against the Wuhan-Hu-1 (D614) isolate.  
It is unclear what effect a reduction in neutralization would have on BNT162b2-elicted protection from Covid-19 caused by the B.1.351 lineage. |
| NEJM 17FEB2021 | Serum Neutralizing Activity Elicited by mRNA-1273 Vaccine — Preliminary Report | Wu K., et al. USA gotopaper | Vaccines - variants | Pseudoviruses bearing the Wuhan-Hu-1 strain, the D614G substitution, the B.1.1.7 and B.1.351 variants and others were tested against sera from mRNA-1273-vaccinated individuals.  
> Both the full panel of mutations in S and a subset of mutations affecting the receptor-binding domain (RBD) region of the B.1.1.7 variant had no significant effect on neutralization.  
> A decrease in titters of neutralizing antibodies against the B.1.351 variant and a subset of its mutations affecting the RBD was observed.  
> In serum samples obtained 1 week after the participants received the second dose of vaccine, we detected reductions by a factor of 2.7 in titters of neutralizing antibodies against the partial panel of mutations and by a factor of 6.4 against the full panel of mutations.  
> Levels of neutralization against the other tested variants that were similar to those against the Wuhan-Hu-1 (D614) isolate.  
Protection against the B.1.351 variant conferred by the mRNA-1273 vaccine remains to be determined. |
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<td>NEJM 18FEB2021</td>
<td>Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults</td>
<td>Libster R., <em>et al.</em> Argentina <a href="https://doi.org/10.1056/NEJMoa2100304">gotopaper</a></td>
<td>Therapeutics</td>
<td>Randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against SARS-CoV-2 in older adult patients within 72 hours after the onset of mild Covid-19 symptoms. <strong>Primary end point:</strong> severe respiratory disease, defined as a respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both. The trial was stopped early at 76% of its projected sample size because cases of Covid-19 in the trial region decreased considerably. <strong>Findings</strong> &gt; A total of 160 patients underwent randomization in the intention-to-treat population, severe respiratory disease developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo (relative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; <em>P</em>=0.03), with a relative risk reduction of 48%. &gt; In the intention-to-treat population, severe respiratory disease developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo (relative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; <em>P</em>=0.03), with a relative risk reduction of 48%. &gt; A modified intention-to-treat analysis that excluded 6 patients who had a primary end-point event before infusion of convalescent plasma or placebo showed a larger effect size (relative risk, 0.40; 95% CI, 0.20 to 0.81). &gt; No solicited adverse events were observed. Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19.</td>
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<td>NEJM 18FEB2021</td>
<td>A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia</td>
<td>Simonovich V.A., <em>et al.</em> Argentina <a href="https://doi.org/10.1056/NEJMoa2100304">gotopaper</a></td>
<td>Therapeutics</td>
<td>Aim: to gather further evidence of whether convalescent plasma improves clinical outcomes. Randomized trial on hospitalized adult patients with severe Covid-19 pneumonia in a 2:1 ratio to receive convalescent plasma or placebo. <strong>Primary outcome:</strong> the patient’s clinical status 30 days after the intervention, as measured on a six-point ordinal scale ranging from total recovery to death. <strong>Findings</strong> &gt; A total of 228 patients were assigned to receive convalescent plasma and 105 to receive placebo. Median time from the onset of symptoms to enrollment in the trial was 8 days, hypoxemia was the most frequent severity criterion for enrollment. &gt; The infused convalescent plasma had a median titer of 1:3200 of total SARS-CoV-2 antibodies (interquartile range, 1:800 to 1:3200). No patients were lost to follow-up. &gt; At day 30 day, no significant difference was noted between the convalescent plasma group and the placebo group in the distribution of clinical outcomes according to the ordinal scale (odds ratio, 0.83; 95% confidence interval [CI], 0.52 to 1.35; <em>P</em>=0.46). &gt; Overall mortality was 10.96% in the convalescent plasma group and 11.43% in the placebo group, for a risk difference of −0.46 percentage points (95% CI, −7.8 to 6.8). &gt; Total SARS-CoV-2 antibody titers tended to be higher in the convalescent plasma group at day 2 after the intervention. &gt; Adverse events and serious adverse events were similar in the two groups. No significant differences were observed in clinical status or overall mortality between patients treated with convalescent plasma and those who received placebo.</td>
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| Nature Commun. 16FEB2021 | Modelling safe protocols for reopening schools during the COVID-19 pandemic in France | Di Domenico L., et al. France gotopaper | Public Health / Epidemiology | **Aim:** to explored scenarios of partial, progressive, or full school reopening, through a stochastic age-structured transmission model.  
> Under a scenario with stable epidemic activity if schools were closed, reopening pre-schools and primary schools would lead to up to 76% ([67, 84]) occupation of ICU beds if no other school level reopened, or if middle and high schools reopened later.  
> Immediately reopening all school levels may **overwhelm the ICU system.** Priority should be given to pre- and primary schools allowing younger children to resume learning and development. Full attendance in middle and high schools is not recommended for stable or increasing epidemic activity.  
> Large-scale **test and trace** is required for epidemic control. |
> Retrospective exploratory analysis using the Hospital Episode Statistics administrative dataset (between March 1 and May 31, 2020)  
> Multilevel logistic regression was used to model the relationship between death and several covariates: age, sex, deprivation (Index of Multiple Deprivation), ethnicity, frailty (Hospital Frailty Risk Score), presence of comorbidities (Charlson Comorbidity Index items), and date of discharge (whether alive or deceased).  
**Findings:**  
> 91,541 adult patients with COVID-19 were discharged during the study period, among which 28,200 (30.8%) in-hospital deaths occurred  
> Significant predictors of in-hospital death included older age, male sex ([1.457 [1.408–1.509]], greater deprivation (1.002 [1.001–1.003]), Asian (1.211 [1.128–1.299]) or mixed ethnicity (1.317 [1.080–1.605]), vs White ethnicity), and most of the assessed comorbidities, including moderate or severe liver disease (5.433 [4.618–6.392]).  
> Later date of discharge was associated with a lower odds of death (0.977 [0.976–0.978]); adjusted in-hospital mortality improved significantly in a broadly linear fashion, from 52.2% in the first week of March to 16.8% in the last week of May => might reflect the impact of changes in hospital strategy and clinical processes.  
**Conclusion:**  
> The reasons for the observed improvements in mortality should be thoroughly investigated to inform the response to future outbreaks.  
> The higher mortality rate reported for certain ethnic minority groups in community-based studies compared with our hospital-based analysis might partly reflect differential infection rates in those at greatest risk, propensity to become severely ill once infected, and health-seeking behaviours. |
| Pediatrics 12FEB2021 | Factors Associated With Severe SARS-CoV-2 Infection | Ouldali N., et al. France gotopaper | Clincs | **Aim:** to analyze the clinical spectrum of hospitalized pediatric SARS-CoV-2 infection and predictors of severe disease evolution.  
**Main outcome:** proportion of children with severe disease, defined by hemodynamic or ventilatory (invasive or not) support requirement.  
> 397 hospitalized children with SARS-CoV-2 infection, with several clinical patterns (paucisymptomatic children, admitted for surveillance, lower respiratory tract infection or multisystem inflammatory syndrome).  
> Children <90 days old accounted for 37% of cases (145 of 397), but only 4 (3%) had severe disease.  
> Excluding children with multisystem inflammatory syndrome in children (n = 29) and hospitalized for a diagnosis not related to SARS-CoV-2 (n = 62), 23 of 306 (11%) children had severe disease, including 6 deaths.  
> **Factors independently associated** with severity were age ≥10 years (odds ratio [OR] = 3.4), hypoxemia (OR = 8.9), C-reactive protein level ≥80 mg/L (OR = 6.6).  
Young age was not an independent factor associated with severe SARS-CoV-2 infection, and children <90 days old were at the lowest risk of severe disease evolution. |
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| Nature Med. 12FEB2021 | Humoral signatures of protective and pathological SARS-CoV-2 infection in children | Bartsch Y.C., et al. USA [gotopaper](#) | Immunology | Aim: identifying immune mechanisms that result in disparate clinical phenotypes in children (largely asymptomatic disease, with rare reports of multisystem inflammatory syndrome in children (MIS-C)).
> Using systems serology, in 25 children with acute mild COVID-19 we observed a functional phagocyte and complement-activating IgG response to SARS-CoV-2, similar to the acute responses generated in adults with mild disease. Conversely, IgA and neutrophil responses were significantly expanded in adults with severe disease.
> Weeks after the resolution of SARS-CoV-2 infection, children who develop MIS-C maintained highly inflammatory monocyte-activating SARS-CoV-2 IgG antibodies, distinguishable from acute disease in children but with antibody levels similar to those in convalescent adults.
These data provide insights into the potential mechanisms of IgG and IgA that might underlie differential disease severity in children infected with SARS-CoV-2. |
| Cell 12FEB2021 | Human neutralizing antibodies against SARS-CoV-2 require intact Fc effector functions for optimal therapeutic protection | Winkler ES., et al. USA [gotopaper](#) | Immunology | Aim: to define correlates of protection of neutralizing human monoclonal antibodies (mAbs) in SARS-CoV-2-infected animals.
Methods: A K18-hACE2 transgenic mouse model of SARS-CoV-2 pathogenesis and a Fc region genetic variant form of IgG (LALA-73 PG) of a potent RBD-binding neutralizing mAb that cannot engage FcγRs or complement were used to define the role of Fc effector functions in antibody protection.
Findings:
> Fc effector functions are dispensable when neutralizing mAbs are administered as prophylaxis, but are required for optimal protection when given as post-exposure therapy.
> When administered after SARS-CoV-2 infection, intact but not LALA-PG mAbs reduce viral burden and lung disease. Fc engagement by Abs decreases immune cell activation and levels of inflammatory cytokines.
> Neutralizing mAbs require monocytes and CD8+ T cells for maximal clinical and virological benefit. In hamsters, Fc effector functions of a neutralizing mAb are required to prevent weight loss, control viral infection, and limit inflammation.
> Fc effector functions of neutralizing antibodies are necessary for optimal therapeutic outcome after SARS-CoV-2 infection |
| BMJ 11FEB2021 | Early initiation of prophylactic anticoagulation for prevention of coronavirus disease 2019 mortality in patients admitted to hospital in the United States: cohort study | Rentsch CT., et al. UK/USA [gotopaper](#) | Therapeutics | Aim: To evaluate whether early initiation of prophylactic anticoagulation compared with no anticoagulation was associated with decreased risk of death among COVID-19 patients admitted to hospital in USA.
Methods: Observational cohort study including 4297 patients admitted to hospital from 1 March to 31 July 2020.
Main outcome: 30 day mortality
Secondary outcomes: inpatient mortality, initiating therapeutic anticoagulation (a proxy for clinical deterioration, including thromboembolic events), and bleeding that required transfusion.
Findings:
> From 4297 patients, 3627 (84.4%) received prophylactic anticoagulation within 24 hours of admission. More than 99% (n=3600) of treated patients received subcutaneous heparin or enoxaparin.
> 622 deaths occurred within 30 days of hospital admission, 513 among those who received prophylactic anticoagulation.
> The cumulative incidence of mortality at 30 days was 14.3% among those who received prophylactic anticoagulation and 18.7% among those who did not.
> Compared with patients who did not receive prophylactic anticoagulation, those who did had a 27% decreased risk for 30 day mortality (hazard ratio 0.73).
> Receipt of prophylactic anticoagulation was not associated with increased risk of bleeding that required transfusion.
Early initiation of prophylactic anticoagulation compared with no anticoagulation among COVID-19 patients admitted to hospital was associated with a decreased risk of 30 day mortality. |
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| Euro Surveill., 11FEB2021 | Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021 | Jabal KA., et al. Israel [gotopaper](#) | Vaccine | Description of one dose immunogenicity of BNT162b2 vaccine in various age and ethnic groups  
**Background:**  
> As at 25 January 2021, Israel had vaccinated 29.2% of its population with a single dose of vaccine (almost exclusively BNT162b2 mRNA from Pfizer/BioNtech)  
> Ziv Medical Center (ZMC), located in Safed, Israel, is a 350-bed hospital, staffed by a multi-ethnic workforce of ca 1,500 persons including Jews, Arabs and Druze among others. ZMC has offered the BNT162b2 mRNA-based vaccine to all its staff, including administrative and support staff, with no specific exclusion for pregnant women. As at 21 January 2021, one-dose uptake was ca 90%.  
**Findings:**  
> 519 participants to the study (19-77 years of age). IgGs levels measured at 21d  
> 475 (92%) had detectable anti-SARS-CoV-2 IgG. Among these, GMC was 68.6 AU/mL (95% CI: 64–73.6). No differences between ethnicity or sex. Titres decreasing with age.  
> 39 non-respondent: median age older than respondent (57 vs 45) and more likely to be Jewish (31/38 non-responders of known ethnicity, 82% vs 291/459 responders of known ethnicity; 63%)  
> IgGs level postvaccination were higher among those with previous evidence of infection (at least one order of magnitude regardless the titre before vaccination) (GMC 573 vs 61.5)  
**Conclusion:**  
> age and ethnicity (but not sex) may be associated with the likelihood of non-response (findings based on 39 observations). |
| PNAS 09FEB2021 | Exhaled aerosol increases with COVID-19 infection, age, and obesity | Edwards D., et al. USA [gotopaper](#) | Public Health / Epidemiology | > Respiratory droplet generation and exhalation in human and nonhuman primate subjects with and without COVID-19 infection to explore whether SARS-CoV-2 infection, and other changes in physiological state, translate into observable evolution of numbers and sizes of exhaled respiratory droplets in healthy and diseased subject  
**Method**  
> Observational cohort study of the exhaled breath particles of 194 healthy human subjects  
> Experimental infection study of 8 nonhuman primates infected, by aerosol, with SARS-CoV-2  
**Findings**  
> Exhaled aerosol particles vary between subjects by three orders of magnitude, with exhaled respiratory droplet number increasing with degree of COVID-19 infection and elevated BMI-years  
> 18% of human subjects (35) accounted for 80% of the exhaled bioaerosol of the group (194), reflecting a superspreader distribution of bioaerosol analogous to a classical 20:80 superspreader of infection distribution  
> The capacity of airway lining mucus to resist breakup on breathing varies significantly between individuals with a trend to increasing with the advance of COVID-19 infection and body mass index multiplied by age (i.e., BMI-years)  
**Conclusion**  
> Our studies of exhaled aerosol suggest that a critical factor in these and other transmission events is the propensity of certain individuals to exhale large numbers of small respiratory droplets.  
> Understanding the source and variance of respiratory droplet generation, and controlling it via the stabilization of airway lining mucus surfaces, may lead to effective approaches to reducing COVID-19 infection and transmission  
> These findings suggest that quantitative assessment and control of exhaled aerosol may be critical to slowing the airborne spread of COVID-19 in the absence of an effective and widely disseminated vaccine |
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| Nature 10FEB2021 | mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants | Wang Z., et al. USA [gotopaper](#) | Vaccines | Antibody and memory B cell responses in volunteers who received either the Moderna (mRNA-1273) or Pfizer-BioNTech (BNT162b2) vaccines  
> Findings:  
> Eight weeks after the second vaccine injection volunteers showed high levels of IgM, and IgG anti-S and anti-RBD  
> Plasma neutralizing activity, and the relative numbers of RBD-specific memory B cells were equivalent to individuals who recovered from natural infection  
> Vaccine-elicited monoclonal antibodies potently neutralize SARS-CoV-2, targeting a number of different RBD epitopes in common with mAbs isolated from infected donors  
> However, neutralization by 14 of the 17 most potent mAbs tested was reduced or abolished by either K417N, or E484K, or N501Y mutations.  
> Activity against SARS-CoV-2 variants encoding E484K or N501Y or the K417N:E484K:N501Y combination was reduced by a small but significant margin.  
> The same mutations were selected when recombinant vesicular stomatitis virus (rVSV)/SARS-CoV-2 S was cultured in the presence of the vaccine elicited mAbs.  
> Conclusion:  
This results suggest that the monoclonal antibodies in clinical use should be tested against newly arising variants, and that mRNA vaccines may need to be updated periodically to avoid potential loss of clinical efficacy. |
| Nature 09FEB2021 | Lasting antibody and T cell responses to SARS-CoV-2 in COVID-19 patients three months after infection | Jiang X.L., et al. China [gotopaper](#) | Immunology | Aim: Longitudinal assessment of 25 SARS-CoV-2-infected patients up to 3–4 months post-infection and analysis of the specific antibody and memory T cell responses over time.  
> Findings:  
> All patients seroconvert for IgG against N, S, or RBD, as well as IgM against RBD, and produce neutralising antibodies (NAb) by 14 days post symptoms onset (PSO) with the peak levels attained by 15–30 days PSO.  
> Anti-SARS-CoV-2 IgG and NAb remain detectable and relatively stable 3–4 months PSO, whereas IgM antibody rapidly decay.  
> 65% of patients have detectable SARS-CoV-2-specific CD4+ or CD8+ T cell responses 3–4 months PSO  
> T cell responses maintain in most recovered patients for at least 3–4 months after infection.  
> Assessment of the duration and resiliency of the SARS-CoV-2 antibody and T cell responses in a large cohort study would be desirable for validation of the results. |
> Follow up of 26 HCW with mild COVID-19 three weeks (D21), two months (M2) and three months (M3) after the onset of symptoms.  
> Findings:  
> All the HCW had anti-receptor binding domain (RBD) IgA at D21, decreasing to 38.5% at M3 (p < 0.0001).  
> Concomitantly a significant decrease in NAb titers was observed between D21 and M2 (p = 0.03) and between D21 and M3 (p < 0.0001).  
> SARS-CoV-2 can elicit a NAb response correlated with anti-RBD antibody levels, however neutralizing activity declines, and may even be lost, in association with a decrease in systemic IgA antibody levels, from two months after disease onset.  
> Conclusions:  
This short-lasting humoral protection supports strong recommendations to maintain infection prevention and control measures in HCW, and suggests that periodic boosts of SARS-CoV-2 vaccination may be required. |
Lancet Child Adolesc Health 08FEB2021

SARS-CoV-2 transmission among children and staff in daycare centres during a nationwide lockdown in France: a cross-sectional, multicentre, seroprevalence study

Lachassiné E., et al. France/go tpaper

Public Health / Epidemiology

Aim: to estimate the seroprevalence of antibodies against SARS-CoV-2 in daycare centres that remained open for key workers’ children during a nationwide lockdown in France (March 15 – May 09, 2020).

> 327 children enrolled (mean age 1·9 years yrs), 197 daycare centre staff (40 yrs), and 164 adults in the comparator group (42 yrs).
> Positive serological tests were observed for 14 children (raw seroprevalence 4·3%) and 14 daycare centre staff (7·7%). After accounting for imperfect sensitivity and specificity of the assay, we estimated that 3·7% of the children and 6·8% of daycare centre staff had SARS-CoV-2 infection.
> The comparator group fared similarly to the daycare centre staff; 9 participants had a positive serological test (raw seroprevalence 5·5%), leading to a seroprevalence of 5·0% after adjusting.
> An exploratory analysis suggested that seropositive children were more likely than seronegative children to have been exposed to an adult household member with laboratory-confirmed COVID-19 (6/14 [43%] vs 19/307 [6%], relative risk 7.1).

The proportion of young children in this sample with SARS-CoV-2 infection was low. Intrafamily transmission seemed more plausible than transmission within daycare centres.

Nature Med. 08FEB2021

Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K and N501Y variants by BNT162b2 vaccine-elicited sera

Xie X., et al. USA/go tpaper

Immunology

Methods
> Engineered three SARS-CoV-2 containing key spike mutations from the newly emerged United Kingdom (UK) and South African (SA) variants
- Mutant N501Y virus contains the N501Y mutation that is shared by both the UK and SA variants
- Mutant Δ69/70 + N501Y +D614G virus contains two additional changes present in the UK variants: amino acid 69 and 70 deletion (Δ69/70) and D614G substitution (D614G mutation is dominant in circulating strains around the world)
- Mutant E484K + N501Y +D614G virus addition-ally contains the E484K substitution, which is also located in the viral RBD
> Neutralization assays with the same 20 sera samples

Findings
> All sera showed equivalent neutralization titers between the WT and mutant viruses, with differences of four-fold or less
> Notably, 10 out of the 20 sera had neutralization titers against mutant Δ69/70 + N501Y + D614G virus that were twice their titers against the WT virus, whereas 6 out of the 20 sera had neutralization titers against mutant E484K + N501Y + D614G virus that were half their titers against the WT virus
> The ratios of the neutralization GMTs of the sera against the N501Y, Δ69/70 + N501Y + D614G and E484K + N501Y + D614G viruses to their GMTs against the USA-WA1/2020 virus were 1.46, 1.41 and 0.81, respectively.
> Neutralization geometric mean titers (GMTs) of 20 BTN162b2 vaccine-elicited human sera against the three mutant viruses were 0.81- to 1.46-fold of the GMTs against parental virus, indicating small effects of these mutations on neutralization by sera elicited by two BTN162b2 doses
> Clinical data are needed for firm conclusions about vaccine effectiveness against variant viruses.
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<td>Eur J Epidemiol. 06FEB2021</td>
<td>Evidence of early circulation of SARS-CoV-2 in France: findings from the population-based “CONSTANCES” cohort</td>
<td>Carrat F., et al. France gotopaper</td>
<td>Public Health / Epidemiology</td>
<td>Analysis of serological status for SARS-CoV-2 antibodies on serum samples routinely collected in 9144 adults from a French general population-based cohort (CONSTANCES). &gt; 353 participants with a positive anti-SARS-CoV-2 IgG test were identified, among whom 13 were sampled between November 2019 and January 2020. &gt; Evidence was confirmed by neutralizing antibodies testing. &gt; Investigations in 11 of these participants revealed evidence of symptoms possibly related to a SARS-CoV-2 infection or situations at risk of potential SARS-CoV-2 exposure. These results suggest early circulation of SARS-CoV-2 in Europe.</td>
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<td>Nature 05FEB2021</td>
<td>SARS-CoV-2 evolution during treatment of chronic infection</td>
<td>Kemp S.A., et al. UK gotopaper</td>
<td>Virology</td>
<td>Aim: to report chronic SARS-CoV-2 with reduced sensitivity to neutralising antibodies in an immune suppressed individual treated with convalescent plasma (whole genome ultradeep sequences over 23 time points spanning 101 days). &gt; Little change was observed in the overall viral population structure following two courses of remdesivir over the first 57 days. &gt; Following convalescent plasma therapy, large, dynamic virus population shifts were observed, with the emergence of a dominant viral strain bearing D796H in S2 and ΔH69/ΔV70 in the S1 N-terminal domain NTD of the Spike protein. &gt; As passively transferred serum antibodies diminished, viruses with the escape genotype diminished in frequency, before returning during a final, unsuccessful course of convalescent plasma. &gt; In vitro, the Spike escape double mutant bearing ΔH69/ΔV70 and D796H conferred modestly decreased sensitivity to convalescent plasma, whilst maintaining infectivity similar to wild type. D796H appeared to be the main contributor to decreased susceptibility but incurred an infectivity defect. The ΔH69/ΔV70 single mutant had two-fold higher infectivity compared to wild type, possibly compensating for the reduced infectivity of D796H. These data reveal strong selection on SARS-CoV-2 during convalescent plasma therapy associated with emergence of viral variants with evidence of reduced susceptibility to neutralising antibodies.</td>
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<td>Nature 05FEB2021</td>
<td>Efficacy and tolerability of bevacizumab in patients with severe Covid-19</td>
<td>Pang J., et al. China gotopaper</td>
<td>Therapeutics</td>
<td>Aim: to evaluate the efficacy of the anti-vascular endothelial growth factor (VEGF) drug bevacizumab for treatment of Covid-19 patients. Single-arm trial (NCT04275414) including 26 patients with severe Covid-19 followed up for 28 days, from 2-centers (China and Italy). Patients received a single dose of bevacizumab. Findings: &gt; PaO2/FiO2 values markedly increased at days 1 and 7 after bevacizumab administration compared to the baseline values. &gt; 24 of 26 patients (92%) showed improvement and 2 patients (8%) showed no change in oxygen-support within 28-day follow-up, 17 (65%) patients are discharged, and none show worsen oxygen-support status nor die. &gt; Significant reduction of lesion areas/ratios are shown in chest computed tomography (CT) or X-ray within 7 days. &gt; Of 14 patients with fever, body temperature normalizes within 72 h in 13 (93%) patients. &gt; Relative to comparable controls, bevacizumab shows clinical efficacy by improving oxygenation and shortening oxygen-support duration. Bevacizumab plus standard care is highly beneficial for patients with severe Covid-19.</td>
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| Lancet Respir Med. 05FEB2021 | Peginterferon lambda for the treatment of outpatients with COVID-19: a phase 2, placebo-controlled randomised trial | Feld J.J., et al. Canada [gotopaper](http://www.gotopaper.com) | Therapeutics       | **Aim** – Test therapeutic effects of Peginterferon lambda (PGL), a type III interferon. Double-blind, placebo-controlled trial, on 60 outpatients with laboratory-confirmed COVID-19 receiving PGL (single subcutaneous injection, 180 μg) or placebo within 7 days of symptoms onset or first positive swab. **Primary endpoint**: proportion of patients who were negative for SARS-CoV-2 RNA on day 7 after the injection.  
> The decline in SARS-CoV-2 RNA was greater in patients treated with PGL than placebo from day 3 onwards, with a difference of 2·42 log copies per mL at day 7 (p=0·0041).  
> By day 7, 24 (80%) participants in the PGL group had an undetectable viral load, compared with 19 (63%) in the placebo group (p=0·15).  
> After controlling for baseline viral load, patients in the PGL group were more likely to have undetectable virus by day 7 than were those in the placebo group (odds ratio [OR] 4·12).  
> Of those with baseline viral load above 106 copies per mL, 15/19 (79%) in the PGL group had undetectable virus on day 7, compared with 6/16 (38%) in the placebo group (OR 6·25).  
> PGL was well tolerated, and adverse events were similar between groups (mild and transient aminotransferase concentration increases more frequently observed in the PGL group).  

Peginterferon lambda accelerated viral decline in outpatients with COVID-19, increasing the proportion of patients with viral clearance by day 7, particularly in those with high baseline viral load. |
Online survey in July 2020, adults aged 18–64 years residing in France, with no history of SARS-CoV-2 infection. Responses were analysed with a two-part model to disentangle outright vaccine refusal from vaccine hesitancy.  
**Findings**:  
Survey responses were collected from 1942 working-age adults, of whom 560 (28·8%) opted for no vaccination (outright vaccine refusal) and 1382 (71·2%) did not.  
>Outright vaccine refusal and vaccine hesitancy were both significantly associated with female gender, age, lower educational level, poor compliance with recommended vaccinations in the past, and no report of specified chronic conditions.  
>Outright vaccine refusal was associated with a lower perceived severity of COVID-19.  
>Vaccine hesitancy was lower when herd immunity benefits were communicated and in working versus non-working individuals, and those with experience of COVID-19 (Symptoms or close contact).  
>For a mass vaccination campaign involving mass vaccination centres and communication of herd immunity benefits, the model predicted outright vaccine refusal in 29·4% of the French working-age population.  
>Predicted hesitancy was highest for vaccines manufactured in China (vaccine acceptance 27·4%), and lowest for a vaccine manufactured in the EU (vaccine acceptance 61·3%). |
Factors associated with the spatial heterogeneity of the first wave of COVID-19 in France: a nationwide geo-epidemiological study

Gaudart J., et al. France gotopaper

Public Health / Epidemiology

> better understand the factors associated with the heterogeneity of in-hospital COVID-19 morbidity and mortality across France

Methods
> Geo-epidemiological analysis was based on data publicly available for the 96 administrative departments of metropolitan France between March 19 and May 11, 2020,
Assessment:
> Multidimensional variables (spatiotemporal spread of the epidemic, national lockdown, demographic population structure, baseline intensive care capacities, ...)
> in-hospital COVID-19 incidence, mortality, and case fatality rates

Findings
> clear spatial heterogeneity of in-hospital COVID-19 incidence and mortality rates, following the spread of the epidemic
> delay between the first COVID-19-associated death and the onset of the national lockdown was positively associated with in-hospital incidence, mortality, and case fatality rates
> Mortality and case fatality rates were higher in departments with older populations (adjusted standardised ratio for populations with a high proportion older than aged >85 years 2.17 [95% CI 1.20–3.90] for mortality and 1.43 [1.08–1.88] for case fatality rate)
> Mortality rate was also associated with incidence rate (1.0004, 1.0002–1.001), but mortality and case fatality rates did not appear to be associated with baseline intensive care capacities
> no association between climate and in-hospital COVID-19 incidence, or between economic indicators and in-hospital COVID-19 incidence or mortality rates

This ecological study highlights the impact of the epidemic spread, national lockdown, and reactive adaptation of intensive care capacities on the spatial distribution of COVID-19 morbidity and mortality

Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial

Wu Z., et al. China gotopaper

Vaccines

> Randomised, double-blind, placebo-controlled, phase 1/2 clinical trial of CoronaVac in healthy adults aged 60 years and older (NCT04383574).
> Vaccine or placebo by IM injection (in two doses, days 0 and 28).
> Phase 1: dose-escalation study. 72 participants (24 per intervention group and 24 in the placebo group; mean age 65.8 years [SD 4.8])
> Block 1: 3 μg inactivated virus in 0.5 mL of aluminium hydroxide
> Block 2 (6 μg per injection).
> Phase 2: 1.5 μg, 3 μg, or 6 μg per dose, or placebo. 350 participants were enrolled in phase 2 (100 in each intervention group and 50 in the placebo group; mean age 66-67 years [SD 4.7] in 349 participants)

Primary safety endpoint: adverse reactions within 28 days after each injection in all participants who received at least one dose.

Primary immunogenicity endpoint was seroconversion rate at 28 days after the second injection (NCT04383574).

Findings:
> Safety: any adverse reaction within 28 days after injection occurred in 20 (20%) of 100 participants in the 1.5 μg group, 25 (20%) of 125 in the 3 μg group, 27 (22%) of 123 in the 6 μg group, and 15 (21%) of 73 in the placebo group.
> All adverse reactions were mild or moderate in severity and injection site pain (39% [9%] of 421 participants) was the most frequently reported event.
> Eight serious adverse events, considered unrelated to vaccination, have been reported by seven (2%) participants.
> In phase 1, seroconversion after the second dose was observed in 24 of 24 participants (100% [95% CI 85.8–100.0]) in the 3 μg group and 22 of 23 (95.7% [78.1–99.9]) in the 6 μg group.
> In phase 2, seroconversion was seen in 88 of 97 participants in the 1.5 μg group (90.7% [83.1–95.7]), 96 of 98 in the 3 μg group (98.0% [92.8–99.8]), and 97 of 98 (99.0% [94.5–100.0]) in the 6 μg group.

Conclusion:
CoronaVac is safe and well tolerated in older adults. Neutralising antibody titres by the 3 μg dose were similar to those of the 6 μg dose, and higher than those of the 1.5 μg dose.
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> The model predicted a median peak viral load that coincided with symptom onset.  
> Patients with age ≥65y had a smaller loss rate of infected cells, leading to a delayed median time to viral clearance occurring 16d after symptom onset as compared to 13 d in younger patients.  
> In multivariate analysis, the risk factors associated with mortality were age ≥65y, male gender, and presence of chronic pulmonary disease (hazard ratio [HR] > 2.0). Using a joint model, viral dynamics after hospital admission was an independent predictor of mortality (HR = 1.31, P < 10−3).  
> Simulation of effectiveness of pharmacological interventions: a treatment able to reduce viral production by 90% upon hospital admission would shorten the time to viral clearance by 2.0 and 2.9d in patients of age <65 y and ≥65y, respectively. Assuming a similar association between viral dynamics and mortality in patients of age ≥65y with risk factors, this could translate into a reduction of mortality from 19 to 14%.  
Viral dynamics is associated with mortality in hospitalized patients. |
| The Lancet 02FEB2021 | Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia | Logunov D.Y., et al. Russia gotopaper | Vaccines | Background  
> Sputnik V: heterologous recombinant adenovirus (rAd)-based vaccine.  
> Good safety profile and strong humoral and cellular immune responses (phase 1/2 clinical trials).  
Preliminary results on the efficacy and safety of this vaccine from the interim analysis of this phase 3 trial. (NCT04530396).  
Methods  
> Randomised, double-blind, placebo-controlled, phase 3 trial (25 hospitals and polyclinics in Moscow, Russia).  
> Participants aged at least 18 years, with negative SARS-CoV-2 PCR and IgG and IgM tests, no infectious diseases in the 14 days before enrolment, and no other vaccinations in the 30 days before enrolment.  
> Randomly assigned (3:1) to receive vaccine or placebo (0.5 mL/dose) IM: prime-boost regimen at 21-day interval  
> First dose (rAd26) and the second dose (rAd5), both vectors carrying the gene for the full-length SARS-CoV-2 glycoprotein S.  
Primary outcome: proportion of participants with PCR-confirmed COVID-19 from day 21 after receiving the first dose.  
SAE: assessed in all participants who had received at least one dose at the time of database lock  
Findings  
> 21,977 adults randomly assigned to the vaccine group (n=16,501) or the placebo group (n=5,476).  
> 19,866 received two doses of vaccine or placebo and were included in the primary outcome analysis.  
> From 21 days after the first dose of vaccine (the day of dose 2): - 16 (0.1%) of 14,964 participants in the vaccine group and 62 (1.3%) of 4,902 in the placebo group were confirmed to have COVID-19: vaccine efficacy was 91.6% (95% CI 85.6–95.2).  
> Most reported AE were grade 1 (7,485 [94.0%] of 7,966 total events).  
> SAE: 45 (0.3%) of 16,427 participants in the vaccine group and 23 (0.4%) of 5,435 participants in the placebo group. None were considered associated with vaccination, with confirmation from the independent data monitoring committee.  
> Four deaths were reported during the study (three (<0.1%) of 16,427 participants in the vaccine group and one (<0.1%) of 5,435 participants in the placebo group), none of which were considered related to the vaccine.  
Conclusion: This interim analysis of the phase 3 trial of Gam-COVID-Vac showed 91.6% efficacy against COVID-19 and was well tolerated in a large cohort. |
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| *Science* 02FEB2021 | Age groups that sustain resurging COVID-19 epidemics in the United States | Monod M., *et al.* UK | Public Health / Epidemiology | > Understanding the age demographics driving transmission and how these affect the loosening of interventions is crucial  
**Methods** > Analyze aggregated, age-specific mobility trends from more than 10 million individuals in the US and link these mechanistically to age-specific COVID-19 mortality data  
**Findings** > Estimation: as of October 2020, individuals aged 20-49 are the only age groups sustaining resurgent SARS-CoV-2 transmission with reproduction numbers well above one, and that at least 65 of 100 COVID-19 infections originate from individuals aged 20-49 in the US  
Targeting interventions – including transmission-blocking vaccines – to adults aged 20-49 is an important consideration in halting resurgent epidemics and preventing COVID-19-attributable deaths. |
| *Cell* 02FEB2021 | Maturation and persistence of the anti-SARS-CoV-2 memory B cell response | Sokal A., *et al.* France | Immunology | Analysis of the longevity and functionality of the anti-SARS-CoV-2 memory B cell response  
**Methods** > longitudinal deep profiling of the anti-SARS-CoV-2 memory B cell response in two parallel cohorts of patients with severe and mild COVID-19 (39 total patients)  
> They combined single cell transcriptomics, single cell culture and IgH VDJ sequencing to track and characterize the cellular and molecular phenotype and clonal evolution of spike-specific MBCs clones from early time points after SARS-CoV-2 infection up to 6 months after the initial symptoms  
**Findings** > Distinct SARS-CoV-2 spike-specific activated B cell clones fueled an early antibody-secreting cell burst as well as a durable synchronous germinal center response  
> While highly mutated memory B cells, including pre-existing cross-reactive seasonal Betacoronavirus-specific clones, were recruited early in the response, neutralizing SARS-CoV-2 RBD-specific clones accumulated with time and largely contributed to the late remarkably stable memory B-cell pool.  
> Seasonal coronavirus-specific memory B cells contribute an early anti-SARS-CoV-2 response  
> Spike-specific memory B cells with a resting phenotype increase up to 6 months  
> Highlighting germinal center maturation, these cells displayed clear accumulation of somatic mutations in their variable region genes over time  
> Longitudinal study reveals a temporal switch to RBD-specific neutralizing memory B cells  
These findings demonstrate that an antigen-driven activation persisted and matured up to 6 months after SARS-CoV-2 infection and may provide long-term protection. |
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| Lancet 02FEB2021 | Azithromycin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial | RECOVERY Collaborative Group UK gotopaper | Therapeutics | **Aim:** to evaluate the safety and efficacy of azithromycin (500 mg once per day by mouth or intravenously for 10 days or until discharge) in patients admitted to hospital with COVID-19.  
**Primary outcome:** 28-day all-cause mortality  
**Results**  
> Between April 7 and Nov 27, 2020, 7763 were included in the assessment of azithromycin. Mean age was 65·3 years, approx. a third were women. 2582 patients were randomly allocated to receive azithromycin and 5181 to usual care alone.  
> Overall, 561 (22%) patients allocated to azithromycin and 1162 (22%) patients allocated to usual care died within 28 days (rate ratio 0·97).  
> No significant difference was seen in duration of hospital stay (median 10 days vs 11 days) or the proportion of patients discharged from hospital alive within 28 days (rate ratio 1·04).  
> Among those not on invasive mechanical ventilation at baseline, no significant difference was seen in the proportion meeting the composite endpoint of invasive mechanical ventilation or death (risk ratio 0·95).  
In patients admitted to hospital with COVID-19, azithromycin did not improve survival or other prespecified clinical outcomes. |
> We identified 314 patients with COVID-19, with 282 (90%) having at least one contact (753 contacts in total), resulting in 282 clusters.  
> 90 (32%) of 282 clusters had at least one transmission event. The secondary attack rate was 17% (125/753 contacts), with a variation from 12% when the index case had a viral load lower than $1 \times 10^6$ copies per mL to 24% when the index case had a viral load of $1 \times 10^{10}$ copies per mL or higher (adjusted odds ratio per log10 increase in viral load 1·3).  
> Increased risk of transmission was also associated with household contact (3·0) and age of the contact (per year: 1·02, 1·01–1·04).  
> 449 contacts had a positive PCR result at baseline. 28 (6%) of 449 contacts had symptoms at the first visit.  
> Of 421 contacts who were asymptomatic at the first visit, 181 (43%) developed symptomatic COVID-19, with a variation from approx. 38% in contacts with an initial viral load lower than $1 \times 10^7$ copies per mL to >66% for those with an initial viral load of $1 \times 10^{10}$ copies per mL or higher (hazard ratio per log10 increase in viral load 1·12).  
> Time to onset of symptomatic disease decreased from a median of 7 days (IQR 5–10) for individuals with an initial viral load lower than $1 \times 10^7$ copies per mL to 6 days (4–8) for those with an initial viral load between $1 \times 10^7$ and $1 \times 10^9$ copies per mL, and 5 days (3–8) for those with an initial viral load higher than $1 \times 10^9$ copies per mL.  
The viral load of index cases was a leading driver of SARS-CoV-2 transmission. The risk of symptomatic COVID-19 was strongly associated with the viral load of contacts at baseline and shortened the incubation time of COVID-19 in a dose-dependent manner. |
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| Nature 01FEB2021 | Immunogenic BNT162b vaccines protect rhesus macaques from SARS-CoV-2 | Vogel A.B., et al. Germany [gotopaper](#) | Immunology / Preclinical model | > Preclinical development of two BNT162b vaccine candidates: lipid-nanoparticle (LNP) formulated nucleoside-modified mRNA encoding SARS-CoV-2 spike glycoprotein-derived immunogens  
> BNT162b1 encodes a soluble, secreted, trimerised receptor-binding domain (RBD-foldon)  
> BNT162b2 encodes the full-length transmembrane spike glycoprotein, locked in its prefusion conformation (PS2)  
> flexibly tethered RBDS of the RBD-foldon bind ACE2 with high avidity  
> Approximately 20% of the P 2S trimers are in the two-RBD ‘down,’ one-RBD ‘up’ state  

Findings  
> In mice, one intramuscular dose of either candidate elicits a dose-dependent antibody response with high virus-entry inhibition titres and strong TH1 CD4+ and IFNγ+ CD8+ T-cell responses  
> Prime/boost vaccination of rhesus macaques with BNT162b candidates elicits SARS-CoV-2 neutralising geometric mean titres 8.2 to 18.2 times that of a SARS-CoV-2 convalescent human serum panel  
> Vaccine candidates protect macaques from SARS-CoV-2 challenge, with BNT162b2 protecting the lower respiratory tract from the presence of viral RNA and with no evidence of disease enhancement |
> Hospitalized patients with laboratory-confirmed COVID-19 from 2 Italian tertiary referral centres (derivation cohort, n = 187 patients; validation cohort, n = 62 patients).  
> Three-day angiopoietin-2 increase of at least twofold from baseline was significantly associated with in-hospital mortality by multivariate analysis (hazard ratio [HR], 6.69) with Area under the receiver operating characteristic curve (AUROC) = 0.845.  
> Ten-day angiopoietin-2 of at least twofold from baseline was instead significantly associated with nonresolving pulmonary condition by multivariate analysis (HR, 5.33) with AUROC = 0.969.  
> Patients with persistent elevation of 10-day angiopoietin-2 levels showed severe reticular interstitial thickening and fibrous changes on follow-up computed tomography scans. Angiopoietin-2 and Tie2 were diffusely colocalized in small-vessel endothelia and alveolar new vessels and macrophages.  

Angiopoietin-2 course is strongly associated with COVID-19 in-hospital mortality and nonresolving pulmonary condition, and may be an early and useful predictor of COVID-19 clinical course.  

Description of disease phenotypes of SARS-CoV-2 exposure occurring around the time of vaccine administration  
- Disease phenotypes of a one-dose regimen given 3 days prior (D-3), 1 (D1) or 2 (D2) days after, or on the day (D0) of virus challenge in golden Syrian hamster  
- Monitoring of serial clinical severity, tissue histopathology, virus burden, and antibody response of the vaccinated hamsters.  

Findings:  
> One-dose vaccinated hamsters had significantly lower clinical disease severity score, body weight loss, lung histology score, nucleocapsid protein expression in lung, infectious virus titres in the lung and nasal turbinate, inflammatory changes in intestines and a higher serum neutralizing antibody or IgG titre against the spike receptor-binding domain or nucleocapsid protein when compared to unvaccinated controls.  
> Improvements particularly noticeable in D-3, but also in D0, D1 and even D2 vaccinated hamsters to varying degrees.  
> No increased eosinophilic infiltration was found in the nasal turbinate, lung, and intestine after virus challenge.  
> Significantly higher serum titre of fluorescent foci microscopy and infection inhibition antibody was detected in D1 and D2 vaccinated hamsters at day 4 post-challenge compared to controls despite undetectable neutralizing antibody titre.  

Vaccination just before or soon after exposure to SARS-CoV-2 does not worsen disease phenotypes and may even ameliorate infection. |
| Clin Infect Dis 30JAN21 | Absence of vaccine-enhanced disease with unexpected positive protection against SARS-CoV-2 by inactivated vaccine given within three days of virus challenge in Syrian hamster model | Li C., et al. China [gotopaper](#) | Vaccines (viral mutants) |  

- Disease phenotypes of a one-dose regimen given 3 days prior (D-3), 1 (D1) or 2 (D2) days after, or on the day (D0) of virus challenge in golden Syrian hamster  
- Monitoring of serial clinical severity, tissue histopathology, virus burden, and antibody response of the vaccinated hamsters.  

Findings:  
> One-dose vaccinated hamsters had significantly lower clinical disease severity score, body weight loss, lung histology score, nucleocapsid protein expression in lung, infectious virus titres in the lung and nasal turbinate, inflammatory changes in intestines and a higher serum neutralizing antibody or IgG titre against the spike receptor-binding domain or nucleocapsid protein when compared to unvaccinated controls.  
> Improvements particularly noticeable in D-3, but also in D0, D1 and even D2 vaccinated hamsters to varying degrees.  
> No increased eosinophilic infiltration was found in the nasal turbinate, lung, and intestine after virus challenge.  
> Significantly higher serum titre of fluorescent foci microscopy and infection inhibition antibody was detected in D1 and D2 vaccinated hamsters at day 4 post-challenge compared to controls despite undetectable neutralizing antibody titre.  

Vaccination just before or soon after exposure to SARS-CoV-2 does not worsen disease phenotypes and may even ameliorate infection. |
### Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine–elicited human sera

**Authors:** Muik M., et al. Germany/USA
gotopaper

**Field of expertise:** Vaccines (viral mutants)

**Journal and date:** Science 29JAN2021

**Title:** Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine–elicited human sera

**Key facts**

- **Background:**
  > The new SARS-CoV-2 lineage called B.1.1.7 emerged in the UK and is reported to spread more efficiently and faster than other strains.
  > This variant contains 10 amino acid changes in the spike protein: ΔH69/V70, ΔY144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H.
  > N501Y mutation is located in the receptor binding site. The spike with this mutation binds more tightly to its cellular receptor ACE-2.

- **Methods:**
  > VSV SARS-CoV-2–S pseudoviruses bearing the Wuhan reference strain or the B.1.1.7 lineage spike protein tested with sera of 40 participants given the BNT162b2 vaccine from Pfizer (phase I/II, DE).
  > The 50% neutralization geometric mean titer (GMT) of sera against the SARS-CoV-2 lineage B.1.1.7 spike-pseudotyped VSV for the younger adult group and the full analysis set were slightly, statistically significantly reduced compared to the GMTs against the Wuhan reference spike-pseudotyped VSV.
  > GMTs were not significantly different for the older adult group (0.78 [0.68;0.89] for the younger and 0.83 [0.65;1.1] for the older adults (0.80 [0.71;0.89] CI 95%).

- **Conclusions:**
  > Based on experience from antibody correlates of disease protection for influenza virus vaccines, a 20% reduced titer does not indicate a biologically significant change in neutralization activity.
  > The largely preserved neutralization of pseudoviruses bearing the B.1.1.7 spike by BNT162b2-immune sera makes it unlikely that the UK variant virus will escape BNT162b2-mediated protection.

### Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios

**Authors:** Flannery D.D., et al. USA
gotopaper

**Field of expertise:** Public Health / Epidemiology

**Journal and date:** JAMA Pediatr. 29JAN2021

**Title:** Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios

**Key facts**

- **Methods:**
  > Maternal and cord blood sera were available for Ab measurement for 1471 mother/newborn dyads (09Apr–08Aug 2020).
  > IgG and IgM to the receptor-binding domain of the SARS-CoV-2 spike protein were measured by enzyme-linked immunosorbent assay.
  > Ab concentrations and placental transfer ratios were analyzed in combination with demographic and clinical data.

- **Findings:**
  > SARS-CoV-2 IgG Ab were transferred across the placenta in 72 of 83 pregnant women who were seropositive.
  > Cord blood IgG concentrations were directly associated with maternal Ab concentrations.
  > IgM antibodies were not detected in any cord blood sera.
  > Transfer ratios were associated with time elapsed from maternal infection to delivery and not associated with severity of maternal infection.

- **Efficient transplacental transfer of SARS-CoV-2 IgG Ab supports potential maternal Ab neonate protection from SARS-CoV-2 infection.

### Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity

**Authors:** Thomson E.C., et al. UK/USA
gotopaper

**Field of expertise:** Virology

**Journal and date:** Cell 28JAN2021

**Title:** Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity

**Key facts**

- **Efficient transplacental transfer of SARS-CoV-2 IgG Ab supports potential maternal Ab neonate protection from SARS-CoV-2 infection.

- **Background:**
  > The SARS-CoV-2 spike (S) receptor binding motif (RBM) is a highly variable region of S, and provide epidemiological, clinical, and molecular characterization of a prevalent, sentinel RBM mutation, N439K.
  > N439K S protein has enhanced binding affinity to the hACE2 receptor, and N439K viruses have similar in vitro replication fitness and cause infections with similar clinical outcomes to wild-type.
  > The N439K mutation confers resistance against several neutralizing monoclonal antibodies, including one authorized for emergency use by the FDA, and reduces the activity of some polyclonal sera from persons recovered from infection.

- **Immune evasion mutations that maintain virulence and fitness such N439K can emerge within SARS-CoV-2 S, highlighting the need for ongoing molecular surveillance.”
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| **Nature Commun. 27JAN2021** | Integrating deep learning CT-scan model, biological and clinical variables to predict severity of COVID-19 patients | Lassau N., et al. France | Diagnostics | Identifying predictors of disease severity is a priority  
> Collect 58 clinical and biological variables, and chest CT scan data, from 1003 coronavirus-infected patients from two French hospitals.  
> Train a deep learning model based on CT scans to predict severity  
> Construct the multimodal AI-severity score that includes 5 clinical and biological variables (age, sex, oxy-genation, urea, platelet) in addition to the deep learning model  
Findings  
Neural network analysis of CT-scans brings unique prognosis information, although it is correlated with other markers of severity (oxygenation, LDH, and CRP) explaining the measurable but limited 0.03 increase of AUC obtained when adding CT-information to clinical variables.  
When comparing AI-severity with 11 existing severity scores, we find significantly improved prognosis performance; AI-severity can therefore rapidly become a reference scoring approach. |
| **JAMA Netw Open 27JAN2021** | Respiratory and Psychophysical Sequelae Among Patients With COVID-19 Four Months After Hospital Discharge | Bellan M., et al Italy | Public Health / Epidemiology - Long Covid | Aim: Evaluate the prevalence of lung function anomalies, exercise function impairment, and psychological sequelae among patients hospitalized for COVID-19, 4 months after discharge  
Methods  
> Prospective cohort study at an academic hospital  
> Patients ≥18 years old (or their caregivers) hospitalized with SARS-CoV-2 infection (March 1-June 29, 2020)  
> Confirmed via RT-PCR testing, bronchial swab, serological testing, or suggestive computed tomography results  
To describe proportion of patients with:  
> Diffusing lung capacity for carbon monoxide (DLCO) <80% of expected value  
> Severe lung function impairment (DLCO <60% expected value)  
> Posttraumatic stress symptoms (measured using the Impact of Event Scale–Revised total score)  
> Functional impairment (assessed using the Short Physical Performance Battery (SPPB) score and 2-minute walking test);  
> Identification of factors associated with DLCO reduction and psychosocial functional sequelae  
Findings  
> 238/767 patients (31.0%) (median age, 61 [50-71] years; 142 [59.7%] men, median comorbidities, 2 [1-3]) had sequelae.  
> 219 patients were able to complete both pulmonary function tests and DLCO measurement. DLCO was reduced to <80% of the estimated value in 113 patients (51.6%) and <60% in 34 patients (15.5%).  
> The SPPB score was suggested limited mobility (score <11) in 53 patients (22.3%).  
> Patients with normal SPPB scores scores underwent a 2-minute walk test, which was outside reference ranges of expected performance for age and sex in 75 patients (40.5%) → 128 patients (53.8%) had functional impairment. Posttraumatic stress symptoms were reported in a total of 41 patients (17.2%)  
4 months after discharge, respiratory, physical, and psychological sequelae were common among patients who had been hospitalized for COVID-19. |
| **Cell 26JAN2021** | Two-component spike nanoparticle vaccine protects macaques from SARS-CoV-2 infection | Brouwer P.J.M., et al. The Netherlands | Vaccines | > Two-component protein nanoparticles display multiple copies of the SARS-CoV-2 Spike protein potentially protecting from infection  
Immunization studies:  
> Vaccination induces potent neutralizing antibody responses in mice, rabbits and cynomolgus macaques  
> Spike protein nanoparticles enhance cognate B cell activation in vitro  
> Vaccination protects macaques against a high-dose SARS-CoV-2 challenge, resulting in strongly reduced viral infection and replication in upper and lower airways.  
These nanoparticles are a promising vaccine candidate. |
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**Methods:** whole-blood preserving single-cell analysis to integrate contributions from all major cell types including neutrophils, monocytes, platelets, lymphocytes and the contents of serum.

**Findings:**
> Patients with mild COVID-19 disease display a coordinated pattern of interferon-stimulated gene (ISG) expression across every cell population and these cells are systemically absent in patients with severe disease
> Severe COVID-19 patients paradoxically produce very high anti-SARS-CoV-2 antibody titers and have lower viral load as compared to mild disease eve two weeks beyond symptom onset.
> Examination of the serum from severe patients demonstrates that they uniquely produce Abs that functionally block the production of the mild disease-associated ISG-expressing cells, by engaging conserved signaling circuits that dampen cellular responses to interferons

Global targeting of ISG archetypes might be addressable with drugs such as rituximab to reduce B cell responses, perhaps in the presence of convalescent serum, through introduction of IVIG to compete with serum antibodies for FcR engagement, or with rapid development of antibodies that clinically block FCyRlb.

| Science 25JAN2021 | Prospective mapping of viral mutations that escape antibodies used to treat COVID-19 | Starr T.N., et al. USA [gtopaper](#) | Immunology | Aim: mapping how all mutations to SARS-CoV-2’s receptor-binding domain (RBD) affect binding by the antibodies in the REGN-COV2 cocktail and the antibody LY-CoV016.

**Methods:** To validate the antigenic effects of key mutations, neutralization assays using spike-pseudotyped lentiviral particles were made.

**Findings:**
> Regarding REGN-COV2 antibodies: a mutation at site 486 escaped neutralization only by REGN10933, whereas mutations at sites 439 and 444 escaped neutralization only by REGN10987.
> One mutation (E406W) strongly escapes the cocktail of both antibodies
> E406W is not accessible by a single-nucleotide change, which may explain why it was not identified by the Regeneron cocktail
> Mutations at RBD residues that contact antibody do not always mediate escape, and several prominent escape mutations occur at residues not in contact with antibody.
> The maps reveal that mutations escaping the individual antibodies are already present in circulating SARS-CoV-2 strains.

| Science 25JAN21 | Plitidepsin has potent preclinical efficacy against SARS-CoV-2 by targeting the host protein eEF1A | White K.M., et al. International [gtopaper](#) | Therapeutics | Previous author’s work on SARS-CoV-2 highlighted 332 host proteins that are likely to play a role in the viral life cycle of SARS-CoV-2. Drugs modulating these host proteins were tested and those that targeted the eukaryotic translation machinery (eIF4H interacts with SARS-CoV-2 Nsp9) demonstrated particularly potent antiviral activities.

In this study, the eEF1A inhibitor plitidepsin was tested.

Plitidepsin has been clinically developed for the treatment of multiple myeloma with a well-established safety profile and pharmacokinetics.

**Findings:**
> Antiviral activity (IC90 = 0.88 nM) 27.5-fold more potent than remdesivir against SARS-CoV-2 in vitro, limiting toxicity
> The dynamics between the antiviral effects of plitidepsin and remdesivir when used together in vitro suggests that plitidepsin has an additive effect with remdesivir
> The antiviral activity of plitidepsin against SARS-CoV-2 is mediated through inhibition of the known target eEF1A.
> In vivo studies in mouse models of SARS-CoV-2 infection showed a reduction of viral replication in the lungs by two orders of magnitude when using Plitidepsin in prophylactic treatment.

**Conclusions:**
This study establishes plitidepsin as a host-targeted anti-SARS-CoV-2 agent with in vivo efficacy. Phase II/III study to come.
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<tr>
<td>Int J Infect Dis 24JAN2021</td>
<td>Is there a need to widely prescribe antibiotics in patients hospitalized for COVID-19?</td>
<td>Moretto F., et al. France gotopaper</td>
<td>Clinics</td>
<td>Comparison of the characteristics and outcomes between patients with and without antibiotics using propensity score matching. &gt; Among the 222 patients included, 174 (78%) were on antibiotics. &gt; Univariate analysis: patients with antibiotics were significantly older, frailer and with a more severe presentation at admission. &gt; An unfavorable outcome was more frequent in patients with antibiotic therapy (HR = 2.94). &gt; In multivariate analysis and on propensity score, antibiotic therapy was not significantly associated with outcome (HR = 1.612). Antibiotics were frequently prescribed in our study and associated with a more severe presentation at admission. However, receiving antibiotics was not associated with outcome.</td>
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<td>Lancet Resp Med. 22JAN2021</td>
<td>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</td>
<td>The CORIMUNO-19 Collaborative group France gotopaper</td>
<td>Therapeutics</td>
<td>Aim: to determine whether anakinra, a recombinant human IL-1 receptor antagonist, could improve outcomes in patients in hospital with mild-to-moderate COVID-19 pneumonia. - Usual care + anakinra (200 mg twice a day on days 1–3, 100 mg twice on day 4, 100 mg once on day 5) vs usual care only. Two coprimary outcomes: proportion of patients who had died or needed non-invasive or mechanical ventilation by day 4 (ie, a score of &gt;5 on the WHO-CPS) and survival without need for mechanical or non-invasive ventilation (including high-flow oxygen) at day 14. Results &gt; 116 patients recruited: 59 in the anakinra group, and 57 in the usual care group (2 withdrew). Median age was 66 years, 70% were men. &gt; In the anakinra group, 21/59 (36%) patients had a WHO-CPS score &gt;5 at day 4 versus 21/55 (38%) in the usual care group (median posterior absolute risk difference [ARD] −2.5%), with a posterior probability of ARD of less than 0 (ie, anakinra better than usual care) of 61.2%. &gt; At day 14, 28 (47%) patients in the anakinra group and 28 (51%) in the usual care group needed ventilation or died, with a posterior probability of any efficacy of anakinra (hazard ratio [HR] &lt;1) of 54.5% (median posterior HR 0.97). &gt; At day 90, 16 (27%) patients in the anakinra group and 15 (27%) in the usual care group had died. Serious adverse events occurred in 27 (46%) patients in the anakinra group and 21 (38%) in the usual care group (p=0.45). Anakinra did not improve outcomes in patients with mild-to-moderate COVID-19 pneumonia.</td>
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<td>JAMA 21JAN2021</td>
<td>Effect of Bamlanivimab as Monotherapy or in Combination With Etesevimab on Viral Load in Patients With Mild to Moderate COVID-19</td>
<td>Gottlieb R.L., et al. USA gotopaper</td>
<td>Therapeutics</td>
<td>Aim: to determine the effect of bamlanivimab monotherapy and combination therapy with bamlanivimab and etesevimab on SARS-CoV-2 viral load in mild to moderate COVID-19 (BLAZE-1 study). - Bamlanivimab: a single infusion of 700 mg (n = 101), 2800 mg (n = 107), or 7000 mg (n = 101) - Combination treatment: 2800 mg of bamlanivimab and 2800 mg of etesevimab [n = 112] - Placebo (n = 156). Primary end point: change in SARS-CoV-2 log viral load at D11 (±4 dys). &gt; Among the 577 randomized (mean age, 44.7 years; 54.6% women), 533 (92.4%) completed the efficacy evaluation period (day 29). &gt; Change in log viral load from baseline at D11 was −3.72 for 700 mg, −4.08 for 2800 mg, −3.49 for 7000 mg, −4.37 for combination treat, and −3.80 for placebo. Compared with placebo, differences in the change in log viral load at D11 were 0.09 for 700 mg, −0.27 for 2800 mg, 0.31 for 7000 mg, and −0.57 for combination treatment. &gt; Among the secondary outcome measures, differences between each treatment group vs the placebo group were statistically significant for 10 of 84 end points. The proportion of patients with COVID-19–related hospitalizations or ED visits was 5.8% (9 events) for placebo, 1.0% (1 event) for 700 mg, 1.9% (2 events) for 2800 mg, 2.0% (2 events) for 7000 mg, and 0.9% (1 event) for combination treatment. &gt; Immediate hypersensitivity reactions were reported in 9 patients (6 bamlanivimab, 2 combination treatment, and 1 placebo). &gt; No deaths occurred during the study treatment. In nonhospitalized patients with mild to moderate COVID-19, bamlanivimab and etesevimab treatment, compared with placebo, was associated with a reduction in SARS-CoV-2 viral load at day 11.</td>
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**Lancet Infect Dis** 21JAN21

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<tr>
<td><strong>Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial</strong></td>
<td>Ella R., et al.  India <a href="#">gotopaper</a></td>
<td>Vaccines</td>
<td>Background&lt;br&gt;BBV152: whole-virion inactivated SARS-CoV-2 vaccine formulated with a toll-like receptor 7/8 agonist molecule adsorbed to alum (Algel-IMDG) or alum (Algel).&lt;br&gt;&lt;br&gt;<strong>Methods</strong>&lt;br&gt;&gt; Double-blind, multicentre, randomised, controlled phase 1 trial to assess the safety and immunogenicity of BBV152 at 11 hospitals across India. (NCT04471519).&lt;br&gt;&gt; Healthy adults aged 18–55 years Individuals with positive SARS-CoV-2 nucleic acid and/or serology tests excluded.&lt;br&gt;&gt; Participants randomly assigned to receive either one of three vaccine formulations:&lt;br&gt;-3 μg with Algel-IMDG / 6 μg with Algel-IMDG group, 6 μg with Algel / Algel only&lt;br&gt;&gt; Two IM doses at d0 et d14&lt;br&gt;&gt; Primary outcomes: solicited local and systemic reactogenicity events at 2 h and 7 days after vaccination&lt;br&gt;&gt; Secondary outcome: seroconversion&lt;br&gt;&gt; Cell-mediated responses were evaluated by intracellular staining and ELISPOT.&lt;br&gt;&lt;br&gt;<strong>Findings</strong>&lt;br&gt;&gt; 375 participants enrolled: 100 each were randomly assigned to the three vaccine groups, and 75 were randomly assigned to the control group (Algel only).&lt;br&gt;&gt; Solicited local and systemic adverse reactions after 2 doses: 17 (17%; 95% CI 10.5–26.1) participants in the 3 μg with Algel-IMDG group, 21 (21%; 13.8–30.5) in the 6 μg with Algel-IMDG group, 14 (14%; 8.1–22.7) in the 6 μg with Algel group, and ten (10%; 6.9–23.6) in the Algel-only group.&lt;br&gt;&gt; Most common solicited adverse events: injection site pain (17 [%] of 375 participants), headache (13 [%]), fatigue (11 [%]), fever (nine [2%]), and nausea or vomiting (seven [2%]). All solicited adverse events were mild or moderate, and more frequent after the first dose.&lt;br&gt;&gt; One SAE (viral pneumonitis) reported in the 6 μg with Algel group, unrelated to the vaccine.&lt;br&gt;&gt; Seroconversion rates (%) of 87.9, 91.9, and 82.8 in the 3 μg with Algel-IMDG, 6 μg with Algel-IMDG, and 6 μg with Algel groups, respectively.&lt;br&gt;&gt; CD4+ and CD8+ T-cell responses were detected in a subset of 16 participants from both Algel-IMDG groups.&lt;br&gt;<strong>BBV152 led to tolerable safety outcomes and enhanced immune responses. Both Algel-IMDG formulations were selected for phase 2 immunogenicity trials.</strong></td>
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**Science Immunol.** 21JAN2021

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<tr>
<td><strong>Severely ill COVID-19 patients display impaired exhaustion features in SARS-CoV-2-reactive CD8+ T cells</strong></td>
<td>Kusnadi A., et al.  USA <a href="#">gotopaper</a></td>
<td>Immunology</td>
<td>Aim: Understand anti-viral immune responses. Report from data generated by single-cell RNA sequencing of virus-reactive CD8+ T cells from COVID-19 patients with different clinical severity.&lt;br&gt;&lt;br&gt;<strong>Methods:</strong> single-cell transcriptomes of &gt;80,000 virus-reactive CD8+ T cells, obtained using a modified Antigen-Reactive T cell Enrichment (ARTE) assay, from 39 COVID-19 patients and 10 healthy subjects.&lt;br&gt;&gt; Recent reports from COVID-19 patients have suggested the presence of exhaustion-related markers in global CD8+ T cell populations. COVID-19 patients were segregated into two groups based on whether the dominant CD8+ T cell response to SARS-CoV-2 was &quot;exhausted&quot; or not.&lt;br&gt;&gt; CD8+ T-cell exhaustion defined by high expression of two exhaustion-related markers in the dominant T cell population in the tested patient samples.&lt;br&gt;&gt; Analysis of CD8+ T cell exhaustion in COVID-19 patients with different clinical severities.&lt;br&gt;&gt; CD8+ T cells from patients with severe disease showed enrichment of transcripts linked to co-stimulation, pro-survival NF-κB signaling, and anti-apoptotic pathways, suggesting the generation of robust CD8+ T cell memory responses in patients with severe COVID-19 illness&lt;br&gt;&gt; Overall, the single-cell analysis revealed substantial diversity in the nature of CD8+ T cells responding to SARS-CoV-2.</td>
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| Lancet Public Health 20JAN2021 | Quarantine and testing strategies in contact tracing for SARS-CoV-2: a modelling study | Quilty B.J., et al. UK gotopaper | Public Health / Epidemiology | Aim: to assess the merit of testing contacts to avert onward transmission and to replace or reduce the length of quarantine for uninfected contacts.  
> Assuming moderate levels of adherence to quarantine and self-isolation, self-isolation on symptom onset alone can prevent 37% of onward transmission potential from secondary cases.  
> 14 days of post-exposure quarantine reduces transmission by 59%.  
> Quarantine with release after a negative PCR test 7 days after exposure might avert a similar proportion (54%; risk ratio [RR] 0.94), as would quarantine with a negative lateral flow antigen test 7 days after exposure (50%; RR 0.88) or daily testing without quarantine for 5 days after tracing (50%; RR 0.88) if all tests are returned negative.  
Testing might allow for a substantial reduction in the length of, or replacement of, quarantine with a small excess in transmission risk. Decreasing test and trace delays and increasing adherence will further increase the effectiveness of these strategies. |
| BMJ 20JAN21 | Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial | V.C. Veiga, et al. Brazil gotopaper | Therapeutics | Does tocilizumab improve clinical outcomes for patients with severe or COVID-19?  
Methods:  
> Randomised, open label trial (NCT04403685)  
> Nine hospitals in Brazil, 8 May to 17 July 2020.  
> Adults with confirmed Covid-19 who were receiving supplemental oxygen or mechanical ventilation and had abnormal levels of at least two serum biomarkers (C reactive protein, D dimer, lactate dehydrogenase, or ferritin).  
> Interventions Tocilizumab (single intravenous infusion of 8 mg/kg) plus standard care (n=65) versus standard care alone (n=64).  
> Main outcome: clinical status measured at 15 days, analysed as a composite of death or mechanical ventilation (assumption of odds proportionality was not met).  
> The data monitoring committee recommended stopping the trial early, after 129 patients had been enrolled, because of an increased number of deaths at 15 days in the tocilizumab group.  
Findings:  
> 129 patients enrolled (mean age 57 years; 68% men) and all completed follow-up.  
> All patients in the tocilizumab group and two in the standard care group received tocilizumab.  
> 18 of 65 (28%) patients in the tocilizumab group and 13 of 64 (20%) in the standard care group were receiving mechanical ventilation or died at day 15 (odds ratio 1.54).  
> Death at 15 days occurred in 11 (17%) patients in the tocilizumab group compared with 2 (3%) in the standard care group (odds ratio 6.42).  
> Adverse events were reported in 29 of 67 (43%) patients who received tocilizumab and 21 of 62 (34%) who did not receive tocilizumab.  
In patients with severe or critical Covid-19, tocilizumab plus standard care was not superior to standard care alone in improving clinical outcomes at 15 days, and it might increase mortality. |
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<td>Lancet Microbe  19JAN2021</td>
<td>Insight into the practical performance of RT-PCR testing for SARS-CoV-2 using serological data: a cohort study</td>
<td>Zhang Z., et al. China <a href="#">gotopaper</a></td>
<td>Diagnostics</td>
<td>Aim: Assess the practical performance of RT-PCR-based surveillance protocols and determine the extent of undetected SARS-CoV-2 infection in Shenzhen, China. <strong>Methods:</strong> cohort study in Shenzhen, China. All RT-PCR-(-) close contacts (defined as those who lived in the same residence as, or shared a meal, travelled, or socially interacted with, an index case within 2 days before symptom onset) of all RT-PCR- (+) cases of SARS-CoV-2 detected since January, 2020. <strong>Findings:</strong> &gt; Serological samples from 2345 of 4422 RT-PCR (-) close contacts of cases of RT-PCR-confirmed SARS-CoV-2. &gt; 80 of 880 RT-PCR (-) close contacts were positive on total antibody ELISA. &gt; The seropositivity rate with total Ab ELISA among RT-PCR (-) close contacts, adjusted for assay performance, was 4.1%, which was significantly higher than among individuals residing in neighbourhoods with no reported cases &gt; RT-PCR (+) individuals were 8-0 times more likely to report symptoms than those who were RT-PCR (-) but seropositive. &gt; RT-PCR did not detect 48 of 134 infected close contacts, and false-negative rates appeared to be associated with stage of infection. <strong>Even rigorous RT-PCR testing protocols might miss a substantial proportion of SARS-CoV-2 infections, perhaps in part due to difficulties in determining the timing of testing in asymptomatic individuals for optimal sensitivity.</strong></td>
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<td>Ann Intern Med.  19JAN2021</td>
<td>Characteristics, Outcomes, and Trends of Patients With COVID-19–Related Critical Illness at a Learning Health System in the United States</td>
<td>Anesi G.L., et al. USA <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td>Aim: to describe the epidemiology, trends outcomes and care delivery of COVID-19–related critical illness. Single–health system, multihospital retrospective cohort study. <strong>Primary outcome:</strong> all-cause 28-day in-hospital mortality. <strong>Secondary outcomes:</strong> all-cause death at any time, receipt of mechanical ventilation (MV), readmissions. &gt; Among 468 patients with COVID-19–related critical illness, 319 (68.2%) were treated with MV and 121 (25.9%) with vasopressors. &gt; All-cause 28-day in-hospital mortality rate was 29.9%, median ICU stay was 8 days (IQR, 3-17), median hospital stay was 13 days (IQR, 7-25), and all-cause 30-day readmission rate (among nonhospice survivors) was 10.8%. &gt; Mortality decreased over time, from 43.5% (CI, 31.3-53.8) to 19.2% (CI, 11.6-26.7) between the first and last 15-day periods in the core adjusted model, whereas patient acuity and other factors did not change. Among patients with COVID-19–related critical illness admitted to ICUs, mortality seemed to decrease over time despite stable patient characteristics.</td>
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<td>Nature  18JAN2021</td>
<td>Evolution of antibody immunity to SARS-CoV-2</td>
<td>Gaebler C., et al. USA <a href="#">gotopaper</a></td>
<td>Immunology</td>
<td>Aim: Assess the humoral memory response in a cohort of 87 individuals assessed at 1.3 and 6.2 months after infection. <strong>Findings:</strong> &gt; IgM, and IgG anti-SARS-CoV-2 spike protein receptor binding domain (RBD) antibody titres decrease significantly with IgA being less affected. &gt; The number of RBD-specific memory B cells is unchanged. Memory B cells display clonal turnover after 6.2 months, and the antibodies they express have greater somatic hypermutation, increased potency and resistance to RBD mutations. &gt; Analysis of intestinal biopsies obtained from asymptomatic individuals, revealed persistence of SARS-CoV-2 nucleic acids and immunoreactivity in the small bowel (7/14 volunteers). &gt; The memory B cell response to SARS-CoV-2 evolves between 1.3 and 6.2 months after infection in a manner that is consistent with antigen persistence. Individuals who are infected with SARS-CoV-2 could mount a rapid and effective response to the virus upon re-exposure.</td>
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<td>&gt; 385 references, 16 unique studies (5922 unique patients). Significant variability in patient selection, study design, setting and stage of illness at which patients were enrolled.</td>
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<td>&gt; In the primary analysis, the <strong>saliva NAAT</strong> pooled sensitivity was 83.2% (95% credible interval [CrI], 74.7%-91.4%) and the pooled specificity was 99.2% (95% CrI, 98.2%-99.8%). &gt; The <strong>nasopharyngeal swab NAAT</strong> had a sensitivity of 84.8% (95% CrI, 76.8%-92.4%) and a specificity of 98.9% (95% CrI, 97.4%-99.8%).</td>
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<td>&gt; Results were similar in secondary analyses (on peer-reviewed studies, and on ambulatory settings).</td>
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<td><strong>Saliva NAAT diagnostic accuracy is similar to that of nasopharyngeal swab NAAT</strong>, especially in the ambulatory setting, supporting larger-scale research on the use of saliva NAAT as an alternative.</td>
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<td><strong>Methods:</strong> &gt; Multicenter, placebo-controlled, phase 1–2a trial, randomised &gt; Healthy adults: between the ages of 18 and 55 years (cohort 1) and those 65 years of age or older (cohort 3) (≥ 805 participants) &gt; Cohorte 1 &amp; 3: receive the Ad26.COV2.S vaccine at a dose of 5x1010 viral particles (low dose) or 1x1011 viral particles (high dose) per milliliter or placebo in a single-dose or two-dose schedule &gt; <strong>Cohorte 2:</strong> Longer-term data comparing a single-dose regimen with a two-dose regimen are being collected</td>
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<td><strong>Findings related to safety &amp; reactogenicity</strong> &gt; After first vaccine dose in cohorts 1 &amp; 3 and after second dose in cohort 1: &gt; Most frequent solicited adverse events (AE) were fatigue, headache, myalgia, and injection-site pain &amp; most frequent systemic AE = fever &gt; Systemic adverse events were less common in cohort 3 than in cohort 1 and in those who received the low vaccine dose than in those who received the high dose. &gt; Reactogenicity was lower after the second dose.</td>
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<td><strong>Findings related to immunogenicity profiles</strong> &gt; Neutralizing-antibody titers against wild-type virus were <strong>detected in 90%</strong> 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 in cohort 1a. &gt; <strong>Titers remained stable until at least day 71.</strong> A second dose provided an increase in the titer by a factor of 2.6 to 2.9 (GMT, 827 to 1266). Spike-binding antibody responses were similar to neutralizing-antibody responses. &gt; On day 14, CD4+ T-cell responses were detected in 76 to 83% of the participants in cohort 1 and in 60 to 67% of those in cohort 3, with a clear skewing toward type 1 helper T cells. CD8+ T-cell responses were robust overall but lower in cohort 3. <strong>The safety and immunogenicity profiles of Ad26.COV2.S support further development of this vaccine candidate.</strong></td>
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primary outcome: death within 30 days after plasma transfusion.  
> of the 3082 patients included in the analysis, death within 30 days after plasma transfusion occurred in 115 of 515 patients (22.3%) in the high-titer group, 549 of 2006 patients (27.4%) in the medium-titer group, and 166 of 561 patients (29.6%) in the low-titer group.  
> association of anti-SARS-CoV-2 antibody levels with risk of death from Covid-19 was moderated by mechanical ventilation status --> a lower risk of death within 30 days in the high-titer group than in the low-titer group was observed among patients who had not received mechanical ventilation before transfusion (relative risk, 0.66), and no effect on the risk of death was observed among patients who had received mechanical ventilation (relative risk, 1.02).  
In patients hospitalized with Covid-19 who were not receiving mechanical ventilation, transfusion of plasma with higher anti-SARS-CoV-2 IgG antibody levels was associated with a lower risk of death than transfusion of plasma with lower antibody levels. |
| Science 12JAN2021 | Mosaic nanoparticles elicit cross-reactive immune responses to zoonotic coronaviruses in mice | Cohen A.A., et al. USA [gotopaper](#) | Immunology | Construction of homotypic nanoparticles displaying the RBD of SARS-CoV-2 or co-displaying SARS-CoV-2 RBD along with RBDs from animal betacoronaviruses (mosaic nanoparticles; 4-8 distinct RBDs).  
> Mice immunized with RBD-nanoparticles, but not soluble antigen, elicited cross-reactive binding and neutralization responses.  
> Mosaic-RBD-nanoparticles elicited antibodies with superior cross-reactive recognition of heterologous RBDs compared to sera from immunizations with homotypic SARS-CoV-2–RBD-nanoparticles or COVID-19 convalescent human plasmas.  
> sera from mosaic-RBD–immunized mice neutralized heterologous pseudotyped coronaviruses equivalently or better after priming than sera from homotypic SARS-CoV-2–RBD-nanoparticle immunizations -->  
> no immunogenicity loss against particular RBDs resulting from co-display.  
A single immunization with mosaic-RBD-nanoparticles provides a potential strategy to simultaneously protect against SARS-CoV-2 and emerging zoonotic coronaviruses. |
methods: Analysis of viral loads, neutralizing antibody titers (nAb), detection of the subgenomic RNAs from 129 hospitalized individuals diagnosed with COVID-19 by RT-PCR  
findings:  
> infectious virus shedding was detected by virus cultures in 23/129 patients (17.8%) hospitalized with COVID-19.  
> the median duration of shedding infectious virus is 8 days post onset of symptoms and drops below 5% after 15.2 days post onset of symptoms.  
> The probability of isolating infectious virus was less than 5% when the nAb titer was 1:80 or higher  
> a serum nAb titre of at least 1:20 (OR of 0.01) is independently associated with non-infectious SARS-CoV-2.  
> quantitative viral RNA load assays and serological assays could be used in test-based strategies to discontinue or de-escalate infection prevention and control precautions.  
> Detection of viral subgenomic RNA correlated poorly with shedding of infectious virus |
The Lancet

**6-month consequences of COVID-19 in patients discharged from hospital: a cohort study**

Huang C.H., *et al.*

Public Health / Epidemiology - Long COVID

**Aim:** to describe the long-term health consequences of patients with COVID-19 who have been discharged from hospital and investigate the associated risk factors.

> 1733 discharged patients with COVID-19 enrolled: median age of 57 years and 52% were men. The median follow-up time after symptom onset was 186·0 days.

> **Fatigue or muscle weakness** (63%, 1038/1655) and **sleep difficulties** (26%, 437/1655) were the most common symptoms. **Anxiety or depression** was reported among 23% (367/1617) of patients.

> The proportions of median 6-min walking distance less than the lower limit of the normal range were 24% for those at severity scale 3, 22% for severity scale 4, and 29% for severity scale 5–6.

> The corresponding proportions of patients with **diffusion impairment** were 22% for severity scale 3, 29% for scale 4, and 56% for scale 5–6, and median CT scores were 3·0 for severity scale 3, 4·0 for scale 4, and 5·0 for scale 5–6.

> After multivariable adjustment, patients showed an odds ratio (OR) 1·61 for scale 4 versus scale 3 and 4·60 for scale 5–6 versus scale 3 for diffusion impairment; OR 0·88 for scale 4 versus scale 3 and OR 1·77 for scale 5–6 versus scale 3 for anxiety or depression, and OR 0·74 for scale 4 versus scale 3 and 2·69 for scale 5–6 versus scale 3 for fatigue or muscle weakness.

> Of 94 patients with **blood antibodies** tested at follow-up, the seropositivity (96·2% vs 58·5%) and median titres (19·0 vs 10·0) of the neutralising antibodies were significantly lower compared with at the acute phase.

> 107 of 822 participants without acute kidney injury and with **eGFR** 90 mL/min per 1·73 m2 or more at acute phase had **eGFR** less than 90 mL/min per 1·73 m2 at follow-up.

**At 6 months after acute infection, COVID-19 survivors were mainly troubled with fatigue or muscle weakness, sleep difficulties, and anxiety or depression. Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations.**

JAMA Netw. Open

**SARS-CoV-2 Transmission From People Without COVID-19 Symptoms**


Public Health/Epidemiology

**Aim:** to assess the proportion of SARS-CoV-2 transmissions in the community that likely occur from persons without symptoms.

Baseline assumptions for the model: incubation period at 5 days, infectious period of 10 days, peak infectiousness occurred at the median of symptom onset, 30% of individuals with infection never develop symptoms and are 75% as infectious as those who do develop symptoms. This implies that persons with infection who never develop symptoms may account for approximately 24% of all transmission.

> In this base case, **59% of all transmission came from asymptomatic transmission**, comprising 35% from presymptomatic individuals and 24% from individuals who never develop symptoms.

> Under a broad range of values for each assumption, **at least 50% of new infections** was estimated to have originated from exposure to individuals with infection but without symptoms.

**In this decision analytical model, transmission from asymptomatic individuals was estimated to account for more than half of all transmissions.** Measures such as wearing masks, hand hygiene, social distancing, and strategic testing of people who are not ill will be foundational to slowing the spread of COVID-19.
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> Retrospective cohort study, adults with acute inpatient hospital admission (March - August 2020)  
> confirmed or suspected COVID-19  
> chronic immunosuppression was defined as prescriptions for immunosuppressive drugs current at the time of admission.  
> Outcomes: mechanical ventilation, in-hospital mortality, and length of stay.  
Findings:  
> 2121 patients admitted with laboratory-confirmed (1967; 93%) or suspected (154; 7%) COVID-19  
> median age of 55 years (40–67).  
> of these, 108 (5%) were classified as immunosuppressed before COVID-19, primarily with prednisone (>7.5 mg/day), tacrolimus, or mycophenolate mofetil.  
> Among the entire cohort, 311 (15%) received mechanical ventilation  
> The median (interquartile range) length of stay was 5.2 (2.5–10.6) days  
> 1927 (91%) survived to discharge  
> no significant differences in the risk of mechanical ventilation, in-hospital mortality or length of stay among individuals with immunosuppression and counterparts.  
Chronic use of immunosuppressive drugs was neither associated with worse nor better clinical outcomes among adults hospitalized with COVID-19 in this setting. |
> Diagnostic study conducted in a COVID-19 screening center in France (March-April, 2020)  
> Participants: health care workers or outpatients with symptoms or with close contact with an index case.  
> Participants interviewed to ascertain their symptoms and then Clinical Olfactory Dysfunction Assessment (CODA) (ad hoc test developed for a simple and fast evaluation of olfactory function).  
Assessment followed a standardized procedure in which participants identified and rated the intensity of 3 scents (lavender, lemongrass, and mint) to achieve a summed score ranging from 0 to 6. The COVID-19 status was assessed using RT PCR.  
Findings:  
> 809 participants, female to male sex ratio: 2.8. Mean age: 41.8 years (18-94).  
> Asymptomatic or mild disease patients; 58 (7.2%) tested positive for SARS-CoV-2.  
> Chemosensory dysfunction was reported by 20 of 58 participants (34.5%) with confirmed COVID-19 vs 29 of 751 participants (3.9%) who tested negative for COVID-19  
> Olfactory dysfunction, either self-reported or clinically ascertained (CODA score ≤3), yielded similar sensitivity and specificity for COVID-19 diagnosis.  
> Concordance was high between reported and clinically tested olfactory dysfunction, with a Gwet AC1 of 0.95 (95% CI, 0.93-0.97).  
> Of 19 participants, 15 (78.9%) with both reported olfactory dysfunction and a CODA score of 3 or lower were confirmed to have COVID-19.  
> The CODA score also revealed 5 of 19 participants (26.3%) with confirmed COVID-19 who had previously unperceived olfactory dysfunction.  
Olfactory dysfunction was suggestive of COVID-19, particularly when clinical testing confirmed anamnesis. However, normal olfaction was most common among patients with COVID-19. |
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| NEJM 07JAN2021   | Antibody Status and Incidence of SARS-CoV-2 Infection in Health Care Workers | Lumley S.F., et al. UK gotopaper | Immunology | > Study relationship between the presence of antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the risk of subsequent reinfection.  
> Incidence of SARS-CoV-2 infection confirmed by polymerase chain reaction (PCR) in seropositive and seronegative HCW attending testing of asymptomatic and symptomatic staff at Oxford University Hospitals.  
> Baseline antibody status was determined by anti-spike (primary analysis) and anti-nucleocapsid IgG assays.  
> Followed for up to 31 weeks.  
> 12,541 health care workers participated having anti-spike IgG measured.  
Findings:  
> A total of 223 anti-spike–seronegative health care workers had a positive PCR test (1.09 per 10,000 days at risk), 100 during screening while they were asymptomatic and 123 while symptomatic, whereas 2 anti-spike–seropositive health care workers had a positive PCR test (0.13 per 10,000 days at risk), and both workers were asymptomatic when tested (adjusted incidence rate ratio, 0.11; 95% confidence interval, 0.03 to 0.44; P = 0.002).  
> The presence of anti-spike or anti-nucleocapsid IgG antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection in the ensuing 6 months. |
| NEJM 06JAN21     | Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults | Libster R., et al. Argentina/USA gotopaper | Therapeutics | Convalescent plasma administration at early COVID19 patients  
> Randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against SARS-CoV-2 in older adult patients within 72 hours after the onset of mild Covid-19 symptoms.  
> 160 patients randomized  
Primary end point: severe respiratory disease (respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both)  
Trial stopped early at 76% of projected sample size because a decrease in Covid-19.  
Findings:  
> Severe respiratory disease developed in 13 of 80 patients (16%) who received convalescent plasma and 25 of 80 patients (31%) who received placebo (relative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; P=0.03), with a relative risk reduction of 48%.  
> No solicited adverse events were observed.  
Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19. |
| Nature 06JAN2021 | A longitudinal study of SARS-CoV-2-infected patients reveals a high correlation between neutralizing antibodies and COVID-19 severity | Legros V., et al. France gotopaper | Immunology | Cohort study of 140 SARS-CoV-2 qPCR-confirmed infections, including patients with mild symptoms and more severe forms (intensive care included).  
The neutralizing antibody (nAb) responses were assessed using either live SARS-CoV-2 particles or retroviruses pseudotyped with the SARS-CoV-2 S viral surface protein (Spike).  
Findings:  
> ICU patients displayed high nAb activity compared to other groups with milder disease symptoms. nAb titers correlated strongly with disease severity and with anti-spike IgG levels.  
The anti-S IgG response can be used as a marker of neutralizing activity in individuals.  
> Serum from individuals diagnosed with OC43, 229E, NL63, and HKU1 coronavirus infections but not infected with SARS-CoV-2 failed to cross-neutralize SARS-CoV-2 suggesting the absence of cross-neutralization between SARS-CoV-2 and endemic coronaviruses.  
The D614G mutation did not affect the nAb activity of the serum samples from our cohort indicating that this highly prevalent mutation is not associated with SARS-CoV-2 resistance to neutralization. |
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<td>Science 06JAN2021</td>
<td>Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection</td>
<td>Dan J.M., et al. USA gotopaper</td>
<td>Immunology</td>
<td>&gt; Understanding immune memory to SARS-CoV-2 and for assessing the likely future course of the COVID-19 pandemic.</td>
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<td>&gt; 2254 samples from 188 COVID-19 cases, including 43 samples at ≥ 6 months post-infection</td>
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<td><strong>Findings</strong></td>
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<td>&gt; IgG to the Spike protein was relatively stable over 6+ months</td>
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<td>&gt; Spike-specific memory B cells were more abundant at 6 months than at 1 month post symptom onset</td>
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<td>&gt; SARS-CoV-2-specific CD4+ T cells and CD8+ T cells declined with a half-life of 3-5 months</td>
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<td>Each component of SARS-CoV-2 immune memory exhibited distinct kinetics</td>
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<td>Clin Infect Dis. 06JAN2021</td>
<td>The duration, dynamics and determinants of SARS-CoV-2 antibody responses in individual healthcare workers</td>
<td>Lumley S.F., et al. USA gotopaper</td>
<td>Immunology</td>
<td>&gt; SARS-CoV-2 IgG antibody measurements used to estimate the proportion of a population exposed or infected and may be informative about the risk of future infection</td>
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<td>&gt; 6 months of data from a longitudinal seroprevalence study of 3276 UK healthcare workers with measurements of SARS-CoV-2 anti-nucleocapsid and anti-spike IgG</td>
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<td>&gt; Interval censored survival analysis was used to investigate the duration of detectable responses</td>
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<td>&gt; Bayesian mixed linear models were used to investigate anti-nucleocapsid waning</td>
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<td>&gt; SARS-CoV-2 anti-nucleocapsid antibodies wane within months (Anti-nucleocapsid IgG levels rose to a peak at 24 (95% credibility interval, CrI 19-31) days post first PCR-positive test, before beginning to fall), and faster in younger adults and those without symptoms</td>
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<td>&gt; Higher maximum observed anti-nucleocapsid titres were associated with longer estimated antibody half-lives</td>
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<td>&gt; Anti-spike IgG remains stably detected.</td>
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<td>Ongoing longitudinal studies are required to track the long-term duration of antibody levels and their association with immunity to SARS-CoV-2 reinfection</td>
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<td>JAMA Netw. 05JAN2021</td>
<td>Estimation of US SARS-CoV-2 Infections, Symptomatic Infections, Hospitalizations, and Deaths Using Seroprevalence Surveys</td>
<td>Angulo F.J., et al. USA gotopaper</td>
<td>Public Health / Epidemiology</td>
<td>Cross-sectional study of respondents of all ages, data from 4 regional and 1 nationwide Centers for Disease Control and Prevention (CDC) seroprevalence surveys between April and August 2020 were used to estimate infection and symptomatic underreporting multipliers.</td>
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<td><strong>Main Outcomes:</strong> SARS-CoV-2 infections, symptomatic infections, hospitalizations, and deaths.</td>
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<td><strong>Findings:</strong></td>
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<td>&gt; 14.3% of the US population was infected with SARS-CoV-2 and 8.6% had a symptomatic infection, with an infection hospitalization ratio of 2.0% and symptomatic fatality ratio of 1.1% through Nov 15, 2020.</td>
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<td>The US population remains a long way from herd immunity. The number of estimated COVID-19 deaths is also remarkably more than the reported deaths in the US through Nov 15, 2020, supporting the conclusion that approximately 35% of COVID-19 deaths are not reported.</td>
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<td><strong>Limitations:</strong> Estimate the COVID-19 disease burden in the US using underreporting multipliers derived from the 10 specific states may not be nationally representative.</td>
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| BMJ Thorax 05JAN2021 | Current smoking and COVID-19 risk: results from a population symptom app in over 2.4 million people | Hopkinson N.S., et al. UK | Public Health / Epidemiology | Main study outcome: development of ‘classic’ symptoms of COVID-19 during the pandemic defined as fever, new persistent cough and breathlessness and their association with current smoking.  
> UK users of the Zoe COVID-19 Symptom Study app provided baseline data including demographics, anthropometrics, smoking status and medical conditions, and were asked to log their condition daily.  
> Participants who reported that they did not feel physically normal were then asked by the app to complete a series of questions, including 14 potential COVID-19 symptoms and about hospital attendance.  
> The number of concurrent COVID-19 symptoms was used as a proxy for severity and the pattern of association between symptoms was also compared between smokers and non-smokers.  
Findings: Data on 2,401,982 participants, mean (SD) age 43.6 (15.1) years, 63.3% female, overall smoking prevalence 11.0%.  
> 834,437 (35%) participants reported being unwell and entered one or more symptoms.  
> Current smokers were more likely to report symptoms suggesting a diagnosis of COVID-19; classic symptoms adjusted OR (95% CI) 1.14 (1.10 to 1.18); >5 symptoms 1.29 (1.26 to 1.31); >10 symptoms 1.50 (1.42 to 1.58).  
> The pattern of association between reported symptoms did not vary between smokers and non-smokers.  
Data are consistent with people who smoke being at an increased risk of developing symptomatic COVID-19. |
Main Outcome: Death due to any cause within 30 days of the 1st positive SARS-CoV-2 test result.  
Findings:  
> Compared with residents aged 75 to 79 years, the odds of death were 1.46 times higher for residents aged 80 to 84 years, 1.59 times higher for residents aged 85 to 89 years, and 2.14 times higher for residents aged 90 years or older.  
> Women had lower risk for 30-day mortality than men (odds ratio 0.69).  
> Comorbidities associated with 30-day mortality: diabetes (OR, 1.21) and chronic kidney disease (OR, 1.33).  
> Fever (OR, 1.66), shortness of breath (OR, 2.52), tachycardia (OR, 1.31), and hypoxia (OR, 2.05).  
> Compared with intact cognitively residents: the odds of death among residents with moderate cognitive impairment (CI) were 2.09 times higher, and 2.79 times higher for residents with severe CI.  
> Compared with residents with no or limited impairment in physical function (IPF), the odds of death among residents with moderate IPF were 1.49 times higher, and 1.64 times higher among residents with severe IPF.  
Once infected, those with baseline functional limitations, cognitive impairment, and disease severity are at heightened risk for mortality. |
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<tr>
<td>Science 04JAN2021</td>
<td>Neutralizing antibody titres in SARS-CoV-2 infections</td>
<td>Lau E.H.Y., et al. USA <a href="#">gotopaper</a></td>
<td>Immunology</td>
<td><strong>Characterization of neutralizing antibody persistence in infected patients.</strong> Testing of 293 sera from an observational cohort of 195 reverse transcription polymerase chain reaction (RT-PCR) confirmed SARS-CoV-2 infections collected from 0 to 209 days after onset of symptoms. <strong>Findings:</strong> &gt; Of 115 sera collected ≥61 days after onset of illness tested using plaque reduction neutralization (PRNT) assays, 99.1% remained seropositive for both 90% (PRNT90) and 50% (PRNT50) neutralization endpoints. &gt; PRNT50 titres dropping to the detection limit of a titre of 1:10 for severe, mild and asymptomatic patients takes at least 372, 416 and 133 days &gt; At day 90 after onset of symptoms (or initial RT-PCR detection in asymptomatic infections), it took 69, 87 and 31 days for PRNT50 antibody titres to decrease by half (T1/2) in severe, mild and asymptomatic infections, respectively. &gt; Patients with severe disease had higher peak PRNT90 and PRNT50 antibody titres than patients with mild or asymptomatic infections. &gt; Age did not appear to compromise antibody responses, even after accounting for severity. <strong>SARS-CoV-2 infection elicits robust neutralizing antibody titres in most individuals.</strong></td>
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<td>Nature Commun. 04JAN2021</td>
<td>Dose-dependent response to infection with SARS-CoV-2 in the ferret model and evidence of protective immunity</td>
<td>Ryan K.A., et al. UK <a href="#">gotopaper</a></td>
<td>Immunology / Preclinical model</td>
<td><strong>Findings:</strong> &gt; Understand if ferrets are a suitable species for a model of human SARS-CoV-2 infection &gt; Dose titration study of SARS-CoV-2 in the ferret model &gt; Animals are challenged intranasally with a range of titres of SARS-CoV-2 (5 × 10², 5 × 10⁴ and 5 × 10⁶ pfu) in 1 ml volume <strong>Findings</strong> &gt; After a high (5 × 10⁶ pfu) and medium (5 × 10⁴ pfu) dose of virus is delivered, intranasally, viral RNA shedding in the upper respiratory tract (URT) is observed in 6/6 animals &gt; Only 1/6 ferrets show similar signs after low dose (5 × 10² pfu) challenge &gt; Ferrets re-challenged, after virus shedding ceased, are fully protected from acute lung pathology &gt; The endpoints of URT viral RNA replication &amp; distinct lung pathology are observed most consistently in the high dose group &gt; This ferret model of SARS-CoV-2 infection presents a mild clinical disease</td>
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<td>&gt; cohort of 99 patients with COVID-19</td>
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<td>&gt; Expression and distribution of ACE2 and lung progenitor cells examinations: combination of public single-cell RNA-seq datasets, lung biopsies, and ex vivo infection of lung tissues with SARS-CoV-2 pseudovirus in children and older adults</td>
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<td>&gt; Compared to children, <strong>ACE2 positive cells are generally decreased in older adults</strong> and mainly presented in the lower pulmonary tract (alveolar region) and rarely in airway regions in the older adults (<strong>p &lt; 0.01</strong>).</td>
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<td>&gt; The lung progenitor cells are also decreased. These risk factors may impact disease severity and recovery from pneumonia caused by SARS-CoV-2 infection in older patients.</td>
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<td>NEJM 30DEC2020</td>
<td>Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine</td>
<td>Baden L.R., et al. USA <a href="#">gotopaper</a></td>
<td>Vaccine</td>
<td><strong>Phase 3 randomized, observer-blinded, placebo-controlled trial conducted at 99 centers across the United States.</strong></td>
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<td>&gt; <strong>Population:</strong> Persons at high risk for SARS-CoV-2 infection or its complications</td>
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<td>&gt; <strong>Intervention:</strong> 2 administration of vaccine (100 μg each) or placebo 28 days apart. 30,420 volunteers enrolled; 15,210 participants in each group</td>
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<td>&gt; <strong>Primary end point:</strong> prevention of Covid-19 illness with onset at least 14 days after the second injection in participants who had not previously been infected with SARS-CoV-2.</td>
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<td><strong>Findings</strong></td>
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<td>&gt; More than 96% of participants received both injection</td>
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<td>&gt; 2.2% had evidence (serologic, virologic, or both) of SARS-CoV-2 infection at baseline.</td>
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<td>&gt; Symptomatic Covid-19 illness was confirmed in 185 participants in the placebo group (56.5 per 1000 person-years; 95% confidence interval [CI], 48.7 to 65.3) and in 11 participants in the mRNA-1273 group (3.3 per 1000 person-years; 95% CI, 1.7 to 6.0);</td>
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<td>&gt; Vaccine efficacy was 94.1% (95% CI, 89.3 to 96.8%; ( P &lt; 0.001 )).</td>
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<td>&gt; Efficacy was similar across key secondary analyses, including assessment 14 days after the first dose, analyses that included participants who had evidence of SARS-CoV-2 infection at baseline, and analyses in participants 65 years of age or older.</td>
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<td>&gt; Severe Covid-19 occurred in 30 participants, with one fatality; all 30 were in the placebo group.</td>
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<td>&gt; Moderate, transient reactogenicity after vaccination occurred more frequently in the mRNA-1273 group.</td>
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<td>&gt; Serious adverse events were rare, and the incidence was similar in the two groups.</td>
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<td>The mRNA-1273 vaccine showed 94.1% efficacy at preventing Covid-19 illness, including severe disease. Aside from transient local and systemic reactions, no safety concerns were identified.</td>
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<td>Science 23DEC2020</td>
<td>Afucosylated IgG characterizes enveloped viral responses and correlates with COVID-19 severity</td>
<td>Larsen M.D., et al. Netherlands gotopaper</td>
<td>Immunology</td>
<td>Analysis of afucosylated IgG role in immune responses to enveloped viruses, including COVID-19. Afucosylated IgG (~6% of total IgG in humans) are specifically formed against enveloped viruses but generally not against other antigens. This mediates stronger FcγRIIIa responses, but also amplifies brewing cytokine storms and immune-mediated pathologies. Findings: &gt; Critically ill COVID-19 patients had high levels of afucosylated IgG antibodies against SARS-CoV-2, amplifying pro-inflammatory cytokine release and acute phase responses. &gt; Afucosylation may potentially help predict disease trajectories and guide future treatments aimed at minimizing FcγRIIIa stimulus. Attempts to generate high-titer immunoglobulin treatments should preferably use plasma enriched in fucosylated anti-SARS-CoV-2 Abs. This may avoid the escalation of symptoms and promote virus neutralization in patients preferentially before developing afucosylated IgG responses.</td>
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<tr>
<td>Science Immunol. 23DEC2020</td>
<td>Discordant neutralizing antibody and T cell responses in asymptomatic and mild SARS-CoV-2 infection</td>
<td>Reynolds C.J., et al. UK gotopaper</td>
<td>Immunology</td>
<td>Analysis of T cell and neutralizing antibody responses in 136 healthcare workers (HCW) 16-18 weeks after UK lockdown, 76 of whom had mild/asymptomatic SARS-CoV-2 infection captured by serial sampling. &gt; Neutralizing antibodies (nAb) were present in 89% of previously infected HCW. &gt; T cell responses tended to be lower following asymptomatic infection than in those reporting case-definition symptoms of COVID-19, while nAb titers were maintained irrespective of symptoms. &gt; T cell and antibody responses were sometimes discordant. 11% lacked nAb and had undetectable T cell responses to spike protein but had T cells reactive with other SARS-CoV-2 antigens. The majority of individuals with mild or asymptomatic SARS-CoV-2 infection carry nAb complemented by multispecific T cell responses at 16-18 weeks after infection.</td>
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<td>Cell Host Microbe 23DEC2020</td>
<td>Intranasal vaccination with a lentiviral vector protects against SARS-CoV-2 in preclinical animal models</td>
<td>Ku M.W., et al. France gotopaper</td>
<td>Vaccine</td>
<td>Vaccine candidate against (COVID-19) based on a lentiviral vector (LV) eliciting neutralizing antibodies against the Spike glycoprotein of SARS-CoV-2. Findings: &gt; Systemic vaccination by this vector in transgenic mice expressing the SARS-CoV-2 receptor hACE2 by transduction of respiratory tract cells by an adenoviral vector, confers only partial protection despite highlevels of serum neutralizing activity. &gt; Eliciting an immune response in the respiratory tract through an intranasal boost results in a &gt;3 log10 decrease in the lung viral loads and reduces local inflammation. &gt; Both integrative and non-integrative LV platforms display strong vaccine efficacy and inhibit lung dele-terious injury in golden hamsters, which are naturally permissive to SARS-CoV-2 replication and closely mirror human COVID-19 physiopathology.</td>
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| Science Immunol. 23DEC2020 | Discordant neutralizing antibody and T cell responses in asymptomatic and mild SARS-CoV-2 infection | Reynolds C.J., et al. UK gotopaper | Immunology | Analysis of T cell and neutralizing antibody responses in 136 healthcare workers (HCW) 16-18 weeks after UK lockdown, 76 of whom had mild/asymptomatic SARS-CoV-2 infection captured by serial sampling.  
> Neutralizing antibodies (nAb) were present in 89% of previously infected HCW.  
> T cell responses tended to be lower following asymptomatic infection than in those reporting case-definition symptoms of COVID-19, while nAb titers were maintained irrespective of symptoms.  
> T cell and antibody responses were sometimes discordant. 11% lacked nAb and had undetectable T cell responses to spike protein but had T cells reactive with other SARS-CoV-2 antigens. The majority of individuals with mild or asymptomatic SARS-CoV-2 infection carry nAb complemented by multispecific T cell responses at 16-18 weeks after infection. |
> 127 pregnant women enrolled, 64 with RT-PCR results positive for SARS-CoV-2 and 63 with RT-PCR results negative for SARS-CoV-2.  
> Of women with SARS-CoV-2 infection, 23 (36%) were asymptomatic, 22 (34%) had mild disease, 7 (11%) had moderate disease, 10 (16%) had severe disease, and 2 (3%) had critical disease.  
> In viral load analyses among 107 women, there was no detectable viremia in maternal or cord blood and no evidence of vertical transmission.  
> Among 77 neonates tested in whom SARS-CoV-2 antibodies were quantified in cord blood, 1 had detectable IgM to nucleocapsid.  
> Among 88 placentas tested, SARS-CoV-2 RNA was not detected in any.  
> In antibody analyses among 37 women, anti–receptor binding domain IgG was detected in 24 women (65%) and anti-nucleocapsid was detected in 26 women (70%).  
> Mother-to-neonate transfer of anti–SARS-CoV-2 antibodies was significantly lower than transfer of anti-influenza hemagglutinin A antibodies (mean [SD] cord-to-maternal ratio: anti–receptor binding domain IgG, 0.72 [0.57]; anti-nucleocapsid, 0.74 [0.44]; anti-influenza, 1.44 [0.80]).  
> Nonoverlapping placental expression of SARS-CoV-2 receptors angiotensin-converting enzyme 2 and transmembrane serine protease 2 was noted.  
> In this cohort study, there was no evidence of placental infection or definitive vertical transmission of SARS-CoV-2. Transplacental transfer of anti-SARS-CoV-2 antibodies was inefficient. Lack of viremia and reduced coexpression and colocalization of placental ACE2 and transmembrane serine protease 2 may serve as protective mechanisms against vertical transmission. |
> 36 blood samples from 25 COVID-19 patients between 4 and 242 days post-symptom onset including 11 paired samples.  
> While serum IgG to RBD and NCP was identified in all patients, antibody levels began declining at 20 days post-symptom onset.  
> RBD- and NCP-specific Bmem cells predominantly expressed IgM+ or IgG+ and continued to rise until 150 days. RBD-specific IgG+ Bmem were predominantly CD27+, and numbers significantly correlated with circulating follicular helper T cell numbers. The SARS-CoV-2 antibody response contracts in convalescence with persistence of RBD- and NCP-specific Bmem cells. |
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| NEJM 22DEC2020   | A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19 | ACTIV-3/TICO LY-CoV555 Study Group International [gotopaper](#) | Therapeutics | Effect of LY-CoV555 (Eli Lilly mAb) antibody in patients who are hospitalized with Covid-19. LY-CoV555 has already been associated with a decrease in viral load and the frequency of hospitalizations or emergency department visits among outpatients with.  
METHODS  
> Hospitalized patients who had Covid-19 without end-organ failure  
> LY-CoV555 (700 mg and 1h infusion) or matching placebo + high-quality supportive care as background therapy, including the antiviral drug remdesivir and, when indicated, supplemental oxygen and glucocorticoids.  
Primary outcome: sustained recovery during a 90-day period, as assessed in a time-to-event analysis.  
**RESULTS**  
> On October 26, 2020, the trial DSMB recommended stopping enrollment for futility after randomization and infusion of 314 patients (163 LY-CoV555 and 151 placebo)  
> Median interval since onset of symptoms: 7 days (interquartile range, 5 to 9).  
> At day 5, 81 patients (50%) in the LY-CoV555 group and 81 (54%) in the placebo group were in one of the two most favorable categories of the pulmonary outcome.  
> Across the seven categories, the odds ratio of being in a more favorable category in the LY-CoV555 group than in the placebo group was 0.85 (95% confidence interval [CI], 0.56 to 1.29; P=0.45).  
> The percentage of patients with the primary safety outcome (a composite of death, serious adverse events, or clinical grade 3 or 4 adverse events through day 5) was similar in the LY-CoV555 group and the placebo group (19% and 14%, respectively; odds ratio, 1.56; 95% CI, 0.78 to 3.10; P=0.20).  
> The rate ratio for a sustained recovery was 1.06 (95% CI, 0.77 to 1.47).  
**CONCLUSIONS**  
Monoclonal antibody LY-CoV555, when coadministered with remdesivir, did not demonstrate efficacy among hospitalized patients who had Covid-19 without end-organ failure. | |
**Methods:**  
Multiplex serological assay measuring IgG and IgM antibody responses to 7 SARS-CoV-2 spike or nucleoprotein antigens, 2 antigens for the nucleoproteins of the 229E and NL63 seasonal coronaviruses, and 3 non-coronavirus antigens. Machine learning classifiers were trained with the multiplex data to classify individuals with previous SARS-CoV-2 infection.  
> IgG antibody responses to trimeric spike protein (Stri) identified individuals with previous SARS-CoV-2 infection with 91·6% sensitivity and 99·1% specificity. Using a serological signature of IgG and IgM to multiple antigens, it was possible to identify infected individuals with 98·8% sensitivity and 99·3% specificity.  
> It is estimated that 1 year after infection, a monoplex assay with optimal anti-Stri IgG cutoff has 88·7% sensitivity and that a four-antigen multiplex assay can increase sensitivity to 96·4%.  
> When applied to population-level serological surveys, statistical analysis of multiplex data allows estimation of seroprevalence levels less than 2%, below the false-positivity rate of many other assays.  
Serological signatures based on antibody responses to multiple antigens can provide accurate and robust serological classification of individuals with previous SARS-CoV-2 infection. | |
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<tr>
<td>Nature 21DEC2020</td>
<td>Underdetection of COVID-19 cases in France threatens epidemic control</td>
<td>Pullano G., et al. France gotopaper</td>
<td>Public Health / Epidemiology</td>
<td><strong>Aim:</strong> to estimate the rate of detection of COVID-19 symptomatic cases in France after lockdown by virological and participatory syndromic surveillance data coupled with mathematical transmission models calibrated to regional hospitalizations.</td>
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<td>&gt; Around 90,000 incident symptomatic infections, corresponding to 9 out 10 cases, <strong>were not ascertained by the surveillance system</strong> in France during the respective study periods. (May 11 - June 28 2020), although the test positivity rate did not exceed WHO recommendations (5%).</td>
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<td>&gt; The median detection rate increased from <strong>7% to 38% over time</strong>, with large regional variations, owing to a strengthening of the system as well as a decrease of epidemic activity.</td>
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<td>&gt; According to participatory surveillance data, only 31% of individuals with COVID-19-like symptoms consulted a doctor in the study period. <strong>Encouraging awareness and same-day healthcare-seeking behaviour</strong> in suspect cases is critical to improve detection.</td>
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<td>&gt; The capacity of the system remained insufficient even at the low levels of viral circulation achieved after lockdown, and was predicted to deteriorate rapidly with increasing epidemic activity.</td>
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<td>Substantially more aggressive, targeted, and efficient testing with easier access is required to act as a pandemic-fighting tool.</td>
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<td><strong>RESULTS</strong> 66,646 (6.5%) admissions with COVID-19, 613 U.S. hospitals: &gt; 12,388 (18.6%) died in-hospital.</td>
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<td>&gt; male sex was independently associated with 30% higher mortality risk (aRR, 1.30, 95% CI: 1.26 – 1.34).</td>
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<td>&gt; Diabetes without chronic complications was not a risk factor at any age (aRR 1.01, 95% CI: 0.96 – 1.06).</td>
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<td>&gt; Hypertension without chronic complications was only a risk factor in 20-39 year-olds (aRR 1.68, 95% CI: 1.17 – 2.40).</td>
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<td>&gt; 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-values ≤ 0.002).</td>
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<td>Hospitalized men with COVID-19 are at increased risk of death across all ages. Hypertension, diabetes with chronic complications, and obesity demonstrated age-dependent effects, with the highest relative risks among adults aged 20-39.</td>
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<td>&gt; 89,530 patients with COVID-19 and 45,819 patients with influenza were hospitalised in France during the respective study periods (March-April 2020; Dec 2018-Feb 2019).</td>
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<td>&gt; The median age of patients was 68 years for COVID-19 and 71 years for influenza. Patients with COVID-19 were more frequently obese or overweight, and more frequently had diabetes, hypertension, and dyslipidaemia than patients with influenza.</td>
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<td>Patients with influenza more frequently had heart failure, chronic respiratory disease, cirrhosis, and deficiency anaemia.</td>
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<td>&gt; <strong>Patients admitted to hospital</strong> with COVID-19 more frequently developed acute respiratory failure, pulmonary embolism, septic shock, or haemorrhagic stroke than patients with influenza, but less frequently developed myocardial infarction or atrial fibrillation.</td>
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<td>&gt; <strong>In-hospital mortality</strong> 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 and an age-standardised mortality ratio of 2.82.</td>
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<td>&gt; Of the patients hospitalised, the proportion of paediatric patients (&lt;18 yrs) was smaller for COVID-19 than for influenza (1.4% vs 19.5%), but a larger proportion of patients &lt;5 yrs needed intensive care support for COVID-19 than for influenza (2.3% vs 0.9%).</td>
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<td>&gt; <strong>In adolescents</strong> (11–17 years), the in-hospital mortality was ten-times higher for COVID-19 than for influenza (1.1% vs 0.1%), and patients with COVID-19 were more frequently obese or overweight.</td>
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| NEJM 17DEC2020   | Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia | Salama C., et al. USA [gotopaper](#) | Therapeutics | **Aim:** to test the safety and efficacy of tocilizumab (8 mg/kg IV) in patients from underserved and racial and ethnic minority populations who are hospitalized with Covid-19 pneumonia.  
**Primary outcome:** mechanical ventilation or death by day 28.  
> 389 patients randomized: 249 patients in the tocilizumab group, 128 patients in the placebo group; 56.0% were Hispanic or Latino, 14.9% were Black, 12.7% were American Indian or Alaska Native, 12.7% were non-Hispanic White, and 3.7% were of other or unknown race or ethnic group.  
> The cumulative percentage of patients who had received mechanical ventilation or who had died by day 28 was **12.0%** in the tocilizumab group and **19.3%** in the placebo group (HR, 0.56).  
> Clinical failure as assessed in a time-to-event analysis favored tocilizumab over placebo (HR, 0.55).  
> **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.  
> In the safety population, serious adverse events occurred in **15.2%** in the tocilizumab group and **19.7%** in the placebo group.  
In hospitalized patients with Covid-19 pneumonia who were not receiving mechanical ventilation, tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival. |
| NEJM 17DEC2020   | Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults | Anderson E.J., et al. USA [gotopaper](#) | Vaccines | Results of mRNA 1273 Vaccine (Moderna) phase I trial in older adults  
**METHODS:**  
Phase 1, dose-escalation, open-label trial in healthy adults, expanded to 40 older adults (stratified according to age: 56 to 70 years or ≥71 years).  
Two doses of either 25 µg or 100 µg of vaccine at 28 days apart  
**RESULTS**  
- Solicited adverse events:  
> fatigue, chills, headache, myalgia, and pain at the injection site  
> dose-dependent and more common after the second immunization  
> mild to moderate in severity  
- Binding-antibody responses increased rapidly after the first immunization  
- Anti–S-2P GMTs 28d after second vaccination:  
> Vaccination with 2x25 µg in 323,945 (56 and 70 years of age) and 1,128,391 (71 years of age or older)  
> Vaccination with 2x100 µg in 1,183,066 (56 and 70 years of age) and 3,638,522, (71 years of age or older)  
- After the second immunization, serum neutralizing activity was detected in all the participants  
- Binding- and neutralizing-antibody responses appeared similar to those previously reported among vaccine recipients between the ages of 18 and 55 years  
- Vaccine elicited a strong CD4 cytokine response involving type 1 helper T cells.  
**CONCLUSIONS**  
Safety profile acceptable. Better responses at the 100-µg dose reinforcing dose selection for Phase III. |
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| Nature Med. 17DEC2020 | Phase 1/2 trial of SARS-CoV-2 vaccine ChAdOx1 nCoV-19 with a booster dose induces multifunctional antibody responses | Barrett J.R., et al. UK | Vaccines | Safety and exploratory humoral and cellular immunogenicity of the AZD1222 vaccine  
> Animal studies suggest that while neutralizing antibodies against the viral spike protein may correlate with protection, additional antibody functions may also be important in preventing infection.  
> Early immunogenicity and safety outcomes already published |
METHODS  
Intervention: two fully human, neutralizing monoclonal antibodies against SARS-CoV-2 S protein, used in a combined cocktail (REGN-COV2) to reduce the risk of the emergence of treatment-resistant mutant virus  
> Double-blind, phase 1–3 trial involving nonhospitalized patients with Covid-19  
> 1:1:1: placebo: 2.4 g of REGN-COV2: 8.0 g of REGN-COV2  
> Time-weighted average change from baseline in viral load from day 1 through day 7 and the percentage of patients with at least one Covid-19–related medically attended visit through day 29. |

RESULTS  
275 patients.  
> The least-squares mean difference in the time-weighted average change in viral load from day 1 through day 7 was  
> \(-0.56 \log_{10}\) copies per milliliter (95% confidence interval [CI], \(-1.02\) to \(-0.11\)) among patients who were serum antibody–negative at baseline  
> \(-0.41 \log_{10}\) copies per milliliter (95% CI, \(-0.71\) to \(-0.10\)) in the overall trial population.  
> patient reporting at least one medically attended visit (overall trial population): 6% of the patients in the placebo group; 3% of the patients in the combined REGN-COV2 dose groups  
> among patients who were serum antibody–negative at baseline, 15% of the patients in the placebo group and 6% of the patients in the combined REGN-COV2 dose groups (difference, \(-9\) percentage points; 95% CI, \(-29\) to \(-11\)).  
> the percentages of patients with hypersensitivity reactions, infusion-related reactions, and other adverse events were similar in the combined REGN-COV2 dose groups and the placebo group. |

CONCLUSIONS  
REGN-COV2 antibody cocktail reduced viral load, with a greater effect in patients whose immune response had not yet been initiated or who had a high viral load at baseline. Safety outcomes were similar in the combined REGN-COV2 dose groups and the placebo group. |
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| Science 15DEC2020 | Inferring the effectiveness of government interventions against COVID-19 | Brauner J.M., et al. UK gotopaper | Public Health / Epidemiology | Estimation of the effectiveness of NPIs, ranging from limiting gathering sizes, business closures, and closure of educational institutions to stay-at-home orders in several countries (Europe and others).  
**METHODS:**  
Bayesian hierarchical model that links NPI implementation dates to national case and death counts and supported the results with extensive empirical validation  
**RESULTS:**  
> percentage of reduction in $R_t$ (with 95% prediction interval) associated with each NPI was:  
• limiting gatherings to 1000 people or less: 23% (0 to 40%); to 100 people or less: 34% (12 to 52%); to 10 people or less: 42% (17 to 60%);  
• closing some high-risk face-to-face businesses: 18% (−8 to 40%); closing most nonessential face-to-face businesses: 27% (−3 to 49%); closing both schools and universities in conjunction: 38% (16 to 54%); and issuing stay-at-home orders (additional effect on top of all other NPIs): 13% (−5 to 31%).  
> In combination, the NPIs in this study reduced $R_t$ by 77% (67 to 85%).  
**CONCLUSIONS:**  
Business closures and gathering bans both seem to have been effective at reducing COVID-19 transmission. Closing most nonessential face-to-face businesses was only somewhat more effective than targeted closures, which only affected businesses with high infection risk (bars, restaurants, nightclubs). Issuing a stay-at-home order had a small effect when a country had already closed educational institutions and nonessential businesses, and banned gatherings -->some countries may have been able to reduce $R_t$ to below 1 without a stay-at-home order by issuing other NPIs. |
Analysis of clinical history and associated plasma and cerebrospinal fluid of children encephalopathy related (SARS-CoV-2) infection  
**RESULTS**  
> 38 children with neurological disease related to SARS-CoV-2 infection were identified (France, 13; UK, 8; USA, 5; Brazil, 4; Argentina, 4; India 2; Peru 1; Saudi Arabia, 1).  
> Most common imaging patterns were:  
• postinfectious immune-mediated acute disseminated encephalomyelitis-like changes of the brain (16 patients),  
• myelitis (eight patients),  
• neural enhancement (13 patients).  
> Cranial nerve enhancement could occur in the absence of corresponding neurological symptoms.  
> Splenial lesions (7 patients) and myositis (4 patients) were predominantly observed in children with multisystem inflammatory syndrome.  
> Cerebrovascular complications in children were less common than in adults. However, fatal atypical CNS co-infections developed in 4 previously healthy children infected with SARS-CoV-2.  
Acute-phase and delayed-phase SARS-CoV-2-related CNS abnormalities are seen in children. |
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| Lancet Infect Dis. 15DEC2020 | 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 | Poustchi H., et al. Iran gotopaper | Public Health / Epidemiology | AIM: to assess the seroprevalence of antibodies against SARS-CoV-2 in 18 cities of Iran as an indicator of the infection rate.  
> 8902 individuals included in the analysis, 5372 had occupations with a high risk of exposure to SARS-CoV-2 and 3530 were recruited from the general population.  
> The overall population weight-adjusted and test performance-adjusted prevalence of antibody seropositivity in the general population was 17.1% -> 4 265 542 individuals from the 18 cities included were infected by the end of April, 2020.  
> The adjusted seroprevalence of SARS-CoV-2-specific antibodies varied greatly by city. Highest estimates: Rasht (72.6%) and Qom (58.5%).  
> The overall population weight-adjusted and test performance-adjusted seroprevalence in the high-risk population was 20.0% (with little variation between the occupations included).  
> Seroprevalence is likely to be much higher than the reported prevalence of COVID-19 based on confirmed COVID-19 cases in Iran. |
> Antibody responses in 113 COVID-19 patients analysed  
> Severe cases (resulting in intubation or death) exhibited increased inflammatory markers, lymphopenia, pro-inflammatory cytokines, and high anti-RBD antibody levels.  
> Anti-RBD IgG levels generally correlated with neutralization titers and neutralization potency was a predictor of survival.  
> Wild-type SARS-CoV-2 patient sera were also able to neutralize the recently emerged SARS-CoV-2 mutant D614G (cross-protection from reinfection)  
> SARS-CoV-2 sera generally lacked cross-neutralization to a highly-homologous pre-emergent bat coronavirus, WIV1-CoV  
> Great importance of neutralizing humoral immunity on disease progression is showed. |
| NEJM 11DEC2020 | Baricitinib plus Remdesivir for Hospitalized Adults with Covid-19 | Kalil A.C., et al. USA gotopaper | Therapeutics | Double-blind, randomized, placebo-controlled trial evaluating baricitinib (≤14 days) plus remdesivir (≤10 days) vs. remdesivir alone in hospitalized adults with Covid-19.  
Primary outcome: time to recovery  
Secondary outcome: clinical status at day 15  
RESULTS  
> 1033 patients randomized (515 to combination treatment, 518 to control).  
> Patients receiving baricitinib had a median time to recovery of 7 days, as compared with 8 days in control group (rate ratio for recovery, 1.16), and a 30% higher odds of improvement in clinical status at day 15 (odds ratio, 1.3).  
> Patients receiving high-flow oxygen or non-invasive ventilation at enrolment had a time to recovery of 10 days with combination treatment and 18 days with control (rate ratio for recovery, 1.51).  
> 28-day mortality was 5.1% in the combination group and 7.8% in the control group (hazard ratio for death, 0.65).  
> Serious adverse events were less frequent in the combination group than in the control group (16.0% vs. 21.0%), as were new infections (5.9% vs. 11.2%).  
> Baricitinib plus remdesivir was superior to remdesivir alone in reducing recovery time and accelerating improvement in clinical status among patients with Covid-19, notably those receiving high-flow oxygen or non-invasive ventilation. The combination was associated with fewer serious adverse events. |
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<td>NEJM 10DEC2020</td>
<td>Efficacy of Tocilizumab in Patients Hospitalized with Covid-19</td>
<td>Stone J.H., et al. USA <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Randomized, double-blind, placebo-controlled trial involving patients with confirmed SARS-CoV-2 infection, hyper inflammatory states, and at least two of the following signs: fever, pulmonary infiltrates, or the need for supplemental oxygen. Study groups: standard care plus tocilizumab (1 dose, 8 mg/kg of body weight) or placebo. Primary outcome: intubation or death. Secondary outcomes: clinical worsening and discontinuation of supplemental oxygen.</td>
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<td>JAMA Netw Open 10DEC2020</td>
<td>Risk Factors Associated With In-Hospital Mortality in a US National Sample of Patients With COVID-19</td>
<td>Rosenthal N., et al. USA <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td>AIM: to examine risk factors (patient characteristics, acute complications, comorbidities, and medications) associated with in-hospital mortality in patients with COVID-19 treated in US hospitals (April 1 – May 31 2020). Outcomes and measures: in-hospital mortality, intensive care unit (ICU) admission, use of invasive mechanical ventilation, total hospital length of stay (LOS), ICU LOS, acute complications, and treatment patterns. &gt; 64 781 patients with COVID-19 (29 479 [45.5%] outpatients; 35 302 [54.5%] inpatients) analysed. &gt; Median age was 46 (33-59) yrs for outpatients and 65 (52-77) years for inpatients; 49.3% men, 39.9% White US residents, 22.1% were Black US residents. &gt; In-hospital mortality was 20.3% among inpatients. 15.9% inpatients received invasive mechanical ventilation, and 19.4% were admitted to the ICU. Median inpatient LOS was 6 (3-10) days. Median ICU LOS was 5 (2-10) days. Common acute complications among inpatients included acute respiratory failure (55.8%), acute kidney failure (33.9%), and sepsis (33.7%). &gt; Older age was the risk factor most strongly associated with death (eg, age 280 years vs 18-34 years: odds ratio [OR], 16.20). &gt; Receipt of statins (OR, 0.60), angiotensin-converting enzyme inhibitors (OR, 0.53), and calcium channel blockers (OR, 0.73) was associated with decreased odds of death. &gt; Patients with both azithromycin and hydroxychloroquine had increased odds of death (OR, 1.21), compared with patients who did not receive such treatment. COVID-19 was associated with high ICU admission and in-hospital mortality rates. Use of statins, angiotensin-converting enzyme inhibitors, and calcium channel blockers were associated with decreased odds of death.</td>
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| Lancet Infect Dis. 08DEC2020 | 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 | Voysey M., et al. UK/International [gotopaper](#) | Vaccines | METHODS:  
> Ongoing blinded, randomised, controlled trials (UK, Brazil, and South Africa).  
> Randomization to ChAdOx1 nCoV-19 vaccine or control (meningococcal group A, C, W, and Y conjugate vaccine or saline).  
> Two doses of 5 × 10¹⁰ viral particles. A subset in the UK trial received a half dose as their first dose and a standard dose as their second dose (LD/SD cohort).  
> Primary efficacy analysis: symptomatic COVID-19 in seronegative participants with a nucleic acid amplification test-positive swab more than 14 days after a second dose of vaccine.  

FINDINGS:  
> 23 848 participants enrolled; 11 636 participants (7548 in the UK, 4088 in Brazil) included in the interim primary efficacy analysis.  
> Participants receiving two standard doses, vaccine efficacy:  
  - 62·1% [95% CI 41·0–75·7; 27 [0·6%] of 4440 in the ChAdOx1 nCoV-19 group vs 71 [1·6%] of 4455 in the control group]  
> Participants receiving a low dose followed by a standard dose, vaccine efficacy:  
  - 90·0% [67·4–97·0; three [0·2%] of 1367 vs 30 [2·2%] of 1374; pinteraction = 0·010).  
> Overall vaccine efficacy:  
  - 70·4% [95% CI 54·8–80·6; 30 [0·5%] of 5807 vs 101 [1·7%] of 5829].  
> Ten cases hospitalized for COVID-19, all in the control arm;  
  - Two were classified as severe COVID-19  
  - 175 severe adverse events occurred in 168 participants  
  - 84 events in the ChAdOx1 nCoV-19 group  
  - 91 in the control group  
  - 3 events were classified as possibly related to a vaccine: one in the ChAdOx1 nCoV-19 group, one in the control group, and one in a participant who remains masked to group allocation.  

INTERPRETATION:  
ChAdOx1 nCoV-19 has an acceptable safety profile and has been found to be efficacious against symptomatic COVID-19 in this interim analysis of ongoing clinical trials.
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<td>Lancet Infect Dis. 08DEC2020</td>
<td>SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England</td>
<td>Ismail S.A., et al. UK gotopaper</td>
<td>Public Health / Epidemiology</td>
<td>Rate of SARS-CoV-2 infection and outbreaks among staff and students in educational settings, June–July, 2020, in England. Public Health England national surveillance in educational settings after the first national lockdown, from June 1 to July 17, 2020. &gt; Early years settings (&lt;5-year-olds) &gt; Primary schools (5–11-yr-olds; only yrs 1 and 6 allowed to return), &gt; Secondary schools (11–18-year-olds; only years 10 and 12) &gt; Mixed-age settings (spanning a combination of the above). FINDINGS: &gt; Median of settings open each day: 38 000 early years settings (IQR 35 500–41 500), 15 600 primary schools (13 450–17 300), 4000 secondary schools (3700–4200) &gt; Overall median daily attendance: 928 000 students (630 000–1 230 000) &gt; 113 single cases of SARS-CoV-2 infection, nine coprimary cases, and 55 outbreaks &gt; Risk of outbreak increased by 72% (95% CI 28–130) for every five cases per 100 000 population increase in community incidence (p=0·0001) &gt; higher incidence in staff than in students: 27 cases [95% CI 23–32] per 100 000 per day among staff, 18 cases [14–24] in early years students, 6·0 cases [4·3–8·2] in primary schools students, 6·8 cases [2·7–14] in secondary school students) &gt; Direction of transmission: staff to staff in 26 outbreaks, staff to student in 8 outbreaks, student to staff in 16 outbreaks, student to student in 5 outbreaks INTERPRETATION SARS-CoV-2 infections and outbreaks were uncommon in educational settings during the summer half-term in England. Interventions should focus on reducing transmission among staff.</td>
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<td>Lancet Psychiatry 08DEC2020</td>
<td>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</td>
<td>Pan K.Y., et al. Netherlands gotopaper</td>
<td>Public Health / Epidemiology</td>
<td>Aim: to compare the perceived mental health impact and coping and changes in depressive symptoms, anxiety, worry, and loneliness before and during the COVID-19 pandemic between people with (n=1181) and without (n=336) lifetime depressive, anxiety, or obsessive-compulsive disorders. &gt; The number and chronicity of disorders showed a positive graded dose–response relation, with greater perceived impact on mental health, fear, and poorer coping. &gt; Although people with depressive, anxiety, or obsessive-compulsive disorders scored higher on all four symptom scales than did individuals without these mental health disorders, both before and during the COVID-19 pandemic, they did not report a greater increase in symptoms during the pandemic. &gt; 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. People with depressive, anxiety, or obsessive-compulsive disorders are experiencing a detrimental impact on their mental health from the COVID-19 pandemic. Yet, the COVID-19 pandemic does not seem to have further increased symptom severity compared with their pre-pandemic levels.</td>
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<td>Science 08DEC2020</td>
<td>Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic</td>
<td>Buss L.F., et al. Brazil gotopaper</td>
<td>Public Health / Epidemiology</td>
<td>The SARS-CoV-2 attack rate in the Brazilian Amazon is an estimate of the final size of a largely unmitigated epidemic. &gt; By June, 1 month after the epidemic peak in Manaus, capital of Amazonas state, 44% of the population had detectable IgG Abs.. &gt; Correcting for cases without a detectable antibody response and antibody waning, we estimate a 66% attack rate in June, rising to 76% in October. &gt; This calculated rate is higher than in São Paulo, in southeastern Brazil, where the estimated attack rate in October is 29%. When poorly controlled, COVID-19 can infect a high fraction of the population causing high mortality.</td>
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- Among 12 780 RT-PCR tests for SARS-CoV-2 performed, 24.0% had positive results.  
- 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 in critically ill patients and 18.0 days in non-critically ill patients. Being critically ill was an independent risk factor for longer viral positivity (hazard ratio, 0.700).  
- 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. Similar antibody responses were seen in clinically diagnosed cases.  
- Serum inflammatory markers remained higher in critically ill patients. Among non-critically ill patients, a higher proportion of those with persistent viral positivity had low IgM titers (<100 AU/mL) during the entire course compared with those with short viral positivity.  
- Limitation: Retrospective study and irregular viral and serology testing. |
| Science Transl Med. 07DEC2020 | IgA dominates the early neutralizing antibody response to SARS-CoV-2 | Stelin S., et al. France [gotopaper](#) | Immunology | RESULTS:  
- Early specific humoral responses are dominated by IgA antibodies.  
- Peripheral expansion of IgA plasmablasts with mucosal-homing potential detected shortly after the onset of symptoms and peaked during the third week of the disease.  
- Virus-specific antibody responses include IgG, IgM and IgA.  
- IgA contribute to virus neutralization to a greater extent compared with IgG  
- Specific IgA serum concentrations decrease one month after the onset of symptoms  
- Neutralizing IgA remain detectable in saliva for a longer time (days 49 to 73 post symptoms). |
| Science Transl Med. 07DEC2020 | Enhanced SARS-CoV-2 neutralization by dimeric IgA | Wang Z., et al. USA [gotopaper](#) | Immunology | RESULTS:  
- IgA responses in plasma correlated with IgG responses.  
- Clones of IgM-, IgG-, and IgA-producing B cells were derived from common progenitor cells.  
- Plasma IgA monomers specific to SARS-CoV-2 proteins are two-fold less potent than IgG equivalents.  
- IgA dimers, the primary form of antibody in the nasopharynx, were on average fifteen times more potent than IgA monomers  
- Dimeric IgA responses may be particularly valuable for protection against SARS-CoV-2 an for vaccine efficacy.  
- SARS-CoV-2 primarily infects cells at mucosal surfaces.  
- Induced IgG antibodies can neutralize the virus  
- What about secretory antibodies such as IgA, that might impact the initial viral spread and transmissibility from the mucosa? |
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| Science Immunol. 07DEC2020 | Defining the features and duration of antibody responses to SARS-CoV-2 infection associated with disease severity and outcome | Roeltgen K., et al. USA gotopaper | Immunology | Analysis of longitudinal plasma samples to identify serological response features affecting clinical outcome of COVID-19 patients.  
> 983 samples from 79 hospitalized COVID-19 patients and 175 SARS-CoV-2-infected outpatients and asymptomatic individuals. 25 patients died of their illness.  
> As compared to severely ill patients, outpatients who had mild illness presented higher ratios of IgG antibodies targeting S1 or RBD domains of spike compared to nucleocapsid antigen.  
> Plasma antibody increases correlated with decreases in viral RNAemia, but antibody responses in acute illness were insufficient to predict inpatient outcomes.  
> Pseudovirus neutralization assays and a scalable ELISA measuring antibodies blocking RBD-ACE2 interaction were well correlated with patient IgG titers to RBD.  
Outpatient and asymptomatic individuals’ SARS-CoV-2 antibodies, including IgG, progressively decreased during observation up to five months post-infection. |
| Cell 04DEC2020 | Amplification-free detection of SARS-CoV-2 with CRISPR-Cas13a and mobile phone microscopy | Fozouni P., et al. USA gotopaper | Diagnostics | Aim: report the development of an amplification-free CRISPR-Cas13a assay for direct detection of SARS-CoV-2 from nasal swab RNA that can be read with a mobile phone microscope.  
> CRISPR-Cas13a can quantitatively detect SARS-CoV-2 RNA without pre-amplification.  
> The assay achieved 100 copies/μL sensitivity in under 30 minutes of measurement time and accurately detected pre-extracted RNA from a set of positive clinical samples in under 5 minutes.  
> Combined of crRNAs targeting SARS-CoV-2 RNA to improve sensitivity and specificity, and direct quantification of viral load using enzyme kinetics was applied.  
> Integrated with a reader device based on a mobile phone, this assay has the potential to enable rapid, low-cost, point-of-care screening for SARS-CoV-2. |
| Nature 04DEC2020 | Correlates of protection against SARS-CoV-2 in rhesus macaques | McMahan K., et al. USA gotopaper | Immunology | Importance of humoral and cellular immunity for protection against SARS-CoV-2 infection  
> Transfer of purified IgG from convalescent macaques protects naïve recipient rhesus macaques against SARS-CoV-2 challenge in a dose dependent fashion.  
> Depletion of CD8+ T cells in convalescent animals partially abrogated the protective efficacy of natural immunity against SARS-CoV-2 re-challenge  
- importance of cellular immunity in the context of waning or subprotective antibody titers.  
> Higher antibody titers are required for therapy of SARS-CoV-2 infection in macaques.  
Relatively low antibody titers are sufficient for protection against SARS-CoV-2 in rhesus macaques, and cellular immune responses may also contribute to protection if antibody responses are suboptimal. |
| NEJM 03DEC2020 | Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination | Widge A.T., et al. USA gotopaper | Vaccines | mRNA 1273 vaccine immunogenicity 3 months after second vaccination  
> 34 healthy adult participants  
> two injections of vaccine at a dose of 100 μg (D1, D28)  
> Stratification according to age (18-55, 56-70, or ≥71 years)  
RESULTS:  
> Binding antibody responses to the RBD at 3 months after 2nd vaccination: 235,228 in participants (18 to 55), 151,761 (56 to 70), 157,946 (≥ 71 years)  
> Serum neutralizing antibodies continued to be detected (live virus PRV8N80): 430 (18 to 55), 269 (56 to 70), 165 (≥ 71 years)  
> Binding and neutralizing GMTs exceeded the median GMTs in a panel of 41 controls who were convalescing from Covid-19  
Binding and neutralizing antibodies induced by mRNA 1273 declined slightly over time, but they remained elevated in all participants 3 months after the booster vaccination. |
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<tr>
<td>NEJM 02DEC2020</td>
<td>Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results</td>
<td>WHO Solidarity Trial Consortium gotopaper</td>
<td>Therapeutics</td>
<td>WHO mortality trial of four repurposed antiviral drugs — remdesivir, hydroxychloroquine (HCQ), lopinavir, and interferon beta-1a (IFN) — in patients hospitalized with Covid-19. Cohorts: 405 hospitals in 30 countries, 11,330 adults underwent randomization. - 2750 were assigned to receive remdesivir (IV - 200 mg on day 0 and 100 mg on days 1 through 9) - 954 to HCQ (4 x200mg tablets at hour 0, 4 tablets at hour 6, and, starting at hour 12, 2 tablets twice daily for 10 days - 1411 to lopinavir (without IFN) (two tablets twice daily for 14 days) - 2063 to IFN (including 651 to IFN plus lopinavir) (3 doses of 44 μg, subcutaneous, over 6 days) - 4088 to no trial drug. Results &gt; In total, 1253 deaths were reported (median day of death, day 8). &gt; The Kaplan–Meier 28-day mortality was 11.8% (39.0% if the patient was already receiving ventilation at randomization and 9.5% otherwise). &gt; Death occurred in 301 of 2743 patients receiving remdesivir and in 303 of 2708 receiving its control (rate ratio, 0.95), in 104 of 947 patients receiving HCQ and in 84 of 906 receiving its control (rate ratio, 1.19), in 148 of 1399 patients receiving lopinavir and in 146 of 1372 receiving its control (rate ratio, 1.00), and in 243 of 2050 patients receiving IFN and in 216 of 2050 receiving its control (rate ratio, 1.16). &gt; No drug definitely reduced mortality, overall or in any subgroup, or reduced initiation of ventilation or hospitalization duration. These remdesivir, HCQ, lopinavir, and IFN 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.</td>
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<td>Nature 01DEC2020</td>
<td>A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate</td>
<td>Sanchez-Felipe L., et al. Belgium gotopaper</td>
<td>Vaccines</td>
<td>Aim: to describe a live virus-vectored SARS-CoV-2 vaccine candidate using the yellow fever 17D (YF17D) vaccine as vector to express a non-cleavable prefusion form of the SARS-CoV-2 Spike antigen. &gt; Vaccine candidate YF-S0 has outstanding safety profile and induces high levels of SARS-CoV-2 neutralizing antibodies in hamsters, mice and cynomolgus macaques. &gt; Concomitantly a protective immunity against YFV. &gt; Humoral immunity is complemented by a favourable Th1 cell-mediated immune response as profiled in mice. &gt; In a stringent hamster model and non-human primates, YF-S0 prevents infection with SARS-CoV-2. &gt; In hamsters, a single dose confers protection from lung disease in most vaccinated animals within 10 days. Further development this potent SARS-CoV-2 vaccine candidate is warranted.</td>
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> Presence of SARS-CoV-2 RNA and protein in anatomically distinct regions of the nasopharynx and brain is demonstrated.  
> Morphological changes associated with infection such as thromboembolic ischemic infarction of the CNS and evidence of SARS-CoV-2 neurotropism are shown.  
SARS-CoV-2 can enter the nervous system by crossing the neural-mucosal interface in olfactory mucosa, exploiting the close vicinity of olfactory mucosal, endothelial and nervous tissue. Subsequently, SARS-CoV-2 appears to follow neuroanatomical structures, penetrating defined neuroanatomical areas including the primary respiratory and cardiovascular control center in the medulla oblongata. |
> Longitudinal study: symptoms registered during the acute phase as well as long COVID.  
> Demographic and clinical characteristics and self-reported acute and persistent symptoms were assessed using a standardized detailed questionnaire administered at enrollment (phone interviews)  
Results  
Of the 180 participants:  
> 53.1% reported persistence of at least one symptom after a mean of 125 days after symptoms onset  
> 33.3% reported one or two symptoms  
> 19.4% three or more symptoms.  
At the last follow-up, 46.7% were asymptomatic compared with 4.4% during the acute phase. The most prevalent persistent symptoms were fatigue, loss of smell and taste, and arthralgias  
=> It might take months for symptoms to resolve, even among non-hospitalized persons with mild illness course in the acute phase. Continued monitoring for long COVID is needed. |
Findings:  
> The overall SARS-CoV-2 seroprevalence was 4.9%, which corresponded to 2.3 million community dwelling individuals in Spain with antibodies against SARS-CoV-2 by 22 June 2020. Seroprevalence was similar in men and women and increased with age up to 20-29, with a smooth decline at older ages.  
> The overall infection fatality risk was 0.8% (19 228 of 2.3 million infected individuals) for confirmed COVID-19 deaths and 1.1% (24 778 of 2.3 million infected individuals) for excess deaths.  
> The infection fatality risk was 1.1% to 1.4% in men and 0.6% to 0.8% in women. The infection fatality risk increased sharply after age 50, ranging from 11.6% to 16.4% in men aged 80 or more and from 4.6% to 6.5% in women aged 80 or more. The estimates of infection fatality risk do not apply to people living in nursing homes in Spain (about 334 000 residents; 76% aged 80 or older29) where more than 19 000 people died during the study period.  
The overall infection fatality risk estimates (0.83-1.07%) were about 10 times larger than those for seasonal influenza. The increase in SARS-CoV-2 infection fatality risk after age 50 appeared to be more noticeable in men than in women. |
### Table of Studies

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**Methods**  
> Simple probabilistic multiplier model  
> Laboratory-confirmed case counts that were reported nationally were adjusted for sources of under-detection based on testing practices in inpatient and outpatient settings and assay sensitivity  
**Results**  
> 1 of every 2.5 (95% Uncertainty Interval (UI): 2.0–3.1) hospitalized infections and 1 of every 7.1 (95% UI: 5.8–9.0) non-hospitalized illnesses may have been nationally reported  
> 2.4 million hospitalizations, 44.8 million symptomatic illnesses, and 52.9 million total infections may have occurred in the U.S. population from February 27–September 30, 2020. |
**Methods**  
Analysis of electronic health records for a large (68,466-case), international COVID-19 cohort, in 5-year age strata. The primary outcome for estradiol therapy was death. Odds ratios and Kaplan-Meier survival curves were analyzed for 37,086 COVID-19 women in two age groups: pre- (15–49 years) and peri-/post-menopausal (>50 years).  
**Findings:**  
> The study revealed age-dependent sex differences. Incidence of SARS-CoV-2 infection is higher in women than men (by about +15%) and, in contrast, the fatality rate is higher in men (about +50%).  
> Pre-adolescent girls and boys had the same risk of infection and fatality rate, while adult premenopausal women had a significantly higher risk of infection than men in the same 5-year age stratum (about 16,000 vs. 12,000 cases).  
The hormone 17β-estradiol influences expression of the human ACE2 protein, involved in SARS-CoV-2 cellular entry, propensity score matching was performed for the women’s sub-cohort, comparing users vs. non-users of estradiol.  
> The fatality risk for women > 50 years receiving estradiol therapy (user group) is reduced by more than 50% (odds ratio: 0.33, hazard ratio: 0.29). For younger, pre-menopausal women (15–49 years), the risk of COVID-19 fatality is the same irrespective of estradiol treatment, probably because of higher endogenous estradiol levels.  
**Chief finding:** strong positive effect of regular estradiol hormone therapy on the survival rates of post-menopausal women. |
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**Methods:**  
- Open-label, cluster-randomized trial involving asymptomatic contacts of patients with PCR–confirmed Covid-19  
- Clusters of contacts assigned to the HCQ group (800 mg once, followed by 400 mg daily for 6 days) or usual-care group (no specific therapy)  
**Primary outcome:** PCR–confirmed, symptomatic Covid-19 within 14 days  
**Secondary outcome:** SARS-CoV-2 infection, defined by symptoms compatible with Covid-19 or a positive PCR test regardless of symptomsIT  
- Adverse events assessed for up to 28 days  
**Results:**  
> 2314 healthy contacts of 672 index case patients with Covid-19  
- 1116 contacts received HCQ  
- 1198 received usual care.  
> Results were similar in the HCQ and usual-care groups with respect to the incidence of PCR–confirmed, symptomatic Covid-19 (5.7% and 6.2%, respectively; risk ratio, 0.86).  
> HCQ was not associated with a lower incidence of SARS-CoV-2 transmission than usual care (18.7% and 17.8%, respectively).  
> The incidence of adverse events was higher in the HCQ group than in the usual-care group (56.1% vs. 5.9%), but no treatment-related serious adverse events were reported.  
**Postexposure therapy with HCQ did not prevent SARS-CoV-2 infection or symptomatic Covid-19 in healthy persons exposed to a PCR-positive case patient.** |
**Primary outcome:** clinical status 30 days after the intervention, as measured on a six-point ordinal scale ranging from total recovery to death.  
**Results:**  
> 228 patients received convalescent plasma and 105 received placebo. Infused convalescent plasma had a median titer of 1:3200 of total SARS-CoV-2 antibodies.  
> The median time from the onset of symptoms to enrolment in the trial was 8 days, and hypoxemia was the most frequent severity criterion for enrolment.  
> At day 30 day, no significant difference was noted between the convalescent plasma group and the placebo group in the distribution of clinical outcomes according to the ordinal scale (odds ratio, 0.83).  
> Overall mortality was 10.96% in the convalescent plasma group and 11.43% in the placebo group, for a risk difference of −0.46 percentage points.  
> Total SARS-CoV-2 antibody titers tended to be higher in the convalescent plasma group at day 2 after the intervention.  
> Adverse events and serious adverse events were similar in the two groups.  
No significant differences were observed in clinical status or overall mortality between patients treated with convalescent plasma and those who received placebo. |
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> Recovered individuals developed SARS-CoV-2-specific IgG antibodies, neutralizing plasma, memory B and memory T cells that persisted for at least three months.  
> SARS-CoV-2-specific IgG memory B cells increased over time.  
> SARS-CoV-2-specific memory lymphocytes exhibited characteristics associated with potent antiviral function: memory T cells secreted cytokines and expanded upon antigen re-encounter, memory B cells expressed receptors capable of neutralizing virus when expressed as monoclonal antibodies.  
Mild COVID-19 elicits memory lymphocytes that persist and display functional hallmarks of antiviral immunity. |
| Clin Infect Dis. 21NOV2020 | Evidence of Severe Acute Respiratory Syndrome Coronavirus 2 Reinfection After Recovery from Mild Coronavirus Disease 2019 | Lee J., et al. South Korea [gotopaper](#) | Public Health / Epidemiology | Aim: to report evidence that supports reinfection with SARS-CoV-2, by characterising the difference in viral genome between initial infection and positive retest (after first recovery).  
> Phylogenetic analysis of the second specimen of a 21-year-old previously healthy woman showed that the viral RNA of positive retest was clustered into a subgroup distinct from that of the initial infection. This suggests that there was a reinfection of SARS-CoV-2 with a different subtype than the primary strain.  
> The spike protein D614G substitution that defines the clade "G" emerged in reinfection, while mutations that characterize the clade "V" were present at initial infection.  
Reinfection with a genetically distinct SARS-CoV-2 strain may occur in an immunocompetent patient. SARS-CoV-2 infection may not confer immunity against a different SARS-CoV-2 strain. |
> 124 patients (age 59±14 years, 60% male) were included; 27 with mild, 51 with moderate, 26 with severe and 20 with critical disease.  
> Lung diffusion capacity was below lower limit of normal in 42% of discharged patients.  
> 99% of discharged patients had reduced ground-glass opacification on repeat CT imaging, and normal chest X-rays were found in 93% of patients with mild diseases.  
> Residual pulmonary parenchymal abnormalities were present in 91% of discharged patients, and correlated with reduced lung diffusion capacity.  
> 22% had low exercise capacity, 19% low fat-free mass index, and problems in mental and/or cognitive function were found in 36% of the patients. Health status was generally poor, particularly in the domains functional impairment (64%), fatigue (69%) and quality of life (72%).  
This study showed severe problems in several health domains many ex-COVID-19 patients. |
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> Of 375 hospitalized patients included, 128 had a sBSI during the hospitalization.  
> 117 (91.4%) infections were bacterial and 7 (5.5%) were fungal.  
> Those with sBSI were more likely to have altered mental status, lower mean percent oxygen saturation on room air, have septic shock and be admitted to the ICU compared to the controls.  
> In-hospital mortality was higher in those with a sBSI versus controls (53.1% vs 32.8%).  
Hospitalized adult patients with severe COVID-19 and sBSI had a more severe initial presentation, prolonged hospital course, and worse clinical outcomes. A better characterization of risk factors and prediction modelling to identify need of empirical treatment for sBSI in severe COVID-19 is needed. |
| Science Adv. 20NOV2020 | Test sensitivity is secondary to frequency and turnaround time for COVID-19 screening | Larremore E., et al., USA [gotopaper](http://example.com) | Diagnosis | **Aim:** modelling the effectiveness of repeated population screening considering test sensitivities, frequency, and sample-to-answer reporting time.  
> Repeated population screening of asymptomatic individuals can be used to limit the spread of SARS-CoV-2, and it can be expressed as a reduction of the reproductive number R.  
> Some repeated population screening subject individuals to unnecessary quarantine days (e.g. those in the recovery period, with detectable virus or RNA but below the infectious threshold) while having no impact on viral spread.  
**Limitations:**  
- Test sensitivity may depend on factors beyond LOD (manufacturer variation, improper clinical sampling)  
- Differences between testing schemes depend on whether the model truly captures viral kinetics and infectiousness profiles, particularly during the acceleration phase between exposure and peak viral load.  
- Participation was modelled in screening regimens (or refusal thereof) as statistically independent between individuals, but health-related behaviors have been shown to be socially and geographically correlated.  
> Effective screening depends largely on frequency of testing and the speed of reporting, and is only marginally improved by high test sensitivity. |
**Methods:**  
> Serology assays from Roche, Abbott, Diasorin, BioMerieux, Beckman-Coulter, Siemens, and Mt.-Sinai EUSA.  
> 2391 control individuals and 698 SARS-CoV-2 PCR positive patients  
**Results:**  
> Immunoassays sensitivities between 81.5%-89.4% and specificities between 97.7%-100% resulted in a profound impact on the expected Positive Predictive Value (PPV) in low (<15%) prevalence scenarios.  
> Positive correlation between disease severity and antibody titers  
> No decrease in antibody titers in first 8 weeks after PCR-positivity  
> A subgroup of symptomatic SARS-CoV-2 positive patients (~5% of patients) remained seronegative across a wide range of antigens, isotypes, and technologies  
The commercially available automated immunoassays exhibit significant differences in performance and expected PPV in low prevalence scenarios. |
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<td><strong>Lancet Microbe</strong>&lt;br&gt;19NOV2020</td>
<td>SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis</td>
<td>Cevik M., et al. UK gotopaper</td>
<td>Public Health / Epidemiology</td>
<td>Characterization of viral load dynamics, duration of viral RNA shedding, and viable virus shedding of SARS-CoV-2 in various body fluids. Methods: Systematic review and meta-analysis: 79 studies (5340 individuals) on SARS-CoV-2, 8 studies (1858 individuals) on SARS-CoV, and 11 studies (799 individuals) on MERS-CoV were included. Findings: &gt; Mean duration of SARS-CoV-2 RNA shedding: - 17·0 days (95% CI 15·5–18·6; 43 studies, 3229 individuals) in upper respiratory tract, - 14·6 days (9·3–20·0; seven studies, 260 individuals) in lower respiratory tract, - 17·2 days (14·4–20·1; 13 studies, 586 individuals) in stool - 16·6 days (3·6–29·7; two studies, 108 individuals) in serum samples. &gt; Maximum shedding duration: - 83 days in the upper respiratory tract, - 59 days in the lower respiratory tract, - 126 days in stools, - 60 days in serum. &gt; Pooled mean SARS-CoV-2 shedding duration is positively associated with age &gt; No study detected live virus beyond day 9 of illness, despite persistently high viral loads. &gt; SARS-CoV-2 viral load in the upper respiratory tract peaks in the first week of illness.</td>
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<td><strong>The Lancet</strong>&lt;br&gt;18NOV2020</td>
<td>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</td>
<td>Ramasamy M., et al. UK gotopaper</td>
<td>Vaccines</td>
<td>Safety and immunogenicity of ChAdOx1 nCoV-19 in a wide range of participants, including adults aged ≥70 yrs (single-dose and two-dose schedule). Methods Phase 2 component: 2 UK clinical research facilities. Recruitment in an age-escalation manner (18–55 yrs, 56–69 yrs, and 70 yrs and older) - Low-dose cohort: either intramuscular ChAdOx1 nCoV-19 (2·2 × 1010 virus particles) or control vaccine, MenACWY. One or two doses (28 days apart) - Standard-dose cohort (3·5–6·5 × 1010 virus particles of ChAdOx1 nCoV-19) Findings &gt; 560 participants enrolled: 160 aged 18–55 yrs; 160 aged 56–69 yrs; 240 aged ≥70 yrs. &gt; Local and systemic reactions were more common in the ChAdOx1 nCoV-19 group than in the control group (injection-site pain, feverish, muscle ache, headache), but were less common in older adults (aged ≥65 years) than younger adults. &gt; 13 serious adverse events occurred during the study period, none of which were considered to be related to either study vaccine. &gt; In participants who received two doses of vaccine, median anti-spike SARS-CoV-2 IgG responses 28 days after the boost dose were similar across the three age cohorts (standard-dose groups: 18–55 years, 20·713 arbitrary units [AU]/mL, n=39; 56–69 years, 16·170 AU/mL, n=26; and ≥70 years, 17·561 AU/mL, n=47; p=0·68. &gt; Neutralising antibody titres after a boost dose were similar across all age groups (median MNA80 at day 42 in the standard-dose groups: 18–55 years, 193, n=39; 56–69 years, 144, n=20; and ≥70 years, 161, n=47; p=0·40). &gt; T-cell responses peaked at day 14 after a single standard dose of ChAdOx1 nCoV-19 (18–55 years: median 1187 spot-forming cells [SFCs] per mln peripheral blood mononuclear cells, n=24; 56–69 years: 797 SFCs, n=29; and ≥70 years: 977 SFCs, n=48). 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.</td>
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- RCT, double-blind  
- Healthy adults aged 18–59 years, 144 participants enrolled in phase 1 trial and 600 in phase 2.  
- Two vaccination schedule cohorts (days 0 and 14 cohort, days 0 and 28 cohort)  
- 2 doses tested: 3 μg per 0·5 mL or 6 μg per 0·5 mL of aluminium hydroxide diluent.  
Primary immunogenic outcome: seroconversion rates of neutralising antibodies to live SARS-CoV-2  
Results  
Phase 1  
> Adverse reactions for the days 0 and 14 cohort was 7/24 participants (29%) in the 3 μg group, 9/24 (38%) in the 6 μg group, and 2/24 (8%) in the placebo group, and for the days 0 and 28 cohort was 3/24 (13%) in the 3 μg group, 4/24 (17%) in the 6 μg group, and 3/23 (13%) in the placebo group.  
> Seroconversion of neutralising antibodies on day 14 in the days 0 and 14 cohort was seen in 11/24 (46%) in the 3 μg group, 12/24 (50%) in the 6 μg group, and 0/24 (0%) in the placebo group; whereas at day 28 after the days 0 and 28 cohort, seroconversion was seen in 20/24 (83%) in the 3 μg group, 19/24 (79%) in the 6 μg group, and 1/24 (4%) of 24 in the placebo group.  
Phase 2  
> Adverse reactions for the days 0 and 14 cohort was 40/120 participants (33%) in the 3 μg group, 42/120 (35%) in the 6 μg group, and 13/60 (22%) in the placebo group, and for the days 0 and 28 cohort was 23/120 (19%) in the 3 μg group, 23/120 (19%) in the 6 μg group, and 11/60 (18%) in the placebo group.  
> Seroconversion of neutralising antibodies was seen for 109/118 (92%) in the 3 μg group, 117/119 (98%) in the 6 μg group, and 2/60 (3%) in the placebo group at day 14 in the days 0 and 14 cohort; whereas at day 28 in the days 0 and 28 cohort, seroconversion was seen in 114/117 (97%) in the 3 μg group, 118/118 (100%) in the 6 μg group, and 0/59 (0%) in the placebo group.  
The 3 μg dose of CoronaVac is the suggested dose for efficacy assessment in future phase. |
> Of the 1396 COVID-19 patients included, 37 patients (2.7%) had clinically important bacterial co-infection within 48 hours of admission.  
> The majority of patients (36/37 in those with co-infection and 98/100 in those without co-infection) received empirical antibiotic treatment. There was no significant difference in age, gender, pre-existing illnesses, ICU admission or 30 day all-cause mortality in the two groups.  
> White cell count, neutrophil count and CRP on admission were significantly higher in patients with bacterial co-infections.  
Bacterial co-infection was infrequent in hospitalized COVID-19 patients within 48h of admission, suggesting that empirical antimicrobial treatment may not be necessary in all admitted COVID-19 patients. The decision could be guided by high inflammatory markers. |
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> 71% mortality benefit in 83 patients with moderate-severe SARS-CoV-2 pneumonia with few drug-induced adverse events, including elderly.  
> A further 48 cases with mild-moderate pneumonia recovered uneventfully.  
> By viral load quantifications and super-resolution microscopy, baricitinib exerts activity rapidly through the inhibition of host proteins (numb associated kinases), uniquely amongst anti-virals.  
JAK-1/2 inhibitor baricitinib targets viral entry, replication and the cytokine storm, and is associated with beneficial outcomes including in severely ill elderly patients. |
| JAMA 12NOV2020 | Fluvoxamine vs Placebo and Clinical Deterioration in Outpatients With Symptomatic COVID-19 A Randomized Clinical Trial | Lenze, E.J., et al. USA gotopaper | Therapeutics | Aim: to determine whether fluvoxamine, given during mild COVID-19 illness, prevents clinical deterioration and decreases the severity of disease. Double-blind, randomized, fully remote (contactless) clinical trial of fluvoxamine 100 mg vs placebo on non-hospitalized adults with confirmed SARS-CoV-2 infection, symptomatic COVID-19 and O2 saturation of >92%.  
Primary outcome: was clinical deterioration within 15 days of randomization defined by both shortness of breath or hospitalization for shortness of breath or pneumonia, and O2 saturation <92% on room air or need for supplemental O2.  
Results: > 152 patients randomized, 115 (76%) completed the trial.  
> Clinical deterioration occurred in 0 of 80 patients in the fluvoxamine group and in 6 of 72 patients in the placebo group (absolute difference, 8.7%).  
> The fluvoxamine group had 1 serious adverse event and 11 other adverse events, the placebo group had 6 serious adverse events and 12 other adverse events.  
In this preliminary study, patients treated with fluvoxamine had a lower likelihood of clinical deterioration over 15 days. |
Methods: - RCT, double-blind, placebo-controlled, phase 2 trial  
- Adults aged >18 years and admitted to hospital with COVID-19 symptoms and positive test  
- Tretamenet: SNG001 (6 MIU) or placebo by inhalation via a mouthpiece daily for 14 days.  
Primary outcome: change in clinical condition on WHO Ordinal Scale for Clinical Improvement (OSCI)  
Findings: > 101 patients randomly assigned to SNG001 (n=50) or placebo (n=51).  
> (67%) patients required oxygen supplementation at baseline: 29 in the placebo group and 37 in the SNG001 group.  
> Patients receiving SNG001 had greater odds of improvement on the OSCI scale (odds ratio 2.32) on day 15 or 16 and were more likely than those receiving placebo to recover to an OSCI score of 1 during treatment (hazard ratio 2.19). SNG001 was well tolerated.  
> The most frequently reported adverse event was headache  
> There were three deaths in the placebo group and none in the SNG001 group.  
Patients who received SNG001 had greater odds of improvement and recovered more rapidly from SARS-CoV-2 infection |
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<td>Clin Infect Dis. 12NOV2020</td>
<td>Susceptibility to Sars-COV-2 Infection Among Children And Adults: A Seroprevalence Study of Family Households in the Barcelona Metropolitan Region, Spain</td>
<td>Brotons P., et al. Spain <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td>Cross-sectional seroprevalence study on families with at least 1 first-reported adult positive to SARS-CoV-2 PCR and at least 1 child &lt;15 years living in the same household under strict confinement.  &gt; 381 family households including 381 first-reported PCR-positive adult cases and 1,084 contacts (672 children, 412 adults) enrolled  &gt; Infection seroprevalence rates were 17.6% (118/672) in children and 18.7% (77/335) in adult contacts  &gt; Among first-reported cases, seropositivity rates varied from 84.0% in adults previously hospitalized and tested within 6 weeks since the first positive PCR result to 31.5% in those not hospitalized and tested after that lag time.  &gt; Nearly all (99.9%) positive pediatric contacts were asymptomatic or had mild symptoms.  Children seem to have similar probability as adults to be infected by SARS-CoV-2 but remain largely asymptomatic. Adult antibody protection against SARS-CoV-2 seems weak at early convalescence and &gt;6 weeks post-infection, especially in mild disease cases.</td>
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<td>Blood 12NOV2020</td>
<td>Convalescent plasma therapy for B-cell–depleted patients with protracted COVID-19</td>
<td>Huseo T., et al. France <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Treatment of 17 patients with 4 units of COVID-19 convalescent plasma. (Patients had profound B-cell lymphopenia, prolonged COVID-19 symptoms, seronegatives, RT PCR positive)  &gt; Within 48 hours of transfusion, all but 1 patient experienced an improvement of clinical symptoms.  &gt; The inflammatory syndrome abated within a week.  &gt; Only 1 patient who needed mechanical ventilation for severe COVID-19 disease died of bacterial pneumonia.  &gt; SARS-CoV-2 RNAemia decreased to below the sensitivity threshold in all 9 evaluated patients.  &gt; In 3 patients, virus-specific T-cell responses were analyzed using immunospot assay before convalescent plasma transfusion: all showed a maintained SARS-CoV-2 T-cell response and poor cross-response to other coronaviruses, no adverse event was reported.  Convalescent plasma with anti-SARS-CoV-2 antibodies appears as promising approach in patients unable to mount a specific humoral response to SARS-CoV-2 and with protracted COVID-19.</td>
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<td>Ann Intern Med. 11NOV2020</td>
<td>Sixty-Day Outcomes Among Patients Hospitalized With COVID-19</td>
<td>Chopra V., et al. USA <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td>Aim: to describe 60-day post-discharge clinical, financial, and mental health outcomes of patients with COVID-19.  &gt; Of 1648 patients with COVID-19 admitted to 38 hospitals, 398 (24.2%) died during hospitalization and 1250 (75.8%) survived. Of the latter, 975 (78.0%) went home, 158 (12.6%) were discharged to a skilled nursing or rehabilitation facility.  &gt; By 60 days after discharge, 84 more patients (6.7% of hospital survivors and 10.4% of ICU survivors) had died. Overall mortality rate for the cohort was 29.2%, 63.5% for the ICU (405 patients).  &gt; Within 60 days of discharge, 189 patients (15.1% of hospital survivors) were rehospitalized.  &gt; Of patients alive 60 days after discharge, 488 (41.8%) were successfully contacted. 265 reported seeing a primary care physician within 2 weeks. 304/382 visits occurred virtually (161 by videoconference, 143 by telephone), 77 occurred in person.  &gt; Cardiopulmonary symptoms were reported by 159 patients, including 92 with new or worsening symptoms and 65 with persistent loss of taste or smell. 58 patients reported new or worsening difficulty completing activities of daily living.  &gt; 117/195 employed patients had returned to work, 78 could not because of ongoing health issues or job loss. 30/117 reported reduced hours or modified duties due to health reasons.  &gt; Nearly half of all patients (238/488) reported being emotionally affected by their health, and 28 sought mental health care.  &gt; 179 patients reported at least mild financial impacts from their hospitalization. 47 reported use of most or all of their savings and 35 rationing food, heat, housing, or medications due to cost. The study conveys that adverse events after COVID-19 hospitalization are common.</td>
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Participants: 2847 key workers (healthcare staff, fire and rescue or police officers - 268 with a PCR positive result, 2579 with unknown infection status); and pre-pandemic blood donors. AbC-19 sensitivity and specificity was estimated using known negative (pre-pandemic) and known positive (PCR confirmed) samples as reference standards. > Test result bands were often weak, with positive/negative discordance by 3 trained laboratory staff for 3.9% of devices. > Using consensus readings, for known positive and negative samples sensitivity was 92.5% and specificity was 97.9%. > Using an immunoassay reference standard, sensitivity was 94.2% among PCR confirmed cases but 84.7% among other people with antibodies. This is consistent with AbC-19 being more sensitive when antibody concentrations are higher, as people with PCR confirmation tended to have more severe disease whereas only 62% (218/354) of seropositive participants had had symptoms. > If 1 million key workers were tested with AbC-19 and 10% had actually been previously infected, 84 700 true positive and 18 900 false positive results would be projected. The probability that a positive result was correct would be 81.7%. AbC-19 sensitivity was lower among unselected populations than among PCR confirmed cases (endorsing overestimation of assay performance in studies involving only PCR confirmed cases). If 10% of the tested population have had SARS-CoV-2 infection, around 1/5 key workers testing positive with AbC-19 would be false positives. |
| Ann Intern Med. 11NOV2020 | Insights From Rapid Deployment of a “Virtual Hospital” as Standard Care During the COVID-19 Pandemic | Sitammagari K., et al. USA gotopaper | Public Health / Epidemiology | Development and rapid deployment of a virtual hospital program, Atrium Health hospital at home (AH-HaH), within a large health care system. - Virtual hospital model providing proactive home monitoring and hospital-level care through a virtual observation unit (VOU) and a virtual acute care unit (VACU) in the home setting for eligible patients with COVID-19.  
Results: > 1477 COVID-19 patients received care in either the AH-HaH VOU or VACU or both settings - median length of stay: 11 days. > 1293 (88%) patients received care in the VOU only, with 40 (3%) requiring inpatient hospitalization. Of these, 16 (40%) went to the ICU, 7 (18%) needed ventilator support, 2 (5%) died. > 184 (12%) patients were ever admitted to the VACU, during which 21 patients (11%) required intravenous fluids, 16 (9%) received antibiotics, 40 (22%) required respiratory inhaler or nebulizer treatments, 41 (22%) used supplemental oxygen, and 24 (13%) were admitted as an inpatient to a conventional hospital. Of these 24 patients, 10 (42%) required ICU admission, 1 (3%) required a ventilator, and none died during their hospital admission.  
Virtual hospital programs have the potential to provide health systems with additional inpatient capacity. |
<p>| Science 11NOV2020 | Seroprevalence of anti–SARS-CoV-2 IgG antibodies in Kenyan blood donors | Uyoga S., et al. Kenya/UK gotopaper | Public Health / Epidemiology | Description of the prevalence of anti–SARS-CoV-2 IgG among blood donors in Kenya in April-June 2020. - Crude seroprevalence was 5.6% (174/3098) - Population-weighted, test-performance-adjusted national seroprevalence was 4.3% - Prevalence was highest in urban counties, Mombasa (8.0%), Nairobi (7.3%) and Kisumu (5.5%) SARS-CoV-2 exposure is more extensive than indicated by case-based surveillance. |</p>
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| Science          | Transmission of SARS-CoV-2 on mink farms between humans and mink and back to humans | Oude Munnink B.B., et al. Netherlands [gotopaper](#)                               | Public Health / Epidemiology | Whole genome sequencing of SARS-CoV-2 outbreaks on 16 mink farms and the humans living or working on these farms.  
> virus was initially introduced from humans to the farms  
> widespread circulation among mink in the beginning of the infection period several weeks prior to detection.  
> transmission occurred between mink farms in three big transmission clusters with unknown modes of transmission  
> 68% of the tested mink farm residents, employees and/or contacts had evidence of SARS-CoV-2 infection.  
> humans were infected with strains with an animal sequence signature, providing evidence of animal to human SARS-CoV-2 transmission within mink farms. |
| Science          | Preexisting and de novo humoral immunity to SARS-CoV-2 in humans     | Ng K.W., et al. UK [gotopaper](#)                                                  | Immunology         | Detection of pre-existing humoral immunity against SARS-CoV-2  
> SARS-CoV-2 S protein reactive antibodies in uninfected individuals, particularly prevalent in children and adolescents.  
> These antibodies were predominantly of the IgG class targeting the S2 subunit.  
> SARS-CoV-2 infection induces high titers of IgG targeting both the S1 and the S2 subunits as well as IgM and IgA.  
> sera coming of uninfected donors exhibited SARS-CoV-2/S pseudotypes specific neutralizing activity. |
> Marked, asynchronous reductions of the basic reproductive number occurred throughout the US in association with social distancing and other control measures.  
> Counterfactual simulations indicate that if the same measures had been implemented 1-2 weeks earlier, substantial cases and deaths could have been averted.  
> Delayed responses to future increased incidence will facilitate a stronger rebound of infections and death.  
Our findings underscore the importance of early intervention and aggressive control in combatting the COVID-19 pandemic. |
| Clin Infect Dis.  | COVID-19 seropositivity and asymptomatic rates in healthcare workers are associated with job function and masking | Sims M.D., et al. USA [gotopaper](#)                                               | Public Health / Epidemiology | Detection of antibodies against SARS-CoV-2 may be useful for determining prior exposure to the virus and assessing mitigation strategies (isolation, masks, and other PPE).  
Methods: online assessment including demographic, clinical, and exposure information, and blood sample from 20,614 participants at Beaumont Health (8 hospitals in the Detroit metropolitan area). The presence of anti-SARS-CoV-2 IgG was determined using the EUROIMMUN assay.  
Results  
> 1,818 (8.8%) participants were seropositive between April 13 and May 28, 2020. Among them, 44% reported being asymptomatic during the month prior to blood collection.  
> Healthcare roles such as phlebotomy, respiratory therapy, and nursing/nursing support exhibited significantly higher seropositivity.  
> Among participants reporting direct exposure to a COVID-19 positive individual, those wearing an N95/PAPR mask had a significantly lower seropositivity rate (10.2%) compared to surgical/other masks (13.1%) or no mask (17.5%).  
Direct contact with COVID-19 patients increased the likelihood of seropositivity but participants who wore a mask during exposures were less likely to be seropositive. |
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Study groups: remdesivir (200 mg on day 1, then 100 mg daily for up to 9 additional days); placebo for up to 10 days.  
Primary outcome: time to recovery (either discharge from the hospital or hospitalization for infection-control purposes only).  

Results  
> 1062 patients randomized (541 to remdesivir and 521 to placebo).  
> The remdesivir cohort had a median recovery time of 10 days, as compared with 15 days of the placebo cohort (rate ratio for recovery, 1.29).  
> Patients who received remdesivir were found to be more likely than those who received placebo to have clinical improvement at day 15.  
> The Kaplan–Meier estimates of mortality were 6.7% with remdesivir and 11.9% with placebo by D15 and 11.4% with remdesivir and 15.2% with placebo by D29 (hazard ratio 0.73).  
> Serious adverse events were reported in 131/532 patients of the remdesivir cohort (24.6%) and in 163/516 of the placebo cohort (31.6%).  

In this study, remdesivir was superior to placebo in shortening the time to recovery in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection. |
| NEJM 05NOV2020  | Remdesivir for 5 or 10 Days in Patients with Severe Covid-19 | Goldman J.D., et al. USA/International | Therapeutics | Randomized, open-label, phase 3 trial involving hospitalized patients with confirmed SARS-CoV-2 infection, oxygen saturation of 94% or less while they were breathing ambient air, and radiologic evidence of pneumonia.  

Study groups: intravenous remdesivir for either 5 or 10 days (200 mg on day 1 and 100 mg once daily on subsequent days).  
Primary end point: clinical status on day 14 (7-point ordinal scale).  

Results  
> 397 patients randomized (200 patients for 5 days and 197 for 10 days). The median duration of treatment was 5 days in the 5-day group and 9 days in the 10-day group.  
> At baseline, the 10-day group had significantly worse clinical status than those assigned to the 5-day group.  
> By day 14, a clinical improvement of 2 points or more on the ordinal scale occurred in 64% of patients in the 5-day group and in 54% in the 10-day group. After adjustment for baseline clinical status, the 10-day group had a distribution in clinical status at day 14 that was similar to that of the 5-day group.  
> The most common adverse events were nausea (9% of patients), worsening respiratory failure (8%), elevated alanine aminotransferase level (7%), and constipation (7%).  

This trial did not show a significant difference between a 5-day course and a 10-day course of remdesivir. With no placebo control, the magnitude of benefit cannot be determined. |
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| Nature 03NOV2020 | Repeated cross-sectional sero-monitoring of SARS-CoV-2 in New York City | Stadlbauer D., et al. USA | Public Health / Epidemiology | Study on SARS CoV 2 seroprevalence dynamics  
Retrospective, repeated cross-sectional analysis of anti-SARS-CoV-2 spike antibodies in weekly intervals from the beginning of February to July 2020  
> More than 10,000 plasma samples from patients at Mount Sinai Hospital in NYC.  
> Seroprevalence increased at different rates in ‘urgent care’ (UC) group, enriched for COVID-19 cases during the epidemic, and a ‘routine care’ group (RC), which more closely represents the general population.  
> Seropositive samples detected as early as mid-February, and levelled out at slightly above 20% in both groups after the epidemic wave (end of May).  
> From May to July seroprevalence stayed stable, suggesting lasting antibody levels in the population. |
> Antibody responses to SARS-CoV-2 are unimodally distributed over a broad range, with symptom severity correlating directly with virus-specific antibody magnitude.  
> 76 subjects followed longitudinally to ~100 days demonstrated marked heterogeneity in antibody duration dynamics.  
> Virus-specific IgG decayed substantially in most individuals, whereas a distinct subset had stable or increasing antibody levels in the same timeframe despite similar initial antibody magnitudes.  
> These individuals with increasing responses recovered rapidly from symptomatic COVID-19 disease, harbored increased somatic mutations in virus-specific memory B cell antibody genes, and had persistent higher frequencies of previously activated CD4+ T cells. |
| Clin Infect Dis. 03NOV2020 | SARS-CoV-2 Infections Among Children in the Biospecimens from Respiratory Virus-Exposed Kids (BRAVE Kids) Study | Hurst J.H., et al. USA | Public Health / Epidemiology | Prospective cohort study of children and adolescents (<21 years of age) with a SARS-CoV-2-infected close contact.  
> Of 382 children, **293 (77%)** were SARS-CoV-2-infected. SARS-CoV-2-infected children were more likely to be Hispanic, less likely to have asthma, and more likely to have an infected sibling contact than uninfected children.  
> Children **ages 6-13 years were frequently asymptomatic** (39%) and had respiratory symptoms less often than younger children (29% vs. 48%) or adolescents (29% vs. 60%).  
> Compared to children ages 6-13 years, **adolescents more frequently reported** influenza-like (61% vs. 39%), gastrointestinal (27% vs. 9%), and sensory **symptoms** (42% vs. 9%), and had **more prolonged illnesses** (median (IQR) duration: 7 vs. 4 days).  
> Despite the age-related variability in symptoms, we found **no differences in nasopharyngeal viral load** by age or between symptomatic and asymptomatic children.  
**Age-related differences in the clinical manifestations of SARS-CoV-2 infection must be considered when evaluating children for COVID-19 and in screening strategies for schools and childcare settings.** |
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<td>Cell 03NOV2020</td>
<td>Compromised humoral functional evolution tracks with SARS-CoV-2 mortality</td>
<td>Zohar T., et al. USA <a href="#">gotopaper</a></td>
<td>Immunology</td>
<td>Analysis of the evolution of the humoral response in 193 hospitalized individuals ranging from moderate-to-severe.</td>
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<td>&gt; Robust IgM and IgA responses both in survivors and non-survivors with severe disease</td>
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<td>&gt; However, non-survivors showed attenuated IgG responses and compromised Fcγ-receptor binding and Fc-effector activity</td>
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<td>--&gt; deficient humoral development rather than disease-enhancing humoral immunity</td>
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<td>&gt; Individuals with moderate disease exhibited delayed responses that ultimately matured.</td>
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<td>These data highlight distinct humoral trajectories associated with resolution of SARS-CoV-2 infection and the need for early functional humoral immunity.</td>
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<td>Science Transl Med. 02NOV2020</td>
<td>Prothrombotic autoantibodies in serum from patients hospitalized with COVID-19</td>
<td>Zuo Y., et al. USA <a href="#">gotopaper</a></td>
<td>Immunology</td>
<td>Aim: to measure 8 types of pathogenic autoantibodies targeting phospholipids and phospholipid-binding proteins (aPL antibodies) in serum samples from 172 patients hospitalized with COVID-19. aPL antibodies included anticardiolipin IgG, IgM and IgA; anti-β2 glycoprotein I IgG, IgM, and IgA; and anti-phosphatidylserine/prothrombin (aPS/PT) IgG and IgM.</td>
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<td>&gt; aPS/PT IgG were detected in 24% of samples, anticardiolipin IgM in 23% of samples, and aPS/PT IgM in 18% of samples.</td>
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<td>&gt; Antiphospholipid autoantibodies were present in 52% of samples using the manufacturer’s threshold and in 30% using a more stringent cutoff (≥40 ELISA-specific units).</td>
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<td>&gt; Higher titers of aPL antibodies were associated with neutrophil hyperactivity including release of neutrophil extracellular traps (NETs), higher platelet counts, more severe respiratory disease, and lower clinical estimated glomerular filtration rate.</td>
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<td>&gt; IgG fractions isolated from COVID-19 patients promoted NET release from neutrophils isolated from healthy individuals. Injection of IgG purified from COVID-19 patient serum into mice accelerated venous thrombosis in two mouse models.</td>
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<td>Half of COVID-19 hospitalised patients seem to become at least transiently positive for aPL antibodies, potentially pathogenic.</td>
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<td>&gt; 7770 close contacts (1863 household contacts, 2319 work contacts, and 3588 social contacts) linked to 1114 PCR-confirmed index cases were identified. Symptom-based PCR testing detected 188 COVID-19 cases, and 7582 close contacts completed quarantine without a positive SARS-CoV-2 PCR test.</td>
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<td>&gt; Among 7518 (96.8%) close contacts with complete data, secondary clinical attack rate (derived from prevalence of PCR-confirmed SARS-CoV-2 among close contacts) was 5.9% for 1779 household contacts, 1.3% for 2231 work contacts, and 1.3% for 3508 social contacts.</td>
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<td>&gt; Bayesian analysis of serology and symptom data from 1150 close contacts estimated that a symptom-based PCR-testing strategy missed 62% of COVID-19 diagnoses, and 36% of individuals with SARS-CoV-2 infection were asymptomatic.</td>
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<td>&gt; Sharing a bedroom (odds ratio 5.38) and being spoken to by an index case for &gt;30 min (7.86) were associated with SARS-CoV-2 transmission among household contacts.</td>
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<td>&gt; Among non-household contacts, exposure to &gt;1 case (OR 3.92), being spoken to by an index case for &gt;30 min (2.67), and sharing a vehicle with an index case (3.07) were associated with SARS-CoV-2 transmission.</td>
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<td>&gt; Among both household and non-household contacts, indirect contact, meal sharing, and lavatory co-usage were not independently associated with SARS-CoV-2 transmission.</td>
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| Nature 02NOV2020 | Age-specific mortality and immunity patterns of SARS-CoV-2 | O’Driscoll M., et al. France/UK | Public Health / Epidemiology | **Background:** estimating size and infection severity of the SARS-CoV-2 epidemic, and comparing them across countries, is challenging due to inconsistencies in available data.  
**Aim:** to investigate the consistency of COVID-19 infection and fatality patterns using age-specific death data from 45 countries and the results of 22 seroprevalence studies.  
> The age **distribution of deaths in younger age groups** (<65 yrs) is **very consistent** across different settings, providing robust estimates of share of the population that has been infected.  
> The infection-to-fatality ratio (IFR) is **lowest among 5-9 years old**, with a log-linear increase by age among individuals older than 30 years.  
> Population age-structures and heterogeneous burdens in nursing homes explain some but not all of the heterogeneity between countries in IFR.  
> Among 45 countries, **approximately 5% of populations had been infected by Sept. 01 2020**, with much higher transmission likely to have occurred in Latin American countries.  
This simple modelling framework can help countries assess the progression of the pandemic and can be applied wherever reliable age-specific death data exists. |
| Lancet Digit Health 28OCT2020 | Evaluating the effect of demographic factors, socioeconomic factors, and risk aversion on mobility during the COVID-19 epidemic in France under lockdown: a population-based study | Pullano G., et al. France | Public Health / Epidemiology | **Aim:** using mobile phone data to study mobility changes in mainland France before and during lockdown in March 2020. Temporally resolved travel flows among 1436 administrative areas were reconstructed.  
> Lockdown caused a **65% reduction** in countrywide number of displacements (from 57 million to 20 million trips per day). It was particularly effective in reducing work-related short-range mobility, especially during rush hour, and long trips.  
> Geographical heterogeneities showed **anomalous increases in long-range movements** even before lockdown announcement that were tightly localised in space.  
> During lockdown, **mobility drops were unevenly distributed** across regions (eg, Île-de-France, went from 585 000 to 117 000 outgoing trips per day). They were strongly associated with active populations, workers employed in sectors highly affected by lockdown, and number of hospitalisations per region, and moderately associated with the socioeconomic level of the regions.  
> Major cities largely **shrunk their pattern of connectivity**, reducing it mainly to short-range commuting (95% of traffic leaving Paris was contained in a 201 km radius before lockdown and reduced to 29 km during lockdown).  
Lockdown was effective in reducing population mobility across scales. Caution should be taken in the timing of policy announcements and implementation. Socioeconomic and demographic constraints to restriction efficacy were identified. |
| Science 28OCT2020 | Robust neutralizing antibodies to SARS-CoV-2 infection persist for months | Wajnberg A., et al. USA | Immunology | **Study on robustness, functionality, and longevity of the antibody response to SARS CoV 2 infection**  
> Data from 30,082 individuals screened at Mount Sinai Health System in New York City  
> The vast majority of infected individuals with mild-to-moderate COVID-19 experience robust IgG antibody responses against the viral spike protein  
> Titers are relatively stable for at least a period approximating 5 months  
> The anti-spike binding titers significantly correlate with **neutralization** of authentic SARS-CoV-2.  
> More than 90% of seroconverters make **detectable neutralizing antibody responses**. These titers remain relatively stable for several months after infection. |
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- 452 patients  
- a single intravenous infusion of neutralizing antibody LY-CoV555 in one of three doses (700 mg, 2800 mg, or 7000 mg) or placebo  
- Quantitative virologic end points and clinical outcomes were evaluated.  
Primary outcome: change from baseline in the viral load at day 11. The results of a preplanned interim analysis as of 05/09/2020 are reported here.  
RESULTS  
> The observed mean decrease from baseline in the log viral load for the entire population was $-3.81$, for an elimination of more than 99.97% of viral RNA.  
> For patients who received the 2800-mg dose of LY-CoV555, the difference from placebo in the decrease from baseline was $-0.53$, for a viral load that was lower by a factor of 3.4.  
> Smaller differences from placebo in the change from baseline were observed among the patients who received the 700-mg dose ($-0.20$) or the 7000-mg dose ($0.09$).  
> On days 2 to 6, patients who received LY-CoV555 had a slightly lower severity of symptoms than those who received placebo. The percentage of patients who had a Covid-19–related hospitalization or visit to an emergency department was 1.6% in the LY-CoV555 group and 6.3% in the placebo group.  
One of three doses of neutralizing antibody LY-CoV555 appeared to accelerate the natural decline in viral load over time, whereas the other doses had not by day 11. |
| Clin Infect Dis. 27OCT2020 | Repeat COVID-19 Molecular Testing: Correlation of SARS-CoV-2 Culture with Molecular Assays and Cycle Thresholds | Gniazdowski V., et al. USA [gotopaper](#) | Diagnostics | Cohort of retrospective data (2months) and consecutively collected specimens (29,686) from 2194 COVID-19 patients to understand the correlation between prolonged viral RNA positive test results, cycle threshold (Ct) values and growth of SARS-CoV-2 in vitro.  
Methods:  
Whole genome sequencing was used to confirm virus genotype in patients with prolonged viral RNA detection. Droplet digital PCR (ddPCR) was used to assess the rate of false negative COVID-19 diagnostic tests.  
Results:  
> The Ct value average from SARS-CoV-2 target genes was 18.8 ± 3.4. Low Ct values in SARS-CoV-2 diagnostic tests were associated with virus growth in Vero E6 cells.  
> Prolonged viral RNA shedding was associated with positive virus growth in vitro in specimens collected up to 20 days after the first positive result but mostly in individuals symptomatic at time of sample collection.  
> ddPCR was positive in 5.6% of negative specimens collected from COVID-19 confirmed or clinically suspected patients.  
Symptomatic patients with prolonged viral RNA shedding can also be infectious. |
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| Ann Intern Med. 27OCT2020 | Effect of Timing of and Adherence to Social Distancing Measures on COVID-19 Burden in the United States - A Simulation Modeling Approach | Alagoz O., et al. USA gotopaper | Public Health / Epidemiology | AIM: To determine the effect of social distancing measures in 3 unique regions in the USA. The model represented the social network and interactions among persons in a region, considering demographic characteristics, limited testing availability, “imported” infections, asymptomatic disease transmission, and age-specific adherence to social distancing measures.  
> In NYC, implementing social distancing measures **1 week earlier** would have reduced the total number of confirmed cases from 203 261 to 41 366 as of 31 May 2020, whereas a **1-week delay** could have increased the number of confirmed cases to 1 407 600.  
> A delay in implementation had a differential effect on the number of cases in the Milwaukee metro area versus Dane County, indicating that the effect of social distancing measures varies even within the same state.  
The timing of implementing and easing social distancing measures has major effects on the number of COVID-19 cases. |
> D614G enhances replication on human lung epithelial cells and primary human airway tissues through an improved infectivity of virions.  
> Hamsters infected with the G614 variant produced higher infectious titers in nasal washes and trachea, but not lungs, confirming clinical evidence that the D614G mutation enhances viral loads in the upper respiratory tract of COVID-19 patients and may increases transmission.  
> Sera from D614-infected hamsters exhibit modestly higher neutralization titers against G614 virus than against D614 virus. This indicates that the mutation may not reduce the protective effect of vaccines, and that therapeutic antibodies should be tested against the circulating G614 virus. |
> 464 adults (≥18 years) with PCR-confirmed moderate Covid-19  
> 235 patients: intervention arm - convalescent plasma (2 x 20 mL doses, transfused 24 hours apart) + best standard of care.  
> 229 Patients: control arm - best standard of care only.  
Main outcome measure: Composite of progression to severe disease (PaO2/ FiO2 <100 mm Hg) or all cause mortality at 28 days post-enrolment (D28).  
RESULTS:  
- Progression to severe disease or all cause mortality at D28 occurred in **44 (19%)** participants in the intervention arm and **41 (18%)** in the control arm.  
- **No difference** in 28-day mortality or progression to severe disease among patients with moderate Covid-19 treated with convalescent plasma + best standard of care compared with best standard of care alone.  
- **Neutralising antibody titres did not differ** between the two trial arms despite the transfusion of convalescent plasma.  
- Potentially no benefit of convalescent plasma from young survivors of mild Covid-19 administered to elderly patients with moderate/severe disease and robust antibody response.  
- No differences in the levels of inflammatory markers such as ferritin, C reactive protein, D-dimer, or lactate dehydrogenase between the arms.  
Limitations of the study: open label design, susceptible to anchoring bias of the treating doctors in outcome ascertainment. Some level of heterogeneity across the trial sites for best standard of care and participant enrolment. |
### Journal and date

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<th>Journal and date</th>
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<th>Field of expertise</th>
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<tr>
<td>JCM 22OCT2020</td>
<td>Comparison of upper respiratory viral load distributions in asymptomatic and symptomatic children diagnosed with SARS-CoV-2 infection in pediatric hospital testing programs</td>
<td>Kociolek L.K., et al. USA</td>
<td>Public Health / Epidemiology</td>
<td><strong>AIM:</strong> to delineate the distribution of SARS-CoV-2 viral loads in upper respiratory samples from asymptomatic and symptomatic children diagnosed to identify the role asymptomatic of children in the transmission of SARS-CoV-2. A robust dataset across all age brackets for extensive analysis were assembled to determine whether viral load distributions are consistent across age categories, SARS-CoV-2 assays, and institutions. <strong>METHODS:</strong> Data from asymptomatic (n=339) and symptomatic (n=478) children from 9 hospital in USA and Canada (March to July, 2020). Each institution provided viral load estimate (copies/mL sample) for each Ct value by age bracket (0-4y, 5-9y, 10-13y, 14-17y) and date of testing. Ct values for each assay were adjusted by centering each value around the institutional symptomatic median. <strong>RESULTS:</strong> &gt; Ct values were significantly higher in asymptomatic children of all ages compared to symptomatic children matched by age bracket and test collection date range. &gt; Timing of infection impacted the viral load distribution among asymptomatic children, with patients more likely to have recent infections showing higher viral loads than those more likely to have remote infections. &gt; Symptomatic children with diabetes (OR 6.5, p = 0.01), recent contact with a COVID-19 case (OR 2.3, p = 0.02), and testing for surveillance (OR 2.7, p = 0.005) had higher estimated risk of having a Ct value in the lowest quartile. &gt; Asymptomatic children tested for surveillance had significantly lower median adjusted Ct values/higher estimated viral loads than those tested for pre-op/AGP or pre-admission.</td>
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<td>Lancet Infect Dis. 22OCT2020</td>
<td>The temporal association of introducing and lifting non-pharmaceutical interventions (NPIs) with the time-varying reproduction number (R) of SARS-CoV-2: a modelling study across 131 countries</td>
<td>Li Y., et al. UK</td>
<td>Public Health / Epidemiology</td>
<td><strong>Modelling study,</strong> first to assess the temporal association between changing the status of a range of NPIs and the transmission of SARS-CoV-2 as measured by R. <strong>AIM:</strong> To understand the association of introducing and lifting NPIs with the level of transmission of SARS-CoV-2, as measured by the time-varying reproduction number (R). <strong>METHODS:</strong> By linking a global dataset of country-level daily R values with a global dataset of country-level policies on NPIs, we modelled the change in R values (as R ratio using log-linear regression) from day 1 to day 28 following the introduction and relaxation of eight individual NPIs among 131 countries. This study quantified the change in transmission of SARS-CoV-2, as measured by R, following the introduction and relaxation of individual NPIs by considering 4 candidates strategies for reintroduction (ban public event, workplace closure, ...). <strong>RESULTS</strong> &gt; Effect of introducing and lifting NPIs was not immediate and that the time required to reach certain levels of effect differed by NPI. &gt; The relaxation of school closure was associated with the greatest increase in R on day 7 (R ratio 1.05, 95% CI 0.96–1.14) and day 14 (1.18, 1.02–1.36). &gt; Reopening schools, lifting bans on public events, lifting bans on public gatherings of more than ten people, lifting requirements to stay at home, and lifting internal movement limits were associated with an increase in R of 11–25% on day 28 following the relaxation. &gt; The introduction of a public events ban was associated with the highest reduction in R; the R ratio was 0.90 (95% CI 0.82–0.99) on day 7, 0.83 (0.68–1.00) on day 14, and 0.76 (0.58–1.00) on day 28.</td>
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<td>NEJM 21OCT2020</td>
<td>Efficacy of Tocilizumab in Patients Hospitalized with Covid-19</td>
<td>Stone J.H., et al. USA</td>
<td>Therapeutics</td>
<td>Randomized, double-blind, placebo-controlled trial involving patients with SARS-CoV-2 infection, hyperinflammatory states, and at least two of the following signs: fever, pulmonary infiltrates, or the need for supplemental oxygen. Patients were administered either tocilizumab (TCZ, 8 mg/kg) or placebo. <em>Primary outcome:</em> intubation or death.</td>
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<td><a href="#">gotopaper</a></td>
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<td>&gt; 243 patients; 58% men, 42% women. The median age: 59.8 years, 45% of the patients were Hispanic or Latino.</td>
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<td>&gt; The hazard ratio (HR) for intubation or death in the TCZ group vs placebo group was 0.83, and the HR for disease worsening was 1.11. At D14, 18.0% of the patients in the TCZ group and 14.9% of the placebo group had had worsening of disease.</td>
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<td>&gt; Median time to discontinuation of supplemental oxygen was 5.0 days TCZ group and 4.9 days in placebo group. At D14, 24.6% of the patients in the TCZ group and 21.2% of the placebo group were still receiving supplemental oxygen.</td>
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<td>&gt; Patients who received TCZ had fewer serious infections than patients who received placebo.</td>
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<td><strong>TCZ was not effective for preventing intubation or death</strong> in moderately ill hospitalized patients with Covid-19. Some benefit or harm cannot be ruled out, however, because the confidence intervals for efficacy comparisons were wide.</td>
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<td>JAMA Intern Med. 20OCT2020</td>
<td>Effect of Tocilizumab vs Usual Care in Adults Hospitalized With COVID-19 and Moderate or Severe PneumoniaA Randomized Clinical Trial</td>
<td>Hermine O., et al. France</td>
<td>Therapeutics</td>
<td>Aim: to determine whether tocilizumab (TCZ, 2 doses: D1 and D3, 8 mg/kg) improves outcomes of patients hospitalized with moderate-to-severe COVID-19 pneumonia (requiring oxygen but no ventilation or ICU) compared to usual care (UC). <strong>Primary outcomes:</strong> scores &gt;5 on the WHO 10-point Clinical Progression Scale (WHO-CPS) on D4 and survival without need of ventilation at D14. <strong>Secondary outcomes:</strong> clinical status at D7 and D14, overall survival, time to discharge, time to oxygen supply independency, biological factors, adverse events.</td>
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<td><a href="#">gotopaper</a></td>
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<td>&gt; 130 patients analysed - 63 in TCZ group, 67 in UC group. 32% were women, median age was 64 years.</td>
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<td>&gt; In the <strong>TCZ group,</strong> 12 patients had a WHO-CPS score &gt;5 at D4 vs <strong>19 in the UC group,</strong> with a posterior probability of negative absolute risk difference of 89.0% not achieving the 95% predefined efficacy threshold.</td>
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<td>&gt; At day 14, <strong>12 fewer patients needed noninvasive ventilation (NIV) or mechanical ventilation (MV) or died in the TCZ group</strong> than in the UC group (24% vs 36%) with a posterior probability of hazard ratio (HR) less than 1 of 95.0%, achieving the predefined efficacy threshold. The HR for MV or death was 0.58.</td>
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<td>&gt; At D28, 7 patients had died in the TCZ group and 8 in the UC group. Serious adverse events occurred in 20 (32%) patients in the TCZ group and 29 (43%) in the UC group.</td>
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<td>In this clinical trial, <strong>TCZ did not reduce WHO-CPS scores ≤5 at D4 but might have reduced the risk of NIV, MV, or death by D14.</strong> No difference on D28 mortality was found.</td>
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<td>JAMA Intern Med.</td>
<td>Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized With COVID-19 PneumoniaA Randomized Clinical Trial</td>
<td>Salvarani C., et al. Italy <a href="https://doi.org/10.1001/jama.2020.18774">gotopaper</a></td>
<td>Therapeutics</td>
<td>AIM: to evaluate the effect of early tocilizumab (TCZ) administration (2 doses, 8 mg/kg up to 800 mg max) vs standard therapy in preventing clinical worsening in patients hospitalized with COVID-19 pneumonia. Primary outcome: entry into ICU with invasive mechanical ventilation, death from all causes, or clinical aggravation (PaO2/FIO2 ratio less than 150 mm Hg). &gt; 126 patients randomized (60 to the TCZ group; 66 to the control group). The median age was 60.0 years, 61.1% males. 3 patients withdrew from the study (123 patients analysed). &gt; 17/60 patients (28.3%) in the TCZ arm and 17/63 (27.0%) in the standard care group showed clinical worsening within 14 days since randomization. &gt; 2 patients in the TCZ group and 1 in the control group died before 30 days from randomization, and 6 and 5 patients were intubated in the 2 groups, respectively. &gt; The trial was prematurely interrupted after an interim analysis for futility. In this clinical trial, no benefit on disease progression was observed with TCZ treatment compared with standard care.</td>
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<tr>
<td>JAMA Intern Med.</td>
<td>Association Between Early Treatment With Tocilizumab and Mortality Among Critically Ill Patients With COVID-19</td>
<td>Gupta S., et al. USA <a href="https://doi.org/10.1001/jama.2020.18774">gotopaper</a></td>
<td>Therapeutics</td>
<td>Aim: to test whether tocilizumab (TCZ, administered the first 2 days of ICU admission) decreases mortality in patients with severe COVID-19 illness admitted to ICU. Primary outcome: time to death and 30-day mortality. &gt; 3924 patients analysed (62.8% males; median age, 62): 433 (11.0%) received TCZ. Patients treated with TCZ were younger (median age 58) and had a higher prevalence of hypoxemia on ICU admission (47.3% vs 37.9% with mechanical ventilation and a ratio of arterial pO2 to fraction of inspired oxygen of &lt;200 mm Hg) than the control group. &gt; 1544 patients (39.3%) died, including 125 (28.9%) treated with TCZ and 1419 (40.6%) of control group. &gt; During a median follow-up of 27 days, patients treated with TCZ had a lower risk of death compared with the control (HR, 0.71; 95% CI, 0.56-0.92). The estimated 30-day mortality was 27.5% in the TCZ group and 37.1% in the control group (risk difference, 9.6%). The risk of in-hospital mortality in this study was lower in patients treated with TCZ compared with the control group.</td>
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<td>Clin Infect Dis.</td>
<td>Clinical Characteristics and Outcomes of COVID-19 Patients Receiving Compassionate Use Leronlimab</td>
<td>Yang B., et al. USA <a href="https://doi.org/10.1093/cid/ciaa602">gotopaper</a></td>
<td>Therapeutics</td>
<td>Use of Leronlimab (Mab blocker of CCR5) administered as an open label compassionate use therapeutic for COVID-19. METHODS 23 hospitalized severe/critical COVID-19 patients &gt; 700mg leronlimab subcutaneously, repeated after 7 days in 17/23 patients still hospitalized. &gt; 18/23 received other experimental treatments (convalescent plasma, hydroxychloroquine, steroids, and/or tocilizumab). &gt; 5/23 received leronlimab after blinded placebo-controlled trials of remdesivir, sarilumab, selinexor, or tocilizumab. RESULTS &gt; Mean age: 69.5±14.9 years. 20/23 had significant co-morbidities. 22/23 receiving supplemental oxygen &gt; Blood showed markedly elevated inflammatory markers and elevated neutrophil/lymphocyte ratio. &gt; By day 30 after initial dosing, 17/23 were recovered, 2/23 were still hospitalized, and 4/23 had died. Of the 7 intubated at baseline, 4/7 were fully recovered off oxygen, 2/7 were still hospitalized, and 1/7 had died. CONCLUSIONS &gt; Leronlimab appeared safe and well tolerated. High recovery rate suggesting benefit.</td>
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Hydroxychloroquine as pre-exposure prophylaxis for COVID-19 in healthcare workers: a randomized trial
Rajasingham R., et al. USA
Therapeutics

Randomized, double-blind, placebo-controlled clinical trial of healthcare workers (HCW) with ongoing exposure to SARS-CoV-2 in the US and Canada. Randomized to hydroxychloroquine (HCQ) 400mg once weekly or twice weekly for 12 weeks.

Primary endpoint: confirmed or probable Covid-19-compatible illness.

- 1483 HCW, of which 79% reported performing aerosol-generating procedures.
- Incidence of Covid-19 (lab-confirmed or symptomatic compatible illness) was 0.27 events per person-year with once-weekly and 0.28 events per person-year with twice-weekly HCQ compared with 0.38 events per person-year with placebo.
- For once weekly HCQ prophylaxis, the hazard ratio was 0.72, for twice-weekly was 0.74 as compared with placebo.
- Median HCQ concentrations in whole blood were 98 ng/mL (IQR, 82–120) with once-weekly and 200 ng/mL (IQR, 159–258) with twice-weekly dosing. HCQ concentrations did not differ between participants who developed Covid-19-compatible illness (154 ng/mL) versus participants without Covid-19 (133 ng/mL; P=0.08).

Pre-exposure prophylaxis with HCQ once or twice weekly did not significantly reduce laboratory-confirmed Covid-19 or Covid-19-compatible illness among HCW.

Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial
Xia S., et al. China
Vaccines

METHODS
Randomised, double-blind, placebo-controlled, phase 1/2 trial in China.

- phase 1, 18–59 and ≥60 years old healthy volunteers (seronegative). Vaccine or placebo in a two-dose schedule of 2 μg, 4 μg, or 8 μg on days 0 and 28.
- phase 2, 18–59 years old healthy volunteers. Vaccine or placebo in a single-dose schedule of 8 μg on day 0 or on a two-dose schedule of 4 μg on days 0 and 14, 0 and 21, or 0 and 28.

Primary outcomes: safety and tolerability.
Secondary outcome: immunogenicity, assessed as the neutralizing antibody (nAb) responses against infectious SARS-CoV-2.

FINDINGS
- phase 1: 192 participants (mean age 53.7 years). Adverse reactions were mild or moderate in severity. No serious adverse event within 28 days post vaccination. nAb mean titres were higher at day 42 in the group aged 18–59 years (87.7 2μg group; 211.2 4μg group; and 228.7 8μg group) and the group aged 60 years and older (80.7 2μg group; 131.5 4μg group; and 170.8 7 8μg group) compared with the placebo group (2·0).
- phase 2: 448 participants (mean age 41.7 years). Adverse reactions were mild or moderate in severity. The most common systematic adverse reaction was fever. nAb titres on day 28 were significantly greater in the 4 μg days 0 and 14 (169·5), days 0 and 21 (282·7), and days 0 and 28 (218·0) schedules than the 8 μg day 0 schedule (14·7).

CONCLUSION
- BBIBP-CorV vaccine is safe and well tolerated.
- Two-dose immunization with 4 μg vaccine on days 0 and 21 or days 0 and 28 achieved higher nAb titers than the single 8 μg dose or 4 μg dose on days 0 and 14.
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METHODS  
NHP receiving 10 or 100 μg of mRNA-1273 (encoding prefusion-stabilized S protein of SARS-CoV-2), or no vaccine.  
> Assessment of T-cell responses before upper- and lower-airway challenge with SARS-CoV-2.  
> Active viral replication and viral genomes in bronchoalveolar-lavage (BAL) fluid and nasal  
> Histopathological analysis and viral quantification on lung-tissue specimens.  
RESULTS  
> Vaccination induces antibody levels exceeding those in human convalescent-phase serum in the 10-μg dose group in the 100-μg dose group.  
> Vaccination induced type 1 helper T-cell (Th1)-biased CD4 T-cell responses  
> Viral replication was not detectable in BAL fluid by day 2 after challenge in 7/8 animals, nor in the nose of any of the 8 animals in the 100-μg dose group by day 2 after challenge  
> Limited inflammation or detectable viral genome or antigen was noted in lungs of animals in either vaccine group.  
CONCLUSIONS  
Vaccination of NHP with mRNA-1273 induced robust SARS-CoV-2 neutralizing activity, rapid protection in the upper and lower airways, and no pathologic changes in the lung. |
| NEJM 14OCT2020           | Safety and Immunogenicity of Two RNA-Based Covid-19 Vaccine Candidates | Walsh E.E., et al. USA gotopaper | Vaccines          | > Safety and immunogenicity of 2 mRNA vaccines (BNT162b1 and b2) developed by BioNTech and Pfizer  
METHODS  
> Placebo-controlled, observer-blinded, dose-escalation, phase 1 trial conducted in the USA.  
> Healthy adults 18-55 and 65-85 years of age receiving placebo or BNT162b1 vaccine (encoding a secreted trimimerized SARS-CoV-2 receptor–binding domain); or BNT162b2 (encoding a membrane-anchored SARS-CoV-2 full-length spike, stabilized in the prefusion conformation).  
Primary outcome: safety; Secondary outcome: immunogenicity  
> Vaccine dose level (10 μg, 20 μg, 30 μg, and 100 μg).  
> In all groups but one, participants received two doses, with a 21-day interval between doses; in one group (100 μg of BNT162b1), participants received one dose.  
RESULTS  
195 participants. In both younger and older adults, the two vaccine candidates elicited similar dose-dependent SARS-CoV-2-neutralizing geometric mean titers, which were similar to or higher than the geometric mean titer of a panel of SARS-CoV-2 convalescent serum samples.  
CONCLUSIONS  
The safety and immunogenicity data from this study added to earlier interim safety and immunogenicity data regarding BNT162b1 in younger adults from trials in Germany and the US, supporting advancement of BNT162b2 to a phase 2–3 safety and efficacy evaluation. |
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| Lancet Infect Dis.       | Genomic evidence for reinfection with SARS-CoV-2: a case study       | Tillet R., et al. USA gotopaper | Virology          | The protective immunity conferred by infection with SARS-CoV-2 is currently unknown and the possibility of reinfection is not well understood.  
> A 25-year-old man who presented to health authorities on two occasions with symptoms of viral infection (April and end of June 2020)  
> Nasopharyngeal swabs at each presentation and twice during follow-up: two positive tests for SARS-CoV-2 in April and June, separated by two negative tests done during follow-up  
> Viral genetically significant differences at each infection.  
> The second infection was symptomatically more severe than the first.  
> Previous exposure to SARS-CoV-2 might not guarantee total immunity in all cases. The implications of reinfections could be relevant for vaccine development and application. |
| JAMA Pediatr.            | Outcomes of Neonates Born to Mothers With Severe Acute Respiratory Syndrome Coronavirus 2 Infection at a Large Medical Center in New York City | Dumitriu D., et al. USA gotopaper | Public Health / Epidemiology | AIM: To describe the outcomes of 101 neonates born to 100 mothers with perinatal asymptomatic/mild or severe/critical SARS-CoV-2 infection.  
- 141 tests obtained from 101 newborns (53.5% girls) on 0-25 days of life - 2 had indeterminate test results (low viral load), 1 never underwent retesting but remained well, the others had negative results on retesting.  
- Maternal severe/critical COVID-19 was associated with newborns born approximately 1 week earlier (37.9 vs 39.1 weeks) and at increased risk of requiring phototherapy (3/10 vs 6/91) compared with newborns of mothers with asymptomatic/mild COVID-19.  
- 55 newborns were followed up in a Follow-up Clinic at DOL 3-10 and remained well. 20 of them plus 3 followed up elsewhere had 32 nonroutine encounters documented at DOL 3-25, and none had evidence of SARS-CoV-2 infection, including 6 with negative retesting results.  
No clinical evidence of vertical transmission was identified in this study, despite most newborns rooming-in and direct breastfeeding practices. |
| Nature Comm.             | Analysis of SARS-CoV-2 vertical transmission during pregnancy         | Fenizia C., et al. Italy gotopaper | Public Health / Epidemiology | Analysis of SARS-CoV-2 genome on maternal and newborns nasopharyngeal swabs, vaginal swabs, maternal and umbilical cord plasma, placenta and umbilical cord biopsies, amniotic fluids and milk from 31 mothers with SARS-CoV-2 infection. Specific anti-SARS-CoV-2 antibodies and expression of genes involved in inflammatory responses in placentas, and in maternal and umbilical cord plasma were also tested.  
> SARS-CoV-2 genome was detected in one umbilical cord blood and in two at-term placentas, in one vaginal mucosa and in one milk specimen.  
> Specific anti-SARS-CoV-2 IgM and IgG antibodies were detected in one umbilical cord blood and in one milk specimen.  
> In the three documented cases of vertical transmission, SARS-CoV-2 infection was accompanied by a strong inflammatory response.  
These data support the hypothesis that in utero SARS-CoV-2 vertical transmission, while low, is possible. |
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> in-hospital mortality  
> time to hospital discharge  
(Matched cohort analysis of hospitalized patients with severe COVID-19),  
RESULTS:  
64 patients receiving CP a median of 7 days after symptom onset compared to a matched control group of 177 patients.  
> Incidence of in-hospital mortality: 12.5% and 15.8% in the CP and control groups, respectively (p = 0.52).  
> no significant difference in the risk of in-hospital mortality between the two groups.  
> overall rate of hospital discharge was not significantly different between the two groups, although there was a significantly increased rate of hospital discharge among patients 65-years-old or greater who received CP.  
Not a significant difference in risk of mortality or rate of hospital discharge between the CP and control groups, with a signal for improved outcomes among the elderly. |
| Science 09OCT2020       | REGN-COV2 antibodies prevent and treat SARS-CoV-2 infection in rhesus macaques and hamsters | Baum A. et al. USA gotopaper | Therapeutics                   | The group previously described REGN-COV2, a cocktail of two potent neutralizing antibodies (REGN10987+REGN10933) targeting non-overlapping epitopes on the SARS-CoV-2 spike protein.  
AIM: evaluation of the in vivo efficacy of this antibody cocktail in both rhesus macaques (model of mild disease), and golden hamsters (model of more severe disease).  
- REGN-COV-2 can greatly reduce virus load in lower and upper airways and decrease virus induced pathological sequelae when administered prophylactically or therapeutically in rhesus macaques.  
- Administration in hamsters limits weight loss and decreases lung titers and evidence of pneumonia in the lungs.  
These results provide evidence of the therapeutic potential of this antibody cocktail. |
- 499 patients were recruited to the point-of-care testing group, and 555 were included in the control group and tested by laboratory PCR. The two groups were similar with regard to the distribution of sex, age, and ethnicity.  
- 197 (39%) patients in the point-of-care testing group and 155 (28%) in the control group tested positive for COVID-19.  
- Median time to results was 1·7 h in the point-of-care testing group and 21·3 h in the control group.  
Point-of-care testing is associated with shorter time to results and could improve infection control measures and patient flow compared with centralised laboratory PCR testing. |
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<tr>
<td>NEJM 08OCT2020</td>
<td>Remdesivir for the Treatment of Covid-19 — Final Report</td>
<td>Beigel J.H., et al., ACTT-1 Study Group International gotopaper</td>
<td>Therapeutics</td>
<td>Double-blind, randomized trial of intravenous remdesivir (200 mg loading dose on day 1, followed by 100 mg daily for up to 9 additional days) vs placebo for 10 days in hospitalised adult Covid-19 patients who had evidence of lower respiratory tract infection.</td>
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<td>- 541 patients assigned to remdesivir and 521 to placebo.</td>
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<td>- Patients who received remdesivir had a median recovery time of 10 days as compared with 15 days among those who received placebo.</td>
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<td>- Patients who received remdesivir were found to be more likely than those who received placebo to have clinical improvement at day 15.</td>
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<td>- The Kaplan–Meier estimates of mortality were 6.7% with remdesivir and 11.9% with placebo by day 15 and 11.4% with remdesivir and 15.2% with placebo by day 29.</td>
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<td>- Serious adverse events were reported in 131 of the 532 patients who received remdesivir (24.6%) and in 163 of the 516 patients who received placebo (31.6%).</td>
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<td>Remdesivir was superior to placebo in shortening the time to recovery in this cohort.</td>
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<td>NEJM 08OCT2020</td>
<td>Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19</td>
<td>The RECOVERY Collaborative Group gotopaper</td>
<td>Therapeutics</td>
<td>METHODS RCT, open-label platform trial comparing a range of possible treatments with usual care in patients hospitalized with Covid-19.</td>
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<td>&gt; 1561 patients received hydroxychloroquine</td>
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<td>&gt; 3155 to receive usual care.</td>
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<td>Primary outcome: 28-day mortality.</td>
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<td>RESULTS &gt; No significative difference in primary outcome: death within 28 days occurred in 421 patients (27.0%) in the hydroxychloroquine group and in 790 (25.0%) in the usual-care group.</td>
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<td>&gt; Patients in the hydroxychloroquine group were less likely to be discharged from the hospital alive within 28 days than those in the usual-care group (59.6% vs. 62.9%).</td>
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<td>&gt; Among the patients who were not undergoing mechanical ventilation at baseline, those in the hydroxychloroquine group had a higher frequency of invasive mechanical ventilation or death (30.7% vs. 26.9%).</td>
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<td>&gt; Small numerical excess of cardiac deaths (0.4 percentage points) but no difference in the incidence of new major cardiac arrhythmia among the patients who received hydroxychloroquine.</td>
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<td>CONCLUSIONS Among patients hospitalized with Covid-19, those who received hydroxychloroquine did not have a lower incidence of death at 28 days than those who received usual care.</td>
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- 34,128 (US: 8362, South Korea: 7341, Spain: 18,425) COVID-19 patients, summarising 4811 - 11,643 unique aggregate characteristics (available at http://evidence.ohdsi.org/Covid19CharacterizationHospitalization/). COVID-19 patients have been majority male in the US and Spain, but predominantly female in South Korea. Age profiles vary across data sources. 
- Many comorbidities were common among COVID-19 patients (i.e. 37–70% of the US cohort, 30–46% of the Spanish and 24% South Korean had hypertension). 
- Prior medication use was common (i.e. 18–39% in the US, 27% in Spain and 14% in South Korea took ACE inhibitors and ARBs in the 30 days prior to hospitalisation). 
- Compared to 84,585 individuals hospitalised with influenza in 2014-19, COVID-19 patients have more typically been male, younger, and with fewer comorbidities and lower medication use. 
Protecting groups vulnerable to influenza is useful in the response to COVID-19, but broader strategies are needed to reflect the particular characteristics of COVID-19 patients. |
| The Lancet 05OCT2020 | Lopinavir–ritonavir in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial | RECOVERY Collaborative Group UK gotopaper | Therapeutics | Effects of usual care plus lopinavir-ritonavir (400mg-100mg by mouth for 10 days) vs usual care only in RECOVERY clinical trial (randomised, controlled, open-label, platform trial, includes 176 hospitals in the UK). Primary outcome was 28-day all-cause mortality. 
Data collectection: March 19 - June 29, 2020. 1616 hospitalised patients received lopinavir-ritonavir, 3424 received usual care. 
- 374 (23%) lopinavir–ritonavir patients and 767 (22%) usual care patients died within D28. 
- No significant difference in time until discharge alive from hospital (median 11days) or the proportion of patients discharged from hospital alive within D28. 
- Among patients not on invasive mechanical ventilation at baseline, there was no significant difference in the proportion who required invasive mechanical ventilation or died. 
These findings do not support the use of lopinavir–ritonavir for treatment of patients admitted to hospital with COVID-19. |
- Fresh territorial ischaemic lesions were detected in six (14%) patients. 37 (86%) patients had astrogliosis in all assessed regions. 
- Activation of microglia and infiltration by cytotoxic T lymphocytes was most pronounced in the brainstem and cerebellum, and meningeal cytotoxic T lymphocyte infiltration was seen in 34 (79%) patients. 
- SARS-CoV-2 was detected in the brains of 21 (53%) of 40 patients, with SARS-CoV-2 viral proteins found in cranial nerves originating from the lower brainstem and in isolated cells of the brainstem. SARS-CoV-2 in the CNS was not associated with severity of neuropathological changes. 
Neuropathological changes in patients with COVID-19 seem to be mild, pronounced neuroinflammatory changes in the brainstem being common. There was no evidence for CNS damage directly caused by SARS-CoV-2. |
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<tr>
<td>BMJ Open Respir Res. 05OCT2020</td>
<td>Association of smoking status with outcomes in hospitalised patients with COVID-19</td>
<td>Adrish M., et al. USA <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td>Retrospective analysis of adults hospitalised with COVID-19 (9 March - 18 May 2020) to determine association of smoking and severity of illness. - Of 1173 patients, 837 never smoked and 336 were current or past smoker (grouped in smokers group). Patients in smokers group were more likely to be male and had higher incidence of COPD (19% vs 6%), HIV infection (11% vs 5%), cancer (11% vs 6%), congestive heart failure (15% vs 8%), coronary artery disease (15% vs 9%), chronic kidney disease (11% vs 8%) and end-stage renal disease (10% vs 6%), compared with non-smokers. - Smokers were more likely to develop critical illness requiring mechanical ventilation (47% vs 37%). Among smokers, only current smokers had higher risk of death compared with never smokers. - Female sex, young age, low serum lactate dehydrogenase and systemic steroid use were associated with overall improved survival. In this single-centre retrospective, smoking was associated with development of critical illness and higher likelihood of death.</td>
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<td>Clin Infect Dis. 03OCT2020</td>
<td>Survival of SARS-CoV-2 and influenza virus on the human skin: Importance of hand hygiene in COVID-19</td>
<td>Hirose R., et al. Japan <a href="#">gotopaper</a></td>
<td>Virology</td>
<td>The stability of the severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) on human skin remains unknown. &gt; Model allowing the evaluation of the stability of SARS-CoV-2 and influenza A virus (IAV), mixed with culture medium or upper respiratory mucus, on human skin surfaces and the dermal disinfection effectiveness of 80% (w/w) ethanol against SARS-CoV-2 and IAV. &gt; Results: &gt; SARS-CoV-2 and IAV were inactivated more rapidly on skin surfaces than on other surfaces (stainless steel/glass/plastic); &gt; the survival time was significantly longer for SARSCoV-2 than for IAV [9.04 h (95% confidence interval: 7.96–10.2 h) vs. 1.82 h (1.65–2.00 h)]. &gt; Both SARS-CoV-2 and IAV in the mucus/medium on human skin were completely inactivated within 15 s by ethanol treatment. &gt; Conclusions: The 9-h survival of SARS-CoV-2 on human skin may increase the risk of contact transmission in comparison with IAV, thus accelerating the pandemic. Proper hand hygiene is important to prevent the spread of SARS-CoV-2 infections.</td>
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<td>Clin Infect Dis. 03OCT2020</td>
<td><strong>SARS-CoV-2 seroprevalence survey among 17,971 healthcare and administrative personnel at hospitals, pre-hospital services, and specialist practitioners in the Central Denmark Region</strong></td>
<td>Jespersen S., et al. Denmark <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td>Seroprevalence survey on SARS-CoV-2 among Danish healthcare workers (HCW) to identify high-risk groups. <strong>Methods</strong>&lt;br&gt;SARS-CoV-2 total antibody ELISA tests to the HCW and administrative personnel at 7 hospitals, pre-hospital services and specialist practitioner clinics in Central Denmark Region <strong>Results</strong>&lt;br&gt;25,950 participants&lt;br&gt; &gt; 17,971 underwent SARS-CoV-2 antibody testing. Of the 668 seropositive participants, 433 (64.8%) had previously been tested for SARS-CoV-2 RNA by RT-PCR, and 50.0% resulted positive.&lt;br&gt; &gt; Overall seroprevalence: 3.4% (CI: 2.5%-3.8%).&lt;br&gt; &gt; Higher seroprevalence in the western part of the region than in the eastern part (11.9% vs 1.2%).&lt;br&gt; &gt; In the high prevalence area, the emergency departments had the highest seroprevalence (29.7%), while departments without patients or with limited patient contact had the lowest seroprevalence (2.2%). <strong>Conclusions</strong>&lt;br&gt;Large differences in the prevalence of SARS-CoV-2 antibodies in HCW within a small geographical area of Denmark. Regular testing of HCW should be considered to identify areas with increased transmission.</td>
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<p>| Blood 01OCT2020 | <strong>Waning of SARS-CoV-2 RBD antibodies in longitudinal convalescent plasma samples within four months after symptom onset</strong> | Perreault J., et al. Canada <a href="#">gotopaper</a> | Public Health / Epidemiology | Transfusion of COVID-19 convalescent plasma (CCP) is used as a mean to reduce COVID-19 severity and help resolve the infection more rapidly&lt;br&gt; &gt; One of the main hypotheses to explain the potential clinical benefits of CCP is the presence of SARS-CoV-2 neutralizing antibodies (nAb)&lt;br&gt; &gt; Analysis of SARS-CoV-2 spike RBD antibodies using ELISA represents a valuable tool for the initial characterization of CCP. <strong>Methods:</strong>&lt;br&gt; &gt; Potential donors were recruited after at least 14 days of resolution of COVID-19 symptoms (Hema-Quebec; CONCOR-1 study)&lt;br&gt; &gt; presence of antibodies against SARS-CoV-2 RBD was determined using a semi-quantitative ELISA <strong>Results:</strong>&lt;br&gt; &gt; 262 patients; 6.9% seronegative at recruitment, up to 15% when considering only donors who had waited &gt;11-12 weeks after symptom onset before donating&lt;br&gt; &gt; level of anti-RBD antibodies at the first donation varies greatly between donors.&lt;br&gt; &gt; a decrease in anti-RBD antibody level between first and last donation was observed for all donors (not correlated with number of donations, but correlated with the time elapsed between the onset of symptoms and the time of the last donation)&lt;br&gt; &gt; anti-RBD response is relatively stable during the first 10 weeks after disease onset |</p>
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| Nature 30SEP2020 | COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T-cell responses | Sahin U., et al. Germany gotopaper | Vaccines | Phase1/2 vaccine trial:  
> Safety and tolerability of BNT162b1, a lipid nanoparticle formulated nucleoside-modified messenger RNA (mRNA) encoding the receptor binding domain (RBD) of the SARS-CoV-2 spike protein.  
> Vaccine groups:  
2 x 1 μg (n = 12); 2 x 10 μg (n = 12); 2 x 30 μg (n = 12); 2 x 50 μg (n = 12); 1 x 60 μg (n = 12)  
>60 participants; 18-55 years of age  
RESULTS:  
> Safety  
Local AE: Injection site pain (33–100% at dose 1, 27–92% at dose 2), swelling (0–25% at dose 1), redness (0–25% at dose 1)  
Systemic AE: Headache (25–83% at dose 1, 45–83% at dose 2), fatigue (33–83% at dose 1, 33–81% at dose 2), chills (8–83% at dose 1, 17–73% at dose 2), muscle pain (8–83% at dose 1, 27–67% at dose 2), joint pain (0–33% at dose 1, 17–58% at dose 2), fever (0–33% at dose 1, 9–54% at dose 2)  
> Immunogenicity  
Anti-RBD IgGs in vaccinated participants increased in a dose-dependent manner from twenty-one days after the priming, with a boosting effect after the 2nd dose (GMC at day 21: 265-1,672 U/mL; day 29: 2,015-25,006 U/mL; day 43: 3,920-18,289 U/mL. GMC from convalescent patients: 602 U/mL)  
High serum-neutralising GMTs were achieved on day 29 (after the booster dose) reaching 36 (1 µg dose level), 158 (10 µg dose level), 308 (30 µg dose level), and 578 (50 µg dose level), compared to 94 for the convalescent serum panel.  
BNT162b1 vaccine induces functional and proinflammatory CD4+/CD8+ T cell responses in almost all participants, with Th1 polarization. |
| NEJM 29SEP2020 | Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults | Andetson E.J., et al. USA gotopaper | Vaccines | BACKGROUND  
Testing immunogenicity and reactogenicity of mRNA-1273 from Moderna (encoding the stabilized prefusion SARS-CoV-2 spike protein) in older adults  
METHODS  
> Phase 1, dose-escalation, open-label trial 1273  
> 40 older adults, stratified according to age (56 to 70 years or ≥71 years).  
> 2x 25 µg or 2x 100 µg of vaccine administered 28 days apart.  
RESULTS  
> Safety  
SAE: mild or moderate and dose dependent and more common after second vaccination (fatigue, chills, headache, myalgia, and pain at the injection site).  
> Immunogenicity  
Anti-antibodies induction  
25 µg: GMT was 323,945 for the 56 and 70 years and 1,128,391 for the 71 years of age or older  
100 µg: GMT in the two age subgroups was 1,183,066 and 3,638,522, respectively  
Serum neutralizing-antibody responses appeared to be similar to those previously reported among vaccine recipients between the ages of 18 and 55 years and were above the median of a panel of controls who had donated convalescent serum.  
The vaccine elicited a strong CD4 cytokine response involving type 1 helper T cells. |
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<td>- The sampled population had similar age, sex, and race and ethnicity distribution to the US dialysis population.</td>
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<td>- Seroprevalence of SARS-CoV-2 was 8·0% in the sample, 8·3% when standardised to the US dialysis population (ranging from 3·5% in the west to 27·2% in the northeast), and 9·3% when standardised to the US adult population.</td>
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<td>- Comparing seroprevalent and case counts per 100 000 population, 9·2% of seropositive patients were diagnosed.</td>
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<td>- Residents of non-Hispanic Black and Hispanic neighbourhoods had higher odds of seropositivity (odds ratio 3·9 and 2·3, respectively) compared with predominantly non-Hispanic white neighbourhoods. Residents of neighbourhoods in the highest population density quintile had increased odds of seropositivity (10·3) compared with lowest density quintile.</td>
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<td>- County mobility restrictions of &gt;5% in March 2020 were associated with lower odds of seropositivity in July 2020, compared with mobility reduction of &lt;5%.</td>
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<td>During the first wave of the COVID-19 pandemic, &lt;10% of the US adult population formed antibodies against SARS-CoV-2, and &lt;10% of those with antibodies were diagnosed.</td>
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<td>- 67 patients (6%) remained hospitalised, 311 (30%) were discharged home or to an acute rehabilitation centre, 101 (10%) were discharged to a long-term acute care centre or unspecified location, 176 (17%) were discharged to another hospital, and 380 (37%) died.</td>
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<td>- The est. cumulative incidence of in-hospital mortality 90 days after the initiation of ECMO was 37·4%. Mortality was 39% in patients with a final disposition of death or hospital discharge.</td>
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<td>- The use of ECMO for circulatory support was independently associated with higher in-hospital mortality. In the subset of patients receiving respiratory (venovenous) ECMO and with ARDS, the est. cumulative incidence of in-hospital mortality 90 days after the initiation of ECMO was 38·0%.</td>
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<td>These data provide a generalisable estimate of ECMO mortality in the setting of COVID-19.</td>
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<td>Clin Infect Dis. 25SEP2020</td>
<td>Mass screening of asymptomatic persons for SARS-CoV-2 using saliva</td>
<td>Yokota I., et al. Japan gotopaper</td>
<td>Diagnostics</td>
<td>The utility of saliva as an alternative specimen for SARS-CoV-2 detection in asymptomatic persons is yet to be determined.</td>
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<td>METHODS Mass-screening study to compare the utility of nucleic acid amplification, such as RT-PCR testing, using nasopharyngeal swabs (NPS) and saliva samples from 1,924 individuals in two cohorts of asymptomatic individual from 2 cohorts (contact tracing and airport)</td>
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<td>RESULTS Sensitivity of nucleic acid amplification testing with nasopharyngeal and saliva specimens were 86% and 92%, respectively, with specificities greater than 99.9%.</td>
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<td>The true concordance probability between the nasopharyngeal and saliva tests was estimated at 0.998 on the estimated airport prevalence at 0.3%. In positive individuals, viral load was highly correlated between NPS and saliva.</td>
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<td>CONCLUSION Self-collected saliva is a valuable specimen to detect SARS-CoV-2 in mass screening of asymptomatic persons.</td>
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| Lancet Rheumatol. 25SEP2020 | Anti-C5a antibody IFX-1 (vilobelimab) treatment versus best supportive care for patients with severe COVID-19 (PANAMO): an exploratory, open-label, phase 2 randomised controlled trial | Vlaar A.P.J., et al. Netherlands gotopaper | Therapeutics | **BACKGROUND**
Analysis of the potential benefit and safety of selectively blocking the anaphylatoxin and complement protein C5a with the monoclonal antibody IFX-1 (vilobelimab) (in severe COVID19)

**METHODS**
- Open-label, randomised phase 2 trial (part of the adaptive phase 2/3 PANAMO trial)- ClinicalTrials.gov (NCT04333420).
- Intravenous IFX-1 in adults with severe COVID-19 (randomly assigned 1:1):
  - up to seven doses of 800 mg intravenously plus best supportive care (IFX-1 group) - or best supportive care only (control group).

**Primary outcome:** the percentage change in PaO2/FiO2 in the supine position between baseline and day 5.

**Other outcomes:** mortality at 28 days and SAE

**RESULTS**
- 30 patients enrolled (15 per group)
- Mean of PaO2/FiO2: 158 mm Hg (SD 63; range 84–265) in the IFX-1 group vs 189 mm Hg (89; 71–329) in the control group (day 5).
- Analyses of the least squares mean relative change in PaO2/FiO2 at day 5 showed no differences between treatment groups
- Similar frequency of SAE I both groups ([60%] vs [47%])
- No deaths related to treatment assignment, but a smaller proportion of patients had pulmonary embolisms classed as serious in the IFX-1 group
- Serious infections reported 20% of patients in the IFX-1 group vs 33% in the control group.

C5a inhibition with IFX-1 appears to be safe in patients with severe COVID-19.

- At least 101 of 987 patients with life-threatening COVID-19 pneumonia had neutralizing IgG auto-Abs against IFN-ω (13 patients), the 13 types of IFN-α (36), or both (52), at the onset of critical disease; a few also had auto-Abs against the other three type I IFNs.
- The auto-Abs neutralize the ability of the corresponding type I IFNs to block SARS-CoV-2 infection in vitro.
- These auto-Abs were not found in 663 individuals with asymptomatic or mild SARS-CoV-2 infection and were present in only 4 of 1,227 healthy individuals. Patients with auto-Abs were aged 25-87 years and 95 were men.

A B cell auto-immune phenocopy of inborn errors of type I IFN immunity underlies life-threatening COVID-19 pneumonia in at least 2.6% of women and 12.5% of men. |
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- Enrichment in rare variants predicted to be loss-of-function (LOF) at the 13 human loci known to govern TLR3- and IRF7-dependent type I interferon (IFN) immunity to influenza virus, in 659 patients with life-threatening COVID-19 pneumonia, relative to S34 subjects with asymptomatic or benign infection.  
- Experimental definition of LOF variants in 23 patients (3.5%), aged 17 to 77 years, underlying autosomal recessive or dominant deficiencies.  
- Human fibroblasts with mutations affecting this pathway are vulnerable to SARS-CoV-2.  
Inborn errors of TLR3- and IRF7-dependent type I IFN immunity can underlie life-threatening COVID-19 pneumonia in patients with no prior severe infection. |
| Science 24SEP2020 | Ultrapotent human antibodies protect against SARS-CoV-2 challenge via multiple mechanisms | Tortorici M.A., et al. USA | Therapeutics | Reported findings:  
- Isolation and characterization of two ultrapotent SARS-CoV-2 human neutralizing antibodies (S2E12 and S2M11) that protect hamsters against SARS-CoV-2 challenge.  
- Cryo-electron microscopy structures show that S2E12 and S2M11 competitively block ACE2 attachment and that S2M11 locks the spike in a closed conformation.  
- Cocktails including S2M11, S2E12 or the previously identified S309 antibody broadly neutralize a panel of circulating SARS-CoV-2 isolates and activate effector functions.  
These results pave the way to implement antibody cocktails for prophylaxis or therapy. |
METHODS  
- Analysis of prevalence of SARS CoV-2 RNAemia (presence of SARS-CoV-2 RNA in blood) and the strength of its association with clinical severity variables.  
- Paired nasopharyngeal and plasma samples were included from 85 patients (Median age: 55 years)  
RESULTS  
> Individuals with RNAemia were older than those with undetectable SARS-CoV-2 RNA in plasma (63 vs 50 years; P = .04).  
> Comorbidities were frequent including obesity (37.6%), hypertension (30.6%), and diabetes mellitus (22.4%).  
> RNAemia was detected in 28/85 (32.9%) of patients, including 22/28 (78.6%) who required hospitalization.  
> In models adjusted for age, RNAemia was detected more frequently in individuals who developed severe disease including ICU admission (32.1 vs 14.0%; P = .04) and invasive mechanical ventilation (21.4% vs 3.5%; P = .02).  
> All 4 deaths occurred in individuals with detectable RNAemia.  
> An additional 121 plasma samples from 28 individuals with RNAemia were assessed longitudinally, and RNA was detected for a maximum duration of 10 days.  
CONCLUSIONS  
This study demonstrated a high proportion of SARS-CoV-2 RNAemia, and an association between RNAemia and clinical severity suggesting the potential utility of plasma viral testing as a prognostic indicator for COVID-19. |
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The model allows the:
- Characterization of the effect of temporal changes in viral transmission rate produced by climate and NPI deployment
- Evaluation of the impact of a transmission-reducing vaccine of varying efficacy relative to natural immunity
- Estimation of postpandemic immunity landscape and clinical case burden in different scenarios shaped by virus biology, presence or absence of external drivers, interventions and vaccine refusal

**CONCLUSIONS:**
> Variation in the immune response to primary SARSCoV2 infection and a potential vaccine can lead to different immune landscapes and burden of critically severe cases, ranging from sustained epidemics to almost elimination.

> Accurately characterizing the individual life stories and cumulative immune landscape of the population to primary and secondary infection and vaccination will be critical for the management and control of pandemic. |


**Methods:** prospective, randomized, controlled, open-label trial on 24 hospitalized adult COVID-19 patients with prolonged PCR positivity. Leflunomide + IFN α-2a versus IFN α-2a alone for 10 days were tested.

- Treatment with leflunomide was not associated with a difference from the IFN α-2a alone group in the duration of viral shedding.
- Patients given leflunomide did not have a substantially shorter length of hospital stay than patients treated with interferon alone (median: 29.0 and 33.0 days, respectively).
- Two leflunomide recipients presented adverse events.

In this cohort, no benefit in terms of the duration of viral shedding was observed with leflunomide treatment. |


- Within 48 hours, all patients except one experienced amelioration of clinical symptoms. The inflammatory syndrome abated within a week. One patient who needed mechanical ventilation for severe COVID-19 disease died of bacterial pneumonia.
- SARS-CoV-2 RNAemia decreased to below the sensitivity threshold in 9 out of 9 evaluated patients.
- Virus-specific T-cell responses was analyzed before convalescent plasma transfusion in 3 patients. All showed a conserved SARS-CoV-2 T-cell response and poor cross-response to other coronaviruses. No adverse event was reported.

In COVID-19 patients unable to mount a specific humoral response to SARS-CoV-2 and presenting protracted symptoms, convalescent plasma with anti-SARS-CoV-2 antibodies could be a promising approach. |
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<td>Lancet Microbe 17SEP2020</td>
<td>Assessing a novel, lab-free, point-of-care test for SARS-CoV-2 (CovidNudge): a diagnostic accuracy study</td>
<td>Gibani M.M., et al. UK <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>Diagnostic accuracy assessment of a novel, rapid point-of-care real time RT-PCR CovidNudge test, which requires no laboratory handling or sample pre-processing. Nasopharyngeal swabs are inserted directly into a cartridge with all reagents and components required for RT-PCR reactions. - 386 paired samples tested: 73% self-referred health-care workers, 4% from patients in the emergency department, 23% hospital inpatient admissions. - 67 samples tested positive on the CovidNudge point-of-care platform and 71 with standard laboratory RT-PCR. - Overall sensitivity of the point-of-care test compared with laboratory-based testing was 94%, and overall specificity was 100%. Test sensitivity varied by group (self-referred healthcare workers 93%, patients in the emergency department 100%; hospital inpatient admissions 100%). Specificity was consistent between groups (100%). - Point of care testing performance was similar during a period of high (25%) and low (3%) prevalence of laboratory positive tests. - Amplification of viral nucleocapsid (n1, n2, and n3) and envelope protein gene (e-gene) were most sensitive for detection of spiked SARS-CoV-2 RNA. The CovidNudge platform is a sensitive, specific, and rapid point of care test for the presence of SARS-CoV-2. The device has been implemented in UK hospitals since May, 2020.</td>
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<td>JAMA Otolaryngol. Head Neck Surg, 17SEP2020</td>
<td>In Vitro Efficacy of a Povidone-Iodine Nasal Antiseptic for Rapid Inactivation of SARS-CoV-2</td>
<td>Frank S., et al. USA <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Aim: to evaluate the in vitro efficacy of PVP-I nasal antiseptic for the inactivation of SARS-CoV-2, testing 3 concentrations (0.5%, 1.25%, and 2.5%) at clinically significant contact times of 15 and 30 seconds. - Povidone-iodine nasal antiseptics at concentrations tested completely inactivated SARS-CoV-2 within 15 seconds of contact (log reduction value of greater than 3 log10 of the 50% cell culture infectious dose of the virus). - The ethanol, 70%, positive control did not completely inactivate SARS-CoV-2 after 15 seconds of contact, performing worse than the tested nasal antiseptics in these experimental conditions. - No cytotoxic effects on cells were observed after contact with each of the nasal antiseptics tested. Povidone-iodine nasal antiseptic solutions rapidly inactivate SARS-CoV-2 and may play an adjunctive role in mitigating viral transmission beyond personal protective equipment.</td>
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<td>Cell 16SEP2020</td>
<td>Antigen-specific adaptive immunity to SARS-CoV-2 in acute COVID-19 and associations with age and disease severity</td>
<td>Rydzynski Moderbacher C., et al. USA <a href="#">gotopaper</a></td>
<td>Immunology</td>
<td>Aim: explore the relationship between antigen-specific immune responses and COVID-19 disease severity, by examining SARS-CoV-2-specific CD4+ and CD8+ T cell and neutralizing antibody responses in acute and convalescent subjects. - Adaptive immune responses limit COVID-19 disease severity. Both SARS-CoV-2-specific CD4+ and CD8+ T cells, as well as coordinated adaptive responses, were each associated with milder disease, suggesting roles for CD4+ and CD8+ T cells in protective immunity in COVID-19. - Coordination of SARS-CoV-2 antigen-specific responses was disrupted in individuals &gt; 65 years old. Scarcity of naïve T cells was also associated with ageing and poor disease outcomes. - CXCL10 may be a biomarker of impaired T cell responses in acute COVID-19. Possibly, coordinated CD4+ T cell, CD8+ T cell, and antibody responses are protective, but uncoordinated responses frequently fail to control disease.</td>
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- Oxygen requirements on day 14 after transfusion worsened in 17.9% of plasma recipients versus 28.2% of propensity score–matched controls hospitalized with COVID-19.  
- Survival improved in plasma recipients.  
Convalescent plasma is potentially effective against COVID-19, but adequately powered, randomized controlled trials are needed. |
Randomized clinical trial – open-label intervention – 200 participants no comorbidities  
2 arms:  
- Usual care (n=100)  
- Usual care + 3 doses of recombinant human granulocyte colony-stimulating factor (rhG-CSF) (n=100).  
Primary endpoint: time from randomization to improvement of at least 1 point on a 7-category disease severity score.  
RESULTS:  
- Time to clinical improvement was similar between groups (rhG-CSF group median 12 days vs 13 days; HR=1,28 IC95%[0,95 – 1,71], p=0,06).  
Secondary endpoint:  
- Proportion of patient progressing to ARDS, sepsis or septic shock was lower in rhG-CSF group (2% vs 15%).  
- At 21 days, 2 patients had died in rhG-CSF group vs 10 in usual care group (HR: 0,19 IC95%(0,04 – 0,88)).  
- At day 5: lymphocytes cell count was higher in the rhG-CSF group (1050/µL vs 620/ µL).  
Serious adverse events were similar (14,5% in rhG-CSF group vs 21% in usual care group).  
--> rhG-CSF treatment did not accelerate clinical improvement but number of patients developing critical illness or dying may have been reduced. |
| Lancet Glob. Health 09SEP2020 | Projected health-care resource needs for an effective response to COVID-19 in 73 low-income and middle-income countries: a modelling study | Tan-Torres Edejer, T., et al, Switzerland gotopaper | Public Health / Epidemiology | AIM: estimate the additional health-care costs of a strategic preparedness and response plan (SPRP) in 73 low- and middle-income countries if current transmission levels are maintained in a status quo scenario, or if the transmission is increased or decreased by 50%.  
- The total cost estimate for the COVID-19 response in the status quo scenario was US$52-45 billion over 4 weeks, at $8-60 per capita.  
- For the decreased or increased transmission scenarios, the totals were $33-08 billion and $61-92 billion, respectively.  
- Costs would triple under the status quo and increased transmission scenarios at 12 weeks. The costs of the decreased transmission scenario over 12 weeks was equivalent to the cost of the status quo scenario at 4 weeks.  
- By percentage of the overall cost, case management (54%), maintaining essential services (21%), rapid response and case investigation (14%), and infection prevention and control (9%) were the main cost drivers.  
The sizeable costs of a COVID-19 response in the health sector will escalate, particularly if transmission increases. |
Clinical Outcomes in Young US Adults Hospitalized With COVID-19

Cunningham J.W., et al.
US gotopaper

Public Health / Epidemiology

> GAP: Few studies have included younger patients to better understand their anticipated clinical trajectory.

> METHODS
- Clinical profile and outcomes of 3222 young adults (18-34 years) requiring hospitalization for COVID-19 (419 US hospitals), discharged between April 1, 2020, and June 30, 2020. Pregnant young adults admitted for childbirth (n = 1644) were excluded. - Comorbidities and outcomes during COVID-19 hospitalization were defined using diagnosis, procedure, or billing ICD-10 codes.
- A 2-sided P value of <.05 was considered significant.

> RESULTS
Population characteristics: mean age was 28.3 years, 1849 (57.6%) men, 1187 (36.8%) had obesity, 789 (24.5%) morbid obesity, 588 (18.2%) diabetes, 519 (16.1%) hypertension

During hospitalization: 684 patients (21%) required intensive care, 331 (10%) required mechanical ventilation, 88 (2.7%) died, vasopressors or inotropes were used for 217 patients (7%), central venous catheters for 283 (9%), and arterial catheters for 192 (6%). The median length of stay was 4 days.

Risk factors: Morbid obesity, hypertension and male sex were associated with greater risk of death or mechanical ventilation. Morbid obesity was present in 140 patients (41%) who died or required ventilation. Diabetes was associated with increased risk of this outcome in univariable analysis but did not reach statistical significance after adjustment. Patients with multiple risk factors (morbid obesity, hypertension, and diabetes) faced risks similar to 8862 middle-aged (age 35-64 years) nonpregnant adults with COVID-19 infection without these conditions

> CONCLUSIONS
- Morbid obesity, hypertension, and diabetes in young adults are associated with greater risks of adverse event following SARS-CoV2 Infection
- Young adults with more than 1 of these conditions faced risks comparable with those observed in middle-aged adults without them

Comparison of Clinical Features of COVID-19 vs Seasonal Influenza A and B in US Children

Song X., et al., US gotopaper

Public Health / Epidemiology

Aim: Retrospective cohort study to describe the similarities and differences in clinical features between COVID-19 and seasonal influenza in US children.

- 315 Covid-19 patients were included, 52% male, median age 8.3 years. 1402 influenza patients were included, 53% male, median age 3.9 years.
- COVID-19 and seasonal influenza patients had a similar hospitalization rate (17% vs 21%), ICU admission rate (6% vs 7%), and use of mechanical ventilators (3% vs 2%).
- Of hospitalized patients, more of those with COVID-19 than with seasonal influenza reported fever (76% vs 55%), diarrhea or vomiting (26% vs 12%), headache (11% vs 3%), body ache or myalgia (22% vs 7%), and chest pain (11% vs 3%).
- Differences between patients hospitalized with COVID-19 vs influenza who reported cough and shortness of breath were not statistically significant.

In this cohort study there was no difference in hospitalization rates, ICU admission rates, and mechanical ventilator use between the 2 groups. More patients hospitalized with COVID-19 than with seasonal influenza reported clinical symptoms at the time of diagnosis.
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- 57.6% of participants intended to be vaccinated, 31.6% were not sure, and 10.8% did not intend to be vaccinated. 
- Factors independently associated with vaccine hesitancy included younger age, Black race, lower educational attainment, and not having received the influenza vaccine in the prior year. 
- Reasons for vaccine hesitancy included vaccine-specific concerns, a need for more information, antivaccine attitudes or beliefs, and a lack of trust. 
Targeted and multipronged efforts will be needed to increase acceptance of a COVID-19 vaccine when one becomes available. |
| The Lancet 04SEP2020 | Azithromycin in addition to standard of care versus standard of care alone in the treatment of patients admitted to the hospital with severe COVID-19 in Brazil (COALITION II): a randomised clinical trial | Furtado RHM et al. Brazil | Therapeutic | AIM: adding azithromycin to standard of care, which included hydroxychloroquine, would improve clinical outcomes of patients admitted to the hospital with severe COVID-19. 
Multicenter (57) – open label study, randomized Patients hospitalized with COVID-19 and at least one criterion: oxygen supplementation> 4L - high flow nasal canula - non invasive mechanical ventilation - mechanical ventilation 2 arms: 
- azithromycin + SoC (n=214) 
- SoC without macrolide (n=183) The primary endpoint: clinical status at day 15 after randomisation, assessed by a six-point ordinal scale (by an independent adjudication committee) 
RESULTS: 
- No difference for clinical status at day 15 between the azithromycin and control groups (OR 1·36 [95% CI 0·94–1·97], p=0·11). 
- Rate of adverse events were not significantly different between two groups.  
--> adding azithromycin to SoC did not improve clinical outcomes. 
--> patients in the azithromycin group had similar mortality and incidence of secondary infections, duration of hospital stay, and time free from mechanical ventilation compared with patients in the control group. 
--> mortality rate was higher than in previous randomized trials in patients with COVID-19. 
Limitations: absence of difference between two groups was due to type 2 error à sample size based on a large magnitude of effects |
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<tr>
<td>JEM 04SEP2020</td>
<td>Phenotypical and functional alteration of unconventional T cells in severe COVID-19 patients</td>
<td>Jouan Y., et al., France [gotopaper]</td>
<td>Immunology</td>
<td>In blood and airways of severe COVID-19 patients, we serially analyzed unconventional T cells, a class of T lymphocytes (MAIT, γδT, and iNKT cells) with potent antimicrobial and regulatory functions.</td>
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<td>- Circulating unconventional T cells of COVID-19 patients presented with a profound and persistent phenotypic alteration.</td>
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<td>- In the airways, highly activated unconventional T cells were detected, potentially contributing to the regulation of local inflammation.</td>
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<td>- Expression of the CD69 activation marker on blood iNKT and MAIT cells of COVID-19 patients on admission was predictive of clinical course and disease severity.</td>
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<td>Thus, COVID-19 patients present with an altered unconventional T cell biology.</td>
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<td>The Lancet 04SEP2020</td>
<td>Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia</td>
<td>Logunov et al., Russia [gotopaper]</td>
<td>Vaccine</td>
<td>- Heterologous COVID-19 vaccine consisting of two components, a recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector, both carrying the gene for SARS-CoV-2 spike glycoprotein (rAd26-S and rAd5-S).</td>
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<td>- 2 formulations (frozen and lyophilised).</td>
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<td>-76 participants enrolled in two non-randomised phase 1/2 studies (38 in each study)</td>
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<td>- In each study, 9 volunteers received rAd26-S in phase 1, 9 received rAd5-S in phase 1, and 20 received rAd26-S and rAd5-S in phase 2</td>
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<td>Both formulations (frozen and lyophilised) were safe and well tolerated. Most adverse events were mild and no serious adverse events were detected. They both induced strong humoral and cellular immune responses in participants.</td>
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<td>Bayesian randomized clinical trial – open-label intervention – 384 adults admitted to an ICU.</td>
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<td>3 arms:</td>
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<td>- A fixed 7-days course of intravenous hydrocortisone (n=137)</td>
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<td>- A shock-dependent course (n=146)</td>
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<td>- No hydrocortisone (n=101).</td>
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<td>Primary endpoint: organ support-free days (days alive and free of ICU-based respiratory or cardiovascular support) within 21 days.</td>
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<td>RESULTS:</td>
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<td>For the fixed-dose, shock-dependent, and no hydrocortisone groups, respectively:</td>
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<td>- 30%, 26% and 33% mortality rates</td>
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<td>- and 11.5, 9.5, and 6 median organ support–free days among survivors.</td>
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<td>Compared with no hydrocortisone, treatment with a 7-day fixed-dose course of hydrocortisone or shock-dependent dosing of hydrocortisone:</td>
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<td>- 93% and 80% probabilities of superiority with regard to the odds of improvement in organ support-free days within 21 days.</td>
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<td>- Few serious adverse events were reported in the 3 arms: 3%, 3% and 1% respectively.</td>
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<td>Following a press release from the RECOVERY trial on June 16, 2020 --&gt; stop enrollment of patients with COVID-19 in the corticosteroid domain due to a loss of equipoise.</td>
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<td>--&gt; the trial was stopped early and no treatment strategy met prespecified criteria for statistical superiority, precluding definitive conclusions.</td>
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<td>--&gt; No strategy was determined to be optimal.</td>
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| JAMA 02SEPT2020  | Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19. The CoDEX Randomized Clinical Trial | Tomazini B.M. et al., Brazil gotopaper | Therapeutic        | **AIM:** To determine whether intravenous dexamethasone increases the number of ventilator-free days among patients with COVID-19–associated ARDS.  
Randomized, open-label, clinical trial, multicenter- in 41 ICU 299 patients with COVID-19 moderate to severe ARDS (Berlin definition)  
2 arms:  
- Dexamethasone + standard of care  
- Standard of care  
**Primary endpoint:** ventilator-free days during the first 28 days, defined as being alive and free from mechanical ventilation.  
**RESULTS:**  
Mean ventilator free-days for the dexamethasone group and SoC group, respectively:  
- 6,6 IC95% [5 – 8,2] vs 4,0 IC95% [2,9 – 5,4], respectively (p=0,04)  
- No significant difference in all-cause mortality at 28 days (56,3% vs 61,5% in SoC group)  
- Mean SOFA score was significantly lower in dexamethasone group (6,1 vs 7,5, p=0,004).  
- No difference in adverse events: 3,3% vs 6,1%  
--- Intravenous dexamethasone plus standard care, compared with standard of care alone, resulted in a statistically significant increase in the number of days alive and free from mechanical ventilation over 28 days.  
--- **the study was interrupted** before the original sample size was obtained due to external evidence of benefit.  
**Limitations:** open-label design - 35%of the patients in the control group received corticosteroids during the study period. |
| JAMA 02SEPT2020  | Effect of Hydrocortisone on 21-Day Mortality or Respiratory Support | Dequin P.F. et al., France gotopaper | Therapeutic        | **AIM:** the effect of hydrocortisone on treatment failure on day 21 in critically ill patients with SARS-CoV-2 infection and acute respiratory failure.  
Multicenter randomized double-blind sequential trial.  
2 arms:  
- Low dose of hydrocortisone  
- Placebo  
**Primary endpoint:** treatment failure on day 21, was defined as death or persistent dependency on mechanical ventilation or high-flow oxygen therapy.  
The study intended to enroll 290 patients but was stopped early following the recommendation of the data and safety monitoring board.  
**RESULTS:**  
- 149 patients enrolled (99,3% completed the study) – 81,2% mechanically ventilated  
- there were 69 treatment failure events, including 11 deaths in the hydrocortisone group and 20 deaths in the placebo group.  
- Treatment failure on day 21, occurred in 32 of 76 patients (42,1%) in the hydrocortisone group compared with 37 of 73 (50,7%) in the placebo group (p = 0,29).  
- No serious events were related to the study treatment  
--- low-dose hydrocortisone, compared with placebo, did not significantly reduce treatment failure at day 21.  
**Limitations:** the trial was stopped early and lacked power. |
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| JAMA 02SEP2020   | Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19. A Meta-analysis. | Sterne J. et al., UK [gotopaper](#) | Therapeutic Meta-analysis | AIM: estimate the association between administration of corticosteroids compared with usual care or placebo and 28-day all-cause mortality.  
Prospective meta-analysis that pooled data from 7 randomized clinical trials – 1703 critically ill patients with COVID-19.  
Patients received:  
- systemic dexamethasone, hydrocortisone, or methylprednisolone (678 patients),  
- usual care or placebo (1025 patients).  
Primary endpoint: all-cause mortality at 28 days after randomization.  
RESULTS:  
- There were 222 deaths among the 678 patients randomized to corticosteroids and 425 deaths among the 1025 patients randomized to usual care or placebo (summary OR, 0.66 IC95% [0.53-0.82]; p < .001 based on a fixed-effect meta-analysis).  
- Risk of bias was assessed as "low" for 6 of the 7 trials.  
Summary OR for the association with mortality was:  
- For dexamethasone: 0.64 IC95% [0.5 – 0.82]; p<0.001 (3 trials)  
- For hydrocortisone: 0.69 IC95% [0.43 – 1.12]; p=0.13 (3 trials)  
- For methylprednisolone: 0.91 IC95% [0.29 – 2.87]; p=0.87 (1 trial)  
--- In critically ill patients with COVID-19, administration of systemic corticosteroids, compared with usual care or placebo, was associated with lower 28-day all-cause mortality.  
Limitations: follow-up was censured when patient were discharged from the hospital – 1 trial was assessed as "some concerns" about the risk of bias – definition and reporting of serious adverse events were not consistent. |
| NEJM 02SEP2020   | Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine | Keech C et al., USA – Australia [gotopaper](#) | Vaccine | AIM: evaluate the safety and immunogenicity of the rSARS-CoV-2 vaccine (NVX-CoV2373)  
Randomized, placebo-controlled phase 1–2 trial.  
The primary endpoint: reactogenicity; laboratory values (serum chemistry and hematology), according to FDA toxicity scoring, to assess safety; and IgG anti–spike protein response.  
RESULTS:  
- 83 participants in the vaccine with adjuvant group + 25 in the vaccine without adjuvant + 23 placebo.  
- No serious adverse events – reactogenicity was absent or mild in the majority  
- The addition of adjuvant resulted in enhanced immune responses and induced a Th1 response.  
--- At 35 days, NVX-CoV2373 appeared to be safe  
--- It elicited immune responses that exceeded levels in Covid-19 convalescent serum  
--- The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype. |
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<tr>
<td>Nature 26AUG2020</td>
<td>Sex differences in immune responses that underlie COVID-19 disease outcomes</td>
<td>Takahashi et al., USA <a href="#">gotopaper</a></td>
<td>Immunology</td>
<td>Focusing the analysis on patients with moderate disease who had not received immunomodulatory medications; &gt; male patients had higher plasma levels of innate immune cytokines such as IL-8 and IL-18 along with more robust induction of non-classical monocytes. &gt; female patients mounted significantly more robust T cell activation than male patients during SARS-CoV-2 infection, which was sustained in old age. &gt; a poor T cell response negatively correlated with patients’ age and was associated with worse disease outcome in male patients, but not in female patients. &gt; higher innate immune cytokines in female patients associated with worse disease progression, but not in male patients. These findings reveal a possible explanation underlying observed sex biases in COVID-19, and provide an important basis for the development of a sex-based approach to the treatment and care of men and women with COVID-19.</td>
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<td>Clin Infect Dis 25AUG2020</td>
<td>COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing</td>
<td>Kai-Wang To K., et al., China <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>First documented case of re-infection of the same individual by SARS-CoV-2. The second episode of asymptomatic infection occurred 142 days after the first symptomatic episode in an apparently immunocompetent patient. During the second episode, there was serological evidence of elevated C-reactive protein and SARS-CoV-2 IgG seroconversion. Viral genomes from first and second episodes belong to different clades/lineages. The first virus was phylogenetically closely related to strains collected in March/April 2020, while the second virus genome was closely related to strains collected in July/August 2020. Epidemiological, clinical, serological and genomic analyses confirmed that the patient had re-infection instead of persistent viral shedding from first infection.</td>
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<td>LANCET GLOBAL HEALTH 25AUG2020</td>
<td>Immediate impact of stay-at-home orders to control COVID-19 transmission on socioeconomic conditions, food insecurity, mental health, and intimate partner violence in Bangladeshi women and their families: an interrupted time series</td>
<td>Hamadani J D et al., Bangladesh <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>AIM: The immediate impact of COVID-19 lockdown orders on women and their families in rural Bangladesh &gt; Interrupted time series – compare data from families on income / food security/ mental health a median of 1 years and 2 years before the COVID-19 pandemic to data collected during the lockdown. 2424 women provided consent – 2414 of 2417 mothers were aware of and adhering to the stay-at-home advice. Results: &gt; 96% reported a reduction in paid work for the family: median monthly family income fell from US$212 at baseline to $59 during lockdown. &gt; Proportion of families earning less than $1,90/days rose from 0,2% (5) to 47,3% (992). &gt; The number of families experiencing any level of food insecurity increased by 51,7% (p&lt;0,0001). &gt; Mother’s depression and anxiety symptoms increased during the lockdown. &gt; Over half women reported that emotional or moderate physical violence had increase during the lockdown. &gt; COVID-19 lockdown present significant economic, psychosocial and physical risks to the wellbeing of women and their families. Support is needed for all affected families.</td>
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<td>Clin Infect Dis 24AUG2020</td>
<td>BCG vaccination in infancy does not protect against COVID-19. Evidence from a natural experiment in Sweden</td>
<td>Chaisemartin and Chaisemartin, Sweden <a href="#">gotopaper</a></td>
<td>Vaccine</td>
<td>This paper takes advantage of a rare nationwide natural experiment that took place in Sweden in 1975, where discontinuation of newborns BCG vaccination led to a dramatic fall of the BCG coverage rate. - Numbers of COVID-19 cases and hospitalizations were recorded for birth cohorts born just before and just after 1975, representing 1,026,304 and 1,018,544 individuals, respectively. - Regression discontinuity to assess the effect of BCG vaccination on Covid-19 related outcomes. &gt; While the effect of a recent vaccination must be evaluated, we provide strong evidence that receiving the BCG vaccine at birth does not have a protective effect against COVID-19 among middle-aged individuals.</td>
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> - In mice and rhesus macaques, intramuscular injection with Ad5-5-nb2 elicits systemic S-specific antibody and cell-mediated immune (CMI) responses.  
> - Intranasal inoculation elicits both systemic and pulmonary antibody responses but weaker CMI response.  
> - At 30 days after a single vaccination with Ad5-5-nb2 either intramuscularly or intranasally, macaques are protected against SARS-CoV-2 challenge.  
> - A subsequent challenge reveals that macaques vaccinated with a 10-fold lower vaccine dosage (1 x 1010 viral particles) are also protected, demonstrating the effectiveness of Ad5-5-nb2 and the possibility of offering more vaccine dosages within a shorter timeframe. |
| JAMA 21AUG2020 | Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19A Randomized Clinical Trial | Spinner C D et al USA, Europe, Asia [gotopaper](#) | Therapeutic | AIM: does remdesivir provide a benefit on clinical status for patients hospitalized with moderate COVID-19? Efficacy of 5 or 10 days of remdesivir treatment compared with SoC.  
Randomized, open-label, phase 3 trial:  
- With confirmed COVID-19 – 596 patients –  
- 10-day course of remdesivir vs 5-day course of remdesivir vs SoC  
- Endpoint: a 7-point ordinal scale of clinical status on day 11  
Results:  
- Median age: 57 [46 – 66] – 39% women – 91% completed the trial  
- In the 5-day remdesivir group 76% completed therapy whereas only 38% of those to a 10-day remdesivir course completed the full course  
On day 11:  
- Patients in the 5-days group had higher odds of a better clinical status distribution than SoC (OR: 1.65 IC95%[1.09 – 2.48]; p=0.02)  
- 10-day remdesivir and SoC group was not significantly different  
On day 28:  
- 9 patients has died: 2 un the 5-day group + 3 in the 10-day and 4 in SoC group.  
- Patients on the 5-day remdesivir group had a statistically significant difference in clinical status compared with SoC.  
- Median length of treatment in the 10-day remdesivir group was 6 days.  
Lot of limitations: discharge decision may have been influenced by the assigned duration of remdesivir therapy + Clinical importance of the difference in clinical status ? |
- Of 1705 patients with COVID-19, 56.6% were prescribed early empiric antibacterial therapy and 3.5% (59/1705) had a confirmed community-onset bacterial infection.  
- Early (within 2 days of hospitalization) empiric antibacterial use was 27%-84%. It was more likely administered to patients that were older, had a lower body mass index, had more severe illness, had a lobar infiltrate, or were admitted to a for-profit hospital.  
- Over time, COVID-19 test turnaround time (returned ≤1 day) and empiric antibacterial use decreased.  
Despite the low prevalence of community-onset bacterial co-infection, half of patients received early empiric antibacterial therapy. Reducing COVID-19 test turnaround time and supporting stewardship could improve antibacterial use. |
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<tr>
<td>JAMA 21AUG2020</td>
<td>Epidemiology of COVID-19 Among Incarcerated Individuals and Staff in Massachusetts Jails and Prisons</td>
<td>Jiménez M.C. et al. USA <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td>AIM: to describe the COVID-19 burden in Massachusetts county jails and state prisons (MA DOC) in April-July 2020, and its association with decarceration and testing rates. - In a total population of 14 987, 1032 confirmed cases were reported among incarcerated individuals (n = 664) and staff (n = 368). The rate was 44.3 cases per 1000 persons, 2.91 times higher than the Massachusetts general population and 4.80 times the US general population. - Reported incidence was lower in county facilities (35.71 cases/1000) than in MA DOC facilities (52.36 cases/1000). - The proportion of positive tests among incarcerated individuals in county facilities was higher (14%) than in MA DOC facilities (5%) and the general Massachusetts (9%) and US (8%) populations. - Case incidence was higher among systems that released a lower proportion of their baseline population. Rates of COVID-19 in Massachusetts jails and prisons are alarmingly high and require urgent action.</td>
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<td>Lancet Rheumatology 21AUG2020</td>
<td>Risk of hydroxychloroquine alone and in combination with azithromycin in the treatment of rheumatoid arthritis: a multinational, retrospective study</td>
<td>Lane J C E et al USA <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>AIM: Hydroxychloroquine is commonly used in the treatment of rheumatoid arthritis. Studied the safety of HCQ alone and in combination with azithromycin to determine the risk associated with use in routine care in patients with rheumatoid arthritis. Retrospective study – comparaison between initiating HCQ with those initiating sulfasalazine and followed up over 30 days. Propensity score stratification of calibration using negative control outcomes were used to address confoundig. - 956 374 users of HCQ, 310 350 users of sulfasalazine, 323 122 users of HCQ+AZT and 351 956 users of HCQ + amoxicillin. - No excess risk of severe adverse events was identified when 30-day hydroxychloroquine and sulfasalazine use were compared - Long-term use of hydroxychloroquine appeared to be associated with increased cardiovascular mortality (calibrated HR 1,65 [95% CI 1,12–2,44]). - Addition of azithromycin appeared to be associated with an increased risk of 30-day cardiovascular mortality (calibrated HR 2,19 [95% CI 1,22–3,95]), chest pain or angina (1,15 [1,05–1,26]), and heart failure (1,22 [1,02–1,45]). Hydroxychloroquine treatment appears to have no increased risk in the short term among patients with rheumatoid arthritis, but in the long term it appears to be associated with excess cardiovascular mortality -&gt; addition of AZT increase the risk of heart failure and cardiovascular mortality even in the short term.</td>
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<td>Cell 20AUG2020</td>
<td>Longitudinal Isolation of Potent Near-Germline SARS-CoV-2-Neutralizing Antibodies from COVID-19 Patients</td>
<td>Kreer et al., Germany <a href="#">gotopaper</a></td>
<td>Immuno/Therapeutic</td>
<td>- Isolation of highly potent SARS-CoV-2-neutralizing antibodies - Longitudinal sampling reveals early class-switched neutralizing response - SARS-CoV-2 S-protein-reactive antibodies show little somatic mutation over time - Potential antibody precursor sequences identified in SARS-CoV-2-naive individuals -&gt; SARS-CoV-2-neutralizing antibodies are readily generated from a diverse pool of precursors, fostering hope for rapid induction of a protective immune response upon vaccination.</td>
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| **Cell** 20AUG2020 | Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus | Korber et al., USA-UK [gotopaper](#) | Genetics/Virology | - A SARS-CoV-2 variant with Spike G614 has replaced D614 as the dominant pandemic form  
- The consistent increase of G614 at regional levels may indicate a fitness advantage  
- G614 is associated with lower RT PCR Cts, suggestive of higher viral loads in patients  
- The G614 variant grows to higher titers as pseudotyped virions  
- In infected individuals, G614 is associated with lower RT-PCR cycle thresholds, suggestive of higher upper respiratory tract viral loads, but not with increased disease severity.  
-> These findings illuminate changes important for a mechanistic understanding of the virus and support continuing surveillance of Spike mutations to aid with development of immunological interventions. |
| **JAMA** 19AUG2020 | Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women | Chambers C et al USA [gotopaper](#) | Clinic | AIM: Concern about SARS-CoV-2 transmission to infants by breastfeeding. Detection of viral RNA by RT-PCR does not equate with infectivity.  
18 women with confirmed SARS-CoV-2 infection – women provided between 1 and 12 samples = total of 64 samples.  
Results:  
- 1 sample had detectable SARS-CoV-2 RNA (collected on the day of symptom onset)  
- No replication-competent virus was detectable in any sample, including the sample that tested positive for viral RNA.  
- Following Holder pasteurization, viral RNA was not detected by RT-PCR  
-> SARS-CoV-2 RNA does not represent replication-competent virus,  
-> Breast milk may not be a source of infection for infant, BUT small sample / nonrandom sample / self-collection of milk sample |
| **EBioMedicine** 17AUG2020 | SARS-CoV2 vertical transmission with adverse effects on the newborn revealed through integrated immunohistochemical, electron microscopy and molecular analyses of Placenta | Facchetti F et al., Italy [gotopaper](#) | Clinic | AIM: debate around the occurrence of trans-placental transmission of SARS-CoV-2 infection  
Screened for SARS-CoV spike protein expression placenta from 101 women: 15 tested positive for SARS-CoV-2 + 34 tested negative + 52 not evaluated  
Immunostatin for SARS-CoV-2 nucleocapsid was performed in the placenta of all COVID-19 positive women.  
Results:  
- SARS-CoV-2 antigens, RNA and/or particles morphologically consistent with coronavirus were identified in villous syncytiotrophoblast, endothelial cells, fibroblasts, in maternal macrophages, and in Hofbauer cells and fetal intravascular mononuclear cells  
- Absence of villitis was associated with an increase in the number of Hofbauer cells, which expressed PD-L1 □ may have prevented immune cell-driven placenta damage.  
□ We provide first-time evidence for maternal-fetal transmission of SARS-CoV-2, likely propagated by circulating virus-infected fetal mononuclear cells  
□ permissiveness of trans-placental SARS-CoV-2 transmission is rare.  
□ depend on host genetic factor, the infection with a unique SARS-CoV-2 genetic variant and/or the production of a high load of maternal antibody-virus immune complexes |
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<tr>
<td>Cell 14AUG2020</td>
<td>A single-dose intranasal ChAd vaccine protects upper and lower respiratory tracts against SARS-CoV-2</td>
<td>Hassan et al., USA <a href="#">gotopaper</a></td>
<td>Vaccines</td>
<td>Evaluation of protective activity of a chimpanzee adenovirus-vectorized vaccine encoding a pre-fusion stabilized spike protein (ChAd-SARS-CoV-2-S) in challenge studies with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and mice expressing the human angiotensin-converting enzyme 2 receptor.</td>
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<td>JAMA 14AUG2020</td>
<td>Association Between Number of In-Person Health Care Visits and SARS-CoV-2 Infection in Obstetrical Patients</td>
<td>Reale S.C., et al., USA <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td><strong>AIM:</strong> to examine whether the number of in-person health care visits of obstetrical patients from 4 hospitals in Boston (USA) between April and June 2020 was associated with the risk of SARS-CoV-2 infection.</td>
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<td>- Of 2968 deliveries, 111 patients (3.7%) tested positive for SARS-CoV-2 infection, of which 45 tested positive for SARS-CoV-2 infection antenatally and 66 tested positive at the time of admission for labour and delivery.</td>
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<td>- Performing a nested case-control study, 93 cases were matched with 372 control observations. The mean number of in-person visits was 3.1 for cases and 3.3 for controls. For the association between the number of in-person health care visits and SARS-CoV-2 infection, the odds ratio was 0.93 per additional visit.</td>
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<td>There was no meaningful association between the number of in-person health care visits and the rate of SARS-CoV-2 infection in this sample of obstetrical patients, despite the high infection rate in Boston. Necessary, in-person care should be therefore safely performed.</td>
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<td>Cell 14AUG2020</td>
<td>Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19</td>
<td>Sekine et al., Sweden <a href="#">gotopaper</a></td>
<td>Immuno</td>
<td>SARS-CoV-2-specific memory T cells will likely prove critical for long-term immune protection against COVID-19. <strong>Method:</strong> Systematic mapping of the functional and phenotypic landscape of SARS-CoV-2-specific T cell responses in unexposed individuals, exposed family members, and individuals with acute or convalescent COVID-19.</td>
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<td><strong>Results:</strong></td>
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<td>- Acute phase SARS-CoV-2-specific T cells display an activated cytotoxic phenotype</td>
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<td>- Broad and polyfunctional SARS-CoV-2-specific T cell responses in convalescent phase</td>
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<td>- Detection of SARS-CoV-2-specific T cell responses also in seronegative individuals</td>
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<td><strong>Conclusions:</strong> SARS-CoV-2 elicits robust, broad and highly functional memory T cell responses, suggesting that natural exposure or infection may prevent recurrent episodes of severe COVID-19.</td>
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| JAMA 13AUG2020 | Effect of an Inactivated Vaccine Against SARS-CoV-2 on Safety and Immunogenicity Outcomes Interim Analysis of 2 Randomized Clinical Trials | Xia et al., China gotopaper | Vaccine | Interim analysis of 2 randomized placebo-controlled trials in 96 healthy adults in a phase 1 trial of patients randomized to aluminum hydroxide (alum) only and low, medium, and high vaccine doses on days 0, 28, and 56:  
- 7-day adverse reactions occurred in 12.5%, 20.8%, 16.7%, and 25.0%, respectively  
- geometric mean titers of neutralizing antibodies at day 14 after the third injection were 316, 206 and 297 in the low-, medium-, and high-dose groups, respectively  
In 224 healthy adults randomized to the medium dose:  
- 7-day adverse reactions occurred in 6.0% and 14.3% of the participants who received injections on days 0 and 14 vs alum only, and 19.0% and 17.9% who received injections on days 0 and 21 vs alum only, respectively  
- geometric mean titers of neutralizing antibodies in the vaccine groups at day 14 after the second injection were 121 vs 247, respectively.  
-> This inactivated COVID-19 vaccine had a low rate of adverse reactions and demonstrated immunogenicity, but longer-term assessment of safety and efficacy will require phase 3 trials. |
| JAMA 13AUG2020 | Outcomes Associated with Use of a Kinin B2 Receptor Antagonist Among Patients With COVID-19 | Van de Veerdonk et al., Netherlands gotopaper | Therapeutic | AIM: Loss of ACE2 might lead to plasma leakage + activation of the plasma kallikrein-kinin system that could contribute to pulmonary angioedema via stimulation of bradykinin 2 receptors.  
Case-control study: 10 patients - 3 doses of 30 mg of icatibant SC injection at 6-hour intervals (bradykinin 2 receptor antagonist).  
Nine cases were matched to 18 controls for sex, age, body mass index and day of illness.  
Results: 90% were men - mean age was 55 years for case and 58 years for controls.  
After 3 injection: 44% cases were no longer oxygen dependent - 55% with substantial decrease of oxygen supplementation,  
Controls: 17% showed a spontaneous reduction in oxygen supplementation,  
Icatibant was well tolerated – no adverse events  
□ association between receipt of icatibant and improved oxygenation  
□ might be beneficial especially in early stages of disease  
□ icatibant’s short half life  
□ randomized trial? |
| The Lancet Haematology 13AUG2020 | Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicentre, cohort study | Passamonti et al., Italy gotopaper | Clinic | The Italian Hematology Alliance on COVID-19: Collection of data from adult patients with haematological malignancies who required hospitalisation for COVID-19.  
Multicentre, retrospective, cohort study included adult patients (aged ≥18 years) with diagnosis of a WHO-defined haematological malignancy admitted to 66 Italian hospitals between Feb 25 and May 18, 2020, with laboratory-confirmed and symptomatic COVID-19.  
-> 198 (37%) of 536 patients died  
-> When compared with the general Italian population with COVID-19, the standardised mortality ratio was 2.04 in the whole study cohort and 3.72 (2.86–4.64) in individuals younger than 70 years.  
-> When compared with the non-COVID-19 cohort with haematological malignancies, the standardised mortality ratio was 41.3  
Were associated with worse overall survival:  
Older age - Progressive disease status - Diagnosis of acute myeloid leukaemia - Indolent non-Hodgkin lymphoma - Aggressive non-Hodgkin lymphoma - Plasma cell neoplasms - Severe or critical COVID-19 |
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<tr>
<td>Clin Inf Dis 12AUG2020</td>
<td>Methylprednisolone as Adjunctive Therapy for Patients Hospitalized With COVID-19 (Metcovid): A Randomised, Double-Blind, Phase IIb, Placebo-Controlled Trial</td>
<td>Prado Jeronimo CM et al., Brazil gotopaper</td>
<td>Therapeutic</td>
<td>AIM: evaluating the efficacy of methylprednisolone (MP) among hospitalized patients with suspected COVID-19 Double blind, placebo-controlled, randomized (1:1), phase IIb Intravenous MP or placebo twice daily for 5 days. 416 randomized patients and 393 analyzed as mITT: 194 MP &amp; 199 placebo. Results: - No patients received anti IL-6, anti IL-1, remdesivir or convalescent plasma therapy, - No difference on mortality at day 28 between groups: 37.1% in the MP group vs 38.2% in the placebo group (p=0.629), - Subgroup analysis: patient &gt;60 years in the MP group had a lower mortality rate at day 28: 46.6% (MP group) vs 61.9% (placebo) – p=0.039 - Patients &gt; 60 years had higher CRP values: 81.3 vs 74.7 (p=0.0028) - No difference in virus clearance in respiratory secretion until day 7. no evidence of improved survival in the overall population with a short course of intravenous MP in patients hospitalized with COVID-19. lower mortality in patients over 60 years who received MP: more pronounced systemic inflammatory status (higher CRP).</td>
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<td>Nature 12AUG2020</td>
<td>Phase 1/2 study of COVID-19 RNA vaccine BNT162b1 in adults</td>
<td>Mulligan M J et al., USA gotopaper</td>
<td>Vaccine</td>
<td>Safety, tolerability and immunogenicity data - 45 healthy adults. Placebo-controlled, observer-blinded dose escalation study. Randomized to receive 2 doses, separated by 21 days of 10 μg, 30 μg, or 100 μg of BNT162b1. à 12 participants per dose level (10 and 30 μg) were vaccinated with BNT162b1 on D1 &amp; D21 à 12 participants received a 100 μg dose on D1. BNT162b1: nucleoside-modified mRNA vaccine that encodes trimerized SARS-CoV-2 spike glycoprotein receptor-binding domain (RBD). Tolerability and safety profile: - Consistent with those previously observed for mRNA-based vaccines. - AE: 50% of participant who received either 10 or 30 μg of BNT162b1 – 58.3% of those who received 100 μg – 11.1% of placebo recipients. - SAE: 2 patients: Grade 3 fever 2 days after vaccination in the 30 μg group, and sleep disturbance 1 day after vaccination in the 100 μg group. Immunogenicity: - Robust immunogenicity was observed after vaccination. - RDB-binding IgG concentrations and SARS-CoV-2 neutralizing titers in sera increased with dose level and after a second dose. - Geometric mean neutralizing titers reached 1.9- to 4.6-fold that of a panel of COVID-19 convalescent human sera at least 14 days after a positive SARS-CoV-2 PCR. Encouraging and strongly support accelerated clinical development.</td>
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<td>Lancet Global Health 10AUG2020</td>
<td>Effect of the COVID-19 pandemic response on intrapartum care, stillbirth, and neonatal mortality outcomes in Nepal: a prospective observational study</td>
<td>Ashish KC et al., Nepal/Sweden/… <a href="#">gotopaper</a></td>
<td>Epidemiology</td>
<td>Maternal and neonatal health service all over the world are affected by the pandemic. Prospective observational study between Jan 1 and May 30 2020, from 9 hospital in Nepal. à 12,5 weeks before the national lockdown and 9,5 weeks during the lockdown Exclusion: gestational age &lt; 22 weeks, no fetal heart sound at admission, multiple birth 21763 women and 20354 gave birth The mean weekly number of institutional birth decrease: 1261,1 before lockdown to 651,4 birth during lockdown (-52,4%) The institutional stillbirth rate increased from 14 per 1000 total birth before lockdown to 21 per 1000 during lockdown (p=0,0002) The institutional neonatal mortality increased from 13 per 1000 livebirths to 40 per 1000 (p=0,0022) Intrapartum fetal rate monitoring decrease by 13,4% Practice skin-to-skin with their mother increased by 13,2% and heath workers’ hand hygiene practices during childbirth increased by 12,9% during lockdown. - Institutional childbirth reduced by more than half during lockdown - increases in institutional stillbirth rate and neonatal mortality - decrease in quality of care - urgent need exists to protect access to high quality intrapartum care and prevent excess death</td>
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<td>Clinical Infectious Disease 09AUG2020</td>
<td>Clinical Outcomes Associated with Methylprednisolone in Mechanically Ventilated Patients with COVID-19</td>
<td>Nelson B C et al., USA <a href="#">gotopaper</a></td>
<td>Clinic</td>
<td>Evaluation of the association between use or methylprednisolone and key clinical outcomes Case-control study – a subset of patients also underwent propensity-score matching Primary outcome: ventilator-free day by 28 days after admission Characteristics: 117 patients – propensity matching yielded a cohort of 42 well-matched pairs. Median age: 63y – IQR [52 – 71] – 67% male Median BMI: 30 kg/m2 Median SOFA score: 11 [8 – 12] 33 patients died by hospital day 28 Results: - 48 patients received methylprednisolone – median dose: 80 mg/d - The matched group were comparable at baseline - Patients who received steroids were less likely to have received HQC or Azithro - Ventilator-free days was significantly higher in steroid group (6,2 vs 3,14, p=0,044) - Probability of extubation by day 28 was significantly higher in patients who received steroid (45% vs 21%) No significant differences in mortality (19% vs 36%, p=0,087) Multivariable linear regression: - Only methylprednisolone use was associated with higher number of ventilator-free day</td>
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| Nat Med 7AUG2020 | Using a real-world network to model localized COVID-19 control strategies | Firth et al., UK [gotopaper](#) | Public Health / Epidemiol | Simulation of control strategies for SARS-CoV-2 transmission in a real-world social network generated from high-resolution GPS data that were gathered in the course of a citizen-science experiment.  
- Tracing the contacts of contacts reduced the size of simulated outbreaks more than tracing of only contacts, but this strategy also resulted in almost half of the local population being quarantined at a single point in time.  
- Testing and releasing non-infectious individuals from quarantine led to increases in outbreak size, suggesting that contact tracing and quarantine might be most effective as a ‘local lockdown’ strategy when contact rates are high.  
- Combining physical distancing with contact tracing could enable epidemic control while reducing the number of quarantined individuals.  
Conclusion: Our findings suggest that targeted tracing and quarantine strategies would be most efficient when combined with other control measures such as physical distancing. |
| Nature 05AUG2020 | SARS-CoV-2 mRNA vaccine design enabled by prototype pathogen preparedness | Corbett K.S. et al., USA [gotopaper](#) | Vaccine | The release of SARS-CoV-2 sequences triggered immediate rapid manufacturing of an mRNA vaccine expressing the prefusion-stabilized SARS-CoV-2 spike trimer (mRNA-1273).  
Prior to vaccination of the first human subject, expression and antigenicity of the S-2P antigen delivered by mRNA was confirmed in vitro and immunogenicity of mRNA-1273 was documented:  
- mRNA-1273 induced dose-dependent S-specific binding antibodies after prime and boost in all mouse strains,  
- The level of pseudovirus neutralizing activity induced by 1 μg of mRNA-1273 in mice is similar in magnitude to that induced in human subjects by 100 μg  
- 1 μg of mRNA-1273 was sufficient to induce robust pseudovirus neutralizing activity and CD8 T cell responses, balanced Th1/Th2 antibody isotype responses, and protection from viral replication for more than 3 months following a prime/boost regimen  
Protection against SARS-CoV-2 infection in the lungs:  
- Efficacy of mRNA-1273 was dose-dependent, with two 0.1 μg mRNA-1273 doses reducing lung viral load by ~100-fold and two 0.01 μg mRNA-1273 doses reducing lung viral load by ~3-fold  
- mRNA-1273 is currently in Phase 3 efficacy evaluation |
| Cell 5AUG2020 | Elevated calprotectin and abnormal myeloid cell subsets discriminate severe from mild COVID-19 | Silvin et al., France [gotopaper](#) | Immuno | High dimensional flow cytometry and single cell RNA sequencing of COVID-19 patient peripheral blood cells.  
- Detection of the disappearance of non-classical CD14LowCD16High monocytes, the accumulation of HLA-DRLow classical monocytes, and the release of massive amounts of calprotectin (S100A8/S100A9) in severe cases.  
- Immature CD10LowCD101-CXCR4+/- neutrophils with an immuno-suppressive profile accumulated as well in blood and lungs, suggesting emergency myelopoiesis  
- Calprotectin plasma level and a routine flow cytometry assay detecting decreased frequencies of non-classical monocytes could discriminate patients who develop a severe COVID-19 form, suggesting a predictive value that deserves prospective evaluation. |
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| Science          | Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans | Mateus et al., USA and Australia [gotopaper](https://doi.org/10.1016/j.science.2020.04.028) | Immuno            | SARS-CoV-2 reactive CD4+ T cells have been reported in unexposed individuals, suggesting pre-existing cross-reactive T cell memory in 20-50% of people.  
|                  |                                                                       |                                |                   | -> We demonstrate a range of pre-existing memory CD4+ T cells that are cross-reactive with comparable affinity to SARS-CoV-2 and the common cold coronaviruses HCoV-OC43, HCoV-229E, HCoV-NL63, or HCoV-HKU1. Thus, variegated T cell memory to coronaviruses that cause the common cold may underlie at least some of the extensive heterogeneity observed in COVID-19 disease.  
|                  |                                                                       |                                |                   | -> Variegated T cell memory to coronaviruses that cause the common cold may underlie at least some of the extensive heterogeneity observed in COVID-19 disease.  |
| Science          | Engineering human ACE2 to optimize binding to the spike protein of SARS coronavirus 2 | Chan et al., USA [gotopaper](https://doi.org/10.1016/j.science.2020.04.028) | Therapeutic       | The spike protein S of SARS coronavirus 2 (SARS-CoV-2) binds ACE2 on host cells to initiate entry, and soluble ACE2 is a therapeutic candidate that neutralizes infection by acting as a decoy. Using deep mutagenesis, mutations in ACE2 that increase S binding are found across the interaction surface, in the N90-glycosylation motif and at buried sites. The mutational landscape provides a blueprint for understanding the specificity of the interaction between ACE2 and S and for engineering high affinity decoy receptors. Combining mutations gives ACE2 variants with affinities that rival monoclonal antibodies. A stable dimeric variant shows potent SARS-CoV-2 and -1 neutralization in vitro. The engineered receptor is catalytically active and its close similarity with the native receptor may limit the potential for viral escape.  |
| The Lancet Infectious Diseases | SeroTracker: a global SARS-CoV-2 seroprevalence dashboard | Arora, R.K. et al., Canada [gotopaper](https://doi.org/10.1016/j.lix.2020.04.028) | Public Health / Epidemiology | Despite the value of antibody testing, there is no unified resource for seroprevalence estimates. The platform SeroTracker has therefore been created, a custom-built dashboard that systematically monitors and synthesises findings from global SARS-CoV-2 serological studies. The dashboard allows users to visualise seroprevalence estimates on a world map and compare estimates between regions, population groups, and testing modalities. SeroTracker integrates evidence from serosurveillance studies through a live systematic review of published articles (MEDLINE, Embase, Web of Science, and Cochrane), preprints (medRxiv and bioRxiv), government reports, and news articles. SeroTracker has proven useful to researchers, policy makers, and public health officials. SeroTracker will be hosted throughout the COVID-19 outbreak to support evidence-based decision making.  
|                  |                                                                       |                                |                   | - History of macular degeneration and history of coagulation disorders are risk factors for SARS-CoV-2-associated morbidity and mortality, independently from age, sex or history of smoking.  
|                  |                                                                       |                                |                   | - In addition to type-I interferon and interleukin-6-dependent inflammatory responses, infection results in robust engagement of the complement and coagulation pathways.  
|                  |                                                                       |                                |                   | - Putative complement and coagulation-associated loci related to severe disease were identified, including missense, eQTL and sQTL variants of critical complement and coagulation regulators. These data provide evidence that complement function modulates SARS-CoV-2 infection outcome, and point to putative transcriptional genetic markers of susceptibility.  
<p>|                  |                                                                       |                                |                   | The results highlight the value of using a multimodal analytical approach to reveal determinants and predictors of immunity, susceptibility and clinical outcome associated with infection.  |</p>
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<tr>
<td>Clinical Infectious Diseases 03AUG2020</td>
<td>Longitudinal dynamics of the neutralizing antibody response to SARS-CoV-2 infection</td>
<td>Wang, K. et al., China <a href="#">go to paper</a></td>
<td>Public Health / Epidemiology</td>
<td>AIM: studying the longitudinal dynamics of SARS-CoV-2-specific neutralizing antibodies (NAb) and IgG and proinflammatory cytokines in COVID-19 patients, through analysis of 173 blood samples from 30 patients. - SARS-CoV-2-specific NAb titers were low for the first 7-10 days after symptom onset and increased after 2-3 weeks. The median peak time for NAb was 33 days after symptom onset. - NAb titers in 93.3% of the patients declined gradually over the 3-month study period, with a median decrease of 34.8%. - NAb titers increased over time in parallel with the rise in IgG antibody levels, correlating well at week 3. - The NAb titers also demonstrated a significant positive correlation with levels of plasma proinflammatory cytokines, including SCF, TRAIL, and M-CSF.</td>
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<td>Journal of Inf Dis 01AUG2020</td>
<td>Prospective study comparing deep-throat saliva with other respiratory tract specimens in the diagnosis of novel coronavirus disease (COVID-19)</td>
<td>Lai et al., China <a href="#">go to paper</a></td>
<td>Diagnostic</td>
<td>Prospective study in two regional hospitals in Hong Kong - 563 serial samples collected during the virus shedding periods of 50 patients: 150 deep-throat saliva (DTS), 309 pooled-nasopharyngeal (NP) and throat swabs, and 104 sputum - DTS had the lowest overall RT-PCR positive rate (68.7% vs. 89.4% [sputum] and 80.9% [pooled NP and throat swabs]), and the lowest viral RNA concentration (mean log copy/mL 3.54 vs. 5.03 [sputum] and 4.63 [pooled NP and throat swabs]) - Analyses with respect to time from symptom onset and severity also revealed similar results. Virus yield of DTS correlated with that of sputum (Pearson correlation index [95% CI]: 0.76 [0.62 – 0.86]). We estimated the overall false-negative rate of DTS could be 31.3%, and increased 2.7 times among patients without sputum. Conclusion: DTS produced the lowest viral RNA concentration and RT-PCR positive rate compared to conventional respiratory specimens in all phases of illness. Self-collect sputum should be the choice for patients with sputum.</td>
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<td>The Lancet Public Health 31JUL2020</td>
<td>Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study</td>
<td>Nguyen, L.H. et al., USA / UK, <a href="#">go to paper</a></td>
<td>Public Health / Epidemiology</td>
<td>Aim: assess risk of COVID-19 among front-line health-care workers compared with the general community and the effect of personal protective equipment (PPE) on risk, through a prospective, observational cohort study in the UK and the USA using self-reported data from the COVID Symptom Study smartphone application. - Among 2,035,395 community individuals and 99,795 front-line health-care workers, we recorded 5545 incident reports of a positive COVID-19 test over 34,435,272 person-days. - Compared with the general community, front-line health-care workers were at increased risk for reporting a positive COVID-19 test. - Secondary and post-hoc analyses suggested adequacy of PPE, clinical setting, and ethnic background were also important factors. Health-care systems should ensure adequate availability of PPE and develop additional strategies to protect health-care workers from COVID-19, particularly those from Black, Asian, and minority ethnic backgrounds.</td>
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<td>Nature 30JUL2020</td>
<td>Single-shot Ad26 vaccine protects against SARS-CoV-2 in rhesus macaques</td>
<td>Mercadi N B et al., USA <a href="#">gotopaper</a></td>
<td>Vaccine</td>
<td>A vaccine that requires only a single immunization would be optimal. S2 rhesus macaques were immunized with Ad26 vectors encoding S variants or sham control and were challenged with SARS-CoV-2. Animals received a single immunization. Immunogenicity: - Induced robust neutralizing antibody responses and provided complete or near-complete protection following SARS-CoV-2 challenge. Protective efficacy: - Vaccine-elicited neutralizing antibody titres correlated with protective efficacy, suggesting an immune correlate of protection. -&gt; Robust single-shot vaccine protection against SARS-CoV-2 in rhesus macaques. -&gt; Being evaluated in clinical trials</td>
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<td>SCIENCE 30JUL2020</td>
<td>Adaptation of SARS-CoV-2 in BALB/c mice for testing vaccine efficacy</td>
<td>Gu et al., China <a href="#">gotopaper</a></td>
<td>Vaccine</td>
<td>Clinical isolate of SARS-CoV-2 by serial passaging in the respiratory tract of aged BALB/c mice. -&gt; The resulting mouse-adapted strain at passage 6 (termed MASCp6) showed increased infectivity in mouse lung, and led to interstitial pneumonia and inflammatory responses in both young and aged mice following intranasal inoculation. -&gt; Deep sequencing revealed a panel of adaptive mutations potentially associated with the increased virulence. In particular, the NS01Y mutation is located at the receptor binding domain (RBD) of the spike protein. -&gt; The protective efficacy of a recombinant RBD vaccine candidate was validated using this model. This mouse-adapted strain and associated challenge model should be of value in evaluating vaccines and antivirals against SARS-CoV-2.</td>
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<td>EBioMedicine 30JUL2020</td>
<td>Serologic responses to SARS-CoV-2 infection among hospital staff with mild disease in eastern France</td>
<td>Fafi-Kremer, S. et al., France, <a href="#">gotopaper</a></td>
<td>Public Health / Epidemiology</td>
<td>Aim: investigating the serologic response of 160 hospital staff who had recovered from mild forms of PCR-confirmed SARS-CoV-2 (no hospitalization required) using two assays for detection (rapid immunodiagnostic test and S-Flow assay), and an assay for neutralizing activity of the sera. - The median time from symptom onset to blood sample collection was 24. The rapid immunodiagnostic test detected antibodies in 153 (95.6%) of the samples and the S-Flow assay in 159 (99.4%). - Neutralizing antibodies (NAbs) were detected in 79%, 92% and 98% of samples collected 13–20, 21–27 and 28–41 days after symptom onset, respectively. This finding supports the use of serologic testing for the diagnosis of individuals who have recovered from SARS-CoV-2 infection. Future studies will help assess the persistence of the humoral response in recovered patients.</td>
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- School closure was associated with a significant decline in both incidence of COVID-19 (adjusted relative change per week, -62%) and mortality (adjusted relative change per week, -58%).  
- In a model derived from this analysis, it was estimated that closing schools when the cumulative incidence of COVID-19 was in the lowest quartile compared with the highest quartile was associated with 128.7 fewer cases per 100 000 population over 26 days and with 1.5 fewer deaths per 100 000 population over 16 days. |
| Nature 29JUL2020 | Papain-like protease regulates SARS-CoV-2 viral spread and innate immunity | Shin et al., Germany [gotopaper](#) | Therapeutic | Papain-like protease PLpro: an essential coronavirus enzyme required for processing viral polyproteins to generate a functional replicase complex and enable viral spread  
- Biochemical, structural and functional characterization of the SARS-CoV-2 PLpro (SCoV2-PLpro) and outline differences to SARS-CoV PLpro (SCoV-PLpro) in controlling host interferon (IFN) and NF-κB pathways  
- Upon infection, SCoV2-PLpro contributes to the cleavage of ISG15 from interferon responsive factor 3 (IRF3) and attenuates type I interferon responses.  
- Inhibition of SCoV2-PLpro with GRL-0617 impairs the virus-induced cytopathogenic effect, fosters the anti-viral interferon pathway and reduces viral replication in infected cells.  
These results highlight a dual therapeutic strategy in which targeting of SCoV2-PLpro can suppress SARS-CoV-2 infection and promote anti-viral immunity.  
Aim: investigating SARS-CoV-2 spike glycoprotein (S)-reactive CD4(+) T cells in peripheral blood of patients with COVID-19 and SARS-CoV-2-unexposed healthy donors (HD).  
- SARS-CoV-2 S-reactive CD4(+) T cells were detected in 83% of patients with COVID-19 but also in 35% of HD. S-reactive CD4(+) T cells in HD reacted primarily to C-terminal S epitopes, which show a higher homology to spike glycoproteins of human endemic coronaviruses, compared to N-terminal epitopes.  
- S-reactive T cell lines generated from SARS-CoV-2-naive HD responded similarly to C-terminal S of human endemic coronaviruses 229E and OC43 and SARS-CoV-2, demonstrating the presence of S-cross-reactive T cells, probably generated during past encounters with endemic coronaviruses.  
The role of pre-existing SARS-CoV-2 cross-reactive T cells for clinical outcomes remains to be determined in larger cohorts. However, their presence in the general population may affect the dynamics of the current pandemic. |
- An increase in soluble Csα levels proportional to COVID-19 severity and high levels of CsαR1 expression in blood and pulmonary myeloid cells is reported, supporting a role for the Csα-CsαR1 axis in the pathophysiology of acute respiratory distress syndrome (ARDS).  
- Anti-CsαR1 therapeutic monoclonal antibodies prevented Csα-mediated human myeloid cell recruitment and activation, and inhibited acute lung injury in human CsαR1 knockin mice.  
These results suggest that Csα-CsαR1 axis blockade might be used to limit myeloid cell infiltration in damaged organs and prevent excessive lung inflammation associated with ARDS in COVID-19 patients. |
<p>| Nature 29JUL2020 | Association of COVID-19 inflammation with activation of the Csα-CsαR1 axis | Caravelli, J. et al, France <a href="#">gotopaper</a> | Public Health / Epidemiology | |</p>
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| NEJM 28JUL2020   | Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates | Kizzmekia S. Corbett et al., USA goto.paper        | Vaccine            | Method: Nonhuman primates received 10 or 100 μg of mRNA-1273, a vaccine encoding the prefusion-stabilized spike protein of SARS-CoV-2, or no vaccine. Antibody and T-cell responses were assessed before upper- and lower-airway challenge with SARS-CoV-2. Active viral replication and viral genomes in bronchoalveolar-lavage (BAL) fluid and nasal swab specimens were assessed by PCR, and histopathological analysis and viral quantification were performed on lung-tissue specimens.  

Results:  
- The mRNA-1273 vaccine candidate induced antibody levels exceeding those in human convalescent-phase serum, with live-virus reciprocal 50% inhibitory dilution (ID50) geometric mean titers of 501 in the 10-μg dose group and 3481 in the 100-μg dose group. -- Vaccination induced type 1 helper T-cell (Th1)-biased CD4 T-cell responses and low or undetectable Th2 or CD8 T-cell responses.  
- Viral replication was not detectable in BAL fluid by day 2 after challenge in seven of eight animals in both vaccinated groups. No viral replication was detectable in the nose of any of the eight animals in the 100-μg dose group by day 2 after challenge  
- Limited inflammation or detectable viral genome or antigen was noted in lungs of animals in either vaccine group.  

Conclusion: The results reported here provide data on mRNA-1273 immunogenicity and protection of the upper and lower airways in nonhuman primates that complement the immunogenicity and safety data established by a phase 1 clinical study involving humans. Studies are now under way to determine the durability of immunity and protection over 1 year after vaccination. |

| Cell Systems 27JUL2020 | Computationally Optimized SARS-CoV-2 MHC Class I and II Vaccine Formulations Predicted to Target Human Haplotype Distributions | Ge Liu et al., USA goto.paper | Vaccine            | Aim Validation of combinatorial machine learning method to evaluate and optimize peptide vaccine formulations for SARS-CoV-2  

Method By testing human HLA haplotype frequencies of three major populations and using recent advances in machine learning, the authors have evaluated completed designs models to provide a conservative evaluation of vaccine peptide presentation.  

Results:  
- SARS-CoV-2 MHC class I vaccine formulations provide 93.21%-predicted population coverage with at least five vaccine peptide-HLA average hits per person (≥ 1 peptide: 99.91%),  
- MHC class II vaccine formulations provide 97.21%-predicted coverage with at least five vaccine peptide-HLA average hits per person with all peptides having an observed mutation probability of ≤ 0.001.  
- OptiVax can be used to augment S protein vaccine designs to increase their population coverage.  

Conclusion EvalVax can be used for vaccine designs that are focused on the expression of entire viral proteins or their subunits to evaluate the level of viral peptide-HLA presentation. |
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| **Nature 27JUL2020** | Longitudinal analyses reveal immunological misfiring in severe COVID-19 | Lucas, Carolina et al., USA [gotopaper](#) | Immunology | Immune profiling in 113 COVID-19 patients with moderate (non-ICU) and severe (ICU) disease revealed:  
- Association between early elevated cytokines and worse disease outcomes.  
  Following early increase in cytokines:  
  - moderate disease COVID-19 patients displayed a progressive reduction in type-1 (antiviral) and type-3 (antifungal) responses.  
  - severe disease patient smaintained elevated type-1 and 3 responses throughout the course of disease, accompanied by increase in multiple type 2 (anti-helminths) effectors (IL-5, IL-13, IgE, eosinophils).  
  -> Identified 4 immune signatures correlating with distinct disease trajectories of patients:  
    (A) enriched growth factors, (B) type-2/3 cytokines, (C) mixed type-1/2/3 cytokines, and (D) chemokines.  
  -> Patients who recovered with moderate disease = immune signature A (enriched tissue reparative growth factors).  
  -> Patients with worsened disease trajectory = elevated levels of all 4 signatures. |
| **Nature 24JUL2020** | Discovery of SARS-CoV-2 antiviral drugs through large-scale compound repurposing | Riva, Laura et al., USA/China [gotopaper](#) | Therapeutics | High-throughput reprofiling screen using the ReFRAME (Repurposing, Focused Rescue, and Accelerated Medchem) drug library, a comprehensive open-access library of ~12,000 that have been either FDA-approved or registered outside the US, entered clinical trials, or undergone significant pre-clinical characterization, to identify existing drugs that harbor antiviral activity against SARS-CoV-2 in a cell-based assay.  
Results:  
Identification of 100 molecules that inhibit SARS-CoV-2 replication in mammalian cells, including 21 known drugs that exhibit dose response relationships.  
Of these, 13 were found to harbor effective concentrations likely commensurate with achievable therapeutic doses in patients, including the PIKfyve kinase inhibitor apilimod2–4, and the cysteine protease inhibitors MDL-28170, Z LVG CHN2, VBY-825, and ONO 5334.  
Notably, MDL-28170, ONO 5334, and apilimod were found to antagonize viral replication in human iPSC-derived pneumocyte-like cells, and the PIKfyve inhibitor also demonstrated antiviral efficacy in a primary human lung explant model.  
Publicly disclosed and relevant preclinical and clinical properties of the most advanced among these molecules will enable prioritization of known drugs for in vivo preclinical and clinical evaluation for the treatment of SARS-CoV-2. |
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| Nature Communications 24JUL2020 | Structural basis of RNA cap modification by SARS-CoV-2 | Viswanathan, Thiruselvam et al., USA | Therapeutics | Report of the high-resolution structure of a ternary complex of SARS-CoV-2 nsp16 and nsp10 in the presence of cognate RNA substrate analogue and methyl donor, S-adenosyl methionine (SAM).  
**Results**  
- This enzyme is specifically adapted to bind and methylate the RNA cap.  
- The structure provides a snapshot of pre-catalytic state of methyl transfer from SAM to 2′-OH of ribose of the first transcribing nucleotide of the mRNA cap.  
- Large conformational changes associated with substrate binding are observed as the enzyme transitions from a binary to a ternary state. This induced fit model provides mechanistic insights into the 2′-O methylation of the viral mRNA cap.  
- A distant (25 Å) ligand-binding site unique to SARS-CoV-2 was discovered in nsp16 with distinct capability to accommodate small molecule ligands. It could alternatively be targeted, in addition to RNA cap and SAM pockets, for antiviral development.  
- The acquired mutations in SARS-CoV-2 nsp16 were mapped. One of these mutation hotspots showed high frequency in COVID-19 strains associated with New York City outbreak.  
**Conclusion**  
Solid framework from which therapeutic modalities may be designed by targeting different ligand-binding sites of nsp16, including RNA cap and SAM pockets, for the treatment of COVID-19 and emerging coronavirus illnesses. |
Inclusion criteria were similar between studies: confirmed SARS-CoV-2 infection, hospitalized patients, with oxygen saturation 94% or lower on room air or required supplemental oxygen, and pulmonary infiltrates.  
**Primary endpoint:** proportion of patients with recovery on day 14, dichotomized from a 7-point clinical status ordinal scale. A key secondary endpoint was mortality.  
**Results**  
312 and 818 patients were counted in the remdesivir- and non-remdesivir-cohorts, respectively.  
At day 14, 74.4% of patients in the remdesivir-cohort had recovered versus 59.0% in the non-remdesivir-cohort (adjusted odds ratio 2.03: 95% confidence interval 1.34–3.08, p<0.001).  
At day 14, 7.6% of patients in the remdesivir-cohort had died versus 12.5% in the non-remdesivir-cohort (adjusted odds ratio 0.38, 95% confidence interval: 0.22–0.68, p=0.001).  
**Conclusions**  
In this comparative analysis, by day 14, remdesivir was associated with significantly greater recovery and 62% reduced odds of death versus standard-of-care treatment in patients with severe COVID-19.  
**Limitations**  
Comparison was not randomized; open-label design of Study 5773 |
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| **Cell** 23JUL2020 | A thermostable mRNA vaccine against COVID-19 | Zhang, Na-Na et al., China [gotopaper](#) | Vaccine | Development of a lipid-nanoparticle-encapsulated mRNA (mRNA-LNP) encoding the receptor binding domain (RBD) of SARS-CoV-2 as a vaccine candidate (ARCoV).  
**Results:**  
- Intramuscular immunization of ARCoV mRNA-LNPs elicited robust neutralizing antibodies against SARS-CoV-2 as well as Th1-biased cellular response in mice and non-human primates.  
- Two doses of ARCoV immunization in mice conferred complete protection against the challenge of a SARS-CoV-2 mouse adapted strain.  
- ARCoV was manufactured in liquid formulation and can be stored at room temperature for at least one week.  
**Conclusion:** Thermostable mRNA vaccine candidate against SARS-CoV-2, with first line evidence of immunogenicity and efficacy in multiple animal models, and currently being evaluated in phase 1 clinical trials. |
| **Science** 23JUL2020 | Structural basis for neutralization of SARS-CoV-2 and SARS-CoV by a potent therapeutic antibody | Lv, Zhe et al., China [gotopaper](#) | Vaccine/Therapeutics | The RBDs of SARS-CoV and SARS-CoV-2 have an amino-acid sequence identity of around 75%, raising the possibility that RBD-targeting cross-neutralizing NAbs could be possibly identified. Using phage display technique, an antibody library was generated from RNAs extracted from peripheral lymphocytes of mice immunized with recombinant SARS-CoV RBD. SARS-CoV-2 RBD was used as the target for screening the phage antibody library for potential hits.  
**Results:**  
- Humanized monoclonal antibody, H014, efficiently neutralizes SARS-CoV-2 and SARS-CoV pseudoviruses as well as authentic SARS-CoV-2 at nM level by engaging the S receptor binding domain (RBD).  
- H014 administration reduced SARS-CoV-2 titers in the infected lungs and prevented pulmonary pathology in HACE2 mouse model.  
- Cryo-EM characterization of the SARS-CoV-2 S trimer in complex with the H014 Fab fragment unveiled a novel conformational epitope, which is only accessible when the RBD is in open conformation.  
- Biochemical, cellular, virological and structural studies demonstrated that H014 prevents attachment of SARS-CoV-2 to its host cell receptors.  
**Conclusion:** The molecular features of H014 epitopes facilitate the discovery of broad cross-neutralizing epitopes within lineage B and pose interesting targets for structure-based rational vaccine design, as well as for the promise of antibody-based therapeutic interventions for the treatment of COVID-19. |
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<td>NEJM 23JUL2020</td>
<td>Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19</td>
<td>Cavalcanti, Alexandre B. et al., Brazil</td>
<td>Therapeutics</td>
<td>Multicenter, randomized, open-label, 3-group, controlled trial in Brazil involving hospitalized patients with suspected or confirmed Covid-19 who were receiving either no supplemental oxygen or a maximum of 4 liters per minute of supplemental oxygen. Patients were randomly assigned in a 1:1:1 ratio to receive standard care, standard care + HCQ (400 mg twice daily), or standard care + HCQ (400 mg twice daily) + azithromycin (500 mg once daily) for 7 days. <strong>Primary outcome</strong>: clinical status at 15 days as assessed with the use of a seven-level ordinal scale in the modified intention-to-treat population (patients with a confirmed diagnosis of Covid-19). Safety was also assessed. A total of 667 patients underwent randomization; 504 patients had confirmed Covid-19 and were included in the modified intention-to-treat analysis. As compared with standard care, the proportional odds of having a higher score on the seven-point ordinal scale at 15 days was <strong>not affected by</strong> either hydroxychloroquine alone (odds ratio, 1.21; 95% confidence interval [CI], 0.69 to 2.11; P=1.00) or hydroxychloroquine plus azithromycin (odds ratio, 0.99; 95% CI, 0.57 to 1.73; P=1.00). - Prolongation of the corrected QT interval and elevation of liver-enzyme levels were more frequent in patients receiving hydroxychloroquine, alone or with azithromycin, than in those who were not receiving either agent. =&gt; Among patients hospitalized with mild-to-moderate Covid-19, the use of hydroxychloroquine, alone or with azithromycin, did not improve clinical status at 15 days as compared with standard care.</td>
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<td>Science 23JUL2020</td>
<td>Evolution and epidemic spread of SARS-CoV-2 in Brazil</td>
<td>Candido, Darlan S. et al., UK-Brazil</td>
<td>Public Health/ Epidemio</td>
<td>Brazil currently has one of the fastest growing SARS-CoV-2 epidemics in the world. - A mobility-driven transmission model showed non-pharmaceutical interventions reduced reproduction number from &gt;3 to 1–1.6 in São Paulo and Rio de Janeiro. Sequencing of 427 new genomes identified: - Over 100 international virus introductions in Brazil. - Most (76%) of Brazilian strains fell in 3 clades introduced from Europe between 22 February and 11 March 2020. - During the early epidemic phase, SARS-CoV-2 spread mostly locally and within-state borders. After this period, despite sharp decreases in air travel, multiple exportations from large urban centers coincided with a 25% increase in average travelled distances in national flights. =&gt; Study sheds light on the epidemic transmission and evolutionary trajectories of SARS-CoV-2 lineages in Brazil, and provide evidence that current interventions remain insufficient to keep virus transmission under control in the country.</td>
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<td>Nature structural &amp; molecular biology 22JUL2020</td>
<td>Controlling the SARS-CoV-2 spike glycoprotein conformation</td>
<td>Henderson, Rory et al. USA <a href="#">gotopaper</a></td>
<td>Vaccine</td>
<td>To better understand S-protein mobility, a structure-based vector analysis of available β-CoV S-protein structures was implemented. - S-proteins from different β-CoVs display distinct configurations. - Two soluble ectodomain constructs for the SARS-CoV-2 S-protein were developed, in which the highly immunogenic and mobile receptor binding domain (RBD) is either locked in the all-RBDs ‘down’ position or adopts ‘up’ state conformations more readily than the wild-type S-protein. =&gt; The conformation of the S-protein can be controlled via rational design and can provide a framework for the development of engineered CoV S-proteins for vaccine applications.</td>
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<td>Nature 22JUL2020</td>
<td>Hydroxychloroquine use against SARS-CoV-2 infection in non-human primates</td>
<td>Maisonnasse, Pauline et al. France <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Evaluation of the antiviral activity of HCQ both in vitro and in SARS-CoV-2-infected macaques. - HCQ showed antiviral activity in African green monkey kidney cells (VeroE6) but not in a model of reconstituted human airway epithelium. - Cynomolgus macaques provides a relevant model for studying the early stages of SARS-CoV-2 infection in humans. - In macaques, no antiviral activity nor clinical efficacy of HCQ treatment, alone or in combination with azithromycin (AZTH), was shown, regardless of the timing of treatment initiation, either before infection, early after infection (before viral load peak) or late after infection (after viral load peak). This was in spite of high HCQ concentration in blood and lung and plasma exposure similar to that observed in COVID-19 patients. - When the drug was used as a pre-exposure prophylaxis (PrEP), HCQ did not confer protection against acquisition of infection. =&gt; These findings do not support the use of HCQ, either alone or in combination with AZTH, as an antiviral treatment for COVID-19 in humans.</td>
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<td>Nature 22JUL2020</td>
<td>Potent neutralizing antibodies directed to multiple epitopes on SARS-CoV-2 spike</td>
<td>Liu, Lihong et al., USA/China <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Isolation of 61 SARS-CoV-2-neutralizing monoclonal antibodies from 5 infected patients hospitalized with severe disease. Among these are 19 antibodies that potently neutralized the authentic SARS-CoV-2 in vitro, 9 of which exhibited exquisite potency, with 50% virus-inhibitory concentrations of 0.7 to 9 ng/mL. Epitope mapping showed this collection of 19 antibodies to be about equally divided between those directed to the receptor-binding domain (RBD) and those to the N-terminal domain (NTD), indicating that both of these regions at the top of the viral spike are immunogenic. In addition, 2 other powerful neutralizing antibodies recognized quaternary epitopes that overlap with the domains at the top of the spike. Cryo-electron microscopy reconstructions of one antibody targeting RBD, a second targeting NTD, and a third bridging two separate RBDs revealed recognition of the closed, “all RBD-down” conformation of the spike. =&gt; Collection of SARS-CoV-2-neutralizing mAbs that are not only potent but also diverse. The potency and diversity of our SARS-CoV-2-neutralizing mAbs are likely attributable to patient selection (infected individuals with severe disease developed a more robust virus-neutralizing antibody response). The diversity of these antibodies is also attributable, in part, to the choice of using the 5 trimer to sort from memory B cells, while most groups focused on the use of RBD. RBD and NTD are, no doubt, quite immunogenic. Neutralizing antibodies to the stem region of the 5 trimer remain to be discovered.</td>
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<td>Nature 22JUL2020</td>
<td>Chloroquine does not inhibit infection of human lung cells with SARS-CoV-2</td>
<td>Hoffmann, Markus et al., Germany <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Comparison of chloroquine and hydroxychloroquine-mediated inhibition of SARS-2-S-mediated entry into Vero (kidney), Vero-TMPRSS2 and Calu-3 (lung) cells. Calu-3 cells, like airway epithelium, express low amounts of cathepsin L (CatL) and SARS-CoV-2 entry into these cells is TMPRSS2-dependent. In contrast, Vero cell entry of SARS-CoV-2 is CatL-dependent while both CatL and TMPRSS2 support entry into Vero-TMPRSS2 cells. As control, camostat mesylate, which inhibits TMPRSS2-dependent entry, was used. - Chloroquine and hydroxychloroquine can block SARS-2-S-driven entry but inhibition is cell line-dependent and efficient inhibition is not observed with TMPRSS2+ lung cells. - Chloroquine efficiently blocked SARS-CoV-2 infection of Vero kidney cells, as expected, but failed to efficiently inhibit SARS-CoV-2 infection of Calu-3 lung cells. - Chloroquine failed to efficiently block Calu-3 cell infection with SARS-2-S-bearing pseudotypes and authentic SARS-CoV-2, indicating that in these cells chloroquine does not appreciably interfere with viral entry or the subsequent steps of the viral replication cycle. Confirmation of the results with primary respiratory epithelium is pending. =&gt; These results indicate that chloroquine targets a pathway for viral activation that is not operative in lung cells and is unlikely to protect against SARS-CoV-2 spread in and between patients. =&gt; Moreover, they highlight that cell lines mimicking important aspects of respiratory epithelial cells should be used when analyzing the antiviral activity of drugs targeting host cell functions.</td>
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<td>Cell Reports Medicine 21JUL2020</td>
<td>Characterization and Treatment of SARS-CoV-2 in Nasal and Bronchial Human Airway Epithelia</td>
<td>Pizzorno, Andrés et al., France <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Use of reconstituted human airway epithelia to isolate and then characterize the viral infection kinetics, tissue-level remodeling of the cellular ultrastructure, and transcriptional early immune signatures induced by SARS-CoV-2 in a physiologically relevant model. Results emphasize distinctive transcriptional immune signatures between nasal and bronchial HAE, both in terms of kinetics and intensity, hence suggesting putative intrinsic differences in the early response to SARS-CoV-2 infection. Most important, evidence in human-derived tissues was provided on the antiviral efficacy of remdesivir monotherapy and the potential of the remdesivir-diltiazem combination was explored as an option worthy of further investigation to respond to the still-unmet COVID-19 medical need. =&gt; Results expected to provide a benchmark for future studies aimed at further characterizing the local pathophysiology and immune response to SARS-CoV-2 infection, particularly in the lower respiratory tract, with the ultimate objective of providing insight in terms of putative prognostic biomarkers and/or patient management. =&gt; The HAE model of SARS-CoV-2 infection described in this study also constitutes an advantageous physiologic model to evaluate candidate therapeutic approaches, provided that in many cases the inhibitory effects observed in classic reductionist models of immortalized cell lines do not necessarily translate into a real clinical setting.</td>
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<td>Science 21JUL2020</td>
<td>Serial interval of SARS-CoV-2 was shortened over time by nonpharmaceutical interventions</td>
<td>Ali, Sheikh Taslim et al., UK-France-USA-China <a href="#">gotopaper</a></td>
<td>Public Health/ Epidemio</td>
<td>A database of 677 COVID-19 transmission pairs (in mainland China) (symptom onset dates and social relationships available for both the infector and infectee) show that: - Mean serial intervals of COVID-19 have shortened substantially from 7.8 days to 2.6 days within a month (January 9 to February 13, 2020). This change is driven by enhanced non-pharmaceutical interventions, in particular reduction of case isolation delay period. - Using real-time estimation of serial intervals allowing for variation over time, provides more accurate estimates of reproduction numbers than using conventionally fixed serial interval distributions. =&gt; Findings could improve assessment of transmission dynamics, forecasting future incidence, and estimating the impact of control measures.</td>
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<td>PLoS Med 21JUL2020</td>
<td>Impact of self-imposed prevention measures and short-term government-imposed social distancing on mitigating and delaying a COVID-19 epidemic: A modelling study</td>
<td>Teslya, Alexandra et al., Netherlands-Portugal</td>
<td>Public Health/Epidemiology</td>
<td>Effectiveness of self-imposed measures and short-term government-imposed social distancing in mitigating COVID-19 epidemic (transmission model in population stratified by disease status and disease awareness status). Principles: Self-imposed measures assumed in disease-aware individuals (handwashing, mask-wearing, social distancing). Government-imposed social distancing reduced contact rate of individuals irrespective of disease or awareness status.  - For fast awareness spread in population, self-imposed measures can significantly reduce the attack rate and diminish and postpone the peak number of diagnoses. Estimated: large epidemic preventable if efficacy of these measures exceeds 50%.  - For slow awareness spread, self-imposed measures reduce peak number of diagnoses and attack rate but do not affect the timing of the peak.  - Early implementation of short-term government-imposed social distancing alone is estimated to delay (by at most 7 months for a 3-month intervention) but not reduce the peak. Delay can be longer and height of peak further reduced if combined with self-imposed measures that continue after government-imposed distancing is lifted. Limitations: analyses do not account for stochasticity, demographics, heterogeneities in contact patterns or mixing, spatial effects, imperfect isolation of individuals with severe disease, and reinfection.  - Suggests that information dissemination and disease awareness, which mobilise people to adopt effective self-imposed control measures, can be an effective strategy to mitigate and delay the epidemic.  - Early initiated short-term government-imposed social distancing can buy extra time.</td>
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<td>Science Translational Medicine 20JUL2020</td>
<td>An alphavirus-derived replicon RNA vaccine induces SARS-CoV-2 neutralizing antibody and T cell responses in mice and nonhuman primates</td>
<td>Erasmus, Jesse H et al., USA</td>
<td>Vaccine</td>
<td>Development of an alphavirus-derived replicon RNA vaccine candidate, repRNA-CoV25, encoding the SARS-CoV-2 spike (S) protein. The RNA replicons were formulated with Lipid InOrganic Nanoparticles (LION) that were designed to enhance vaccine stability, delivery, and immunogenicity.  <strong>Results:</strong>  - A single intramuscular injection of the LION/repRNA-CoV25 vaccine in mice elicited robust production of anti-SARS-CoV-2 S protein IgG antibody isotypes indicative of a Type 1 T helper cell response.  - A prime/boost regimen induced potent T cell responses in mice including antigen-specific responses in lung and spleen. Prime-only immunization of aged (17-month old) mice induced smaller immune responses compared to young mice, but this difference was abrogated by booster immunization.  - In nonhuman primates, prime-only immunization in one intramuscular injection site or prime/boost immunizations in 5 intramuscular injection sites elicited modest T cell responses and robust antibody responses. The antibody responses persisted for at least 70 days and neutralized SARS-CoV-2 at titers comparable to those in human serum samples collected from individuals convalescing from COVID-19.  <strong>Conclusion:</strong> Potential for LION/repRNA-CoV25, which will enter clinical development under the name HDT-301, to induce rapid immune protection from SARS-CoV-2 infection. <strong>Limitations:</strong> Absence of challenge data; limited number of animals; time points after vaccination where observed responses, especially T-cell responses, exhibited great variability</td>
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<td>Gut 20JUL2020</td>
<td>Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19</td>
<td>Zuo, Tao et al., China <a href="#">gotopaper</a></td>
<td>Gut Microbiota</td>
<td>Longitudinal faecal microbiome alterations in patients with COVID-19 (RNA metagenomics sequencing on faecal viral extractions from 15 hospitalised patients with COVID-19):  - 7 of 15 COVID-19 patients (46.7%) had SARS-CoV-2 positive stool (viral RNA). Even in absence of GI manifestations, all 7 patients showed strikingly higher 3’ vs 5’ end SARS-CoV-2 genome coverage and density in their faecal viral metagenome profile.  - 3 patients continued to display active fecal viral infection signature up to 6 days after clearance of SARS-CoV-2 from respiratory samples.  - Faecal samples with high SARS-CoV-2 infectivity signature -&gt; higher abundances of bacterial species <em>Collinsella aerofaciens</em>, <em>Collinsella tanakaei</em>, <em>Streptococcus infantis</em>, <em>Morganella morganii</em>, and higher capacity for nucleotide <em>de novo</em> biosynthesis, amino acid biosynthesis and glycolysis.  - Faecal samples with low-to-no SARS-CoV-2 infectivity signature -&gt; higher abundances of short-chain fatty acid producing bacteria, <em>Parabacteroides merdae</em>, <em>Bacteroides stercoris</em>, <em>Alistipes onderdonkii</em> and <em>Lachnospiraceae bacterium</em>.  - Gut microbiota of patients with active SARS-CoV-2 GI infection was characterised by enrichment of opportunistic pathogens, loss of salutary bacteria and increased functional capacity for nucleotide and amino acid biosynthesis and carbohydrate metabolism.</td>
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| LANCET 20JUL2020 | Immunogenicity and safety of a recombinant adenovirus type-5-vecteded COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo controlled, phase 2 trial | Feng-Cai Zhu et al., China [gotopaper](#) | Vaccine | PROTOCOLE DESIGN (NCT04341389):  
> Vaccine: Ad5-vecteded COVID 19 vaccine from CanSino  
> Phase 2 clinical trial; randomized, double blindered, placebo controlled.  
> 508 participants > 18 years of age (seronegatifs for SARS-CoV-2 infection). Recruited in one single site (Wuhan)  
> Doses: either 1x10exp11 vp/mL, 5x10exp10vp/mL or placebo (2:1:1). One single administration IM  
Primary endpoints:  
> Mean geometric titers of specific ELISA antibody responses to the receptor binding domain (RBD)  
> Neutralizing antibody responses at day 28  
> Incidence of adverse reactions within 14 days.  
RESULTS:  
Cohort characteristics: 50% male; mean age 39.7 years, SD 12.5  
RDB specific antibodies induction et seroconversion rates at day 28:  
> Dose 1x10exp11 vp/mL: 656.5 (95% CI 575.2–749.2); 96% (95% CI 93–99)  
> Dose 5x10exp10vp/mL: 571.0 (467.6–697.3); 97% (92–99)  
Neutralizing antibodies induction:  
> Dose 1x10exp11 vp/mL: GMTs of 19.5 (95% CI 16.8–22.7)  
> Dose 5x10exp10vp/mL: GMTs of 18.3 (14.4–23.3)  
Specific interferon-γ enzyme-linked immunospot assay responses post vaccination observed in:  
> 227/253 participants (90%, 95% CI 85–93) (Dose 1x10exp11vp/mL)  
> 113/129 participants (88%, 81–92) (Dose 5x10exp10vp/mL)  
Solicited adverse reactions were reported by:  
> 183/253 participants (72%) (Dose 1x10exp11 vp/mL)  
> 96/129 participants (74%) (Dose 5x10exp10vp/mL)  
Severe adverse reactions were reported by:  
> 24/253 participants (9%) (Dose 1x10exp11 vp/mL)  
> 1/129 participant (1%) (Dose 5x10exp10vp/mL)  
No severe adverse reactions documented |
| LANCET 20JUL2020 | Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial | Folegatti P et al., [gotopaper](#) | Vaccine | PROTOCOLE DESIGN (NCT04324606):  
> Vaccine: ChAdOx1-vecteded COVID 19 vaccine from Oxford/AstraZeneca  
> Phase 1/2 clinical trial; randomized, single blindered, - controlled.  
> 1077 participants between 18 and 55 years of age (seronegative for SARS-CoV-2 infection). Recruited in 5 sites across UK  
> Dose: 5x10exp10vp/mL of ChAdOx1-nCov19 . MenACWY used as control (1:1). One single administration IM  
-10 participants received ChAdOx1 nCoV-19 end prime boost (administration at 28d)  
> Prophylactic paracetamol administered in 2/3 sites  
Primary outcomes:  
> Measurement of humoral (Total and NAbs) and cellular responses  
> Assessment of efficacy and safety  
RESULTS:  
Local and systemic reactions were more common in the ChAdOx1 nCoV-19 group and reduced by use of prophylactic paracetamol  
> In ChAdOx1 nCoV-19 vaccinated participants:  
i. spike-specific T-cell responses peaked on day 14 (median 856 spot-forming cells per million peripheral blood mononuclear cells, IQR 493–1802; n=43).  
ii. Anti-spike IgG responses rose by day 28 (median 157 ELISA units [EU], 96–317; n=127), and were boosted following a second dose (639 EU, 360–792; n=10).  
iii. Neutralising antibody responses were detected in 32/35 participants (91%) or 35/35 participants (100%) depending on the measuring method after a single dose. After a booster dose, all participants had neutralising activity  
Neutralising antibody responses at day 28:  
> 96/129 participants (74%) (Dose 5x10exp10vp/mL)  
> 183/253 participants (72%) (Dose 1x10exp11 vp/mL)  
Solicited adverse reactions were reported by:  
> 183/253 participants (72%) (Dose 1x10exp11 vp/mL)  
> 96/129 participants (74%) (Dose 5x10exp10vp/mL)  
Severe adverse reactions were reported by:  
> 24/253 participants (9%) (Dose 1x10exp11 vp/mL)  
> 1/129 participant (1%) (Dose 5x10exp10vp/mL)  
No severe adverse reactions documented |
Retrospective multicenter cohort study of 446 COVID-19 patients in China to examine the association between the use and timing of IFN-α2b and clinical outcomes.
- Early IFN use with significantly reduced in-hospital mortality.
- No significant clinical benefit of IFNs was observed in moderately ill COVID-19 patients.
- Late administration of IFN could be associated with longer hospital stay and slower recovery of lung function.
- Using early IFNs with LPV/r is associated with more favorable clinical responses than by using LPV/r alone in COVID-19 patients.
- Early administration of IFN-α2b was associated with reduced in-hospital mortality among severe to critical COVID-19 patients. In contrast, late interferon therapy increased mortality and delayed recovery, suggesting the timing of interferon therapy is crucial for favorable responses in COVID-19 patients.

Limitations:
- retrospective design and non randomized assignment of therapies;
- detailed virologic data were not included in the study that precluded comparison with randomized controlled trials of IFNs;
- regression models did not include location of care as a confounder because of multicollinearity with therapy choices between IFNs and LPV/r;
- adjunctive and supportive therapies were not included in the analyses but could influence the length of hospital stay.

Preliminary results oral or intravenous dexamethasone vs usual care alone in RECOVERY, controlled, open-label trial comparing a range of possible treatments in patients hospitalized with Covid-19. Primary outcome: 28-day mortality.
2104 patients assigned to receive dexamethasone and 4321 to receive usual care.
- 482 patients (22.9%) in the dexamethasone group and 1110 patients (25.7%) in the usual care group died within 28 days after randomization (age-adjusted rate ratio, 0.83; 95% confidence interval [CI], 0.75 to 0.93; P<0.001).
- The proportional and absolute between-group differences in mortality varied considerably according to the level of respiratory support that the patients were receiving at the time of randomization. In the dexamethasone group, the incidence of death was lower than that in the usual care group among patients receiving invasive mechanical ventilation (29.3% vs. 41.4%; rate ratio, 0.64; 95% CI, 0.51 to 0.81) and among those receiving oxygen without invasive mechanical ventilation (23.3% vs. 26.2%; rate ratio, 0.82; 95% CI, 0.72 to 0.94) but not among those who were receiving no respiratory support at randomization (17.8% vs. 14.0%; rate ratio, 1.19; 95% CI, 0.91 to 1.55).
- In patients hospitalized with Covid-19, the use of dexamethasone resulted in lower 28-day mortality among those who were receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support and results were consistent with possible harm in this subgroup.
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<td>Eurosurveillance 16JUL2020</td>
<td>Convalescent plasma treatment for SARS-CoV-2 infection: analysis of the first 436 donors in England, 22 April to 12 May 2020</td>
<td>Harvala, Heli et al., UK <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Serological reactivity was analysed in plasma from 436 individuals with a history of disease compatible with COVID-19, including 256 who had been laboratory-confirmed with SARS-CoV-2 infection. - Over 99% of laboratory-confirmed cases developed a measurable antibody response (254/256) and 88% harboured neutralising antibodies (226/256). - Antibody levels declined over 3 months following diagnosis, emphasising the importance of the timing of convalescent plasma collections. - Finally, the study indicates that commercial ELISA can perform effectively as surrogate assays for predicting neutralising antibody titres and represent a streamlined and rapid way to guide convalescent plasma donor selection.</td>
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<td>Ann Intern Med. 16JUL2020</td>
<td>Hydroxychloroquine in Nonhospitalized Adults With Early COVID-19: A Randomized Trial</td>
<td>Skipper, Caleb P. et al., USA/Canada <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Internet-based multisite, international randomized, double blind, placebo-controlled trial to investigate whether HCQ could reduce COVID-19 severity in symptomatic, non hospitalized adults with laboratory-confirmed COVID-19 or probable COVID-19 and high-risk exposure within 4 days of symptom onset. The primary end point was change in overall symptom severity over 14 days, because the pooled event rate of hospitalization or death was substantially lower than initial 10% expectation. 423 patients contributed primary end point data. Of these, 341 (81%) had lab-confirmed infection with SARS-CoV-2 or epidemiologically linked exposure to a person with lab confirmed infection; 56% (236) were enrolled within 1 day of symptoms starting. - Change in symptom severity over 14 days did not differ between the HCQ and placebo groups (difference in symptom severity: relative, 12%; absolute, -0.27 points [95% CI, -0.61 to 0.07 points]; P = 0.117). - At 14 days, 24% (49 of 201) of participants receiving HCQ had ongoing symptoms compared with 30% (59 of 194) receiving placebo (P = 0.21). - Medication adverse effects occurred in 43% (92 of 212) of participants receiving HCQ versus 22% (46 of 211) receiving placebo (P &lt; 0.001). With placebo, 10 hospitalizations occurred (2 non–COVID-19–related), including 1 hospitalized death. With HCQ, 4 hospitalizations occurred plus 1 non hospitalized death (P = 0.29). =&gt; HCQ did not substantially reduce symptom severity in outpatients with early, mild COVID-19. Limitations: Only 58% of participants received SARS-CoV-2 testing because of severe U.S. testing shortages.</td>
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<td>Clin. Infect. Dis. 16JUL2020</td>
<td>Hydroxychloroquine for Early Treatment of Adults with Mild Covid-19: A Randomized Controlled Trial</td>
<td>Mitja, Oriol et al., Spain <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Multicenter, open label, randomized controlled trial in non hospitalized adult patients with recently confirmed SARS-CoV-2 infection and less than five days of symptoms receiving HCQ or no antiviral treatment (not-placebo controlled). Study outcomes were the reduction of viral RNA load in nasopharyngeal swabs up to 7 days after treatment start, patient disease progression using the WHO scale up to 28 days, and time to complete resolution of symptoms. Adverse events were assessed up to 28 days.</td>
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| **Nature** 16JUL2020 | Reconstruction of the full transmission dynamics of COVID-19 in Wuhan | Hao, Xingjie et al., China, USA [gotopaper](#) | Public Health/Epidemio | Modelling approach to reconstruct the full-spectrum dynamics of COVID-19 (Wuhan China, 1 January to 8 March 2020) across 5 periods marked by events and non-pharmaceutical interventions (based on 32,583 laboratory-confirmed cases), accounting for presymptomatic infectiousness, time-varying ascertainment rates, transmission rates and population movements:  
- High covertness and high transmissibility were key features identified.  
- Estimate 87% (lower bound 53%) of infections before March 8 were unascertained, potentially including asymptomatic and mild-symptomatic cases, and basic reproduction number R0 of 3.54 in the early outbreak (much higher than for SARS and MERS).  
- Positive effects of multi-pronged interventions: decreasing the reproduction number to 0.28, reducing total infections in Wuhan by 96.0% as of March 8.  
- Probability of resurgence following lifting of all interventions after 14 days of no ascertained infections, estimated at 0.32 and 0.06 based on models with 87% and 53% unascertained infections, respectively.  
-> Risk posed by unascertained cases when changing intervention strategies highlight the important implications for continuing surveillance and interventions to eventually contain COVID-19 outbreaks. |
| **Antiviral Research** 15JUL2020 | Lower prevalence of antibodies neutralizing SARS-CoV-2 in group O French blood donors | Gallian, Pierre et al., France [gotopaper](#) | Public Health/Epidemio | Distribution of antibodies neutralizing SARS-CoV-2 according to age, sex or blood group in 998 samples from French blood donors (last week of March or first week of April 2020):  
- At this stage of the outbreak, prevalence was low (2.7%) and criteria for blood donation imply that vast majority of seropositives had asymptomatic or pauci-symptomatic SARS CoV-2 infections.  
- Antibodies neutralizing SARS-CoV-2 found with similar prevalence in men and women.  
- Virus infection may occur at similar incidence in men and women (2.82% vs 2.69%), while severe forms are more frequent in men.  
- Proportion of seropositives significantly lower in group O donors (1.32% vs 3.86% in other donors, p = 0.014).  
-> Blood group O persons are less at risk of being infected by SARS-CoV-2 than other blood groups persons. |
### Physical distancing interventions and incidence of coronavirus disease 2019: natural experiment in 149 countries

**Aim:** To evaluate the incidence of Covid-19 before and after physical distancing intervention using data of 149 countries that implemented one of the five physical distancing interventions (closures of schools, workplaces, and public transport, restrictions on mass gatherings and public events, and restrictions on movement (lockdowns)) between 1 January and 30 May 2020.

- Implementation of any physical distancing intervention was associated with an overall reduction in covid-19 incidence of 13%;
- Closure of public transport was not associated with any additional reduction in covid-19 incidence when the other four physical distancing interventions were in place;
- Data from 11 countries also suggested similar overall effectiveness (pooled IRR 0.85, 0.81 to 0.89) when school closures, workplace closures, and restrictions on mass gatherings were in place;
- Earlier implementation of lockdown was associated with a larger reduction in covid-19 compared with a delayed implementation of lockdown after other physical distancing interventions were in place.

These findings might support policy decisions related to physical distancing measures in current or future epidemic waves.

### Epidemiology and Clinical Presentation of Children Hospitalized with SARS-CoV-2 Infection in Suburbs of Paris

Prospective, observational, multicentre study aimed at identifying the epidemiological characteristics, clinical presentation, and prognosis of 192 children with Covid-19 hospitalized in Paris suburb hospitals from 23 March to 10 May 2020 (lockdown period).

- Median age of children was one year old, sex ratio 1.3:1;
- Fever was recorded in 76.6% children and poorly tolerated in 15.1%. Symptoms ranged from rhinorrhea (34.4%) and gastrointestinal (35.5%) to respiratory distress (25%). Only 5.2% of children had anosmia and 2.6% had chest pain. An underlying condition was identified in almost 30% of cases;
- 24 (12.5%) children were admitted to paediatric intensive care units, 12 required mechanical ventilation, and three died.

Although most Covid-19 paediatric cases showed mild to moderate clinical expression, one-eighth of children were admitted to paediatric intensive care units and three died.
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<tr>
<td>Nature 15JUL2020</td>
<td>Potently neutralizing and protective human antibodies against SARS-CoV-2</td>
<td>Zost, Seth J. et al., USA <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>From a larger panel of human monoclonal antibodies (mAbs) targeting the spike (S) glycoprotein, several were identified that exhibited potent neutralizing activity and fully blocked the receptor-binding domain of S (SRBD) from interacting with human ACE2 (hACE2). - Competition-binding, structural, and functional studies allowed clustering of the mAbs into classes recognizing distinct epitopes on the SRBD as well as distinct conformational states of the S trimer. - Potent neutralizing mAbs recognizing non-overlapping sites, COV2-2196 and COV2-2130, bound simultaneously to S and synergistically neutralized authentic SARS-CoV-2 virus. - In two mouse models of SARS-CoV-2 infection, passive transfer of either COV2-2196 or COV2-2130 alone or a combination of both mAbs protected mice from weight loss and reduced viral burden and inflammation in the lung. - Passive transfer of each of two of the most potently ACE2 blocking mAbs (COV2-2196 or COV2-2381) as monotherapy protected rhesus macaques from SARS-CoV-2 infection. ➞ These results identify protective epitopes on SRBD and provide a structure-based framework for rational vaccine design and the selection of robust immunotherapeutics.</td>
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<td>JAMA 14JUL2020</td>
<td>Rapid implementation of SARS-CoV-2 sequencing to investigate cases of health-care associated COVID-19: a prospective genomic surveillance study</td>
<td>Meredith et al., UK <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Prospective surveillance study Between March 13 and April 24, 2020, collection of clinical data and samples from 5613 patients with COVID-19 from across the East of England ➞ Rapid SARS-CoV-2 nanopore sequencing from PCR-positive diagnostic samples, enabling sample-to-sequence in less than 24 h ➞ Establishment of a weekly review and reporting system with integration of genomic and epidemiological data to investigate suspected health-care associated COVID-19 cases Results : Sequencing of 1000 samples producing 747 high-quality genomes. Combination of epidemiological and genomic analysis of the 299 patients from our hospital and identified 35 clusters of identical viruses involving 159 patients. 92 (58%) of 159 patients had strong epidemiological links and 32 (20%) patients had plausible epidemiological links. These results were fed back to clinical, infection control, and hospital management teams, leading to infection-control interventions and informing patient safety reporting. Conclusions : Benefit of combined genomic and epidemiological analysis for the investigation of health-care associated COVID-19 Possibility to detect cryptic transmission events and identify opportunities to target infection-control interventions to further reduce health-care associated infections. Our findings have important implications for national public health policy as they enable rapid tracking and investigation of infections in hospital and community settings.</td>
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<td>JAMA 14JUL2020</td>
<td>Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers</td>
<td>Wang et al., USA <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Mass General Brigham (MGB) is the largest health care system in Massachusetts, with 12 hospitals and more than 75 000 employees. Using electronic medical records -&gt; identification of HCWs providing direct and indirect patient care who were tested for SARS-CoV-2 with RT PCR between March 1 and April 30, 2020. 3 phases during the study period: 1- A preintervention period before implementation of universal masking of HCWs (March 1-24, 2020) 2- A transition period until implementation of universal masking of patients (March 25–April 5, 2020) 3- An additional lag period to allow for manifestations of symptoms (April 6-10, 2020), as previously defined; and an intervention period (April 11-30, 2020) Results : Of 9850 tested HCWs, 1271 (12.9%) had positive results for SARS-CoV-2 (median age, 39 years; 73% female; 7.4% physicians or trainees, 26.5% nurses or physician assistants, 17.8% technologists or nursing support, and 48.3% other). During the preintervention period, the SARS-CoV-2 positivity rate increased exponentially from 0% to 21.32%, with a weighted mean increase of 1.16% per day and a case doubling time of 3.6 days (95% CI, 3.0-4.5 days). During the intervention period, the positivity rate decreased linearly from 14.65% to 11.46%, with a weighted mean decline of 0.49% per day and a net slope change of 1.65% (95% CI, 1.13%-2.15%; P &lt; .001) more decline per day compared with the preintervention period. Conclusion : Universal masking at MGB was associated with a significantly lower rate of SARS-CoV-2 positivity among HCWs. Randomized trials of universal masking of HCWs during a pandemic are likely not feasible. Nonetheless, these results support universal masking as part of a multirange infection reduction strategy in health care settings.</td>
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<tr>
<td>Nature Comm 14JUL2020</td>
<td>Transplacental transmission of SARS-CoV-2 infection</td>
<td>Vivanti A.J. et al, France <a href="#">gotopaper</a></td>
<td>Clinic Case study</td>
<td>23 years old G1P0: SARS-CoV-2 detected in blood, in nasopharyngeal and vaginal swabs (35±2 weeks of gestation) All routine tests were normal, ultrasound normal. At 35±5 weeks of gestation à cesarean section for pathological fetal heart rate tracing: - Amniotic fluid tested positive for SARS-CoV-2 prior to the rupture of membranes - RT-PCR on the placenta was positive for SARS-CoV-2 (viral load much higher) - No other pathogen agent was detected on the placenta Neonate: - Male, birth weight 2540g - Apgar scores 4 – 2 – 7 (1, 5 and 10 min) à intubation à intensive care unit - Extubated at H6, no sedative or analgesic drug - Echocardiography and lung ultrasound were normal - RT-PCR positive for SARS-CoV-2 on blood and non-bronchoscopic bronchoalveolar lavage fluid - Nasopharyngeal and rectal swabs were positive for SARS-CoV-2: 1h of life, at 2 and 18 days. On the third day: - Irritability, axial hypertonia &amp; opisthotonos - CSF was negative, blood culure was sterile, EEG normal, no signs suspected for metabolic disease - Improved slowly, mild hypotonia and feeding difficulty persisted MRI at 11 day: bilateral gliosis of the deep white periventricular and subcortical matter 2 months of life: improved neurological examination an MRI. Clinical exam normal -&gt; Description of an actual neonatal infection -&gt; A case of congenital infection associated with neurological manifestations following neonatal viremia -&gt; Demonstration that the transplacental transmission of SARS-CoV-2 infection is possible</td>
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<tr>
<td>Nature Communications 14JUL2020</td>
<td>Exploring the SARS-CoV-2 virus-host-drug interactome for drug repurposing</td>
<td>Sadegh, Sepideh et al., Germany gotopaper</td>
<td>Therapeutics</td>
<td>CoVex, a web-based platform for the interactive exploration and network-based analysis of virus–host interactions, aimed towards drug repurposing for the treatment of COVID-19. It integrates virus-human protein interactions, human protein–protein interactions, and drug-target interactions. It allows visual exploration of the virus-host interactome and implements systems medicine algorithms for network-based prediction of drug candidates. Thus, CoVex is a resource to understand molecular mechanisms of pathogenicity and to prioritize candidate therapeutics.</td>
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<td>NEJM 14JUL2020</td>
<td>An mRNA Vaccine against SARS-CoV-2 — Preliminary Report</td>
<td>Jackson LA et al., USA gotopaper</td>
<td>Vaccine</td>
<td>&gt; Phase 1 clinical Trial with mRNA-1273 vaccine from Moderna</td>
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<tr>
<td>Nature structural &amp; molecular biology 13JUL2020</td>
<td>Neutralizing nanobodies bind SARS-CoV-2 spike RBD and block interaction with ACE2</td>
<td>Huo, Jiangdong et al., UK gotopaper</td>
<td>Therapeutics</td>
<td>Using a naïve llama single-domain antibody library and PCR-based maturation, 2 closely related nanobodies, H11-D4 and H11-H4, that bind RBD (KD of 39 and 12 nM, respectively) and block its interaction with ACE2 were produced.</td>
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- Single-particle cryo-EM revealed that both nanobodies bind to all three RBDs in the spike trimer.
- Crystal structures of each nanobody–RBD complex revealed how both nanobodies recognize the same epitope, which partly overlaps with the ACE2 binding surface, explaining the blocking of the RBD–ACE2 interaction.
- Nanobody-Fc fusions showed neutralizing activity against SARS-CoV-2 (4–6 nM for H11-H4, 18 nM for H11-D4) and additive neutralization with the SARS-CoV-1/2 antibody CR3022. Such additive combinations are a well-known strategy to reduce the propensity of the virus to escape by mutating.

- Nanobody maturation technology can be deployed to produce a highly neutralizing agent against an emerging viral threat in real time. The approach may be useful in identifying complementary epitopes to those identified by animal immunization approaches. The H11-H4 and H11-D4 nanobodies may find application in a cocktail of laboratory-synthesized neutralizing antibodies given for passive immunization of severely ill COVID-19 patients. |
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<tr>
<td>Science 13JUL2020</td>
<td>Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients</td>
<td>Hadjadj J et al, France <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Integrated immune analysis – 50 COVID-19 patients and 18 healthy controls were included: mild-to-moderate (n=15) – severe (n=17) – critical (n=18). Immunological transcriptional signature: - Data suggested a severity grade-dependent increase in activation of innate and inflammatory pathways. - IFN response was high in mild-to-moderate patients while it was reduced in more severe patients. - IFN activity in serum was significantly lower in severe/critical patients as compared to mild-to-moderate patients. - Genes specifically up-regulated in severe or critical patients mainly belonged to the NF-κB pathway.</td>
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<tr>
<td>Cell 13JUL2020</td>
<td>Longitudinal isolation of potent near-germline SARS-CoV-2-neutralizing antibodies from COVID-19 patients</td>
<td>Kreer, Christoph et al., Germany <a href="#">gotopaper</a></td>
<td>Vaccines</td>
<td>Longitudinal analysis of the antibody response of 12 COVID-19 patients from 8 to 69 days after diagnosis. - By screening 4,313 SARS-CoV-2-reactive B cells, 255 antibodies were isolated from different time points as early as 8 days after diagnosis. - Of these, 28 potently neutralized authentic SARS-CoV-2 with IC100 as low as 0.04mg/mL, showing a broad spectrum of variable (V) genes and low levels of somatic mutations. - Interestingly, potential precursor sequences were identified in naive B cell repertoires from 48 healthy individuals who were sampled before the COVID-19 pandemic. ➔ These results demonstrate that SARS-CoV-2-neutralizing antibodies are readily generated from a diverse pool of precursors, fostering hope for rapid induction of a protective immune response upon vaccination.</td>
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<tr>
<td>Clin. Infect. Dis. 11JUL2020</td>
<td>Tocilizumab for treatment of mechanically ventilated patients with COVID-19</td>
<td>Somers, Emily C. et al., USA <a href="#">gotopaper</a></td>
<td>Therapeutics</td>
<td>Observational, single-center, controlled study of 154 patients with severe COVID-19 illness requiring mechanical ventilation to assess effectiveness and safety of IL-6 blockade with tocilizumab. Primary endpoint was survival probability post-intubation; secondary analyses included an ordinal illness severity scale integrating superinfections. - In propensity score inverse probability weighting (IPTW)-adjusted models, tocilizumab was associated with a 45% reduction in hazard of death [hazard ratio 0.55 (95% CI 0.33, 0.90)] and improved status on the ordinal outcome scale [odds ratio per 1-level increase: 0.58 (0.36, 0.94)]. - Though tocilizumab was associated with an increased proportion of patients with superinfections (54% vs. 26%; p&lt;0.001), there was no difference in 28-day case fatality rate among tocilizumab-treated patients with versus without superinfection [22% vs. 15%; p=0.42]. Staphylococcus aureus accounted for ~50% of bacterial pneumonia. Limitations: observational study; does not address the potential role of tocilizumab earlier in illness for preventing mechanical ventilation, the optimal dose of tocilizumab, the potential utility of multiple doses, or the role of IL-6 serum concentrations (which were not routinely available) in predicting tocilizumab response; tocilizumab usage in this clinical care setting was not dictated by a firm study protocol, and therefore not completely standardized.</td>
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<td>Nature Med</td>
<td>Rapid isolation and profiling of a diverse panel of human monoclonal antibodies targeting the SARS-CoV-2 spike protein</td>
<td>Zost SJ et al., USA gotopaper</td>
<td>Therapeutic</td>
<td>Use a rapid antibody discovery platform to isolate hundreds of human monoclonal antibodies (mAbs) against SARS-CoV-2 s protein</td>
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<td>à obtain human mAbs from the B cells of some patients in North America (4 patients)</td>
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<td>à used different workflows in parallel</td>
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<td>The antibodies could be grouped into five binding patterns on the basis of domain recognition and cross-reactivity.</td>
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<td>à Most neutralizing mAbs recognizing the receptor-binding domain (RBD) of S</td>
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<td>à the RBD= the principal site of vulnerability for SARS-CoV-2 neutralization</td>
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<td>à RBD of SARS-CoV-2 for vaccine design and therapeutic-antibody development</td>
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<td>PNAS</td>
<td>BCG vaccine protection from severe coronavirus disease 2019 (COVID-19)</td>
<td>Escobar LE et al., USA gotopaper</td>
<td>Vaccine/Public Health</td>
<td>&gt; Epidemiological explorations suggest a negative association between national BCG vaccination policy and the prevalence and mortality of COVID-19</td>
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<td>&gt; But comparisons are difficult due to broad differences between countries:</td>
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<td>- socioeconomic status,</td>
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<td>- demographic structure</td>
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<td>- rural vs. urban settings</td>
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<td>- number of diagnostic tests</td>
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<td>- national control strategies</td>
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<td>RESULTS:</td>
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<td>1. Strong correlation between the BCG index (estimation of the degree of universal BCG vaccination in a country), and COVID19 mortality in different socially similar European countries (r² = 0.88; P = 8 × 10−7 )</td>
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<td>- every 10% increase in the BCG index was associated with a 10.4% reduction in COVID-19 mortality</td>
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<td>2. Results fail to confirm the null hypothesis of no association between BCG vaccination and COVID-19 mortality, and suggest that BCG could have a protective effect</td>
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<td>3. Nevertheless, the analyses should be considered with caution. BCG vaccination clinical trials are required to corroborate the patterns detected</td>
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<td>Eurosurveillance</td>
<td>International external quality assessment for SARS-CoV-2 molecular detection and survey on clinical laboratory preparedness during the COVID-19 pandemic, April/May 2020</td>
<td>Matheeussen, V et al., International gotopaper</td>
<td>Public Health/Epidemi</td>
<td>External quality assessments (EQA) on molecular detection of RT-PCR SARS-CoV-2 tests : based on 521 datasets from 365 of 406 laboratories from 36 countries. 23% of the assays were in-house assays which performed as well or better than commercial ones. The overall qualitative performance of the participating laboratories was at an acceptable level. A lack of standardisation emerges, and extraction and amplification methods were significantly associated with correct classification of all samples. Laboratories should be aware of the limitations of their assays and perform their own validation and verification in line with ISO 15189 or equivalent requirements. EU RECOVER project survey assessing the molecular testing capacity and throughput for SARS-CoV-2 detection of clinical laboratories : almost 80% of the participating laboratories E5(n = 360) are capable of generating a PCR result within 24 h after receiving the sample, 48% of the laboratories could analyse more than 250 samples per day.</td>
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| Nature 08JULY2020 | OpenSAFEly: factors associated with COVID-19 death in 17 million patients | Williamson, EJ et al., gotopaper | Public Health/Epidemiology | OpenSAFEly is a secure health analytics platform covering 40% of all patients in England. Primary care records of 17,278,392 adults were pseudonymously linked to 10,926 COVID-19-related deaths.  
- COVID-19-related death was associated with male sex, older age and deprivation, diabetes, severe asthma and other conditions / Compared with people with white ethnicity, Black and South Asian people were at higher risk.  
Retrospective cohort study on data from COVID-19, SARS and other HCoV patients from Hong Kong, and the association with Alanine aminotransferase (ALT)/aspartate aminotransferase (AST) levels as marker of livel injury.  
- Cohorts : 1040 COVID-19 patients (mean age 38, 54% men), 1670 SARS patients (mean age 44, 44% men) and 675 other HCoV patients (mean age 20, 57% men).  
- ALT/AST was elevated in 50.3% SARS patients, 22.5% COVID-19 patients and 36.0% other HCoV patients.  
- For COVID-19 patients, 53 (5.1%) were admitted to ICU, 22 (2.1%) received invasive mechanical ventilation and 4 (0.4%) died.  
- ALT/AST elevation was independently associated with primary end point (ICU admission, mechanical ventilation and/or death) after adjusted for albumin, diabetes and hypertension. Use of lopinavir-ritonavir +/-ribavirin + interferon and corticosteroids was independently associated with ALT/AST elevation.  |
| CLIN. INFECT. DIS. 08JULY2020 | Evaluating use cases for human challenge trials in accelerating SARS-CoV-2 vaccine development | Nguyen LC et al., USA, CANADA, UK, gotopaper | Vaccine | Human challenge trials (HCTs) have been proposed as a means to accelerate SARS-CoV-2 vaccine development. Potential scenarios where using HCT could generate useful data for rapid vaccine development:  
1. Evaluating efficacy: use of HCT alongside an expanded safety trial to replace Ph3, or in parallel with Ph3 trial to give an early indicator of efficacy. HCT could take as little as two months to conduct and would require far fewer participants than a phase 3 trial due to viral exposure being guaranteed by the challenge  
2. Converging on correlates of protection: HCTs could be used to identify or verify CoPs against disease endpoints. These CoPs could then be used as surrogate endpoints in phase 3 trials (instead of clinical endpoints).  
3. Improving understanding of pathogenesis and the human immune response: A COVID-19 HCM would allow close observation of the participants prior to and from the point of vaccination and infection. This could help resolve the physiological basis for variation in disease severity, the disease’s progression from infection, or the immune response upon re-infection.  
**LIMITATIONS**  
> Timing of viral challenge relative to vaccination (same for all patients in HCT but highly variable in real world) / Method of administration can affect the nature of infection and the immune response.  |
| Cell Reports 07JUL2020 | Remdesivir inhibits SARS-CoV-2 in human lung cells and chimeric SARS-CoV expressing the SARS-CoV-2 RNA polymerase in mice | Pruijssers A et al., USA gotopaper | Therapeutic | Remdesivir (RDV) showed both prophylactic and therapeutic efficacy in mouse models of SARS and MERS.  
**In vitro:**  
- RDV potently inhibits SARS-CoV-2 replication in human lung cells and primary human airway epithelial culture.  
- Different cell lines were tested: Vero E6, Vero CCL-8, Huh7 and Calu3 2B4.  
- Weaker activity is observed in Vero E6 cells (EC50 = 1.65 μM) due to their low capacity to metabolize RDV.  
**In vivo:**  
- SARS-CoV-2 does not bind the murine ortholog of the human entry receptor to enter cells / Constructed a chimeric mouse-adapted SARS-CoV variant encoding the target of RDV antiviral activity, the RdRp, of SARS-CoV-2 / RDV is active against the SARS-CoV-2 RdRp in vivo / Therapeutic RDV administration diminishes lung viral load and improves pulmonary function compared to vehicle treated animals.  
Caution should be exercised when interpreting nucleoside prodrug potency experiments performed using Vero cell lineages. RDV is potently active against SARS-CoV-2 in vitro and in vivo. |
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| Annals of Internal Medicine 06JULY2020 | Clinical Validity of Serum Antibodies to SARS-CoV-2 | Caturegli et al., USA [gotopaper](#) | Public Health/Epidemiology | Case Control Study  
Objective: To determine the clinical validity and utility of SARS-CoV-2 antibodies.  
Serum IgG and IgA antibodies against SARS-CoV-2 spike protein were detected by using ELISA  
Sensitivity and specificity of the SARS-CoV-2 IgG assay were 0.976 (95% CI, 0.928 to 0.995) and 0.988 (CI, 0.974 to 0.995), respectively, when performed 14 days or later after symptom onset, but sensitivity decreased at earlier time points. Immunoglobulin G developed rapidly and was sustained at high levels throughout follow-up (up to 58 days). Antibodies to SARS-CoV-2 predicted the odds of developing acute respiratory distress syndrome, which increased by 62% (CI, 48% to 81%; P < 0.001) for every 2-fold increase in IgG. Of 11 066 NAAT-tested patients, 457 were repeatedly NAAT-negative, and serum samples were obtained for 18 such patients: 6 COVID-19 case patients and 12 non–COVID-19 control patients. Antibodies were present in 5 of 6 case patients and none of the 12 control patients (P = 0.001). Antibodies to SARS-CoV-2 demonstrate infection when measured at least 14 days after symptom onset, associate with clinical severity, and provide valuable diagnostic support in patients who test negative by NAAT but remain clinically suspicious for COVID-19. - 35 883 households were selected  
From April 27 to May 11, 2020, 61 075 participants answered a questionnaire on history of symptoms compatible with COVID-19 and risk factors, received a point-of-care antibody test, and, if agreed, donated a blood sample for additional testing with a chemiluminescent microparticle immunoassay.  
> Seroprevalence was 5-0% (95% CI 4-7–5-4) by the point-of-care test and 4-6% (4-3–5-0) by immunoassay, with a specificity-sensitivity range of 3-7% (3-3–4-0; both tests positive) to 6-2% (5-8–6-6; either test positive), with no differences by sex and lower seroprevalence in children younger than 10 years (<3-1% by the point-of-care test).  
> Substantial geographical variability: higher prevalence around Madrid (>10%) and lower in coastal areas (<3%).  
> In 7273 individuals with anosmia or at least three symptoms, seroprevalence ranged from 15-3% (13-8–16-8) to 19-3% (17-7–21-0). Around a third of seropositive participants were asymptomatic, ranging from 21-9% (19-1–24-9) to 35-8% (33-1–38-5). Only 19% (16-3–23-2) of symptomatic participants who were seropositive by both the point-of-care test and immunoassay reported a previous PCR test.  
> Nasopharyngeal and oropharyngeal swabs were collected from residents and staff in long-term care facilities and sent for real-time PCR testing  
> Data were reported for 2074 LTCFs  
> cross-sectional analysis of data received from the laboratories between April 8, and May 18, 2020  
> 280 427 people were tested, including 142 100 (51%) residents and 138 327 (49%) staff  
> 8343 (3-0%) people tested positive, including 2953 (2-1%) staff and 5390 (3-8%) residents.  
> No symptoms were reported for 6244 (74-8%, 95% CI 73-9–75-8) of 8343 people who tested positive | | | | |
<p>| The Lancet 06JULY2020 | Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study | Pollan et al., Spain and USA <a href="#">gotopaper</a> | Public Health/Epidemiology | | |
| The Lancet ID 03JULY2020 | Asymptomatic SARS-CoV-2 infection in Belgian long-term care facilities | Hoxha et al., Sweden and Belgium <a href="#">gotopaper</a> | Public Health/Epidemiology | | |</p>
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<tr>
<td>Ann Rheum Dis 03JUL2020</td>
<td>Interleukin-6 blockade with sarilumab in severe COVID-19 pneumonia with systemic hyperinflammation: an open-label cohort study</td>
<td>Della-Tore E et al Italy gotopaper</td>
<td>Therapeutic</td>
<td>Open label study of sarilumab (IL-6 blockade) in severe COVID-19 patients with hyperinflammation</td>
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<td>At day 28 of follow-up</td>
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<td>- Survival rate: 93% (sarilumab) vs 82% (control): HR: 0.36 (95%CI[0.08 – 1.68])</td>
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<td>- Median time to death: 19 days (sarilumab) vs 4 (control), p = 0.006</td>
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<td>- Death: 7% (sarilumab) vs 18% (control), p=0.42</td>
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<td>- Clinical improvement: 60% (sarilumab) vs 64% (control), p=0.99</td>
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<td>- Adverse events: similar in both group, 43% (sarilumab) vs 36% (control)</td>
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<td>Independent factors of clinical improvement:</td>
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<td>- Baseline PaO2/FiO2 &gt; 100mmHg</td>
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<td>- Lung consolidation &lt;17% at CT scan</td>
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<td>No difference for clinical improvement and mortality between two group</td>
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<td>Sarilumab was associated with faster recovery in a subset of patient showing minor lung consolidation at baseline</td>
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<td>Lancet Child Adolesc Healt 02JUL2020</td>
<td>Emergence of Kawasaki disease related to SARS-CoV-2 infection in an epicenter of the French COVID-19 epidemic: a time-series analysis</td>
<td>Ouldali N et al France gotopaper</td>
<td>Clinic</td>
<td>Time series analysis over the past 15 years in a pediatric centre in Paris - Estimation of the number of Kawasaki disease (KD) cases over time (quasi-Poisson regression)</td>
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<td>230 patients with KD (dec 2005 to may 2020) à 1,2 case/month (quasi-Poisson model)</td>
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<td>2 peak of hospital admission due to KD April 2020:</td>
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<td>- Increase of KD (497% increase): 6 cases per month</td>
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<td>- Starting 2 weeks after the peak of COVID-19</td>
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<td>- 10 cases between April 15 and May 20</td>
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<td>- 80% of the cases were positive for SARS-CoV-2 (PCR or serology)</td>
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<td>6 cases required intensive care</td>
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<td>Similar characteristics to the patients with KD in Bergamo December 2009:</td>
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<td>- Concomitant with the influenza A H1N1 pandemic – 1 – 3 weeks after the peak in Paris</td>
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<td>6 cases per month (365% increase)</td>
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<td>Characteristics of patients with KD in April 2020 appeared to be different from those diagnosed during the H1N1 epidemics:</td>
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<td>- Older (11,8 years vs 2,1 years, p=0,034)</td>
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<td>- Less inflammatory: CRP à 23,6 mg/dL vs 8,4 mg/dL, p=0,042</td>
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<td>SARS-CoV-2 : only respiratory virus with intense circulation in April 2020 - Viral respiratory infections could be triggers for KD</td>
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<td>Eurosurveillance 02JULY2020</td>
<td>Rapid risk assessment from ECDC: Resurgence of reported cases of COVID-19 in the EU/EEA, the UK and EU candidate and potential candidate countries</td>
<td>Eurosurveillance editorial team, Europe gotopaper</td>
<td>Public Health/Epidemio</td>
<td>From 31.12.2019 to 30.06.2020: 10,273,001 Covid-19 cases reported worldwide, 505,295 deaths. EU/EEA countries and the UK reported 1,556,709 cases (15% of total) and 176,800 deaths (35% of total).</td>
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<td>Decreasing trends in disease incidence are being observed in Europe (12% decrease in 14-day incidence of reported cases, 16-30 June), but community transmission is still reported, as well as a resurgence of observed cases or localised outbreaks. Reasons explaining apparent increase of resurgence vary (changes in case ascertainment, genuine increases in transmission, importation of cases).</td>
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<td>In this risk assessment, ECDC assesses the risks associated with the reported increases of incidence. National authorities should carefully analyse every increase in incidence to assess if these are associated with increases in transmission or involve populations at risk. ECDC does not consider travel restrictions within and to the Schengen area as an efficient way to reduce transmission within the EU.</td>
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| **Eurosurveillance**<br>02JULY2020 | **Introductions and early spread of SARS-CoV-2 in France, 24 January to 23 March 2020** | Gámbaro, F. et al., France<br><a>gotopaper</a> | Public Health/Epidemiology | We sequenced SARS-CoV-2 genomes from clinical cases sampled through surveillance, gaining insights into the initial introductions and spread of the virus in France.  
- Imposed quarantine prevented local transmission. The first cases were imported from China.  
- The Clade V characteristics suggest convergent evolution or a reversion of the V-clade. Subsequent early cases detected in February in the West or East of France had recent history of travel to Italy but also do not appear to have seeded local transmission.  
- All other sequences from northern France fall in clade G. Phylogenetic analysis suggests that the French outbreak was mainly seeded by one or several variants of this clade, unlike what is observed for other European countries.  
- This surveillance allowed to capture one of the earliest representatives of clade G. The mutations in early and late sampling highlight the complexity and risk of inferences based on 1 or 2 nucleotide substitutions.  
It is impossible to infer with confidence how the virus was introduced to France, but these data suggest that SARS-CoV-2 might have been present before the first recorded local cases. |
| **Cellular & Molecular Immunology**<br>01JUL2020 | **Identification of druggable inhibitory immune checkpoints on Natural Killer cells in COVID-19** | Demaria, Olivier et al. France<br><a>gotopaper</a> | Therapeutic | Analysis of NK cells in blood from a cohort of 82 individuals: 10 healthy controls (HC), 10 paucisymptomatic COVID-19 patients (pau), 34 patients with pneumonia (pneumo) and 28 patients with ARDS due to SARS-CoV-2 infection.  
- The absolute numbers of peripheral blood NK cells, B, CD4+, and CD8+ T lymphocytes were lower in the pneumonia and ARDS groups than in healthy controls.  
- Among CD45+CD3−CD56+ total NK cells the proportion of mature NK cells was markedly lower in patients with ARDS. Loss of mature NK cells may contribute to the pulmonary complications occurring in the most severe cases of COVID-19.  
- Presence of a CD39-expressing NK cell population observed in the blood of the COVID-19 patients of the pneumonia and ARDS groups that was absent in the HC and paucisymptomatic groups. Expression of CD39 on NK cells from COVID-19 patients may be explained by the levels of circulating IL-6 that rise with disease severity.  
- PD-1 receptor was upregulated on NK lymphocytes in COVID-19 patients, and several pneumonia and ARDS COVID-19 patients had a particularly large subset of NK cells expressing PD-1.  
- Bronchoalveolar lavage fluid (BALF) analysis showed a lack of CD16+CD57+ mature NK cells in the lungs of ARDS patients, suggesting that the decrease in mature NK cell levels observed in blood is not a consequence of their migration to infected lungs. In addition, high levels of CD39, PD-1, and NKG2A expression were also observed in NK cells isolated from the BALF of ARDS COVID-19 patients.  
- NK cells isolated from the blood of ARDS COVID-19 patients retained cytotoxic functions, and that incubation with monoclonal an anti-NKG2A mAb blocking the inhibitory interaction with HLA-E, was able to unleash their killing ability.  
These data suggest that NK cells do not participate in the exaggerated inflammatory response observed in ARDS. Thus, therapies targeting PD-1/L1, NKG2A and CD39 should be investigated as means of boosting NK cell antiviral immunity in patients at early stages of SARS-CoV-2 infection. |
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<td>J Intern Med 01JUL2020</td>
<td>Treatment with proton pump inhibitors increases the risk of secondary infections and ARDS in hospitalized patients with COVID-19: coincidence or underestimated risk factor?</td>
<td>Luxenburger, H. et al. Germany <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Retrospective study, 152 hospitalized patients with confirmed SARS-CoV-2 infection were included in the analysis. 62 patients (40.8%) received regular treatment with proton pump inhibitors (PPI). 48 patients (31.6%) presented with a secondary infection during hospitalization. - PPI-treated patients with COVID-19 presented more often with secondary infections compared to patients without PPI treatment. This effect remained statistically significant after adjusting for other possible risk factors. - Secondary infections were strongly associated with the development of ARDS indicating an indirect negative impact of PPI treatment on the development of ARDS. - Index mortality was higher in patients with PPI treatment. δ PPI treatment may be a negative predictive factor for development of secondary infections and consecutive ARDS in patients with COVID-19. Limitations: retrospective study, not able to analyse the effect of the duration of PPI treatment on the outcome of SARS-CoV2-infected patients.</td>
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<td>MICROBIOLOGY AND INFECTION 26JUN2020</td>
<td>Childhood COVID-19: a multi-center retrospective study</td>
<td>Chen Z et al <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Description of clinical and epidemiological characteristics of pediatric patients with COVID19 Cohort of 32 children from 3 months to 18 years old (China). - Family aggregation occurred in 87.5% of infant and preschool/school-aged, but only 12.5% of adolescents. - Most common symptoms (mild): fever, cough, fatigue (4/32). - Average duration of viral RNA in respiratory samples 15.8 d - Average duration of viral RNA in gastrointestinal samples: 28.9d - 14 children developed pneumonia, but no statistical significance in the incidence between age groups. Most children with COVID-19 had a mild process and good prognosis. More attention should be paid to household contact history investigation</td>
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<td>LANCET PHYSICIATRY 25JUN2020</td>
<td>Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study</td>
<td>Varatharaj A et al <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>The aim of this study was to investigate the breadth of complications of COVID-19 across the UK that affected the brain METHODS &gt; development of a rapid case report notifications portal across UK neurosciences bodies &gt; clinical syndromes associated with COVID-19 were classified as a cerebrovascular event, altered mental status, peripheral neurology, or other. RESULTS During the study period, platforms received notification of 153 cases that met the clinical case definitions (with an exponential growth in reported cases similar to overall COVID-19 data). Complete clinical datasets were available for 125 (82%) of 153 patients (median age 71 years) &gt; 77 (62%) of 125 patients presented with a cerebrovascular event, &gt; 39 (31%) of 125 patients presented with altered mental status, &gt; 9 (23%) with unspecified encephalopathy &gt; 7 (18%) with encephalitis. &gt; 23 (59%) fulfilled the clinical case definitions for psychiatric diagnoses (mostly new onset disorders)</td>
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<td>JAMA network open 24JUN2020</td>
<td>Effect of Colchicine vs Standard Care on Cardiac and Inflammatory Biomarkers and Clinical Outcomes in Patients Hospitalized With Coronavirus Disease 2019: The GRECCO-19 Randomized Clinical Trial</td>
<td>Deftereos, Spyridon G. et al. Greece gotopaper</td>
<td>Therapeutic</td>
<td>Prospective, open-label, multicenter randomized clinical trial, involving 105 patients hospitalized with COVID-19 randomized in a 1:1 allocation to either standard medical treatment or colchicine with standard medical treatment. Primary endpoints were (1) maximum high-sensitivity cardiac troponin level; (2) time for C-reactive protein to reach more than 3 times the upper reference limit; and (3) time to deterioration by 2 points on a 7-grade clinical status scale, ranging from able to resume normal activities to death. Participants who received colchicine had statistically significantly improved time to clinical deterioration. There were no significant differences in high-sensitivity cardiac troponin or C-reactive protein levels. Limitations: study allowed for co-treatment with other investigational agents; small sample size combined with low event rate make data underpowered and hypothesis generating.</td>
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<td>THE LANCET CHILD &amp; ADOLESCENT HEALTH 25JUN2020</td>
<td>COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study</td>
<td>Götzinger Florian et al. 25 European countries. gotopaper</td>
<td>Public Health/Epidemiology</td>
<td>Factors associated with need for ICU admission and initiation of drug treatment for COVID-19 for children and adolescents with SARS-CoV-2. METHODS - Multicentre cohort (582 individuals). Children under 18 years of age (median 5 IQR 0·5–12·0) with confirmed SARS-CoV2 Infection (PCR). 82 participating health-care institutions; 25 European countries (Paediatric Tuberculosis Network European Trials Group) RESULTS: Four children died. &gt; 145 (25%) had pre-existing medical conditions. &gt; 363 (62%) individuals were admitted to hospital. &gt; 48 (8%) individuals required ICU admission, &gt; 25 (4%) mechanical ventilation &gt; 19 (3%) inotropic support, &gt; 1 (&lt;1%) extracorporeal membrane oxygenation Significant risk factors for requiring ICU admission were: &gt; being younger than 1 month &gt; male sex &gt; pre-existing medical conditions &gt; presence of lower respiratory tract infection signs &gt; symptoms at presentation</td>
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<td>Cell Metabolism 24JUN2020</td>
<td>In-hospital Use of Statins is Associated with a Reduced Risk of Mortality among Individuals with COVID-19</td>
<td>Zhang, Xiao-Jing et al. China gotopaper</td>
<td>Therapeutic</td>
<td>Retrospective multicenter study on 13,981 clinically confirmed cases of COVID-19, among which 1,219 received statins, to determine the association of in-hospital use of statins with clinical outcomes. In a subgroup analysis, the additional effects of combining ACEi/ARB with statins on the clinical outcomes of COVID-19 was investigated. - In-hospital use of statins was associated with a lower risk of all-cause mortality: the risk for 28-day all-cause mortality was 5.2% and 9.4% in the matched statin and non-statin groups, respectively, with an adjusted hazard ratio of 0.58. - The combination of statins and ACEi/ARB utilization was not significantly associated with the risk of all-cause mortality among individuals with COVID-19 and hypertension. - In-hospital usage of statins and combination usage of statins and ACE inhibitors or ARBs did not increase the risk of organ damage and other adverse effects. Limitation: retrospective study</td>
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<td>American Journal of Obstetrics and Gynecology 23JUN2020</td>
<td>Exposure and Seroconversion to SARS-CoV-2 Among Obstetric Healthcare Providers Following a Contained Outbreak</td>
<td>KIEFER MK et al, USA</td>
<td>Public Health/Epidemio</td>
<td>Key question: Exposure and seroconversion to SARS-CoV-2 among obstetric HCWs (in a tertiary care center)</td>
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<td>&gt; Obstetric units are an underestimated hotspot in the pandemic, owing to an asymptomatic population, high patient turnover, integrated workstations, and frequent emergencies requiring response from multiple disciplines and expedient transfer to onsite surgical suites</td>
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<td>STUDY DESIGN - Prospective cohort of HCW: study of SARS-CoV-2 antibody levels</td>
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<td>Collection of Blood samples at two time points four weeks apart (IgM and IgG levels)</td>
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<td>RESULTS - 110 HCW recruited (females, median age 34). 68.2% nurses, 24.5% physicians</td>
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<td>&gt; 90 participants (82%) reported a SARS-CoV-2 exposure</td>
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<td>&gt; 66 (60%) reported one or more COVID-19 symptoms; &gt; 52 (47%) had nasopharyngeal PCR testing, of which 15 (29%) tested positive for the virus, 14 seroconverted</td>
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<td>&gt; 52 (47%) had nasopharyngeal PCR testing, of which 15 (29%) tested positive for the virus, 14 seroconverted</td>
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<td>&gt; at baseline, 3 participants (2.7%) had positive antibodies &gt; 5 participants (4.5%) who reported being asymptomatic, seroconverted</td>
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<td>Blood 23JUN2020</td>
<td>Improved Clinical Symptoms and Mortality on Severe/Critical COVID-19 Patients Utilizing Convalescent Plasma Transfusion</td>
<td>Xia, Xinyi et al, China</td>
<td>Therapeutic</td>
<td>Evaluation of the effectiveness, safety, and indications of convalescent plasma transfusion (CPT) therapy for severe or critical COVID-19 patients, through analysis of the clinical, laboratory, and radiologic characteristics of 1,568 patients from a single center, in which 138 patients received ABO-compatible CPT and 1,430 patients received standard treatment.</td>
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<td>&gt; 2.2% and 4.1% of cases died in the CPT group and in the standard-treatment group, respectively. &gt; 2.4% and 5.1% of patients in the CPT and the standard-treatment group have been admitted to ICU eventually. &gt; 70% of the patients who had severe respiratory symptoms got improved and removed oxygen supports within 7 days after CPT. &gt; The viral loads and C-reactive protein (CRP) concentration significantly decreased (P&lt;0.001), and the percentage of lymphocytes increased (P=0.006), 76.8% of cases received radiological improvements within 14 days after CPT. &gt; Patients with a higher percentage of lymphocytes and a lower percentage of neutrophils and CRP concentration respond better to CPT (P&lt;0.05). &gt; Notably, for the patients who received CPT within 7 weeks after symptom onset, the median time from CPT to clinical improvements was approximately 10 days. But the time to clinical improvements was significantly prolonged for patients who received CPT later than 7 weeks after onset.</td>
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<td>The results suggest CCP, transfused even after two weeks of symptom onset, could improve the symptoms and mortality in severe or critical COVID-19 patients.</td>
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<td>Limitations: single center, retrospective study; complete data on neutralizing antibody titers in CCP units were not available; a stratified analysis of severe and critical patients could not be performed due to the low proportion of critical patients.</td>
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| **CELL** 23JUN2020 | A universal design of betacoronavirus vaccines against COVID-19, MERS and SARS | Lianpan D et al, CHINA [gotopaper](#) | Vaccine | Design of a dimeric form of MERS-CoV RBD inducing high immunogenicity and significantly increased neutralizing antibody (NAb) titers compared to conventional monomeric form.  
> Crystal structures of the RBD-dimer shows fully exposed dual receptor-binding motifs which are the targets of NAbs  
> Strategy (RBD dimers) to design a SARS-CoV2 vaccine candidate  
> Selected sequences: from R319 to K537  
> Dimerization and binding to hACE was demonstrated  
> Immunization of BALB/c mice with RBD +adjuvant induced significantly higher antigen-specific IgG compared to immunization with RBD-monomer  
> RBD dimers elicited ~10-100-fold higher titer of NAb compared to monomer  
> No differences in T-cell responses in of RBDdimers-vaccinated mice compared to the PBS-vaccinated ones.  
Expression on SARS CoV 2 RBD dimers in clinical grade CHO cells line reached expression levels of > 1.5 g/L, with a final yield of 0.67 gram purified antigen per liter  
> Highly scalable production |
| **Science** 23JUN2020 | A mathematical model reveals the influence of population heterogeneity on herd immunity to SARS-CoV-2 | Britton et al., Sweden and UK [gotopaper](#) | Public Health/Epidemiology | Population heterogeneity can significantly impact disease-induced immunity as the proportion infected in groups with the highest contact rates is greater than in groups with low contact rates.  
> if R0 = 2.5 in an age-structured community with mixing rates fitted to social activity then the disease-induced herd immunity level can be around 43%, which is substantially less than the classical herd immunity level of 60% obtained through homogeneous immunization of the population.  
These estimates should be interpreted as an illustration of how population heterogeneity affects herd immunity, rather than an exact value or even a best estimate. |
Vero E6 cells treated with 5,000 to 0.01 IU/mL of IFN-β 1a 1 h after inoculation with the SARS-CoV-2 (MOI of 0.001) and monitored for cytopathic effect and q-RT–PCR evaluation at 48, 72 and 96 hpi.  
- Inhibition of the SARS-CoV-2 by IFN-β 1a was dependent on both time and drug concentration. No altered cell morphology related to drug toxicity was observed on uninfected cells treated with IFN-β 1a at 5000 IU/mL.  
- EC50 calculations at different time points, resulting in 1.971 IU/mL (95% CI: 0.3969 to 4.891 IU/mL) at 48 hpi, 2.071 IU/mL (95% CI: 0.5982 to 5.819 IU/mL) at 72 hpi, and 4.682 IU/mL (95% CI: 3.505 to 6.018 IU/mL) at 96 hpi. Can be easily accessed in the clinical setting.  
=> Shed light for the first time on antiviral activity of IFN-β 1a against SARS-CoV-2 when administered after the infection of cells, highlighting its possible efficacy in an early therapeutic setting. IFN-β 1a activity is retained up to 96 hours after its use on the infected cells.  
Preclinical evaluation of the antiviral activity of a drug, such as IFN-β 1a, is only a partial assessment of its possible clinical role in a disease such as COVID-19 in which the beneficial or detrimental effect of type I IFN is still to be established and in which immune-mediated damage is probably an extremely important factor in determining the development of the worst outcomes of the infection. |
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| VACCINE 19JUN2020 | Recombinant SARS-CoV-2 spike S1-Fc fusion protein induced high levels of neutralizing responses in nonhuman primates | Ren W et al, China [gotopaper](#) | Vaccine | Immunogenicity of SARS-CoV-2 S1 Fc fusion proteins as potential vaccine candidate  
> the S1 is located at the N-terminus of the S protein and contains the RBD  
> the S1 was fused with the Fc region of human IgG1 and expressed as a recombinant protein in CHO-K1 cell line  
> the S1-Fc protein was formulated with different adjuvants and tested as vaccine candidate  
Injection of S1 Fc protein in mice, rabbit and macaques elicited  
> high levels of anti-S1 antibodies in all animal models  
> high neutralizing activities against SARS-CoV-2 (in the antisera of macaques)  
These results indicate that the S1-Fc fusion protein can effectively induce humoral immune responses in various animals models and may be a good vaccine candidate. |
| JAMA 19JUN2020 | Association of Angiotensin-Converting enzyme inhibitor or angiotensin receptor blocker use with COVID-19 diagnosis and mortality | Fosbøl EL et al, Danish [gotopaper](#) | Clinic | Use of ACEI/ARBs was associated with COVID-19 diagnosis and worse outcomes in patients with COVID-19? Retrospective cohort study (data from Danish national administrative registries)  
4480 patients included: 895 users of ACEI/ARBs and 3585 nonusers  
Nested case-control framework: association use of ACEI/ARBs vs other antihypertensive drugs and incidence rate of a COVID-19 diagnosis  
- 571 patients prior hypertension + COVID-19  
- 570 controls with prior hypertension no COVID-19  
Primary outcome: death  
- 18.1% in ACEI/ARBs group vs 7.3% within 30-days, HRa: 0.83 (IC95%[0.67 – 1.03])  
Secondary outcome: death or severe COVID-19  
- 31.9% in ACEI/ARBs group vs 14.2% in nonusers, HRa: 1.04 (IC95%[0.89 – 1.23])  
Nested case-control framework:  
- 86.5% of cases used ACEI/ARBs versus 85.4% of controls  
- ACEI/ARBs not associated with higher incidence of COVID-19, HRa: 1.05 (IC95%[0.80 – 1.36]).  
Limits: observational study – laboratory data were not available – exposure to ACEI/ARBs was defined by prescription fillings – confounding by indication treatment  
Prior use of ACEI/ARBs was not significantly associated with COVID-19 diagnosis among patients with hypertension or with mortality or severe disease |
| Nature Medicine 18JUN2020 | Clinical and immunological assessment of asymptomatic SARS-CoV-2 infections | Long, Quan-Xin, et al, China [gotopaper](#) | Public Health/Epidemiology | AIM: to describe the clinical features of study 37 SARS-CoV-2 positive but asymptomatic individuals in the Wanzhou District.  
- Median duration of viral shedding in the asymptomatic group (19d) significantly longer than in the symptomatic group (14 in patients with mild symptoms).  
- Virus-specific IgG levels in the asymptomatic group significantly lower relative to the symptomatic group in the acute phase. In the early convalescent phase, 93.3% and 81.1% of asymptomatic individuals had reduction in IgG and neutralizing antibody levels respectively, as compared to 96.8% and 62.2% of symptomatic patients.  
- 40% of asymptomatic individuals and 12.9% of the symptomatic group became seronegative in the early convalescent phase. Asymptomatic individuals exhibited lower levels of 18 pro- and anti-inflammatory cytokines.  
These data suggest that asymptomatic individuals had a weaker immune response to SARS-CoV-2 infection, that might have implications for immunity strategy and serological surveys. |
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| EClinicalMedicine 18JUN2020 | Tocilizumab for treatment of patients with severe COVID–19: A retrospective cohort study | Kewan T el al USA gotopaper | Therapeutic        | Retrospective cohort study – hypoxic COVID-19 patients – patients with lung infiltrates and elevated inflammatory markers received a single dose of tocilizumab  
51 patients included: 28 received tocilizumab and 23 did not received  
At baseline:  
- More mechanical ventilation in tocilizumab cohort: 68% vs 22%  
Clinical improvement: tocilizumab vs non tocilizumab cohort  
- All patients: 6,5 days versus 7 days, HR:1,14 IC95%[0,55 – 2,38] / Mechanically ventilated patients: 8 days versus 13 days, HR:1,83 IC95%[0,57 – 5,84]  
Duration of vasopressor support  
- 2 days in tocilizumab cohort versus 5 days (p=0,039)  
Duration of mechanical ventilation / 7 days in tocilizumab cohort versus 10 days (p=0,11)  
Limits: retrospective / single center with small number of patients / tocilizumab cohort was younger / short follow-up / concomitant use of other dugs.  
-> Tocilizumab was associated with shorter duration of vasopressor support and shorter median time to clinical improvement (not statistically significant)  
-> Use of tocilizumab in select patients with severe COVID–19 ? |
- Significant cross-replicating associations with rs11385942 at locus 3p21.31 and with rs657152 at locus 9q34.2 were detected.  
- At locus 3p21.31, the association signal spanned six genes  
- The association signal at locus 9q34.2 coincided with the ABO blood group locus; a blood-group–specific analysis showed a higher risk in blood group A and a protective effect in blood group O, as compared with other blood groups.  
The 3p21.31 gene cluster identified as a genetic susceptibility locus in patients with severe Covid-19 and confirmed a potential involvement of the ABO blood-group system. |
| The Lancet. Infectious diseases 16JUN2020 | Effectiveness of isolation, testing, contact tracing, and physical distancing on reducing transmission of SARS-CoV-2 in different settings: a mathematical modelling study | Kucharski, AJ, et al. UK gotopaper | Public Health/Epidemio | AIM: to estimate the reduction in SARS-CoV-2 transmission under different control measures (testing, isolation, tracing, physical distancing) across settings (household, work, school, or other ) and the number of contacts to quarantine daily in different strategies for a given symptomatic case incidence.  
- Combined isolation and tracing strategies could reduce transmission more than mass testing or self-isolation alone:  
mean transmission reduction of 2% for weekly random testing of 5% of the population. 29% for self-isolation alone of symptomatic cases within the household. 35% for self-isolation alone outside the household, 37% for self-isolation plus household quarantine, 64% for self-isolation and household quarantine plus manual contact tracing of all contacts, 57% plus manual tracing of acquaintances only, 47% plus app-based tracing only.  
- If limiting gatherings outside of home, school, or work, manual contact tracing alone could reduce transmission similarly to detailed contact tracing.  
- If 1000 new symptomatic cases occurred daily, 15 000–41 000 contacts per day would be quarantined through contact tracing.  
Many cases would need to self-isolate and their contacts successfully traced to ensure a R0<1 in the absence of other measures. If combined with moderate physical distancing, self-isolation and contact tracing would be more likely to be effective. |
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<td>Lancet Rheumatol 16JUN2020</td>
<td>GM-CSF blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study</td>
<td>De Lucas G et al Italy gotopaper</td>
<td>Therapeutic</td>
<td>Single center prospective cohort study, open label – Adults patients with severe COVID-19, hypoxemia &amp; systemic hyperinflammation 2 groups: - Standard of care (26 patients) - Standard of care + mavrilimumab IV (13 patients) At inclusion time, none of the patient included was mechanically ventilated Main outcome: time to clinical improvement (ordinal scale of clinical status) At day 28 - 100% clinical improvement in mavrilimumab group vs 65% control group (p=0.03) - Earlier improvement in mavrilimumab group (8 days vs 19 days, p=0.0001) - 0% death in mavrilimumab group vs 27% in control group (p=0.086) - 8% progressed to MV in mavrilimumab group vs 35% in control group (p=0.14) Fever resolution was faster in mavrilimumab group Mavrilimumab was well tolerated. Several limitations - Not randomly assigned - Other clinical variables besides mavrilimumab might have affected clinical outcomes - Patients in mavrilimumab group had a longer duration fever before enrolment Mavrilimumab was associated with clinical improvement compared with standard care in non-mechanically ventilated patients These results require placebo-controlled studies/multicenter/double-blind/randomised</td>
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<td>Nature Medicine 16JUN2020</td>
<td>Age-dependent effects in the transmission and control of COVID-19 epidemics</td>
<td>Davies et al., UK gotopaper</td>
<td>Public Health/Epidemiology</td>
<td>Age-structured mathematical model to epidemic data from China, Italy, Japan, Singapore, Canada and South Korea. <strong>Estimation:</strong> - Susceptibility to infection in individuals under 20 years of age is approximately half that of adults aged over 20 years - Clinical symptoms manifest in 21% (95% credible interval: 12–31%) of infections in 10- to 19-year-olds, rising to 69% (57–82%) of infections in people aged over 70 years -&gt; interventions aimed at children might have a relatively small impact on reducing SARS-CoV-2 transmission, particularly if the transmissibility of subclinical infections is low <strong>Conclusion:</strong> -&gt; In countries with younger population structures such as many low-income countries the expected per capita incidence of clinical cases would be lower than in countries with older population structures, although it is likely that comorbidities in low-income countries will also influence disease severity. -&gt; Without effective control measures, regions with relatively older populations could see disproportionately more cases of COVID-19, particularly in the later stages of an unmitigated epidemic.</td>
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<td>CELL 15JUN2020</td>
<td>Structures of human antibodies bound to SARS-CoV-2 spike reveal common epitopes and recurrent features of antibodies</td>
<td>Christopher O et al, USA/SWITZERLAND</td>
<td>Vaccine/Therapeutics</td>
<td>Characterization of polyclonal IgGs and Fab s from COVID-19 convalescent individuals for recognition of coronavirus spikes. Analysis of purified IgG and Fab s from the plasmas of 10 COVID-19 convalescent individuals showed &gt; binding to trimeric S and monomeric RBD/S1B domains of six human coronaviruses &gt; neutralizing activity against SARS-CoV-2 pseudoviruses By using EM approaches it was shown that: &gt; Fab s recognize both S1A and RBD epitopes on SARS-CoV-2 S protein &gt; the monoclonal Fab-spike neutralizing complex passes through an specific epitope that blocks ACE2 receptor binding Overall, these studies structurally define a recurrent anti-SARS-CoV-2 antibody class derived from VH3-53/VH3-66 and similarity to a SARS-CoV VH3-30 antibody, providing criteria for evaluating vaccine-elicited antibodies.</td>
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<tr>
<td>Science 15JUN2020</td>
<td>Antibody cocktail to SARS-CoV-2 spike protein prevents rapid mutational escape seen with individual antibodies</td>
<td>Baum, Alina et al. USA</td>
<td>Therapeutic</td>
<td>Investigate the development of resistance against 4 antibodies to the spike protein that potently neutralize SARS-CoV-2, individually as well as when combined into cocktails. - Efficacy of antiviral antibodies against the breadth of spike RBD variants represented in publicly available SARS-CoV-2 sequences was assessed using VSV pseudoparticle system expressing the SARS-CoV-2 spike variants =&gt; antibodies remain effective against spike variants that have arisen in the human population. - Escape mutants were selected under pressure of single antibodies, as well as of antibody combinations, by using a replicating VSV-SARS-CoV-2-S virus =&gt; novel spike mutants rapidly appeared following in vitro passaging in the presence of individual antibodies, resulting in loss of neutralization; such escape also occurred with combinations of antibodies binding diverse but overlapping regions of the spike protein. - Escape following treatment with an antibody cocktail (REGN10987+REGN10933) was assessed, cocktail being rationally designed to avoid escape through inclusion of two antibodies that bind distinct and non-overlapping regions of the RBD, and which can thus simultaneously bind and block RBD function =&gt; attempts to grow VSV-SARS-CoV-2-S virus in the presence of this non-competing antibody cocktail did not result in the outgrowth of escape mutants. ⇔ Cocktail therapy may provide a powerful way to minimize mutational escape by SARS-CoV-2; in particular when two antibodies were chosen so as to bind to distinct and non-overlapping regions of the viral target, and thus require the unlikely occurrence of simultaneous mutations at two distinct genetic sites for viral escape</td>
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<tr>
<td>Science 15JUN2020</td>
<td>Potent neutralizing antibodies from COVID-19 patients define multiple targets of vulnerability</td>
<td>Brouwer, Philip J. M. et al. Netherlands/USA gotopaper</td>
<td>Therapeutic</td>
<td>Isolation of monoclonal antibodies from 3 convalescent COVID-19 patients using a SARS-CoV-2 stabilized prefusion spike protein. These antibodies had low levels of somatic hypermutation and showed a strong enrichment in VH1-69, VH3-30-3 and VH1-24 gene usage.</td>
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<tr>
<td>Science 15JUN2020</td>
<td>Studies in humanized mice and convalescent humans yield a SARS-CoV-2 antibody cocktail</td>
<td>Hansen, Johanna et al. USA gotopaper</td>
<td>Therapeutic</td>
<td>Describe parallel efforts using both humanized mice and convalescent patients to generate antibodies against the SARS-CoV-2 spike protein, yielding a large collection of fully-human antibodies that were characterized for binding, neutralization and three dimensional structure.</td>
</tr>
<tr>
<td>Science 15JUN2020</td>
<td>Broad neutralization of SARS-related viruses by human monoclonal antibodies</td>
<td>Wec, Anna Z. et al. USA gotopaper</td>
<td>Therapeutic</td>
<td>Mined the memory B cell repertoire of a convalescent SARS donor and identified 200 SARS-CoV-2 binding antibodies that target multiple conserved sites on the (S) protein.</td>
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- 19 NABs that target a diverse range of antigenic sites on the S protein, of which 2 showed picomolar neutralizing activities (IC50s of 0.007 and 0.009 μg/mL or 47 and 60 pM) against authentic SARS-CoV-2 virus.
- Large-scale SPR-based competition assays allowed to define NABs that target multiple sites of vulnerability on the RBD as well as additional previously undefined non-RBD epitopes on SARS-CoV-2.

- Subsequent structural characterization of these potent NABs will guide vaccine design, while simultaneous targeting of multiple non-RBD and RBD epitopes with mAb cocktails paves the way for safe and effective COVID-19 prevention and treatment.

- A smaller collection of 4 antibodies was chosen for further analyses to determine whether the above binding data to RBD reflected binding to trimeric spike protein, whether neutralization potencies noted in the above assays were consistent with those seen in other assays including with SARS-CoV-2, and whether these antibodies retained neutralization activity against pseudoparticles with mutations in the S1/S2 cleavage site.
- Examined 9 most potent neutralizing antibodies in cross-competition binding assays, identifying several pairs of non-competing mAbs with pM neutralization potency that could potentially be combined to form antibody cocktails.

- Selection of pairs of highly-potent individual antibodies that simultaneously bind the receptor-binding domain of the spike protein, providing ideal partners for a therapeutic antibody cocktail that may deliver optimal antiviral potency while minimizing odds of virus escape.

Such an antibody cocktail is now being tested in human trials (clinicaltrials.gov NCT04426695 and NCT04425629). Mined the memory B cell repertoire of a convalescent SARS donor and identified 200 SARS-CoV-2 binding antibodies that target multiple conserved sites on the (S) protein.

- A large proportion of the non-neutralizing antibodies display high levels of somatic hypermutation and cross-react with circulating HCoVs, suggesting recall of pre-existing memory B cells (MBCs) elicited by prior HCoV infections.
- Several antibodies potently cross-neutralize SARS-CoV, SARS-CoV-2, and the bat SARS-like virus WIV1 by blocking receptor attachment and inducing S1 shedding.

These antibodies represent promising candidates for therapeutic intervention and reveal a target for the rational design of pan-sarbecovirus vaccines.
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| The Lancet GH 15JUN2020 | Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study | Clark et al., UK, China, USA [gotopaper](#) | Public Health/Epidemiology | Aim: Understanding the number of individuals at increased risk of severe COVID-19 and how this varies between countries

**Estimation:**
- > 1.7 billion people, comprising 22% of the global population, have at least one underlying condition that puts them at increased risk of severe COVID-19 if infected
- > 349 million people (4% of the global population) are at high risk of severe COVID-19 and would require hospital admission if infected
- > 6% of males to be at high risk compared with 3% of females.

The share of the population at increased risk was highest in countries with older populations, African countries with high HIV/AIDS prevalence, and small island nations with high diabetes prevalence.

Estimates of the number of individuals at increased risk were most sensitive to the prevalence of chronic kidney disease, diabetes, cardiovascular disease, and chronic respiratory disease.
- About one in five individuals worldwide could be at increased risk of severe COVID-19

| Science 15JUN2020 | Isolation of potent SARS-CoV-2 neutralizing antibodies and protection from disease in a small animal model | Rogers, Thomas F. et al. USA [gotopaper](#) | Therapeutic | Cohort of SARS-CoV-2-recovered participants, neutralization assays to interrogate antibody responses, high-throughput antibody generation pipeline to rapidly screen over 1800 antibodies, and animal model to test protection.

Only a small fraction of these Abs was neutralizing, highlighting the value of deep mining of responses to access the most potent Abs.

- Potent neutralizing antibodies (nAbs) to two epitopes on the receptor binding domain (RBD) and to distinct non-RBD epitopes on the spike (S) protein isolated.
- Passive transfer of a nAb provides protection against disease in high-dose SARS-CoV-2 challenge in Syrian hamsters, as revealed by maintained weight and low lung viral titers in treated animals.

The study suggests a role for nAbs in prophylaxis, and potentially therapy, of COVID-19. The nAbs define protective epitopes to guide vaccine design.

This study identified several potent SARS-CoV-2 Mpro inhibitors with potent enzymatic inhibition as well as cellular antiviral activity.

- Boceprevir, an FDA-approved HCV drug, inhibits the enzymatic activity of Mpro with IC50 of 4.13 µM, and has an EC50 of 1.90 µM against the SARS-CoV-2 virus in the cellular viral CPE assay.
- GC-376, an investigational veterinary drug, showed promising antiviral activity against the SARS-CoV-2 virus (EC50 = 3.37 µM). It has the highest enzymatic inhibition against the Mpro with an IC50 value of 0.03 µM. The X-ray crystal structure of SARS-CoV-2 Mpro in complex with GC-376 provides a molecular explanation of the high binding affinity of aldehyde-containing compounds as they can adopt two configurations R and S.
- 3 calpain/cathepsin inhibitors, MG-132, calpain inhibitors II and XII, are potent inhibitors of Mpro with single-digit to submicromolar efficacy in the enzymatic assay. Calpain inhibitors II and XII also inhibit SARS-CoV-2 in the CPE assay with EC50 values of 2.07 and 0.49 µM, respectively.
- Ritonavir and lopinavir failed to inhibit the SARS-CoV-2 Mpro (IC50 > 20 µM), which might explain why they lack efficacy in clinical trials for COVID-19.
- Camostat has no inhibition against the SARS-CoV-2 Mpro (IC50 > 20 µM). |

| Cell research 15JUN2020 | Boceprevir, GC-376, and calpain inhibitors II, XII inhibit SARS-CoV-2 viral replication by targeting the viral main protease | Ma, Chunlong et al. USA [gotopaper](#) | Therapeutic | Boceprevir, an FDA-approved HCV drug, inhibits the enzymatic activity of Mpro with IC50 of 4.13 µM, and has an EC50 of 1.90 µM against the SARS-CoV-2 virus in the cellular viral CPE assay.

- GC-376, an investigational veterinary drug, showed promising antiviral activity against the SARS-CoV-2 virus (EC50 = 3.37 µM). It has the highest enzymatic inhibition against the Mpro with an IC50 value of 0.03 µM. The X-ray crystal structure of SARS-CoV-2 Mpro in complex with GC-376 provides a molecular explanation of the high binding affinity of aldehyde-containing compounds as they can adopt two configurations R and S.

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<tr>
<td>SCIENCE 12JUN2020</td>
<td>The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries</td>
<td>Walker et al., UK, USA <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Combining data on demography, contact patterns, disease severity, and health care capacity and quality to understand its impact and inform strategies for its control.</td>
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<td>The Lancet 11JUN2020</td>
<td>Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study</td>
<td>Stringhini, S. et al., Switzerland <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>In SEROCoV-POP, a population-based study, we planned a series of 12 consecutive weekly serosurveys of anti-SARS-CoV-2-IgG antibodies among randomly selected participants and their household members in Geneva, Switzerland (2766 participants from 2339 households), and estimated the seroprevalence in the population. We present results from the first 5 weeks of the study.</td>
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<td>The Journal of clinical investigation 11JUN2020</td>
<td>Early safety indicators of COVID-19 convalescent plasma in 5,000 patients</td>
<td>Joyner, Michael J et al. USA <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Analysis of key safety metrics after transfusion of ABO compatible human COVID-19 convalescent plasma in 5,000 hospitalized adults with severe or life threatening COVID-19, with 66% in the intensive care unit, as part of the US FDA Expanded Access Program for COVID-19 convalescent plasma.</td>
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- Incidence of all serious adverse events (SAEs) in the first four hours after transfusion was <1% (n=36), including mortality rate (0.3%).
- Of the 36 reported SAEs, there were 25 reported incidences of related SAES, including mortality (n = 4), transfusion-associated circulatory overload (TACO; n = 7), transfusion-related acute lung injury (TRALI; n = 11), and severe allergic transfusion reactions (n = 3).
- Only 2 (of 36) SAEs were judged as definitely related to the convalescent plasma transfusion by the treating physician.
- The seven-day mortality rate was 14.9%.

- no signal of toxicity beyond what is expected from plasma use in severely ill patients
- mortality rate does not appear excessive

These early indicators suggest that transfusion of convalescent plasma is safe in hospitalized patients with COVID-19.
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| PSYCHOLOGICAL MEDICINE 10JUN2020 | Health-protective behaviour, social media usage, and conspiracy belief during the COVID-19 public health emergency | Allington D et al. UK gotopaper | SHS/SciPo          | > Social media platforms are major disseminators of health misinformation  
> Spread of COVID-19 is subject of conspiracy theories on social media.  
**Methods**  
> 3 questionnaire surveys of social media use, conspiracy beliefs, and health-protective behaviours with regard to COVID-19 (N = 949, 2250 N=2254; UK)  
**Results**  
> negative relationship between COVID-19 conspiracy beliefs and COVID-19 health-protective behaviours,  
**Conclusions**  
Unregulated social media may present a health risk partly reducible to their role as disseminators of health-related conspiracy beliefs. |
| Nature 09JUN2020                  | Clinical benefit of remdesivir in rhesus macaques infected with SARS-CoV-2 | Williamson BN et al USA gotopaper | Therapeutic        | Rhesus macaque model of SARS-CoV-2 infection → develop mild to moderate disease  
2 group of 6 macaque were inoculated:  
- 12 hours after 1 received remdesivir IV and 1 received vehicle solution  
- Assigned a daily clinical score sheet in a blinded fashion, 12 hours after inoculation  
Animal treated with remdesivir → 12 hours after inoculation:  
- Clinical scores were significantly lower than in control animals  
- Reduced pulmonary infiltrate on radiographs  
- Reduced virus titers in bronchoalveolar lavage  
- Reduction in damage to the lung significantly at necropsy  
Absence of resistance mutation in all remdesivir-treated animals  
No reduction in virus shedding  
**The first antiviral treatment with proven efficacy against SARS-CoV-2 in an animal model**  
**Early remdesivir treatment initiation in COVID-19 patients prevent progression to pneumonia** |
| European journal of emergency medicine 08JUN2020 | COVID-19 epidemic in the Seine-Saint-Denis Department of Greater Paris: one month and three waves for a tsunami | Lapostolle, F. et al. France gotopaper | Public Health/Epidemio | It is proposed that the chronology of epidemic spread gives a window of time in which hospitals can act to prevent reaching capacity. The number of patients managed, of patients transferred to emergency departments (ED), and of mobile intensive care units (MICUs) dispatched in the department of Seine-Saint-Denis between February 17th and March 28th was compared to a reference period of 5 years (2015-2019). The alert threshold to indicate a public health crisis was defined as a 20% increase compared to the 5-year mean.  
- The daily numbers of patients managed crossed the threshold on February 25th and increased until the end of the study period.  
- The daily number of patients transferred to ED crossed the threshold on March 16th and increased until the end of the period.  
- The daily number of MICUs dispatched crossed the threshold on March 15th and increased until the end of the period.  
The COVID-19 epidemic reached the department in three consecutive waves, and the first wave preceded by 30 days the massive arrival of critical patients. Health care systems must take advantage of this delay to prepare for the next wave. |
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Oral loading dose: 400 mg or 200 mg if AKI and after 200mg t.i.d or 200mg b.i.d if AKI  
Measure daily blood trough and peak concentration of HCQ  
→ evaluation of PK parameters  
Target HCQ concentration: 1 to 2 mg/L  
8 patients: median age was 59 (IQR:53 – 70) – 5 with AKI and 1 with ECLS – all under MV – SOFA score at admission was 5 [3 – 7]  
Analysis of 212 HCQ levels  
Median HCQ peak concentration after loading dose: 0,5mg/L or 0,22mg/L (AKI)  
Median time to obtain target concentration: 4 days [3 – 7]  
Median duration in therapeutic range: 3,3 days  
Toxic levels were noted after day 5 of treatment → drug accumulation and high volume of distribution  
→ prescribing HCQ in COVID-19 patients if unsafe  
→ monitoring of electrocardiogram and blood concentration daily |
| Chest 08JUN2020 | Tocilizumab treatment for cytokine release syndrome in hospitalized COVID-19 patients: survival and clinical outcomes | Price C et al USA [gotopaper](#) | Therapeutic | Observational study – Patient were treated with tocilizumab using an algorithm that targeted cytokine release syndrome (CRS)  
Algorithm developed by a multidisciplinary team  
239 patients included – age median: 64 years  
153 were treated with tocilizumab  
Patient with severe disease were significantly more likely to:  
- Have higher admission hsCRP levels (120 vs 71 mg/l, p<0,001)  
- Have Abnormal chest radiographs  
- Received tocilizumab (90% vs 44%, p<0,001)  
- Received tocilizumab sooner (2 vs 3 days, p<0,01)  
14-days survival was 84% for patients treated with tocilizumab:  
- Not differ by disease severity (83% vs 91%, p=0,11)  
- Mechanical ventilation (MV) occurred in 31% of patients treated with tocilizumab  
After tocilizumab  
- Improve of inflammatory biomarkers (hsCRP, IL-6) and oxygenation  
- D-dimer increased significantly  
- Few adverse events  
→ Tocilizumab to target CRS may influence MV and survival outcomes  
→ Need for randomized trials |
| Intensive Care Medicine 08JUN2020 | Severe COVID-19 is associated with deep and sustained multifaceted cellular immunosuppression | Jeannet et al., France [gotopaper](#) | Immuno | This French study conducted on13 consecutively recruited patients infected with SARS-CoV-2 virus during their first week of ICU stay with 10 healthy donors used as controls confirms that patients uniformly exhibited deep global and persisting T, NK and B cell lymphopenia from ICU admission to day 7  
Interestingly the report indicated few CD4 T cells transiently expressed CTLA-4 during the first 3 days and expression of PD-1 observed at admission day increased until day 7 whereas CD8 T cells significantly expressed PD-1 from admission day to day 7 and CTLA-4 expression remained unchanged.  
Conclusion: These data strongly suggest a vicious effect of the virus to cause an upregulation of potent T cell killing and immunosuppressive mechanisms in critically-ill COVID-19 patients. This call into question therapies (e.g., anti-IL-6, corticosteroids, JAK inhibitors) that aim to block the ability of the patient to mount an effective immune response to the invading SARS-CoV-2. |
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| PLOS ONE 08 JUN2020 | **Quantify the role of superspreaders - opinion leaders- on COVID-19 information propagation in the Chinese Sina-microblog** | Yin F et al CHINA AND CANADA [gotopaper](#) | SHS/SciPo | **Background:**  
> the success of control of COVID-19 outbreak relies on the resilience of people to follow public health interventions  
➢ evidence shows that opinion leaders play a significant role in the propagation of epidemic information and public health policy and implementations  
**Methods:**  
➢ “Opinion-leader susceptible-forwarding-immune (OL-SFI)” mathematical model to quantify the roles of information “superspreaders”  
➢ analysis of the information propagation dynamics in the Chinese Sina-microblog.  
**Results:**  
The earlier opinion leaders get into the public health intervention, the greater their influence will be on the population. |
| PLoS biology 8JUN2020 | **A unifying structural and functional model of the coronavirus replication organelle: Tracking down RNA synthesis** | Snijder, Eric J. et al. Netherlands [gotopaper](#) | Fundamental research | Which replication organelle (RO) element(s) of infected cells accommodate CoV RNA synthesis remains unclear.  
- 2D and 3D analyses of CoV ROs showed that diverse CoVs induce the same membrane modifications, including the small open double-membrane spherules (DMSs) (previously thought to be restricted to gamma- and delta-CoV infections). But RNA synthesis could not be linked to DMSs or any other cellular or virus-induced structure.  
- Abundant association of newly synthesized viral RNA with double-membrane vesicles (DMVs) detected in cells infected with the beta-CoV MERS-CoV and SARS-CoV, and gamma-CoV infectious bronchitis virus (Metabolic labelling by quantitative EM autoradiography).  
- Provides a unifying model of the CoV replication organelle and establish DMVs as the central hub for viral RNA synthesis and a potential drug target in CoV infection. |
| Lancet 5JUN2020 | **Retraction:** Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis | Mandeep R Mehra et al. USA [gotopaper](#) | Therapeutic | Unable to conduct an independent and private peer review to evaluate the origination of the database elements, to confirm the completeness of the database, and to replicate the analyses presented in the paper “Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis”  
The raw data could not be made available to an independent third-party peer review  
Withdrawal of the article at the request of the authors |
The raw data could not be made available to a third-party auditor  
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<tr>
<td>Nature 8JUN2020</td>
<td>Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe</td>
<td>Flaxman, Seth et al. UK gotopaper</td>
<td>Therapeutic</td>
<td>Study of the impact of major non-pharmaceutical interventions across 11 European countries for the period from the start of COVID-19 until the 4th of May 2020 when lockdowns started to be lifted. These large-scale non-pharmaceutical interventions vary between countries but include social distancing (such as banning large gatherings), border closures, school closures, measures to isolate symptomatic individuals and their contacts, and large-scale lockdowns of populations with all but essential internal travel banned. - Estimate that, for all the countries considered, current interventions have been sufficient to drive the reproduction number Rt below 1 (probability Rt &lt; 1.0 is 99.9%) and achieve epidemic control. - Estimate that, across all 11 countries, between 12 and 15 million individuals have been infected with SARS-CoV-2 up to 4th May, representing between 3.2% and 4.0% of the population. =&gt; Major non-pharmaceutical interventions and lockdown in particular have had a large effect on reducing transmission. Continued intervention should be considered to keep transmission of SARS-CoV-2 under control.</td>
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<td>Blood 08JUN2020</td>
<td>COVID and Coagulation: Bleeding and Thrombotic Manifestations of SARS-CoV2 Infection</td>
<td>Al-Samkari H et al USA gotopaper</td>
<td>Clinic</td>
<td>Multicenter study – rate and severity of hemostatic and thrombotic complications 400 patients COVID-19 receiving standard dose prophylactic anticoagulation Overall population: - Radiographically-confirmed VTE rate: 4.8% [2.9 – 7.3] / Thrombotic complications rate: 9.5% [6.8 – 12.8] / Major bleeding rate: 2.3% [1.0 – 4.2] Critically ill patients: - Radiographically-confirmed VTE rate: 7.6% [3.9 – 13.3] / Major bleeding rate: 5.6% [2.4 – 10.7] Predictive of coagulation-associated complications during hospitalization - Elevated D-dimer at admission / Platelet count &gt; 450x10^9/L / CRP &gt; 100mg/L / Erythrocyte sedimentation rate &gt;40mm/h. ( \Rightarrow ) Randomized trials are needed to determine any potential benefit of intensified anticoagulation prophylaxis 58 children in 8 hospitals in England with PIMS-TS ( \Rightarrow ) Comparison with patients with KD (n=1132), KD shock syndrome (n=45) and toxic shock syndrome (n=37) admitted in US and Europe from 2002 to 2019 Median age: 9 years [5.7 – 14] – 57% female Symptoms - Fever with non-specific symptoms: vomiting – abdominal pain – diarrhea – … / 52% rash &amp; 45% conjunctival injection / 22% children met definition of KD (AHA) Biology - PCR SARS-CoV-2 positive 15/58 &amp; SARS-CoV-2 IgG positive in 40 of 46 - 78% had evidence of current or prior infection of SARS-CoV-2 - High level of inflammatory markers (CRP, ferritin) Outcomes - 50% developed shock with evidence of left ventricular dysfunction whom 79% received mechanical ventilation / 14% developed coronary artery dilatation or aneurysm / No death Comparison with KD and KD shock syndrome - Older (9 vs 2.7 vs 3.8 respectively) - Greater elevation of inflammatory markers - Lower platelet count – higher fibrinogen levels and greater elevation of troponin ( \Rightarrow ) the comparison suggests this disorder differ from other pediatric inflammatory entities</td>
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<td>JAMA 08JUN2020</td>
<td>Clinical Characteristics of 58 Children with a Pediatric Inflammatory Multisystem Syndrome Temporarily Associated With SARS-CoV-2</td>
<td>Whittaker E et al UK gotopaper</td>
<td>Clinic</td>
<td>58 children in 8 hospitals in England with PIMS-TS ( \Rightarrow ) Comparison with patients with KD (n=1132), KD shock syndrome (n=45) and toxic shock syndrome (n=37) admitted in US and Europe from 2002 to 2019 Median age: 9 years [5.7 – 14] – 57% female Symptoms - Fever with non-specific symptoms: vomiting – abdominal pain – diarrhea – … / 52% rash &amp; 45% conjunctival injection / 22% children met definition of KD (AHA) Biology - PCR SARS-CoV-2 positive 15/58 &amp; SARS-CoV-2 IgG positive in 40 of 46 - 78% had evidence of current or prior infection of SARS-CoV-2 - High level of inflammatory markers (CRP, ferritin) Outcomes - 50% developed shock with evidence of left ventricular dysfunction whom 79% received mechanical ventilation / 14% developed coronary artery dilatation or aneurysm / No death Comparison with KD and KD shock syndrome - Older (9 vs 2.7 vs 3.8 respectively) - Greater elevation of inflammatory markers - Lower platelet count – higher fibrinogen levels and greater elevation of troponin ( \Rightarrow ) the comparison suggests this disorder differ from other pediatric inflammatory entities</td>
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| Lancet Infectious Disease 08JUN2020 | Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study | Carsana L et al Italy gotopaper         | Clinic             | Analysis of lung tissue samples from 38 patients who died from COVID-19. **Diffuse alveolar damage:**  
- Capillary congestion (100%)  
- Necrosis of pneumocytes (100%)  
- Type 2 pneumocytes hyperplasia (100%)  
- Necrosis of hyaline membranes (87%)  
- Interstitial & intra-alveolar edema (97%)  
- Platelet-fibrin thrombi (87%)  
→ presence of platelet-fibrin thrombi in small arterial vessels is consistent with coagulopathy  
→ same lesions in patients infected with SARS and MERS-CoV |
| Science 08JUN2020 | Genomic surveillance reveals multiple introductions of SARS-CoV-2 into Northern California | Deng, X. et al, USA gotopaper           | Public Health/Epidemio | Investigation of the genomic epidemiology of SARS-CoV-2 in Northern California from late January to mid-March 2020, using samples from 36 patients spanning 9 counties and the Grand Princess cruise ship.  
- Phylogenetic analyses revealed the cryptic introduction of at least 7 SARS-CoV-2 lineages into California, including epidemic WA1 strains associated with Washington State, with lack of a predominant lineage and limited transmission between communities.  
- Lineages associated with outbreak clusters in 2 counties were defined by a single base substitution in the viral genome.  
These findings support contact tracing, social distancing, and travel restrictions to contain SARS-CoV-2 spread. |
| Nature 08JUN2020 | The effect of large-scale anti-contagion policies on the COVID-19 pandemic | Hsiang S. et al, USA gotopaper           | Public Health/Epidemio | Reduced-form econometric methods are applied to empirically evaluate the effect of policies on the growth rate of infections, using new data on 1,717 local, regional, and national non-pharmaceutical interventions deployed in the Covid-19 pandemic across China, South Korea, Italy, Iran, France, and the US.  
- In the absence of policy actions, early infections exponential growth rates are estimated at roughly 38% per day.  
- Anti-contagion policies have significantly and substantially slowed this growth: interventions prevented or delayed on the order of 62 million confirmed cases, corresponding to averting roughly 530 million total infections.  
These findings may help inform whether or when these policies should be deployed, intensified, or lifted. |
| Journal of the American College of Cardiology 08JUN2020 | Prevalence and Impact of Myocardial Injury in Patients Hospitalized with COVID-19 Infection | Lala A. et al, USA gotopaper            | Public Health/Epidemio | AIM: Describing the degree of myocardial injury and associated outcomes in a hospitalized cohort with COVID-19 (n=2,736), based on troponin-I measures (normal value <0.03ng/mL).  
- Cardiovascular disease (CVD; coronary artery disease, atrial fibrillation, and heart failure), hypertension and diabetes were more prevalent in patients with higher troponin concentrations.  
- 506 (18.5%) patients died during hospitalization. In all, 985 (36%) patients had elevated troponin concentrations.  
- After adjusting for disease severity and relevant clinical factors, even small amounts of myocardial injury (troponin I 0.03-0.09ng/mL) were significantly associated with death, while greater amounts (troponin I>0.09 ng/dL) were significantly associated with higher risk.  
Myocardial injury is prevalent among patients hospitalized with COVID-19 however troponin concentrations were generally low. |
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<tr>
<td>J Med Virol 5JUN2020</td>
<td>Identification of nsp1 gene as the target of SARS-CoV-2 real-time RT-PCR using nanopore whole genome sequencing</td>
<td>Chan, Wan-Mui et al. Hong Kong</td>
<td>Virology</td>
<td>There is an increasing number of SARS-CoV-2 viruses with mutations at the primer or probe binding sites. These mutations may affect the sensitivity of RT-PCR assays targeting the N, E, and ORF1a/b genes. =&gt; Using sequence-independent single-primer amplification (SISPA) and nanopore whole-genome sequencing, we have found that the nsp1 gene, located at the 5’ end of the SARS-CoV-2 genome, was highly expressed in the nasopharyngeal or saliva specimens of 9 COVID-19 patients of different clinical severity. =&gt; we have developed a novel nsp1 real-time RT-PCR assay. The primers and probes are highly specific for SARS-CoV-2. <strong>Results:</strong> Validation with 101 clinical specimens showed that our nsp1 RT-PCR assay has a sensitivity of 93.1% (95% confidence interval, 86.2-97.2%), which was similar to those of N and E gene RT-PCR assays. The diagnostic specificity was 100% (95% CI, 92.9-100%) <strong>Conclusion:</strong> The addition of nsp1 for multi-target detection of SARS-CoV-2 can avoid false negative results due to mutations at the primers/probes binding sites of currently available RT-PCR assays. <strong>Limitations:</strong> There can still be bias during the library preparation which may affect the coverage of each position in the viral genome + our nanopore sequencing did not encompass phylogenetic type C strains, which is mainly found in Europe and in America.</td>
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<td>Med 5JUN2020</td>
<td>Outcomes of hydroxychloroquine usage in United States veterans hospitalized with COVID-19</td>
<td>Magagnoli, Joseph et al. USA</td>
<td>Therapeutic</td>
<td>Retrospective study of electronic health records of 807 US veterans patients hospitalized with confirmed SARS-CoV-2 infection to analyze the associations between hydroxychloroquine and azithromycin use and clinical outcome. The primary outcomes were mortality and use of mechanical ventilation. - Compared to the no HC group, after propensity score adjustment for clinical characteristics, the risk of death from any cause was higher in the HC group (adjusted hazard ratio (aHR), 1.83; 95% CI, 1.16 to 2.89; P=0.009) but not in the HC+AZ group (aHR, 1.31; 95% CI, 0.80 to 2.15; P=0.28). - Both the propensity score-adjusted risks of mechanical ventilation and death after mechanical ventilation were not significantly different in the HC group (aHR, 1.19; 95% CI, 0.78 to 1.82; P=0.42 and aHR, 2.11; 95% CI, 0.96 to 4.62; P=0.06, respectively) or in the HC+AZ group (aHR, 1.09; 95% CI, 0.72 to 1.66; P=0.69 and aHR, 1.25; 95% CI, 0.59 to 2.68; P=0.56, respectively), compared to the no HC group. <strong>Limitations:</strong> non-randomization of treatments; demographic composition of patients (US veterans) with a majority of men and majority of black.</td>
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<td>HEART FAILURE JUN2020</td>
<td>Incidence of New-Onset and Worsening Heart Failure Before and After the COVID-19 Epidemic Lockdown in Denmark</td>
<td>Andersson C et al, DENMARK</td>
<td>Public Health/Epidemiology</td>
<td>Consequences of the lockdown for patients with heart failure (Cohort Study in Denmark) &gt; Incidence of new onset HF and and hospitalizations for worsening HF before and after the lockdown (2019 vs 2020, same period) <strong>Results:</strong> 1. Before lockdown: &gt; Rates of new-onset HF before lockdown were comparable for 2020 and 2019 / Hospitalizations for worsening HF were slightly higher in 2020 versus 2019 in 2. During lockdown: &gt; Rates of new-onset HF diagnoses and of hospitalizations for worsening HF significantly lower in 2020 versus 2019 / Similar mortality before and after lockdown for the population with HF. <strong>Conclusions:</strong> &gt; These data raise concerns for a potential undertreatment of HF currently that may impact prognosis in the longer term</td>
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COVID-19-Related Information Sources and the Relationship With Confidence in People Coping with COVID-19: Facebook Survey Study in Taiwan

Wang PW et al.
TAIWAN
gotopaper

Objectives: to examine major COVID-19 information sources of people in coping with COVID-19 in Taiwan.

Methods:

- 1904 participants (1270 non-health-care workers (HCW) and 634 HCW) recruited from Facebook advertisement.
- surveyed sources of information: internet (blogs, internet news, and social media: Facebook, Line, Twitter, and Plurk), friends, traditional media (television, newspapers, and radio broadcasting) and formal lesson on COVID19
- Participants rated their frequency for each source, and responded to question on self-confidence and worries in coping with COVID19

Results:

- Sources of information by order of acces: internet (80%) followed by traditional media, family members, coworkers, friends, formal lessons, and medical staff. > 50% of participant consulted one or two sources. 10% zero.
- for HCW: the use of formal lessons as an information source was associated with better self-confidence in coping with COVID-19
- association between receiving information from more sources and greater self-confidence found in HCW, but not in other groups

Conclusions:

- internet is a popular and accessible information source, but misinformation on COVID-19 is rife
- severe worry is associated with using more information sources.
- Medical professionals should consider that when delivering information online.

Comparison of virus concentration methods for the RT-qPCR-based recovery of murine hepatitis virus, a surrogate for SARS-CoV-2 from untreated wastewater

Ahmed, Warish et al.
Australia
gotopaper

There is currently a clear benefit for many countries to utilize wastewater-based epidemiology (WBE) as part of ongoing measures to manage the COVID-19 global pandemic. It is imperative to determine the efficiency of the most commonly used methods for the enveloped SARS-CoV-2.

- Municipal wastewater seeded with a human coronavirus (CoV) surrogate, murine hepatitis virus (MHV), was used to test the efficiency of seven wastewater virus concentration methods: (A–C) adsorption-extraction with three different pre-treatment options, (D–E) centrifugal concentration device methods with two different devices, (F) polyethylene glycol (PEG 8000) concentration, and (G) ultrafiltration. MHV was quantified by reverse-transcription quantitative polymerase chain reaction and the concentration efficiency was calculated for each method.

Results: the most efficient methods were (B) Adsorption-extraction methods, with MgCl$_2$ pre-treatment.

CI*: absorption-extraction methods with minimal pretreatment or without manipulation can provide suitably rapid, cost-effective and relatively straightforward recovery of enveloped viruses in wastewater. The MHV is a promising process control for SARS-CoV-2 surveillance and can be used as a quality control measure to support community-level epidemic mitigation and risk assessment.
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| **CELL 4JUN2020** | Development of an inactivated vaccine candidate, BBIBP-CorV, with potent protection against SARS-CoV-2 | Wuang H et al, China | Vaccin | BBIBP-CorV inactivated SARS-CoV-2 vaccine candidate: 3 viral strains isolated from BAL or throat swabs from 3 hospitalized patients in Vero cells.  
> The strain showing the most optimal replication rates and highest virus yield was selected.  
**Immunogenicity tests:**  
In mice: BalbC injected with 2, 4, 8 ug/dose of BBIBP-CorV + aluminium hydroxide adjuvant.  
> One/Two/three dose programmes: High seroconversion rate in the three groups at D7. Better NAb production in three dose program as evaluated at D28  
In rabbits, guinea pigs, rats and NHP: good immunogenicity and seroconversion rates in a two-dose vaccination program.  
**Protection in NHP**  
Immunization of NHP with BBIBP-CorV-2 after intratracheal challenge: 2 doses; 2ug/dose  
> highly efficient protection against SARS-CoV-2  
> viral clearance in lungs, throat and and swabs  
> no side effects on serum biochemical parameters  
> no ADE  
Safety evaluation in rat showed no specific concerns  
BBIBP-CorV exhibits efficient productivity and good genetic stability for vaccine manufacture |
| **Allergy 4JUN2020** | Distribution of ACE2, CD147, CD26 and other SARS-CoV-2 associated molecules in tissues and immune cells in health and in asthma, COPD, obesity, hypertension, and COVID-19 risk factors | Radzikowska, U. et al, Switzerland-Poland-China-Norway-Japan-Germany-USA-Ireland | Fundamental research | Gene expression analysis (RNA sequencing and RNA-Seq databases) of SARS-CoV-2 receptors and related molecules in collection of primary human cells and tissues from healthy (children and adults) and adult patients with risk factors and known comorbidities of COVID-19: (ACE2, CD147 (BSG), CD26 (DPP4), and their direct and indirect molecular partners in primary human bronchial epithelial cells, bronchial and skin biopsies, bronchoalveolar lavage fluid, whole blood, PBMCs, monocytes, neutrophils, DCs, NK cells, ILC1, ILC2, ILC3, CD4+ and CD8+ T cells, B cells and plasmablasts)  
- ACE2 and TMPRSS2 co-expressed at epithelial sites of lung and skin,  
- CD147, cyclophilins (PPIA and PPIB), CD26 and related molecules expressed in both epithelium and in immune cells.  
- Distinct age-related expression profile of these genes in the PBMCs and T cells from healthy children and adults.  
- Higher expression of ACE2- and CD147-related genes generally in asthma, COPD, hypertension, smoking, obesity, and male gender in the bronchial biopsy, BAL or blood.  
- CD147-related genes correlated positively with age and BMI.  
> Different receptor repertoire potentially involved in the SARS-CoV-2 infection at the epithelial barriers and in the immune cells.  
Altered expression of these receptors related with age, gender, obesity and smoking, as well as with the disease status might contribute to COVID-19 morbidity and severity patterns. |
| **The Lancet Rheumatology 4JUN2020** | Canakinumab in a subgroup of patients with COVID-19 | Ucciferri, Claudio et al, Italie/USA | Therapeutic | Retrospective analysis of 10 hospitalized patients with confirmed SARS-CoV-2 infection, bilateral pneumonia, hyperinflammation (defined as serum C-reactive protein ≥50 mg/L), and respiratory failure (requiring supplemental oxygen without invasive ventilation). These patients were treated with canakinumab, a human monoclonal antibody against IL-1β.  
All patients also received hydroxychloroquine and lopinavir-ritonavir.  
Canakinumab was safe, well tolerated, and associated with a rapid reduction in the systemic inflammatory response and an improvement in oxygenation compared to controls. Notably, none of the patients developed neutropenia or bacterial sepsis.  
**Limitations:** small sample size and absence of a random comparison. |
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<td>JAMA 3JUN2020</td>
<td>Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial</td>
<td>Li, Ling et al. China <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Open-label, multicenter, randomized clinical trial including 103 participants with laboratory-confirmed COVID-19 severe (respiratory distress and/or hypoxemia) or life-threatening (shock, organ failure, or requiring mechanical ventilation) treated with Convalescent plasma in addition to standard treatment vs standard treatment alone (stratified by disease severity). The trial was terminated early after 103 of a planned 200 patients were enrolled. Primary outcome was time to clinical improvement within 28 days. Secondary outcomes included 28-day mortality, time to discharge, and the rate of viral PCR results turned from positive at baseline to negative at up to 72 hours. - Clinical improvement occurred within 28 days in 51.9% of the convalescent plasma group vs 43.1% in the control group (difference, 8.8% [95% CI, −10.4% to 28.0%]; hazard ratio [HR], 1.40 [95% CI, 0.79-2.49]; P = .26). Among those with severe disease, the primary outcome occurred in 91.3% (21/23) of the convalescent plasma group vs 68.2% (15/22) of the control group (HR, 2.15 [95% CI, 1.07-4.32]; P = .03); among those with life-threatening disease the primary outcome occurred in 20.7% (6/29) of the convalescent plasma group vs 24.1% (7/29) of the control group (HR, 0.88 [95% CI, 0.30-2.63]; P = .83) (P for interaction = .17). - There was no significant difference in 28-day mortality (15.7% vs 24.0%; OR, 0.65 [95% CI, 0.29-1.46]; P = .30) or time from randomization to discharge (51.0% vs 36.0% discharged by day 28; HR, 1.61 [95% CI, 0.88-2.93]; P = .12). - Convalescent plasma treatment was associated with a negative conversion rate of viral PCR at 72 hours in 87.2% of the convalescent plasma group vs 37.5% of the control group (OR, 0.88 [95% CI, 0.30-2.63]; P = .83) (P for interaction = .17).</td>
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<td>Biosensors and Bioelectronics JUN2020</td>
<td>Homogeneous circle-to-circle amplification for real-time optomagnetic detection of SARS-CoV-2 RdRp coding sequence</td>
<td>Tian, Bo et al. Denmark <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>Circle-to-circle amplification (C2CA) is a specific and precise cascade nucleic acid amplification method consisting of more than one round of padlock probe ligation and rolling circle amplification (RCA). We herein demonstrate a homogeneous and isothermal nucleic acid quantification strategy based on C2CA and optomagnetic analysis of magnetic nanoparticle (MNP) assembly. -&gt; eliminates the need for additional monomerization and ligation steps after the first round of RCA, and combines two amplification rounds in a one-pot reaction. -&gt; Applied for the detection of a synthetic complementary DNA of SARS-CoV-2 RdRp (RNA-dependent RNA polymerase) coding sequence, achieving a detection limit of 0.4 fM with a dynamic detection range of 3 orders of magnitude and a total assay time of ca. 100 min. A mathematical model was set up and validated to predict the assay performance. Conclusion: Reaches a sub-femtomolar level detection limit and significantly simplified the operation by eliminating the labor-intensive and time-consuming operation steps requiring different reaction temperatures. Capability of target quantification in 10% FBS samples was demonstrated with an acceptable loss of sensitivity.</td>
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<td>J. Infect. 3JUN2020</td>
<td>Detection of SARS-CoV-2 antibodies using commercial assays and seroconversion patterns in hospitalized patients</td>
<td>Tuillon, E. et al. France <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>SARS-CoV-2 antibody assays are needed for serological surveys and as a complement to molecular tests to confirm COVID-19. However, the kinetics of the humoral response against SARS-CoV-2 remains poorly described and relies on the performance of the different serological tests. =&gt; Evaluation of performance of six CE-marked point-of-care tests (POC) and three ELISA assays for the diagnosis of COVID-19 by exploring seroconversions in hospitalized patients who tested positive for SARS-CoV-2 RNA. Results: our study is one of the very first to evaluate the performance of commercial SARS-CoV-2 serologic assays. The second week of COVID-19 seems to be the best period for assessing the sensitivity of commercial serological assays. CI: serological assays may be useful in the diagnosis of patients with acute respiratory distress syndrome and a negative PCR assay Seroconversions occur during the second week of the disease. To achieve an early diagnosis of COVID-19 based on antibody detection, a dual challenge must be met: the immunodiagnostic window period must be shortened and an optimal specificity must be conserved Limitations: relatively small number of plasma samples -&gt; the estimation of sensitivity and specificity values are relatively imprecise. Patients with moderate to severe COVID-19 -&gt; intensity of the humoral response to SARS-CoV-2 N or S proteins may be lower in asymptomatic or paucity symptomatic cases.</td>
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<td>NEJM 03JUN2020</td>
<td>A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19</td>
<td>David R. Boulware et al. USA/Canada <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Randomized, double-blind, placebo-controlled trial to evaluate postexposure prophylaxis with hydroxychloroquine after exposure to Covid-19. Participants had known exposure (by participant report) to a person with laboratory-confirmed Covid-19, whether as a household contact, a health care worker, or a person with other occupational exposures. The primary outcome was the incidence of either laboratory-confirmed Covid-19 or illness compatible with Covid-19 within 14 days. 821 asymptomatic adult participants were randomly assigned to the hydroxychloroquine group (414 participants) or the placebo group (407 participants). Overall, 87.6% of the participants (719 of 821) had high-risk exposures without eye shields and surgical masks or respirators. - The incidence of new illness compatible with Covid-19 did not differ significantly between participants receiving hydroxychloroquine (49 of 414 [11.8%]) and those receiving placebo (58 of 407 [14.3%]); the absolute difference was −2.4 percentage points (95% confidence interval, −7.0 to 2.2; P=0.35). - Side effects were more common with hydroxychloroquine than with placebo (40.1% vs. 16.8%), but no serious adverse reactions were reported. Conclusion: high doses of hydroxychloroquine did not prevent illness compatible with Covid-19 when initiated within 4 days after a high-risk or moderate-risk exposure. Limitation: a priori symptomatic case definition used because majority of the participants, including health care workers, were unable to access testing; Internet-based approach used to rapidly recruit participants in the context of a pandemic, data were obtained by means of participant report; predictive power of the case definition is unknown, particularly in the younger populations studied.</td>
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<td>The Lancet Public Health 02JUN2020</td>
<td>Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study</td>
<td>Davies, N.G., et al. UK <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Assessment of the potential impact of control measures for COVID-19 in the UK, using a stochastic age-structured transmission model tracking 664 million people. Interventions modelled were school closures, physical distancing, shielding of people aged &gt;70, and self-isolation of symptomatic cases, a combination of the four, as well as lockdown. Estimations of new cases, patients requiring ICU admission, death and R0 were calculated. - The median unmitigated burden was of 23 million clinical cases and 350 000 deaths in the UK by December 2021. - The four base interventions were each likely to decrease R0, but not sufficiently to prevent ICU demand from exceeding health service capacity. Only lockdown periods were sufficient to bring R0 near or below 1. - The most stringent lockdown scenario resulted in a projected 120 000 cases and 50 000 deaths. Intensive interventions with lockdown periods would need to be in place for a large proportion of the coming year to prevent health-care demand exceeding availability.</td>
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<td>European journal of heart failure 2JUN2020</td>
<td>ACE-inhibitors and Angiotensin-2 Receptor Blockers are not associated with severe SARS-COVID19 infection in a multi-site UK acute Hospital Trust</td>
<td>Bean, Daniel M. et al. UK <a href="#">gotopaper</a></td>
<td>Clinic</td>
<td>Hypothesis: ACE-inhibitors (ACEi) and Angiotensin-2 Blockers (ARB), commonly used in patients with hypertension or diabetes and may raise tissue ACE2 levels, could increase the risk of severe COVID19 infection. Consecutive cohort of 1200 acute COVID19 inpatients (2 hospitals) with multi-ethnic catchment population in London: - Mean age: 68 ± 17 years (57% male); 74% of patients with at least 1 comorbidity. - 34.6% reached the primary endpoint of death or transfer to a critical care unit for organ support within 21-days of symptom onset. - 33.3% were taking ACEi or ARB (significantly older and more comorbidities). - Odds ratio for the primary endpoint in patients on ACEi and ARB, after adjustment for age, sex and co-morbidities, was 0.63 (CI 0.47-0.84, p &lt; 0.01). No evidence for increased severity of COVID19 disease in hospitalised patients on chronic treatment with ACEi or ARB. A trend towards a beneficial effect of ACEi/ARB requires further evaluation in larger meta-analyses and randomised clinical trials.</td>
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<td>Cell Systems 02JUN2020</td>
<td>Ultra-high-throughput clinical proteomics reveals classifiers of COVID-19 infection</td>
<td>Messner et al., UK,Germany,S weden <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>-A standardized, ultra-high-throughput clinical platform for serum and plasma proteomics -Platform enables high precision quantification of 180 patient samples/day at low cost -27 biomarkers are differentially expressed between WHO severity grades for COVID-19 -Biomarkers include proteins not previously associated with COVID-19 infection</td>
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<td>The Lancet Psy 2JUN2020</td>
<td>Global mental health and COVID-19</td>
<td>Lola Kola, Nigeria <a href="#">gotopaper</a></td>
<td>Psy</td>
<td>Disruption of mental health, in particular in LMICs. Two successful global mental health strategies: 1- Task shifting—the use of trained lay health workers to deliver health care in non-specialist settings [can be used to address the urgent need to build a provider base in developing countries 2- Use of digital health technology to strengthen health systems (use of mobile phone for health interventions in LMICs) -&gt; to increase access and coverage in hard-to-reach areas calls for more research on their electiveness in LMICs - &gt; the Lancet Commission on global mental health recommended adoption of digital interventions alongside traditional treatments/ -&gt; Efforts to respond to mental health needs present the urgent need to build a provider base in developing countries.</td>
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<td>Lancet 01JUN2020</td>
<td>Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis</td>
<td>Chu et al, Canada <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Aim: to investigate the effects of physical distance, face masks, and eye protection on virus transmission in healthcare and community settings, through a systematic review and meta-analysis of 172 observational studies (25,697 patients in total). - Transmission of viruses was lower with physical distancing of 1 m or more, compared with a distance of less than 1 m. Protection was increased as distance was lengthened. - Face mask use resulted in a large reduction in risk of infection, with stronger associations with N95 or similar respirators compared with disposable surgical masks or similar. - Eye protection was associated with less infection. These findings support physical distancing of 1 m or more and provide quantitative estimates for models and contact tracing to inform policy.</td>
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<td>Eur. Respir. J. 01JUN2020</td>
<td>Estimates of the ongoing need for social distancing and control measures post-“lockdown” from trajectories of COVID-19 cases and mortality</td>
<td>Lonergan, M., Chalmers, J.D. UK <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Predictions on trajectories, doubling times and R0 of COVID-19 under social distancing and lockdown measures, based on new cases and mortality data in 89 countries up to May 21st 2020. - Estimates of R0 before lockdown was between 2.0 and 3.7 (USA, Italy, Spain, France and UK). There was little evidence that the restrictions had reduced R far below 1 in many places (France showed the most rapid reductions - R0 0.76, based on cases and 0.77 based on mortality). - With an intermittent lockdown strategy, few countries could have even 1 week per month unrestricted without resurgence of the epidemic. - Restoring 20% of the activity that has been prevented by the lockdowns does not reconcile with preventing the resurgence of the disease in most countries.</td>
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<td>Nature Communications 01JUN2020</td>
<td>Two linear epitopes on the SARS-CoV-2 spike protein that elicit neutralizing antibodies in COVID-19 patients</td>
<td>Poh, Chek Meng et al; Singapore <a href="#">gotopaper</a></td>
<td>Immuno</td>
<td>Identification of immunogenic targets against the coronavirus spike glycoprotein - In this study, using pools of overlapping linear B-cell peptides, two immunodominant linear B-cell epitopes on the S glycoprotein of SARS-CoV-2 were identified. SP14P5 is located in close proximity to the receptor binding domain whereas S21P2 is in the region that encompasses the fusion peptide, which is highly conserved among coronaviruses suggesting a potential pan-SARS epitope at this location. - Detection for both S14P5 and S21P2 was consistently and significantly higher in COVID-19 patients. - Interestingly, antibody depletion assays demonstrate that antibodies recognized these two linear epitopes and can neutralise SARS-CoV-2. Conclusion: SP14P5 et S21P2 epitopes can potentially be used in the design of more sensitive serological assays for epidemiological or vaccine efficiency assessments since that antibodies targeting these two linear epitopes account for a significant fraction of the anti-S-neutralising response.</td>
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| Sensors 31MAY2020 | Development of a Portable, Ultra-Rapid and Ultra-Sensitive Cell-Based Biosensor for the Direct Detection of the SARS-CoV-2 S1 Spike Protein Antigen | Mavrikou, Sophie et al. Greece [gotopaper](https://example.com) | Diagnostic | One of the key challenges of the recent COVID-19 pandemic is the ability to accurately estimate the number of infected individuals, particularly asymptomatic and/or early-stage patients. 

**Proof-of-concept development of a biosensor able to detect the SARS-CoV-2 S1 spike protein.** The biosensor is based on membrane-engineered mammalian cells bearing the human chimeric spike S1 antibody. 

**Results:** We demonstrate that the attachment of the protein to the membrane-bound antibodies resulted in a selective and considerable change in the cellular bioelectric properties measured by means of a Bioelectric Recognition Assay. The novel biosensor provided results in an ultra-rapid manner (3 min), with a detection limit of 1 fg/mL and a semi-linear range of response between 10 fg and 1 μg/mL. In addition, the observed high sensitivity of the biosensor could allow for screening the virus in easy-to-obtain patient samples such as saliva. **No cross-reactivity** was observed against the SARS-CoV-2 nucleocapsid protein. Furthermore, the biosensor was configured as a ready-to-use platform, including a portable read-out device operated via smartphone/tablet.

**Conclusion:** The novel biosensor can be potentially applied for the mass screening without prior sample processing. The next step will be the actual clinical validation of the assay using patient samples and comparison to current serological and molecular tests. |
| Int. J. Infect. Dis. 31MAY2020 | Fast SARS-CoV-2 detection by RT-qPCR in preheated nasopharyngeal swab samples | Alcoba-Florez, Julia et al. Spain [gotopaper](https://example.com) | Diagnostic | Performance of three alternative, simple and affordable protocols to rapidly detect SARS-CoV-2, bypassing the long and tedious RNA extraction step and reducing the time to viral detection: three methods based on direct nasopharyngeal swab viral transmission medium (VTM) heating before the RT-qPCR: a) direct without additives; b) in a formamide-EDTA (FAE) buffer, c) in a RNAsnapTM buffer. 

Although with a delay in cycle threshold compared to the gold-standard, we found consistent results in nasopharyngeal swab samples that were subject to a direct 70°C incubation for 10 min.

**CP:** This study provides valuable options to overcome any supply chain issue and help to increase the throughput of diagnostic tests, thereby complementing standard diagnosis. |
| Int. J. Infect. Dis. 31MAY2020 | Aberrant hyperactivation of cytotoxic T-cell as a potential determinant of COVID-19 severity | Kang, Chang Kyung et al. Rep. of Korea [gotopaper](https://example.com) | Immuno | We hypothesized that immune response may contribute to progression of coronavirus disease-19 (COVID-19) at the second week of illness. Therefore, we compared cell-mediated immune (CMI) responses between severe and mild COVID-19 cases. 

We examined peripheral blood mononuclear cells of laboratory-confirmed COVID-19 patients from their first and third weeks of illness.

**CP:** Severe COVID-19 had higher degree of proliferation, activation, and cytotoxicity of T-cells at the late phase of illness without cytotoxic T-cell contraction, which might contribute to the development of severe COVID-19.

**Limitations:** Small numbers of patients. Requires more time points to be examined to elucidate the exact temporal changes of such responses or when the persistent cytotoxic T-cell activity returns to normal in severe cases. The potential immunomodulatory effects of lopinavir/ritonavir could not be adjusted because the drug was prescribed to all severe patients in this study. |
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<tr>
<td>J. Clin. Virol.</td>
<td>Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19</td>
<td>Gombar, Saurabh et al. USA <a href="#">goto paper</a></td>
<td>Diagnostic</td>
<td>Current guidelines for returning health care workers (HCW) to service after a positive SARS-CoV-2 RT-PCR test and ceasing of transmission precautions for patients is based on two general strategies: A test-based strategy that requires negative respiratory RT-PCR tests obtained after the resolution of symptoms; a symptom-based strategy that recommends excluding HCW from the workforce until a fixed period of time has elapsed from symptom recovery.</td>
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<td>Brain, Behavior and Immunity</td>
<td>COVID-19 pandemic and mental health consequences: systematic review of the current evidence</td>
<td>Vindegaard and Eriksen Benros, Denmark <a href="#">goto paper</a></td>
<td>Psy</td>
<td>Objective: to better understand the appropriate length of symptom-based return to work and contact precaution strategies in healthcare workers. Observational analysis of 150 patients and HCW shows that the average time to transition from RT-PCR positive to negative was 24 days after symptom onset and 10% remained positive even 33 days after symptom onset.</td>
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<tr>
<td>Clin. Infect. Dis.</td>
<td>Maximum Daily Temperature, Precipitation, Ultra-Violet Light and Rates of Transmission of SARS-CoV-2 in the United States</td>
<td>Shera T et al., USA <a href="#">goto paper</a></td>
<td>Public Health/Epidemi</td>
<td>COVID-19 patients displayed high levels of PTSS and increased levels of depression. • Patients with preexisting psychiatric disorders reported worsening of psychiatric symptoms. • Higher levels of psychiatric symptoms were found among healthcare workers. • A decrease in psychological well-being was observed in the general public. • However, well conducted large-scale studies are highly needed.</td>
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| Cell Reports         | Structural and biochemical characterization of nsp12-nsp7-nsp8 core polymerase complex from SARS-CoV-2 | Peng, Qi et al. China [goto paper](#) | Structural biology       | Aim: to investigate effects of temperature, precipitation, and UV Light on community transmission of SARS-CoV-2 in the USA.  
- A maximum temperature >52°F on a given day was associated with a lower rate of new cases at 5 days.  
- Below 52°F, there was a significant inverse association between the maximum daily temperature and the rate of cases at 5 days.  
- In a theoretical state with a stable maximum daily temperature >52°F, the rate of new cases is predicted to be of 23-fewer cases per-million per-day by 25 days of the epidemics.  
- A 1-unit higher UV index was associated with a lower rate at 5 days.  
- Precipitation was not associated with a greater rate of cases at 5 days.  
The incidence of disease is lower at warmer versus cooler temperatures, but this association is small, and transmission is likely to remain high at warmer temperatures.  
Cryo-EM structure of SARS-CoV-2 core polymerase complex (nsp12 catalytic subunit + nsp7-nsp8 cofactors):  
- Structure highly resembles SARS-CoV counterpart with conserved motifs for all viral RNA-dependent RNA polymerases, and suggests a mechanism for activation by cofactors.  
- SARS-CoV-2 core complex has lower enzymatic activity than SARS-CoV.  
- SARS-CoV-2 nsp7/8/12 subunits are less thermostable than the SARS-CoV counterpart.  
> Provides insights into RNA synthesis by coronavirus polymerase and indicate adaptation of SARS-CoV-2 towards humans with relatively lower body temperatures than the natural bat hosts. |
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<tr>
<td>Clin. Infect. Dis. 30MAY2020</td>
<td>Surgical mask partition reduces the risk of non-contact transmission in a golden Syrian hamster model for Coronavirus Disease 2019 (COVID-19)</td>
<td>Chan, Jasper Fuk-Woo et al. China gotopaper</td>
<td>Transmission - Animal model</td>
<td>Golden Syrian hamster SARS-CoV-2 model to experimentally address effect of surgical mask on transmission: Surgical mask partition placed between cages of SARS-CoV-2-challenged index hamsters and naïve hamsters (closed system units separated by a polyvinyl chloride air porous partition + unidirectional airflow). - Surgical mask partition for challenged hamsters significantly reduced transmission to 16.7% (2/12, P=0.019) of exposed naïve hamsters compared to exposed naïve hamsters without surgical mask partition (66.7%). - Unlike severe COVID-19 manifestations of challenged hamsters, infected naïve hamsters had lower clinical scores, milder histopathological changes, and lower viral nucleocapsid antigen expression respiratory tract tissues. - SARS-CoV-2 could be transmitted by respiratory droplets or airborne droplet nuclei in the hamster model. Such transmission could be reduced by surgical mask usage, especially when masks were worn by infected individuals.</td>
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<td>J Med Virol 29MAY2020</td>
<td>Serum KL-6 concentrations as a novel biomarker of severe COVID19</td>
<td>d’Alessandro, Miriana et al. Italy gotopaper</td>
<td>Virology</td>
<td>SARS-CoV-2 induced direct cytopathic effects against type I and II pneumocytes mediate lung damage. Krebs von den Lungen-6 (KL-6) is mainly produced by damaged or regenerating alveolar type II pneumocytes. This preliminary study analysed serum concentrations of KL-6 in COVID19 patients to verify its potential as a prognostic biomarker of severity. CI*: NK cell analysis and assay of KL-6 in serum can help identify severe COVID19 patients. Increased KL-6 serum concentrations were observed in patients with severe pulmonary involvement, revealing a prognostic value and supporting the potential usefulness of KL-6 measurement to evaluate COVID19 patients prognosis. Limitations: these results are worthy of further validation in a larger cohort to define the cut-off value for identifying patients at high risk of severe respiratory failure.</td>
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<td>BMJ 29MAY2020</td>
<td>Covid-19: the ethics of clinical research in quarantine</td>
<td>Nicholas G Evans, USA gotopaper</td>
<td>SHS/Sciences Po</td>
<td>Quarantine = an opportunity to gain scientific knowledge of covid-19. Quarantine provides a model community in which to study both the social and epidemiological characteristics of a disease outbreak. As a closed system, quarantine offers the possibility for highly controlled research into the development and transmission of covid-19. But this opportunity is also an ethical risk. This knowledge would be obtained with human rights violation (such as liberty). Moreover, individuals under quarantine seem to me more vulnerable to researchers. Confinement could affect their ability to choose or not to participate into research. Finally, research in this context could be a major opportunity to clarify when quarantine is, or is not, effective and proportionate (with high quality data on COVID-19).</td>
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<td>Journal of Allergy and Clinical Immunology 29MAY2020</td>
<td>Successful use of methylprednisolone for treating severe COVID-19</td>
<td>Liu, Jing et al. China gotopaper</td>
<td>Therapeutic</td>
<td>Case series of 101 consecutive hospitalized patients with confirmed COVID-19 infection, among which 26 were classified as severe or critical (25.74%), with at least 10 patients had a PaO2/FiO2 ratio of less than 150 mmHg, treated with methylprednisolone. -&gt; Timely and appropriate application of glucocorticoid in severe and critical COVID-19 patients may improve outcomes and lung function and could avoid the need for invasive mechanical ventilation, compared with outcomes in reported studies. -&gt; Single-dose pulse methylprednisolone (40-500mg methylprednisolone) had no apparent negative impact on SARS-CoV-2 removal and production of specific IgG.</td>
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<td>Nature Communications 29MAY2020</td>
<td>Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients</td>
<td>Chia, PY et al., Singapore <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Screening for SARS-CoV-2 RNA on surface and air samples from 3 airborne infection isolation rooms (AIIRs) in ICU and 27 AIIRs in the hospital general ward hosting Covid-19 patients. From 245 surface samples collected:  - 56.7% of rooms have at least one surface contaminated  - High touch surface contamination is shown in 10 (66.7%) out of 15 patient environments in the first week of illness, and 3 (20%) beyond the first week of illness  - Air sampling performed in 3 of 27 general ward AIIRs detected SARS-CoV-2 PCR-positive particles of sizes &gt;4 microm and 1-4 microm in two rooms, despite these rooms having 12 air changes per hour. This warrants further study of the particle size distribution and airborne transmission potential of SARS-CoV-2.</td>
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<td>Science 29MAY2020</td>
<td>Introductions and early spread of SARS-CoV-2 in the New York City area</td>
<td>Gonzalez-Reiche et al, USA <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Aim: to identify the early transmission events underlying the rapid spread of the virus in the NYC metropolitan area, by sequencing SARS-CoV-2 from patients. Phylogenetic analysis of 84 distinct SARS-CoV-2 genomes indicated:  - multiple, independent but isolated introductions mainly from Europe and other parts of the United States,  - evidence for community transmission of SARS-CoV-2 as suggested by clusters of related viruses found in patients living in different neighborhoods of the city.</td>
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<td>Science Advances 29MAY2020</td>
<td>Emergence of SARS-CoV-2 through recombination and strong purifying selection</td>
<td>Li, Xiaojun et al. USA - China <a href="#">gotopaper</a></td>
<td>Phylogenetic</td>
<td>Localised genomic analysis of patterns of evolutionary recombination between CoVs from distinct host species that likely originated SARS-CoV-2, reveal:  - Strong purifying selection around the receptor binding motif (RBM) of the spike among bat, pangolin, and human coronaviruses.  - SARS-CoV-2’s entire RBM was introduced through recombination with coronaviruses from pangolins, possibly a critical step in the evolution of SARS-CoV-2’s ability to infect humans.  <strong>Note:</strong> all 3 human CoVs (SARS, MERS and SARS-2) are the result of recombination among CoVs involving the S gene, likely a precondition to zoonosis that enabled efficient binding to human receptors.  -&gt; Similar evolutionary selection in different host species, together with frequent recombination among coronaviruses, suggest a common evolutionary mechanism that could lead to new emerging human coronaviruses.</td>
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<td>Lancet 29MAY2020</td>
<td>Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study</td>
<td>COVIDSurg Collaborative UK <a href="#">gotopaper</a></td>
<td>Clinic</td>
<td>International – multicentre – 235 hospitals – 24 countries Surgery + SARS-CoV-2 positive within 7 before or 30 days after 1128 patients Pulmonary complication: ARDS or pneumonia or unexpected postoperative ventilation 74% had emergency surgery and 24.8% elective surgery 30-day mortality= 23.8%  <strong>Pulmonary complications= 51.2% with 38% of mortality</strong> Association with mortality (adjusted analysis):  - Male sex OR: 1.75 [1.28 – 2.40]  - &gt; or = 70 years OR: 2.30 [1.65 – 3.22]  - ASAS grade 3-5 OR: 2.35 [1.57 – 3.53]  - Malignant diagnosis OR: 1.55 [1.01 – 2.39]  - Emergency surgery OR: 1.67 [1.06 – 2.63]  - Major surgery OR: 1.52 [1.01 – 2.31]  -&gt; pulmonary complication in more than half of patients with perioperative SARS-CoV-2 infection  -&gt; postponing non urgent procedure and promoting non operative treatment</td>
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**Impaired immune cell cytotoxicity in severe COVID-19 is IL-6 dependent**

Mazzoni, Alessio et al., Italy

Gotopaper

**Immu**

**Key facts**

- A flow cytometric characterization of immune cells subsets from 30 COVID-19 patients correlated with clinical outcomes confirms a decreased number of circulating T, B and NK cells and that T CD4+, T CD8+ but also NK cells displayed reduced anti-viral cytokine production capability.
- The study shows a skewing of CD8+ T cells towards a terminally differentiated/senescent phenotype via a TNF-mediated T cell apoptosis. This may contribute to an uncontrolled inflammatory response.
- In a group of patients that required intensive care, serum IL-6 levels are inversely correlated with the frequency of granzyme-expressing NK cells. This underlines that the exposure to high levels of IL-6 inhibits NK cell cytotoxicity and down-regulates the expression of perforin and granzyme.
- In all patients treated with tocilizumab an increased expression of both perforin and granzyme in NK cells was observed as well as a decrease of CRP, which is considered as a marker of IL-6 mediated inflammation. This study points out that tocilizumab might restore the cytotoxic potential of NK cells.

**Conclusion:** This current work endorses that targeting IL-6 cytokine might restore anti-viral mechanisms and the use an anti-IL-6 receptor monoclonal antibody in COVID-19 patients remains a potential therapeutic option.

**Preliminary evidence from a multicenter prospective observational study of the safety and efficacy of chloroquine for the treatment of COVID-19**

Huang, Mingxing et al., China

Gotopaper

**Therapeutic**

**Key facts**

- **Multicenter prospective observational study** to assess the efficacy and safety of chloroquine with different doses in COVID-19.
  - A total of 197 patients completed chloroquine treatment, and 176 patients treated with non-chloroquine therapy were included as historical controls. Across the two treatment groups, the majority patients were classified as moderate cases (93.4% in chloroquine; 89.2% in nonchloroquine).
  - The primary endpoint is the time to undetectable viral RNA. Secondary outcomes include the proportion of patients with undetectable viral RNA by day 10 and 14, hospitalization time, duration of fever, and adverse events.
- Patients in the chloroquine group experienced significantly faster and higher rate of viral suppression comparing to the nonchloroquine group in both the full analysis and the post hoc stratified analysis. Even when the dose reduced to half, the benefit of chloroquine still remained.
- **Duration of fever is shorter** in chloroquine (geometric mean ratio 0.6; 95% CI 0.5 to 0.8).
- **No serious adverse events** were observed in the chloroquine group. Patients treated with half dose experienced lower rate of adverse events than with full dose.
- **No beneficial effect** of chloroquine in the length of hospital stay and the duration of oxygen support.
- Unprecedently, 3 cases of so called “re-positive” patients observed in the chloroquine group.

**Limitations:** observational study; dramatic improvement in the primary outcome in chloroquine could be due to the later treatment initiation since symptom onset; relatively young study population with few patients with severe symptoms that requires ventilation.
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<tr>
<td><strong>Lancet HIV</strong></td>
<td>Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort</td>
<td>Vizcarra P et al Spain <a href="#">gotopaper</a></td>
<td>Clinic</td>
<td>Observational &amp; prospective study: 51 HIV-infected COVID-19+ &amp; 1288 HIV-infected without 1 center in Madrid Mean age of COVID-19= 53.3y (SD:9.5) – 84% of men No difference for age and CD4 cell counts 63% with COVID-19 had at least one comorbidity Clinical presentations similar than in general population 12% critically ill and 4% died Covid-19 vs without COVID-19: - 73% vs 32% received tenofovir before COVID-19 diagnosis (p=0.0036) - 22% vs 14% had previous protease inhibitor (p=0.578) RT-PCR remained positive after a median of 40 days in 6 patients → HIV-infected patients should receive the same treatment to the general population</td>
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<td><strong>Lancet HIV</strong></td>
<td>Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study</td>
<td>Kuderer NM et al USA <a href="#">gotopaper</a></td>
<td>Clinic</td>
<td>Cohort study from the USA, Canada &amp; Spain from the COVID-19 &amp; cancer consortium (CCC19) Patients with active or previous malignancy &amp; SARS-CoV-2 infection: 928 patients included Malignancy: breast cancer (21%) – prostate (16%) – gastrointestinal (12%) – thoracic (10%) ... Status: active cancer (43%) – remission (45%) – anticancer treatment (39%) 13% had died Median age: 66 y IQR [57 – 76] – 50% were male Independent factor associated with increased 30-day mortality: - Increased age per 10 years OR: 1.84 [1.53 – 2.21] - Male OR: 1.63 [1.07 – 2.28] - Former smoker vs never OR: 1.60 [1.03 – 2.47] - Two comorbidities vs none OR: 4.50 [1.33 – 15.28] - Active cancer OR: 5.2 [2.77 – 9.77] - Receipt azithro+hydroxy vs neither OR: 2.93 [1.79 – 4.79] → confounding by indication not excluded Obesity, cancer type, ethnicity, type of anticancer therapy, recent surgery → not associated Limits: regional variations in the primary and secondary outcomes → Hight mortality among patients with cancer + COVID-19 → longer follow-up is needed</td>
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<td>The Lancet ID</td>
<td>Implication of SARS-CoV-2 evolution in the sensitivity of RT-qPCR diagnostic assays</td>
<td>Sampaio Osorio and Correia-Neves, Portugal <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>Reports suggest the virus might be evolving → redesign of the oligonucleotide sequences in use in RT-qPCR assays to circumvent potential primer–sample mismatches? Analysis of all high-coverage SARS-CoV-2 genome sequences (1825 in total) deposited in the Global Initiative on Sharing All Influenza Data (GISAID) database nucleotide diversity (π) WAS CALCULATED in the binding region of each oligonucleotide. → 79% (26 of 33) of the primer binding sites used in the RT-qPCR assays were mutated in at least one genome → at least one of the previously designed primers is now likely to be ineffective at detecting up to 14% of the virus variants in circulation → Oligonucleotide optimisation will be facilitated by global sharing of SARS-CoV-2 genomes and the frequently updated reports on sequence analysis that are available on the GISAID website.</td>
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<td>BMJ 28MAY2020</td>
<td>Kawasaki-like multistystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study</td>
<td>Toubiana J et al France gotopaper</td>
<td>Clinic</td>
<td>21 children in a hospital in Paris: median age: 7,9y [3,7 – 16,6] – 43% male 9 had a recent history of a viral like symptoms – 10 reported a recent contact Children of African ancestry were overrepresented (57%) Symptoms: - 57% presented with Kawasaki disease shock syndrome - 76% presented with myocarditis - 100% gastrointestinal symptoms during the early stage Biology: - High level of inflammatory markers (PCT, CRP, IL-6) - 81% had lymphopenia - 95% had elevated D-dimer (&gt;500 µg/L) - 90% recent SARS-CoV-2 infection (PCR or IgG antibody) Treatment: - All received intravenous Ig - 48% received also corticosteroid Outcomes: - 81% required intensive care - 24% had moderate coronary artery dilations - No death – all discharged home after 8 days of hospital stay → high proportion of children with KD shock syndrome – differ from classic KD → temporal association between the covid-19 pandemic &amp; results of test for SARS-CoV-2 in children with Kawasaki-like disease suggest a causal link → further study is needed</td>
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<td>BMJ 27MAY2020</td>
<td>Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study</td>
<td>Knight M et al UK gotopaper</td>
<td>Clinic</td>
<td>National cohort of pregnant women hospitalized with SARS-CoV-2 427 women Estimated incidence: 4,9 per 1000 maternities [4,5 – 5,4] Comorbidities: - 69% were obese or overweight - 34% had co-existence comorbidities: asthma, hypertension, diabetes, cardiac disease Symptoms: - Have symptom at median of 34 completely weeks' - Most have symptom on the third trimester: fever – cough – breathlessness ... Outcomes: - 62% women admitted gave birth or had a pregnancy loss - 15% women were given corticosteroids for fetal lung maturation - 196 women gave birth at term and 66 preterm 265 infants - 41 needed respiratory support - 5 women died Neonatal: - 5 babies died: 3 stillborn &amp; 2 neonatal period - 12 were positive for SARS-CoV-2 which 6 within the 12 hours → no death → Most women had good outcome → transmission to infant was uncommon</td>
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<td>Gene Reports 2020</td>
<td>COVID-19 target: A specific target for novel coronavirus detection</td>
<td>Kakhki, Reza Kamali et al. Iran gotopaper</td>
<td>Diagnostic</td>
<td>The diagnosis and differentiation of this virus from other types of coronavirus is essential to control of the disease. The analysis of genomics data plays a vital role in introducing a stronger target and consequently provides better results in laboratory examinations. The modified comparative genomics approach helps us to find novel specific targets by comparing two or more sequences on the nucleotide collection database. Unlike previous reported genes (RdRP, E and N genes), ORF8 is entirely specific to the novel coronavirus (COVID-19) and has no cross-reactivity with other kinds of coronavirus. CI*: ORF8 gene can be used as an additional confirmatory assay. Limitations: this study was conducted bioinformatically, and laboratory examinations are needed to confirm ORF8 gene as a potential target using RT-PCR, Real time PCR, or Line probe assay.</td>
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<td>Critical care medicine 27MAY2020</td>
<td>Routine Venous Thromboembolism Prophylaxis May Be Inadequate in the Hypercoagulable State of Severe Coronavirus Disease 2019</td>
<td>Maatman, Thomas K. et al. USA gotopaper</td>
<td>Therapeutic/ Clinic</td>
<td>Observational multicenter study, enrolled 240 consecutive patients among whom 109 critically ill COVID-19 patients admitted to the ICU were included in the analysis. All patients received routine subcutaneous chemical venous thromboembolism prophylaxis. Primary outcome: frequency of venous thromboembolism (VTE) and the degree of inflammatory and coagulation marker elevation associated with venous thromboembolism development. - VTE was diagnosed in 31 patients (28%) 8 ± 7 days after hospital admission, including two patients diagnosed with venous thromboembolism at presentation to the hospital. - Elevated admission D-dimer and peak D-dimer were associated with VTE development (p &lt; 0.05). - D-dimer greater than 2,600 ng/ml predicted VTE with an area under the receiver operating characteristic curve of 0.760 (95% CI, 0.661-0.858; p &lt; 0.0001), sensitivity of 89.7%, and specificity of 59.5%. - Twelve patients (11%) had thromboelastography performed and 58% of these patients had a hypercoagulable study. The calculated coagulation index was hypercoagulable in 50% of patients with thromboelastography. - SARS-CoV-2 infection results in systemic hypercoagulability resulting in VTE. Although current data on outcomes in patients receiving therapeutic anticoagulation in COVID-19 are lacking, it is apparent that routine chemical VTE prophylaxis may be inadequate in preventing thrombotic complications in severe COVID-19. Limitations: Although a relatively large series, it is an observational study; retrospective study; lack of comparator group of ICU patients without COVID-19 in which to compare VTE frequency; degree of viremia not evaluated as a risk factor for VTE.</td>
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<td>NEJM 27MAY2020</td>
<td>Remdesivir for 5 or 10 Days in Patients with Severe Covid-19</td>
<td>Jason D. Goldman et al. gotopaper</td>
<td>Therapeutic</td>
<td>Open-label, randomized, multicenter trial evaluating the efficacy and safety of treatment with remdesivir for 5 or 10 days in 397 patients with severe Covid-19 disease. The primary end point was clinical status on day 14, assessed on a 7-point ordinal scale. =&gt; No significant difference in efficacy between 5-day and 10-day courses of remdesivir. After adjustment for baseline imbalances in disease severity, outcomes were similar as measured by a number of end points: clinical status at day 14, time to clinical improvement, recovery, and death from any cause. Similar percentages of patients experiencing adverse events. Results cannot be extrapolated to critically ill patients receiving mechanical ventilation; further evaluation of this subgroup and of other high-risk groups is needed to determine the shortest effective duration of therapy. Limits: lack of a randomized placebo control group (magnitude of benefit not determined); open-label design.</td>
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**Reducing transmission of SARS-CoV-2**

Prather et al., USA-China

Public Health/Epidemiology

**Key facts**

- Traditional respiratory disease control measures: designed to reduce transmission by droplets produced in the sneezes and coughs of infected individuals. However, a large proportion of the spread: through *airborne transmission of aerosols* produced by asymptomatic individuals during breathing and speaking. Aerosols can accumulate, remain infectious in indoor air for hours, and be easily inhaled deep into the lungs. Contact (direct or indirect) is also a major source of contamination.

- Respiratory droplet size has been shown to affect the severity of disease
- “Silent shedders” (asymptomatic / pre-symptomatic) could be critical drivers. In China, undiagnosed cases, presumably asymptomatic, may be responsible for up to 79% of infections.
- Many countries have not yet acknowledged airborne transmission as a possible pathway

Recommendations for social distancing of 6 ft are based on studies of respiratory droplets carried out in the 1930s, but on large droplets (no technology for submicron aerosols). Intense coughs and sneezes that propel larger droplets more than 20 ft can also create thousands of aerosols that can travel even further (like a cigarette smoke). "6 ft WHO recommendation is likely not enough."

- Viruses can attach to other particles such as dust and pollution, which can modify the aerodynamic characteristics and increase dispersion

Aerosol transmission of viruses must be acknowledged as a key factor leading to the spread of infectious respiratory diseases. Evidence suggests that SARS-CoV-2 is silently spreading in aerosols exhaled by highly contagious individuals with no symptoms.

- It is essential that control measures be introduced to reduce aerosol transmission (face masks +++)

**Dysregulation of type I interferon responses in COVID-19**

Dhiraj Acharya et al, USA

Immuno

**Key facts**

How imbalanced interferon responses may contribute to the pathology of COVID-19:
- The lung injury in patients with severe COVID-19 underlines a possible failure to activate immuno-suppressive mechanisms in a timely manner. One suggestion is that the deficient or dysregulated IFN responses elicited by SARS-CoV-2 infection may influence the generation of regulatory T cells during the recovery phase of COVID-19.
- The use of IFNs as a treatment for COVID-19 remains controversial, particularly regarding the timing of administration in mice model and in human.
- Since ACE2 has been identified as an ISG in human airway epithelial cells. This finding raises the question of whether prophylactic or therapeutic IFN administration enhance the entry and replication of SARS-CoV-2 in target cells during disease progression.

**Conclusion**: a deeper understanding of the spatiotemporal kinetics of IFN responses during clinical SARS-CoV-2 infections is warranted to inform IFN-related therapeutics and vaccine design.
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| Cell Death Discovery 26MAY2020 | **SARS-CoV-2 infection serology: a useful tool to overcome lockdown?** | Nuccetelli, M. et al, Italy [goto paper](#) | Diagnostic | **Aim:** to compare and to evaluate different serological assays analytical performances (two different immunochromatographic cards, an immunofluorescence chromatographic card, and a chemiluminescence-automated immunoassay) on 43 positive samples with RT-qPCR-confirmed SARS-CoV-2 infection and 40 negative control subjects.  

→ excellent IgG/IgM specificities for all the immunocromatographic card tests (100% IgG and 100% IgM) and for the chemiluminescence-automated assay (100% IgG and 94% IgM);  

→ IgG/IgM sensitivities are moderately lower for all methods (94% and 84% for IgG and IgM, respectively), probably due to the assay viral antigen’s nature and/or to the detection time of nasopharyngeal swab RT-qPCR, with respect to symptoms onset. |
| Clinical Infectious Diseases 25MAY2020 | **Characterization of an asymptomatic cohort of SARS-COV-2 infected individuals outside of Wuhan, China** | Wang Y et al China [goto paper](#) | Clinic | **Epidemiologic and clinical characteristics of asymptomatic SARS-CoV-2 infections**  

279 hospitalized SARS-CoV-2+ contacts of COVID-19 patients **63 asymptomatic** included  

Mean time to diagnosis after contact: 16 days  
Mean age: 39.3 - 87.3% had no comorbidities  
Laboratory findings: quasi normal for all  

2 groups: abnormal chest CT findings (29) & normal chest CT findings (34)  
- Patient with abnormal findings were older (p<0.05)  
- Time from exposure to illness shorter in patient with abnormal CT (p>0.05)  

**Outcomes:**  
- 9 transmitted the virus to others with and without abnormal chest CT  
- No one died  

→ asymptomatic infections play a large role in transmission  
→ impact on treatment of symptomatic cases on transmission? |

- Establishment of a medical organisation led by a central crisis medical director and supported by medical directors in each hospital  
- Allocation of human resources to recruit and train specialised staff from a single platform  
- Centralised logistics to adjust to shortages the equipment and consumables daily supply  
- Recruitment of students of various medical branches to support as paramedics, research assistants, operators of a telemedicine platform.  
- Regional centralised ICU bed-allocation system  
- Regularly updated practical guidelines for all hospitals  
- Development of a common research strategy prioritising patient cohorts, biobanking, clinical trial  
- Large scale initiatives: equipment 3D printing, Covidom telemedicine platfor  
- Setup of a region-wide patient-tracing programme |
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| Nature Climate Change 23MAY2020 | Temporary reduction in daily global CO2 emissions during the COVID-19 forced confinement | Le Quéré et al. UK, gotopaper | SHS/SciPo | > Emissions of carbon dioxide rise by about 1% per year over the previous decade  
> COVID-19 imposed confinement leads to drastic changes in energy use, with expected impacts on CO2 emissions. However CO2 emissions are reported as annual values and there is no available real time data  
> An alternative approach using a combination of energy, activity and policy data was used to estimate changes in CO2 daily emissions during the confinement is proposed (69 countries, 50 US states and 30 Chinese provinces; 85% of global population; 87% of global emissions) |
| Biosensors and Bioelectronics 23MAY2020 | Ultra-sensitive and high-throughput CRISPR-Powered COVID-19 diagnosis | Huang, Zhen and al. USA gotopaper | Diagnostic | A rapid, sensitive SARS-CoV-2 diagnostic assay capable of high-throughput operation that can preferably utilize existing equipment to facilitate broad, large-scale screening efforts.  
The developed assay utilizes a custom CRISPR Cas12a/gRNA complex and a fluorescent probe to amplify target amplicons produced by standard RT-PCR or isothermal recombinase polymerase amplification (RPA), to allow sensitive detection at sites not equipped with real-time PCR systems required for qPCR diagnostics.  
The results obtained on nasal swab samples of individuals with suspected COVID-19 cases were comparable to paired results from a CDC-approved qPCR assay performed in a state testing lab, and superior to those produced by same assay in a clinical lab, where the qPCR assay exhibited multiple invalid or inconclusive results. It also demonstrated greater analytical sensitivity and more robust diagnostic performance than other recently reported CRISPR-based assays. |
| BMJ 22MAY2020 | Features of 20 133 UK patients in hospital with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study | Docherty, AB. Et al. UK gotopaper | Clinic | Aim: To characterise the clinical features of 20 133 hospital patients with Covid-19 enrolled in the ISARIC WHO CCP-UK prospective cohort study, and to explore risk factors associated with admission to critical care and mortality in hospital. Patient follow-up time was of two weeks minimum.  
Median age: 73 years (interquartile range (IR) 58-82, range 0-104). 60% of patients were men, 40% women. Median duration of symptoms before admission was 4 days (IR 1-8).  
Comorbidities: chronic cardiac disease (31%), uncomplicated diabetes (21%), non-asthmatic chronic pulmonary disease (18%), chronic kidney disease (16%); 23% had no reported major comorbidity.  
41% of patients were discharged alive, 26% died, 34% continued receiving care as of reporting date. 17% (3001/18 183) required admission to high dependency or ICU; of these, 28% were discharged alive, 32% died, and 41% continued to receive care. Of those receiving mechanical ventilation (1658), 17% were discharged alive, 37% died, and 46% remained in hospital. Increasing age, male sex, and chronic comorbidities were associated with higher mortality in hospital. |
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<td>Circulation 22MAY2020</td>
<td>Cardiovascular Toxicities Associated with Hydroxychloroquine and Azithromycin: An Analysis of the World Health Organization Pharmacovigilance Database</td>
<td>Nguyen, Lee S. et al. France/USA gotopaper</td>
<td>Therapeutic</td>
<td>Observational, retrospective study, that used VigiBase®, the WHO pharmacovigilance database encompassing over 21 million reports from over 130 countries, to compare CV-ADR reporting in patients who received hydroxychloroquine, azithromycin, or their combination with cardiovascular adverse-drug-reactions (CV-ADRs) reported with all other drugs in the full database. Extraction of 76,822 ADR cases associated with hydroxychloroquine alone, 89,692 with azithromycin alone, and 607 with the combination of both drugs. The cases were retrieved from 21,275,867 total ADR reports in VigiBase®. The lower end of the IC’s 95% credibility interval is IC025. It is considered significant when above 0. - Significant greater reporting of prolonged-QT (LQT) and/or ventricular tachycardia including Torsades-de-Pointes (TdP/VT) for each drug individually in suspected cases (IC025=1.67 for azithromycin and IC025=1.04 for hydroxychloroquine). - Hydroxychloroquine was also associated with conduction disorders (atrioventricular and bundle branch blocks) (IC025=1.04) and heart failure (HF, IC025=0.06). - Azithromycin monotherapy was associated with a greater reporting of LQT and/or TdP/VT than hydroxychloroquine monotherapy. The combination of azithromycin and hydroxychloroquine was associated with a greater reporting of LQT and/or TdP/VT than either drug in monotherapy. - The proportion that resulted in death for TdP/VT cases was 8.4% with hydroxychloroquine and 20.2% with azithromycin versus 0% and 5.4% for LQT without TdP/VT with hydroxychloroquine and azithromycin, respectively (p&lt;0.001 for both). - Corresponding death rate was 20.7% for HF associated with hydroxychloroquine. Dose of hydroxychloroquine was higher in HF compared to LQT and/or TdP/VT cases. Main limitation: without data on numbers exposed in Vigibase, this work cannot assess the incidence or risk for QT prolongation with these drugs.</td>
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<td>Annals of Translational Medicine MAY2020</td>
<td>Preliminary study to identify severe from moderate cases of COVID-19 using combined hematology parameters</td>
<td>Wang, Changzheng et al. China gotopaper</td>
<td>Diagnostic</td>
<td>The aim of this study was to investigate the characteristics and rules of hematology changes in patients with COVID-19, and to explore the possibility differentiating moderate and severe patients using conventional hematology parameters or combined parameters. As the disease progressed, white blood cell count (WBC), neutrophil count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), red blood cell distribution width-coefficient of variation (RDW-CV), and red cell volume distribution width-standard deviation (RDW-SD) parameters in the severe group were significantly higher than those in the moderate group. CI*: the combined NLR and RDW-SD parameter is the best hematology index. It may help clinicians to predict the severity of COVID-19 patients and can be used as a useful indicator to help prevent and control the epidemic.</td>
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<td><strong>Gastroenterology 22MAY2020</strong></td>
<td><strong>Famotidine Use is Associated with Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study</strong></td>
<td>Freedberg, Daniel E. et al. USA <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Retrospective cohort study of 1,620 hospitalized patients tested positive for SARS-CoV-2 within 72 hours following admission including 84 patients who received famotidine within 24 hours of hospital admission. <strong>Primary outcome</strong> was a composite of death or endotracheal intubation. Although Famotidine has not previously been studied in patients for antiviral effects, an untargeted computer modelling analysis identified famotidine as one of the highest-ranked matches for drugs predicted to bind 3CLpro, a SARS-CoV-2 protease which generates non-structure proteins critical to viral replication. 340 (21%) patients met the composite study outcome. Famotidine use was significantly associated with a reduced risk of clinical deterioration leading to intubation or death. A randomized controlled trial is currently underway to determine whether famotidine can improve clinical outcomes in hospitalized COVID-19 patients. <strong>Limitations</strong>: observational; no samples were gathered, and mechanism cannot be directly assessed; single center study.</td>
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<td><strong>Clinical infectious diseases 22MAY2020</strong></td>
<td><strong>Association of renin-angiotensin-aldosterone system inhibitors with COVID-19-related outcomes in Korea: a nationwide population-based cohort study</strong></td>
<td>Jung, Sun-Young et al. Korea <a href="#">gotopaper</a></td>
<td>Therapeutic/ Clinic</td>
<td>Nationwide population-based cohort study in Korea comparing the clinical outcomes of confirmed COVID-19 cases between RAAS inhibitor users and nonusers. The study revealed a significantly higher mortality rate among patients with COVID-19 who were using RAAS inhibitors, relative to patients who were not receiving RAAS inhibitors. However, RAAS inhibitor users were older, had more comorbidities, and were more likely to receive in-hospital treatments. The elevated risk of mortality among RAAS inhibitor users disappeared after adjusting for these confounding factors. This study in an Asian population is clinically relevant, given that the East Asian populations have higher ACE2 expression in tissues than other populations under the similar conditions. <strong>Limitations</strong>: accuracy of diagnostic codes may be limited; retrospective observational design.</td>
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<td><strong>Clinical infectious diseases 22MAY2020</strong></td>
<td><strong>Thymosin alpha 1 (Talpha1) reduces the mortality of severe COVID-19 by restoration of lymphocytopenia and reversion of exhausted T cells</strong></td>
<td>Liu, Yueping et al. China <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Retrospective cohort study to evaluate the clinical outcomes of severe or critical COVID 19 hospitalized patients receiving Thymosin alpha 1 (Ta1) supplement. A total of 76 patients were enrolled (36 in the treatment group and 40 in the non treatment group) Compared with untreated group, Ta1 treatment significantly reduces mortality of severe COVID-19 patients (11% vs. 30%, p=0.044). Ta1 timely enhances blood T cell numbers in COVID-19 patients with severe lymphocytopenia. Under such conditions, Ta1 also successfully restores CD8+ and CD4+ T cell numbers in aged patients. Meanwhile, Ta1 reduces PD-1 and Tim-3 expression on CD8+ T cells from severe COVID-19 patients in comparison with untreated cases. <strong>Limitations</strong>: issue with the normalization of TREC levels among individuals; retrospective study and small sample size; mortality as primary clinical outcome and not clinical improvement.</td>
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<td>NEJM 22MAY2020</td>
<td>Remdesivir for the Treatment of Covid-19 — Preliminary Report</td>
<td>Beigel, John H. et al., USA</td>
<td>Therapeutic</td>
<td>Double-blind, randomized, placebo-controlled trial of intravenous remdesivir in 1063 adults hospitalized with Covid-19 with evidence of lower respiratory tract involvement in 60 trial sites in 10 countries. The primary outcome was the time to recovery, defined by either discharge from the hospital or hospitalization for infection-control purposes only. Early unblinding of the results recommended by the DSMB based on findings from an analysis that showed shortened time to recovery in the remdesivir group. Preliminary results from the 1059 patients (538 assigned to remdesivir and 521 to placebo) suggest that a 10-day course of remdesivir was superior to placebo in the treatment of hospitalized patients with Covid-19. - This benefit was seen in the number of days to recovery (median, 11 days, as compared with 15; rate ratio for recovery, 1.32 [95% CI, 1.12 to 1.55]) and in recovery according to the ordinal scale score at day 15 (odds ratio, 1.50; 95% CI, 1.18 to 1.91). - Mortality was numerically lower in the remdesivir group than in the placebo group, but the difference was not significant (hazard ratio for death, 0.70; 95% CI, 0.47 to 1.04; 1059 patients). - Incidence of adverse events was not found to be significantly different between the remdesivir group and the placebo group.</td>
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<td>The Lancet 22MAY2020</td>
<td>Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis</td>
<td>Mandeep R Mehra et al., USA</td>
<td>Therapeutic</td>
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<td>mBio 22MAY2020</td>
<td>Antiviral Efficacies of FDA-Approved Drugs against SARS-CoV-2 Infection in Ferrets</td>
<td>Park, Su-Jin et al. Korea</td>
<td>Therapeutic</td>
<td>FDA-approved drugs lopinavir-ritonavir, hydroxychloroquine sulfate, and emtricitabine-tenofovir were tested against SARS-CoV-2 infection in a highly susceptible ferret infection model. While most of the drug treatments marginally reduced clinical symptoms, they did not reduce virus titers, with the exception of emtricitabine-tenofovir treatment, which led to diminished virus titers in nasal washes at 8 dpi. Further, the azathioprine-treated immunosuppressed ferrets showed delayed virus clearance and low SN titers, resulting in a prolonged infection.</td>
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| BMJ 22MAY2020    | Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study | Pettrilli CM, et al., USA [getpaper](#) | Clinic | **Aim:** To describe outcomes, and clinical and laboratory characteristic associated with severity of illness of 5279 patients admitted with Covid-19 in NYC/Long Island (US).  
→ 48.2% of people tested (5566/11544) were positive for SARS-CoV2; of the 5279 patients included, 51.9% were admitted to hospital. Of these, 69.5% were discharged without hospice care, 24.3% were discharged to hospice care or died. Of 647 (23.6% of hospitalised) patients requiring mechanical ventilation, 60.4% died and 26.2% were extubated or discharged.  
→ Risk for hospital admission was associated with age (odd ratio >2 for age groups >44 years, 37.9 (95% CI[26.1 to 56.0]) for >75 years), heart failure (4.4, 2.6 to 8.0), male sex (2.8, 2.4 to 3.2), chronic kidney disease (2.6, 1.9 to 3.6), increase in body mass index (BMI) (eg, for BMI >40: 2.5, 1.8 to 3.4).  
→ Risk for critical illness besides aged was associated with heart failure (1.9, 1.4 to 2.5), BMI >40 (1.5, 1.0 to 2.2), and male sex (1.5, 1.3 to 1.8). Admission oxygen saturation of <88% (3.7, 2.8 to 4.8), troponin level >1 (4.8, 2.1 to 10.9), C reactive protein level >200 (5.1, 2.8 to 9.2), and D-dimer level >2500 (3.9, 2.6 to 6.0) were more strongly associated with critical illness than age or comorbidities.  
→ Risk of critical illness decreased significantly over the study period, and similar associations were found for mortality alone, potentially suggesting improvement in care. |
| The Lancet 22MAY2020 | Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial | Zhu FC et al. China, [getpaper](#) | Vaccine | Phase 1 vaccine trial using the recombinant non-replicating adenovirus 5 type vectored COVID 19 vaccine expressing the S protein (open label; non randomised; dose escalation- 5x10^10/1x10^11/5x10^11 viral particles). NCT04313127 108 patients recruited (18-60 years; 51% male-49% female)  
**Endpoint for safety:** 7D post vaccination/recording of AE until 28D post-vaccination  
**Humoral immunogenicity endpoints:** The specific ELISA antibody titres to RBD and S protein, and the neutralising antibody amounts against live SARS-CoV-2  
**Positive antibody response (seroconversion):** at least a four-fold increase in post-vaccination titre from baseline  
**SAE and Safety**  
> >83%/83%/75% (related to increasing dose, non-significant difference) of patients had at least an AE of moderate/mild severity within the first 7 days (pain, fever, fatigue, headache or muscle pain)  
> no serious AE were recorded at 28d post vaccination  
**Protection**  
Elisa antibodies and neutralizing antibodies increased at D14 and peaked at D28 post-vaccination. Specific T cells response peaked at D14 post-vaccination  
**Comments**  
> Older age participants could have a negative effect on the vaccine-elicited responses to SARS-CoV-2  
> ADE not evaluated (because of low number of participants)  
> Pre-existing Ad5 immunity might also have a negative effect on the persistence of the vaccine-elicited immune responses.  
**Issues to evaluate in Phase 2** |
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<tr>
<td>Neurology 22MAY2020</td>
<td>Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy</td>
<td>Benussi A et al. Italy gotopaper</td>
<td>Clinic</td>
<td>Outcomes of patients admitted with neurological disorders with and without COVID-19 173 patients included: 56 COVID-19 pos &amp; 117 COVID-19 neg No difference for comorbidities Patients with COVID-19: - Older: 77.0 versus 70.1 years (p=0.006) - More cerebrovascular disorders: 76.8% versus 58.1% (p=0.035) - Higher qSOFA: 0.9 versus 0.5 (p=0.006) - Higher incidence of delirium: 26.8% versus 7.7% (p=0.003) - Higher in-hospital mortality: 75.5% versus 4.3% (p&lt;0.001) - Wider use of high flow oxygenation: 76.8% versus 9.4% (p&lt;0.001) - Prolonged length of stay Potential risk factor of poor prognosis: high qSOFA score – thrombocytopenia – increase lactate deshydrogenase level</td>
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<td>Clinical infectious diseases 22MAY2020</td>
<td>Predicting infectious SARS-CoV-2 from diagnostic samples</td>
<td>Bullard, Jared and al. Canada gotopaper</td>
<td>Diagnostic</td>
<td>RT-PCR detects RNA, not infectious virus, thus its ability to determine duration of infectivity of patients is limited. Objective: to determine the relationship between E gene SARS-CoV-2 RT-PCR cycle threshold (Ct) values from respiratory samples, symptom onset to test (STT) and infectivity in cell culture. =&gt; SARS-CoV-2 Vero cell infectivity was only observed for RT-PCR Ct &lt;24 and STT &lt; 8 days. Infectivity of patients with Ct &gt;24 and duration of symptoms &gt;8 days may be low. CI*: this information can inform public health policy and guide clinical, infection control and occupational health decisions. However, further studies of larger size are needed.</td>
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<td>Analytical chemistry 22MAY2020</td>
<td>A novel one-step single-tube nested quantitative Real-Time PCR assay for highly sensitive detection of SARS-CoV-2</td>
<td>Wang, Ji and al. China gotopaper</td>
<td>Diagnostic</td>
<td>qRT-PCR results could be false-negative due to the inadequate sensitivity of qRT-PCR. In this study, we have developed and evaluated a novel one-step single-tube nested quantitative Real-Time PCR (OSN-qRT-PCR) assay for highly sensitive detection of SARS-CoV-2 targeting the ORF1aband N genes. The sensitivity of the OSN-qRT-PCR assay was 1 copy/reaction and 10-fold higher than that of commercial qRT-PCR kit (10 copies/reaction). CI* : Compared to the qRT-PCR kit, OSN-qRT-PCR assay revealed higher sensitivity and specificity hence better suited to clinical applications for the detection of SARS-CoV-2 in patients with low viral load.</td>
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| **JAMA** 21MAY2020 | Postmortem Examination of Patients With COVID-19 | Schaller, Tina, et al. Germany gotopaper | Clinic | Serial postmortem examinations, 10 patients with proven SARS-CoV-2 infection who died at University Medical Center Augsburg. Median age: 79; range: 64-90 yrs, 7 male; all SARS-CoV-2 +ve by nasopharyngeal swab at hospital admission. Admission median till death: 7.5 days (range, 1-26 days), median of 4 known preexisting comorbidities.  
- At autopsy, SARS-CoV-2 detectable in respiratory tracts of all patients, and PCR +ve in pleural effusion but not in all CSF samples. |
| Nature 21MAY2020 | Structure of replicating SARS-CoV-2 polymerase | Hillen, Hauke S. et al. Germany gotopaper | Structural biology | Cryo-EM structure of SARS-CoV-2 RdRp in active form, mimicking the replicating enzyme:  
- Active site cleft of nsp12 binds first turn of RNA and mediates RdRp activity with conserved residues.  
- Two copies of nsp8 bind to opposite sides of the cleft and position the second turn of RNA.  
- Long helical extensions in nsp8 protrude along exiting RNA, forming +vely charged ‘sliding poles’.  
-> sliding poles can account for known processivity of RdRp required for replicating the long coronavirus genome.  
- Previous study suggested remdesivir functions as ‘immediate’ RNA chain terminator, while this study showed that several more nucleotides can be added to RNA following remdesivir incorporation, leading to ‘delayed’ termination.  
-> mechanism that could explain how remdesivir escapes removal from the RNA 3’-end by the viral exonuclease nsp14. |
| **Cell** 21MAY2020 | Pathogenesis of SARS-CoV-2 in transgenic mice expressing human angiotensin-converting enzyme 2 | Jiang, Ren-Di. et al. China-USA gotopaper | Animal model | Developed a SARS-CoV-2 hACE2 transgenic mouse (HFH4-hACE2 in C3B6 mice) infection model, generating:  
- Typical interstitial pneumonia and pathology, similar COVID-19 patients.  
- Viral quantification: lungs are the major site of infection (viral RNA also found in eye, heart, and brain in some mice).  
- Full-genome sequences of virus identical to SARS-CoV-2 isolated from the infected lung and brain tissues.  
- Pre-exposure to SARS-CoV-2 could protect mice from severe pneumonia.  
-> The hACE2 mouse would be a valuable tool for testing potential vaccines and therapeutics. |
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<td>Nature 20MAY2020</td>
<td>Viral and host factors related to the clinical outcome of COVID-19</td>
<td>Zhang, Xiaonan, et al. China</td>
<td>Clinic</td>
<td>326 confirmed COVID-19 cases in Shanghai. (SARS-CoV-2 genomic sequences assembled from 112 samples + sequences in the Global Initiative on Sharing All Influenza Data (GISAID)). Observations: - stable evolution and 2 major lineages suggested with differential exposure history during the early phase of outbreak in Wuhan (similar virulence and clinical outcomes for both lineages). - Lymphocytopenia predictive of disease progression (especially reduced CD4+ and CD8+ T cell counts upon admission). - High IL-6 and IL-8 levels during treatment in patients with severe/critical disease, which correlated with decreased lymphocyte count. - Determinants of disease severity seemed to stem mostly from host factors (age, lymphocytopenia and associated cytokine storm), whereas viral genetic variation did not significantly affect outcomes.</td>
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<td>Eur. Respir. J. MAY2020</td>
<td>A Fully Automatic Deep Learning System for COVID-19 Diagnostic and Prognostic Analysis</td>
<td>Wang et al., China</td>
<td>Diagnostic</td>
<td>Retrospective collection of 5372 patients with computed tomography images from 7 cities or provinces. Steps: 1st: 4106 patients with computed tomography images were used to pre-train the DL system, making it learn lung features 2nd: 1266 patients from 6 cities or provinces were enrolled to train and externally validate the performance of the deep learning system - Deep learning system achieved good performance in identifying COVID-19 from other pneumonia (AUC=0.87 and 0.88) and viral pneumonia (AUC=0.86). - Succeeded to stratify patients into high-risk and low-risk groups whose hospital-stay time have significant difference (p=0.013 and 0.014) - Without human-assistance, the deep learning system automatically focused on abnormal areas that showed consistent characteristics with reported radiological findings</td>
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<td>Science 20MAY2020</td>
<td>SARS-CoV-2 infection protects against rechallenge in rhesus macaques</td>
<td>Chandrashekar A et al. USA</td>
<td>Vaccine</td>
<td>Infection of macaques with SARS-CoV-2 results in protective immunity against re-exposure? Methods: Infection of 9 rhesus macaques (6-12 years) with SARS-CoV-2 showing high viral loads in the upper and lower respiratory tract, humoral and cellular immune responses and pathologic evidence of viral pneumonia, re-challenged after virus clearance (D35 post initial infection), + 3 naive animals as positive controls in the rechallenge experiment Results: - After primary infection all 9 macaques developed binding antibody responses to S protein and NAb responses and cellular immune responses. - 5 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa compared with primary infection and infected naive animals - All animals developed anamnestic antibody responses following re-challenge→ protection mediated by immunologic control</td>
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<td>Cell 20MAY2020</td>
<td>Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals</td>
<td>Grifoni et al., USA</td>
<td>Immuno</td>
<td>Measuring immunity to SARS-CoV-2 is key for understanding COVID-19 and vaccine development - Epitope pools detect CD4+ and CD8+ T cells in 100% and 70% of convalescent COVID patients - T cell responses are focused not only on spike but also on M, N, and other ORFs - T cell reactivity to SARS-CoV-2 epitopes is also detected in non-exposed individuals</td>
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| The Lancet            | Individual quarantine versus active monitoring of contacts for the mitigation of COVID-19: a modelling study | Peak, C. et al, USA gotopaper | Public Health/Epidemi               | Aim: to estimate the comparative efficacy of individual quarantine and active monitoring of contacts to control SARS-CoV-2, fitting a model to the incubation period distribution (mean 5.2 days) and to two estimates of the serial interval distribution (4.8 and 7.5 days). Two feasibility settings: - high-feasibility (90% of contacts traced, half-day average delay in tracing and symptom recognition, 90% effective isolation) - low-feasibility (50% of contacts traced, 2-day average delay, 50% effective isolation).  
- Mean time of infectiousness onset before symptom onset: 0.77 days (shorter serial interval) and 0.51 days (longer serial interval).  
- Individual quarantine in high-feasibility settings (>75% of infected contacts individually quarantined), contains an outbreak of SARS-CoV-2 with a short serial interval 84% of the time. In low-feasibility setting; the outbreak continues to grow and so does the burden of the number of contacts traced for active monitoring or quarantine, particularly asymptomatic contacts. Conclusion: When resources are prioritised for scalable interventions such as physical distancing, active monitoring or individual quarantine of high-risk contacts, this can contribute synergistically to mitigation efforts. |
| Science               | DNA vaccine protection against SARS-CoV-2 in rhesus macaques          | Yu et al., USA gotopaper | Vaccine                             | Development of a series of DNA vaccine candidates expressing different forms of the SARS-CoV-2 Spike (S) protein and evaluated them in 35 rhesus macaques.  
- > humoral and cellular immune response with neutralizing antibody (titers = those found in convalescent humans and macaques).  
- > challenged with SARS-CoV-2: the vaccine encoding the full-length S protein resulted in >3.1 and >3.7 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa.  
- > Vaccine-elicited neutralizing antibody titers correlated with protective efficacy: suggests an immune correlate of protection. |
| JAMA                  | Nasal Gene Expression of Angiotensin-Converting Enzyme 2 in Children and Adults | Bunyavanich, Supinda, et al. USA gotopaper | Clinic                              | Nasal epithelium from 305 individuals aged 4-60, with or without asthma (Mount Sinai Health System, New York, during 2015-2018) collected using a cytology brush.  
ACE2 gene expression in nasal epithelium:  
- lowest in aged <10 yrs, and significantly higher in older children (10-17 yrs), young adults (18-24 yrs), and adults (≥25 yrs).  
- ACE2 gene expression and age was independent of sex and asthma.  
- > Lower ACE2 expression in children nasal epithelium relative to adults may help explain why COVID-19 is less prevalent in children. Limitation: study did not include individuals older than 60 years. |
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<th>Journal and date</th>
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<tr>
<td>NEJM 19MAY2020</td>
<td>Respecting disability rights – towards improved crisis standards of care</td>
<td>Mello M. et al, US gotopaper</td>
<td>HSS/Politic</td>
<td>Policymakers and hospitals can take key steps to honor commitments to antidiscrimination principles while appropriately stewarding scarce resources during a public health emergency.</td>
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<td>1- Do not use categorical exclusions. Patients must not be categorically excluded from access to treatment because of a disability or diagnosis. Consider not whether someone has a disability but patient’s prospects of benefiting from treatment.</td>
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<td>2- Do not use perceived quality of life = biases in how the public/physicians evaluate the quality of life of persons with disabilities.</td>
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<td>3- Use hospital survival and near-term prognosis but not long-term life expectancy. Predictions of long-term life expectancy are much more uncertain &amp; prone to bias than predictions of short-term survival + affected by social circumstances (poverty). Ignoring near-term prognosis can produce outcomes inconsistent with responsible stewardship of scarce resources.</td>
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<td>4- Designate triage officers as the decision-makers and train them to respect disability rights. Include disability rights advocates in policy development and dissemination = it will also help in avoiding inflammatory language and ensure public understanding for operationalization.</td>
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<tr>
<td>Clinical Infectious Diseases 19MAY2020</td>
<td>Early Short Course Corticosteroids in Hospitalized Patients with COVID-19</td>
<td>Fadel, Raef et al, USA gotopaper</td>
<td>Therapeutic</td>
<td>Multi-center quasi-experimental study of 213 adult patients with confirmed moderate to severe COVID, 81 (38%) and 132 (62%) in SOC and early short course corticosteroid (methylprednisolone) groups, respectively. Outcomes were evaluated with a primary composite endpoint of escalation of care from ward to ICU, new requirement for mechanical ventilation, and mortality.</td>
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<td>- The composite endpoint occurred at a significantly lower rate in the early corticosteroid group (34.9% vs. 54.3%, p=0.005). Treatment effect observed within each individual component of the composite endpoint.</td>
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<td>- Significant reduction in median hospital length of stay was also observed in the early corticosteroid group (8 vs. 5 days, p &lt; 0.001).</td>
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<td>- Multivariate regression analysis demonstrated an independent reduction in the composite endpoint at 14-days controlling for other factors (aOR: 0.41; 95% CI [0.22 – 0.77]).</td>
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<td>Conclusion: An early short course of methylprednisolone in patients with moderate to severe COVID-19 reduced escalation of care and improved clinical outcomes.</td>
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<td>Limitations: pragmatic quasi-experimental design was used and there are some differences in the baseline characteristics of the comparator groups; limited follow up period of 14 days.</td>
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<td><strong>J Infect Dis</strong> 19MAY2020</td>
<td>Influence of storage conditions on SARS-CoV-2 nucleic acid detection in throat swabs</td>
<td>Li, Lin and al. China <a href="#">gotopaper</a></td>
<td>Virology</td>
<td>For the detection of SARS-CoV-2 infection, samples often need to be shipped or inactivated before SARS-CoV-2 testing. In this study, we checked the influence of sample storage conditions on SARS-CoV-2 nucleic acid testing results, including sample inactivation time, storage temperature and the time. All of these conditions caused an increase in the Ct values of the nucleic acid tests and led to the misclassification of at least 10.2% of positive cases as negative or suspected. CL*: results highlight the importance of immediate testing of samples for SARS-CoV-2 nucleic acid and detection.</td>
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<td><strong>Lancet</strong> 19MAY2020</td>
<td>Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study</td>
<td>Cummings MJ et al USA <a href="#">gotopaper</a></td>
<td>Clinic</td>
<td>2 hospitals in NY – critically ill patient with COVID-19 – At least 28 days of observation 1150 adults admitted COVID-19 which 257 (22%) were critically ill (included) Median age: 62 years – 67% male – 82% at least one comorbidity (HTA, diabetes) 46% had obesity Treatment - 72% received hydroxychloroquine and 9% remdesivir - 26% received corticosteroid - 66% received vasopressor - 31% received RRT Outcomes: - 79% received IMV median of 18 days - 39% died (median of 9 days in the hospital) and 37% remained hospitalized Association with in hospital death (significantly) - Older age aHR: 1.31 [1.09 – 1.57] per 10 years increase - Chronic cardiac disease aHR: 1.76 [1.08 – 2.86] - Chronic pulmonary disease aHR: 2.94 [1.48 – 5.84] - Concentration of IL-6 aHR: 1.11 [1.02 – 1.20] per decile increase - Concentration of D-dimer aHR: 1.10 [1.01 – 1.19] per decile increase – high frequency of IMV &amp; in hospital mortality</td>
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<td><strong>Nature Medicine</strong> 19MAY2020</td>
<td>Artificial intelligence–enabled rapid diagnosis of patients with COVID-19</td>
<td>Mei et al., USA <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>Use of artificial intelligence (AI) algorithms to integrate chest CT findings with clinical symptoms, exposure history and laboratory testing to rapidly diagnose patients who are positive for COVID-19. - In a test set of 279 patients, the AI system achieved an area under the curve of 0.92 and had equal sensitivity as compared to a senior thoracic radiologist. - The AI system also improved the detection of patients who were positive for COVID-19 via RT–PCR who presented with normal CT scans, correctly identifying 17 of 25 (68%) patients, whereas radiologists classified all of these patients as COVID-19 negative When CT scans and associated clinical history are available, the proposed AI system can help to rapidly diagnose COVID-19 patients.</td>
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<td>Circulation 19MAY2020</td>
<td>Deep Vein Thrombosis in Hospitalized Patients with Coronavirus Disease 2019 (COVID-19) in Wuhan, China: Prevalence, Risk Factors, and Outcome</td>
<td>Zang L et al, China</td>
<td>Clinic</td>
<td>Investigation of deep vein thrombosis (DVT) in hospitalized patient with COVID-19. 143 patients from Jan 29 and Feb 29. <strong>Demographic</strong>: 51.7% man – median age= 63, 46.1% (66) lower extremity DVT= 23 proximal DVT and 43 distal DVT. <strong>DVT vs no DVT</strong>: - Older - Lower oxygenation index - Higher rate of cardiac injury - Increase death (23 vs 9, p=0.001). <strong>Multivariate analysis, DVT associated with</strong>: - CURB-65 score 3-5, OR: 6.12 - Padua prediction ≥ 4, OR: 4.01 - D-dimer &gt; 1 μg/ml OR: 5.81. <strong>Predicting DVT</strong>: CURB-65 score 3-5, Padua prediction score ≥ 4 + D-dimer &gt; 1 had Se 88% and Spe 61.4% → prevalence of DVT is high → importance of prophylaxis for venous thromboembolism (Padua prediction score ≥ 4).</td>
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<tr>
<td>Science 18MAY2020</td>
<td>Susceptible supply limits the role of climate in the early SARS-CoV-2 pandemic</td>
<td>Baker, Rachel E. et al., USA</td>
<td>Climate</td>
<td>Climate-dependent model to simulate SARS-CoV-2 pandemic, probing different scenarios based on known coronavirus biology. <strong>Results suggest</strong>: - While climate may play a role in details of the size and timescales of an endemic outbreak, population immunity is a much more fundamental driver of pandemic invasion dynamics. - Both tropical and temperate locations should prepare for severe outbreaks and summertime temperatures will not effectively limit spread of infection. - Endemic cycles will likely be tied to climate factors and seasonal peaks may vary with latitude.</td>
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<td>Cell 18MAY2020</td>
<td>Potent neutralizing antibodies against SARS-CoV-2 identified by high-throughput single-cell sequencing of convalescent patients’ B cells</td>
<td>Yunlong Cao et al., China</td>
<td>Immunology</td>
<td>Rapid and efficient identification of SARS-CoV-2 neutralizing antibodies achieved by high-throughput single-cell RNA and VDJ sequencing of antigen-binding B cells from 60 convalescent COVID-19 patients reveal over 8,500 antigen-binding B cell clonotypes expressing IgG1 antibodies. =&gt; among of which, 14 potent neutralizing mAbs were identified =&gt; one of them, BD-368-2, exhibited an IC50 of 1.2 ng/mL and 15 ng/mL against pseudotyped and authentic SARS-CoV-2. =&gt; in vivo experiments confirmed that BD-368-2 provide strong therapeutic efficacy and prophylactic protection against SARS-CoV-2, using the hACE2 transgenic mice model. <strong>Conclusion</strong>: The potent neutralizing antibodies we identified may provide an effective therapeutic and prophylactic solution. <strong>Limitation</strong>: deeper sequencing of the scRNA libraries is needed to further evaluate the effectiveness of removing exhausted memory B cells to improve the identification of neutralizing mAbs.</td>
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<td>Ann. Intern. Med. 18MAY2020</td>
<td>Tocilizumab for Hemophagocytic Syndrome in a Kidney Transplant Recipient With COVID-19</td>
<td>Faguer, Stanislas et al., France</td>
<td>Therapeutic</td>
<td>Case Report describing an immunocompromised patient with COVID-19 and a related hemophagocytic syndrome who was treated with tocilizumab. The cytokine storm and multiorgan failure rapidly reversed, and the patient made a speedy recovery. On hospital day 30, the patient was breathing spontaneously with protective tracheotomy, and rehabilitation is ongoing.</td>
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<td>Circulation 17MAY2020</td>
<td>Acute heart failure in multisystem inflammatory syndrome in children (MIS-C) in the context of global SARS-CoV-2 pandemic</td>
<td>Belhadjer S et al, France gotopaper</td>
<td>Clinic</td>
<td>A series of children admitted to PICU for cardiogenic shock + left ventricular dysfunction + severe inflammatory state (14 centers) 35 children – median age: 10 y [2 – 16] Comorbidities: 28% of the children which 17% were overweight Symptoms: Fever and asthenia (100%) / Gastrointestinal symptoms (83%) / Respiratory distress (65%) – rhinorrhea (43%) Left ventricular ejection at baseline &lt; 30 for 28% / 30 to 50 for 72% Laboratory: cytokine storm → high IL-6 and D-dimer (= macrophage activation) + elevation of CRP and PCT 88% were positive for SARS-CoV-2 (nasopharyngeal swabs or serology) Treatment: 94% Respiratory support: invasive (62%) – noninvasive (32%) / 28% ECMO / 80% inotropic support / 100% IV globuline / 1/3 received steroid therapy At discharge: 25/35 had left ventricular function restored - no death → SARS-COV-2 + severe inflammatory state in children → acute cardiac decompensation</td>
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<td>The Journal of Antimicrobial Chemotherapy 17MAY2020</td>
<td>COVID-19 infection also occurs in patients taking hydroxychloroquine</td>
<td>Lahouati, M et al. France gotopaper</td>
<td>Therapeutic</td>
<td>Report on two severe cases of COVID-19 in patients already using hydroxychloroquine for a long time to treat inflammatory disease. High plasma levels of hydroxychloroquine collected on admission in those cases confirm chronic exposure and adherence to hydroxychloroquine. These values are close to or higher than the EC50 described by Yao et al. not taking into account lung diffusion. Those potentially immunosuppressed patients do not represent the general population exposed to COVID-19. It cannot be excluded that chloroquine and hydroxychloroquine negatively impact the early inflammatory response to the virus and the risk of acquisition of infection owing to their anti-inflammatory activity. These observational data are not in favour of a universal protective effect of hydroxychloroquine, and clinicians should use it carefully, awaiting the results of clinical trials, particularly in the context of prevention.</td>
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<td>Water research 16MAY2020</td>
<td>SARS-CoV-2 RNA in wastewater anticipated COVID-19 occurrence in a low prevalence area</td>
<td>Randazzo et al, Spain <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Faecal shedding of SARS-CoV-2 RNA from COVID-19 patients has extensively been reported. We investigated the occurrence of SARS-CoV-2 RNA in six wastewater treatments plants serving the major municipalities within the Region of Murcia, Spain (low COVID-19 prevalence). -&gt; The estimated quantification of SARS-CoV-2 RNA titers in untreated wastewater waters of 5.4 ± 0.2 log10 genomic copies/L on average. -&gt; Two secondary water samples resulted positive (2/18) and all tertiary water samples tested as negative (0/12). SARS-CoV-2 RNA shedding in stools was present even before the first cases were reported by the authorities. This strategy could be implemented in environmental surveillance as an early indicator of the infection within a specific population.</td>
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<td>Developmental Cell 16MAY2020</td>
<td>Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract</td>
<td>Smith, Joan C. et al., USA <a href="#">gotopaper</a></td>
<td>Fundamental research</td>
<td>Cigarette smoke causes dose-dependent upregulation of ACE2 receptor in rodent and human lungs. Single-cell sequencing data: - ACE2 expressed in a subset of secretory cells in respiratory tract. - Chronic smoke exposure triggers expansion of this cell population and increased ACE2 expression. - Quitting smoking has convers effect (decreases this cell population and ACE2 levels). - ACE2 expression responsive to inflammatory signalling and upregulated by viral infections / interferon treatment. -&gt; May partially explain why smokers are particularly susceptible to severe SARS-CoV-2 infections -&gt; identifies ACE2 as interferon-stimulated gene in lung cells -&gt; possible positive-feedback loops increasing ACE2 levels and facilitating viral dissemination.</td>
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<td>J. Clin. Virol. 16MAY2020</td>
<td>A combined oropharyngeal/nares swab is a suitable alternative to nasopharyngeal swabs for the detection of SARS-CoV-2</td>
<td>LeBlanc, Jason J. and al., Canada <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>Given the global shortage of nasopharyngeal (NP) swabs typically used for respiratory virus detection, alternative collection methods were evaluated during the COVID-19 pandemic. This study showed that a combined oropharyngeal/nares swab is a suitable alternative to NP swabs for the detection of SARS-CoV-2, with sensitivities of 91.7% and 94.4%, respectively. Routinely collected, pseudonymised data for patients in the RCGP Research and Surveillance Centre primary care network +ve for SARS-CoV-2 (Jan 28 - April 4 2020): - 587 SARS-CoV-2 +ve out of 3802 test results. - male sex independently associated with testing +ve (18 vs 13 % for women) Clinical factors and demographics more likely to testing +ve: - Adults, in particular ages 40-64, vs children (19 % in aged 40-64 vs 5 % in children) - People with chronic kidney disease (33 vs 14 % without chronic kidney disease), but no significant association with other chronic conditions. - Obese people (21 vs 13 % for people of normal weight) - Active smoking at decreased odds of testing +ve (11 vs 18 % in non-smokers) - black people vs white (62 vs 16 %) - People living in urban areas vs rural areas (26 vs 5-6% in rural areas) - People living in deprived areas (30 vs 8% in least deprived areas) -&gt; +ve SARS-CoV-2 test results in primary care cohort was associated with similar risk factors as for severe outcomes of COVID-19 in hospital settings, except for smoking. -&gt; Provides evidence of potential sociodemographic factors associated with a +ve test : deprivation, population density, ethnicity and chronic kidney disease.</td>
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<td>The Lancet Infectious Diseases 15MAY2020</td>
<td>Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study</td>
<td>Lusignan, Simon de et al. UK-South Africa <a href="#">gotopaper</a></td>
<td>Clinic</td>
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<td>Gastroenterology 15MAY2020</td>
<td>Associations between Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blocker Use, Gastrointestinal Symptoms, and Mortality among Patients with COVID-19</td>
<td>Tan, Nian-Di et al. China <a href="#">gotopaper</a></td>
<td>Therapeutic/ Clinic</td>
<td>Retrospective cohort study of consecutive patients with COVID-19. Among the 100 participants with hypertension, 31 were classified as ACEI/ARB group and the remaining 69 were classified as non-ACEI/ARB group. Inpatient treatment with ACEI/ARB was associated with lower risk of digestive system involvement and lower risk of all-cause mortality compared with ACEI/ARB non-users in COVID-19 patients with hypertension. Limitations: small sample-size, possible unappreciated confounding effect.</td>
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<tr>
<td>Science 15MAY2020</td>
<td>Serology assays to manage COVID-19</td>
<td>Krammer F., Simon V., USA <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiol</td>
<td>Measurement of antibodies to SARS-CoV-2 will improve disease management if used correctly. This perspective article describes the serological assays available and discusses the potential applications, including: - understand the antibody responses mounted upon SARS-CoV-2 infection and vaccination; - inform on the prevalence of SARS-CoV-2 infection if different populations; - identification of donors for convalescent plasma therapy; - identify individuals who are immune (and the caveats concerning this point). With high-quality serological assays now available, the key challenge will be to apply and deploy these tests in a strategic manner.</td>
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<td>Clinical microbiology and infection 15MAY2020</td>
<td>A multiple center clinical evaluation of an ultra-fast single-tube assay for SARS-CoV-2 RNA</td>
<td>Wang, Ji and al. China <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>To evaluate the performance of an ultra-fast single-tube nucleic acid isothermal amplification detection assay for SARS-CoV-2 RNA using clinical samples from multiple centers. A reverse transcription recombinase-aided amplification (RT-RAA) assay for SARS-CoV-2 was conducted within 15 minutes at 39°C with portable instruments after addition of extracted RNA. The clinical performance of RT-RAA assay was evaluated using 947 clinical samples and the approved commercial real-time fluorescent RT-PCR (qRT-PCR) kits were used for parallel detection. The sensitivity and specificity of RT-RAA were compared and analyzed. CI*: with comparable sensitivity and specificity to the commercial qRT-PCR kits, RT-RAA assay for SARS-CoV-2 exhibited distinctive advantages of simplicity and rapidity in terms of operation and turn-around time.</td>
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<td>Science 15MAY2020</td>
<td>Inferring change points in the spread of COVID-19 reveals the effectiveness of interventions</td>
<td>Dehning et al., Germany <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>By combining an established epidemiological model with Bayesian inference -&gt; analysis of the time dependence of the effective growth rate of new infections. Focusing on COVID-19 spread in Germany, detection of change points in the effective growth rate that correlate well with the times of publicly announced interventions -&gt; Possibility to quantify the effect of interventions, and we can incorporate the corresponding change points into forecasts of future scenarios and case numbers. This code is freely available and can be readily adapted to any country or region.</td>
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<td>Nature 14MAY2020</td>
<td>Proteomics of SARS-CoV-2-infected host cells reveals therapy targets</td>
<td>Bojkova, Denis a et al. Germany <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Identification of the host cell pathways modulated by SARS-CoV-2 infection and inhibition of these pathways showed to prevent viral replication in human cells. A human cell culture model for infection with SARS-CoV-2 clinical isolate was established. Employing this system, the SARS-CoV-2 infection profile was determined by translatome3 and proteome proteomics at different times after infection. These analyses revealed that SARS-CoV-2 reshapes central cellular pathways, such as translation, splicing, carbon metabolism and nucleic acid metabolism. Small molecule inhibitors targeting these pathways prevented viral replication in cells.</td>
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<td>Lancet 14MAY2020</td>
<td>Use of renin–angiotensin–aldosterone system inhibitors and risk of COVID-19 requiring admission to hospital: a case-population study</td>
<td>Abajo, Francisco J. De, et al. Spain</td>
<td>Therapeutic/ Clinic</td>
<td>Case-population study of consecutively selected hospitalized patients with a PCR-confirmed diagnosis of COVID-19, and randomly sampled ten patients per case, individually matched for age, sex, region, and date of admission to hospital as a reference group. <strong>1139 cases and 11 390 population controls.</strong> Despite being matched on sex and age, a significantly higher proportion of cases had pre-existing cardiovascular disease (OR 1.98, 95% CI 1.62–2.41) and risk factors (1.46, 1.23–1.73) than did controls. The current use of RAAS inhibitors is not associated with an increased risk of COVID-19 requiring admission to hospital (including fatal cases and those admitted to an ICU) compared with other antihypertensive drugs. No substantial difference was observed between ACE inhibitors and angiotensin-receptor blockers, nor among short-term and long-term users. Sex, age, and background cardiovascular risk did not significantly affect the results, although use of RAAS inhibitors was associated with a reduced risk of COVID-19 requiring admission to hospital in patients with diabetes. <strong>Limitations:</strong> different data sources to extract information from cases and controls; cases and controls were recorded at different dates; data on smoking and other lifestyle habits not collected; observational study, residual confounding due to unmeasured or unknown confounders cannot be ruled out.</td>
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<tr>
<td>BMJ 14MAY2020</td>
<td>Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial</td>
<td>Tang, Wei et al. China</td>
<td>Therapeutic</td>
<td>Multicentre, randomised, parallel, open label trial of hydroxychloroquine (1200 mg daily for three days, then 800 mg daily) versus standard of care in 150 patients admitted to hospital with covid-19. No evidence to support an increase in the probability of negative conversion of SARS-CoV-2 conferred by the addition of hydroxychloroquine administration to the current standard of care in patients admitted to hospital with mainly persistent mild to moderate covid-19. Adverse events, particularly gastrointestinal events, were more frequently reported in patients receiving hydroxychloroquine. <strong>Limitations:</strong> open label; use of sequential envelopes for randomisation; no patients at the early stage of disease; 148/150 (99%) patients had mild to moderate disease; underpowered sample size due to the lack of enough eligible patients to enrol.</td>
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<td>American journal of obstetrics and gynecology 14MAY2020</td>
<td>Clinical Characteristics of 46 Pregnant Women with a SARS-CoV-2 Infection in Washington State</td>
<td>Lokken EM et al. USA</td>
<td>Clinic</td>
<td>Description of maternal disease and obstetrical outcomes—6 hospital in Washington state <strong>46 pregnant women</strong> <strong>Demographic:</strong> median age: 29y – 6.5% in first &amp; 43.4% second &amp; 50% in third trimester 26.1% had at least one comorbidity: asthma – hypertension – diabetes – .... 28.6% were overweight and 35.7% obese <strong>Symptoms:</strong> 93.5% had one – cough (70%) – fever (51%) – dyspnea – headache .... <strong>Outcomes:</strong> - 15% categorized has severe disease: overweight/obese/comorbidity - 16% hospitalized &amp; 1 to ICU (all severe disease) - 8 delivered during the study period (median: 38.4 week) - 1 stillbirth: unknown etiology <strong>→ higher risk group: chronic comorbidity / obese / overweight</strong></td>
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<td>Clinica Chimica Acta 14MAY2020</td>
<td>The underlying changes and predicting role of peripheral blood inflammatory cells in severe COVID-19 patients: a sentinel?</td>
<td>Sun, Da-wei and al. China <a href="#">gotopaper</a></td>
<td>Virology</td>
<td>The underlying changes of peripheral blood inflammatory cells (PBICs) in COVID-19 patients are little known. Moreover, the risk factors for the underlying changes of PBICs and their predicting role in severe COVID-19 patients remain uncertain.</td>
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<tr>
<td>Journal of Allergy and Clinical Immunology 14MAY2020</td>
<td>Complement activation in patients with COVID-19: a novel therapeutic target</td>
<td>Cugno, Massimo et al. Italy <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Preliminary data providing evidence of complement activation in patients with COVID-19 with different degrees of respiratory failure. Investigation of the plasma levels of sC5b-9 and C5a as markers of complement activation in 31 COVID-19 patients, compared with 27 healthy subjects.</td>
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- **Complement activation** may contribute to the development of lung and endothelial damage in patients. Possibility that the coronavirus may directly cause damage to endothelial cells.

- **Plasma levels of sC5b-9** were significantly higher in the patients with moderate disease and those with severe disease compared to healthy controls, and significantly higher in the patients with severe disease than in those with moderate disease.

- **The plasma levels of C5a** were higher in the patients with moderate disease and those with severe disease compared to healthy controls (P<0.0001 for both), with no statistically significant difference between the two patient groups.

- The cohort of patients had increased levels of acute-phase proteins and coagulation system abnormalities.

The results of this study do not support its use in patients admitted to hospital with covid-19 who require oxygen.

**Limitations:** observational data, centre effect not taken into account; limited sample; only patients admitted to hospital.
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<tr>
<td>Clinical Infectious Disease 14MAY2020</td>
<td>Risk Factors of Severe Disease and Efficacy of Treatment in Patients Infected with COVID-19: A Systematic Review, Meta-Analysis and Meta-Regression Analysis</td>
<td>Zhang, John J. Y et al. Singapore [gotopaper]</td>
<td>Therapeutic/ Clinic</td>
<td>Systematic review and meta-analysis on COVID-19 clinical features and/or treatment outcomes. 45 studies reporting 4203 patients were included. Pooled rates of intensive care unit (ICU) admission, mortality and acute respiratory distress syndrome (ARDS) were 10.9%, 4.3% and 18.4%, respectively. - On meta-regression, ICU admission was predicted by raised leukocyte count (p&lt;0.0001), raised alanine aminotransferase (p=0.024), raised aspartate transaminase (p=0.0040), elevated lactate dehydrogenase (LDH) (p&lt;0.0001) and increased procalcitonin (p&lt;0.0001). - ARDS was predicted by elevated LDH (p&lt;0.0001), while mortality was predicted by raised leukocyte count (p=0.0005) and elevated LDH (p&lt;0.0001). - Treatment with lopinavir-ritonavir showed no significant benefit in mortality and ARDS rates. Corticosteroids were associated with a higher rate of ARDS (p&lt;0.0003). Limitations: possible selection bias (publications in English); only studies from Asia at the time of the literature search; studies included were observational; heterogeneity in the range of symptoms and comorbidities recorded in the different studies.</td>
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<td>Nature 14MAY2020</td>
<td>Infection of dogs with SARS-CoV-2</td>
<td>Sit, Thomas H. C Hong Kong [gotopaper]</td>
<td>Fundamental research</td>
<td>2/15 dogs from households with confirmed human COVID-19 cases in Hong Kong were found to be infected (qRT-PCR, serology, viral genome sequencing, and virus isolation in 1 dog): - a 17yr-old male Pomeranian (SARS-CoV-2 RNA detected from 5 nasal swabs over 13-days). - a 2.Syr-old male German Shepherd dog (SARS-CoV-2 RNA on two occasions and virus isolated from nasal and oral swabs) - Both had antibody responses (plaque reduction neutralization assays). - Viral genetic sequences from both dogs were identical to virus detected in respective human cases. Animals asymptomatic during quarantine. -&gt; These are instances of human-to-animal transmission of SARS-CoV-2. Unclear whether infected dogs can transmit the virus to other animals or back to humans.</td>
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<td>Nature 14MAY2020</td>
<td>Pathogenesis and transmission of SARS-CoV-2 in golden hamsters</td>
<td>Sia, Sin Fun et al. Hong Kong [gotopaper]</td>
<td>Animal model</td>
<td>Pathogenesis and transmissibility of the SARS-CoV-2 in golden Syrian hamsters (intranasal infection): - viral antigens (immunohistochemistry) in nasal mucosa, bronchial epithelial cells and in areas of lung on 2 and 5 dpi, followed by rapid viral clearance and pneumocyte hyperplasia on 7 dpi. - Viral antigen found in duodenum epithelial cells and viral RNA in feces. -&gt; Efficient SARS-CoV-2 transmission from inoculated hamsters to naive by direct contact and via aerosols. Transmission via fomites less efficient. -&gt; Communicable period was short and correlated with detection of infectious virus but not viral RNA. -&gt; Inoculated and naturally-infected hamsters showed apparent weight loss, and all animals recovered with detection of neutralizing antibodies.</td>
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<td>Proc. Natl. Acad. Sci. U. S. A. 13MAY2020</td>
<td>The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission</td>
<td>Stadnytskyi et al. USA [gotopaper]</td>
<td>Public Health/Epidemiology</td>
<td>Speech droplets generated by asymptomatic carriers of SARS-CoV-2 likely to be a mode of disease transmission. - Highly sensitive laser light scattering observations have revealed that loud speech can emit thousands of oral fluid droplets per second. -&gt; In a closed, stagnant air environment, they disappear from the window of view with time constants in the range of 8 to 14 min (droplet nuclei of ca. 4 μm diameter, or 12 to 21-μm droplets prior to dehydration). There is therefore a substantial probability that normal speaking causes airborne virus transmission in confined environments.</td>
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<td>Science 13MAY2020</td>
<td>Estimating the burden of SARS-CoV-2 in France</td>
<td>Salje et al., France <a href="#">gotopaper</a></td>
<td>Public Health/Epidemiology</td>
<td>Using models applied to hospital and death data, we estimate the impact of the lockdown and current population immunity in France. - We find 3.6% of infected individuals are hospitalized and 0.7% die (0.001% in &lt;20 years of age (ya), 10.1% in &gt;80ya). The lockdown reduced the reproductive number from 2.90 to 0.67 (77% reduction). By 11 May 2020, when interventions are scheduled to be eased, we project that 4.4% (range: 2.8–7.2) of the population will have been infected. Population immunity appears insufficient to avoid a second wave if all control measures are released at the end of the lockdown</td>
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<td>Ann. Intern. Med. 13MAY2020</td>
<td>Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure</td>
<td>Kucirka, Lauren M. and al. USA <a href="#">gotopaper</a></td>
<td>Virology</td>
<td>Tests for SARS-CoV-2 based on RT-PCR are being used to “rule out” infection among high-risk persons, such as exposed inpatients and health care workers. It is critical to understand how the predictive value of the test varies with time from exposure and symptom onset to avoid being falsely reassured by negative test results. Objective: To estimate the false-negative rate by day since infection. CI*: care must be taken in interpreting RT-PCR tests for SARS-CoV-2 infection—particularly early in the course of infection—when using these results as a basis for removing precautions intended to prevent onward transmission. If clinical suspicion is high, infection should not be ruled out on the basis of RT-PCR alone, and the clinical and epidemiologic situation should be carefully considered. Autopsy series from 22 patients who died from Covid-19: - 77% had more than 2 coexisting conditions, and greater coexisting conditions associated with SARS-CoV-2 tropism for kidneys. - highest SARS-CoV-2 copies per cell = respiratory tract, - lower viral copies per cell = kidneys, liver, heart, brain, and blood. Kidney tissue microdissection from 6 patients: - 3 = detectable SARS-CoV-2 viral load in all kidney compartments examined, with preferential targeting of glomerular cells. -&gt; SARS-CoV-2 organotropism beyond respiratory tract includes heart, liver, brain, and kidneys. Renal tropism is a potential explanation of commonly reported new clinical signs of kidney injury in Covid-19 patients</td>
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<td>N. Engl. J. Med. 13MAY2020</td>
<td>Multorgan and Renal Tropism of SARS-CoV-2</td>
<td>Puelles, Victor G. et al Germany <a href="#">gotopaper</a></td>
<td>Cellular tropism</td>
<td>The availability of viral transport media (VTM) has become severely limited, contributing to delays in diagnosis and rationing of diagnostic testing. The phosphate buffered saline (PBS) may be a viable transport medium, as an alternative to VTM, for clinical qPCR testing. We assessed the intra- and inter-individual reliability of SARS-CoV-2 qPCR in clinical endotracheal secretion samples transported in VTM or PBS, evaluating the stability of the RT-qPCR signal for three viral targets (N gene, ORF1ab, and S gene) when samples were stored in these media at room temperature for up to 18 hours. Results: using PBS as a transport medium has high intra-and inter-individual reliability, maintains viral stability, and is comparable to VTM in the detection of the three SARS-CoV-2 genes through 18 hours of storage. CI*: PBS as a clinically useful medium for transporting and short-term preservation of specimens containing SARS-CoV-2 has the potential to increase testing capacity for SARS-CoV-2</td>
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<td>The Journal of Molecular Diagnostics 13MAY2020</td>
<td>Detection of SARS-CoV-2 is comparable in clinical samples preserved in saline or viral transport media</td>
<td>Radbel, Jared and al. USA <a href="#">gotopaper</a></td>
<td>Virology</td>
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| Lancet           | An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study | Verdoni L et al. Italy gotopaper       | Clinic             | 29 children with Kawasaki disease Group1(n=19): before SARS-CoV-2 outbreak  
Group2(n=10): after SARS-CoV-2 outbreak  
Group1 versus group2:  
- Higher incidence in group2: 0.3 vs 10/month (p<0.05)  
- Older group2: 3.0 vs 7.5 y (p<0.05)  
- Abnormal echocardiogram: 60%(grp2) vs 10%(grp1), p<0.05  
- More MAS group2: 50% vs 0%  
→ 30-fold increased incidence of KD in the past month  
→ SARS-CoV-2 outbreak is associated with high incidence of severe form of KD |
| Nature Medicine  | Infection of bat and human intestinal organoids by SARS-CoV-2       | Zhou, Jie et al. Hong Kong gotopaper   | Fundamental research | Establishment and characterization of intestinal organoids derived from horseshoe bats (*Rhinolophus sinicus*) can recapitulate bat intestinal epithelium:  
- bat enteroids are fully susceptible to SARS-CoV-2 infection and robust viral replication.  
- human intestinal organoids also sustain active replication of SARS-CoV-2  
-> First expandable organoid culture system of bat intestinal epithelium and evidence that SARS-CoV-2 can infect bat intestinal cells.  
-> Robust SARS-CoV-2 replication in human intestinal organoids suggests that the human intestinal tract might be a transmission route of SARS-CoV-2. |
| JAMA             | SARS-CoV-2 Rates in BCG-Vaccinated and Unvaccinated Young Adult     | Hamiel et al., Israel gotopaper        | Vaccine            | The BCG vaccine was routinely administered to all newborns in Israel as part of the national immunization program between 1955 and 1982  
Since 1982, the vaccine has been administered only to immigrants from countries with high prevalence of tuberculosis. This change allowed comparison of infection rates and propor- tions with severe COVID-19 disease in 2 similar populations with differing BCG status: individuals born during the 3 years before and 3 years after cessation of the universal BCG vaccine program.  
-> This study does not support the idea that BCG vaccination in childhood has a protective effect against COVID-19 in adulthood. |
- Lopinavir trough levels were approximately 2-fold higher in this population than in patients with HIV receiving the same dose (7.1 µg/mL).  
- A correlation of drug concentrations with C-reactive protein, a downstream marker of IL-6, was observed.  
However, approximately 60- to 120-fold higher concentrations are required to reach the assumed EC50 at trough levels, making effective treatment of COVID-19 with lopinavir and ritonavir at the currently used doses unlikely.  
Limitations: only trough levels were quantified, more detailed pharmacokinetics not available ; no data on the half-maximal effective dose of lopinavir for SARS-CoV-2 in vivo. |
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| Nature 12MAY2020 | Respiratory disease in rhesus macaques inoculated with SARS-CoV-2 | Munster, Vincent J. et al. USA [gotopaper](#) | Animal model | SARS-CoV-2 causes respiratory disease in infected rhesus macaques, with disease lasting 8-16 days: 
- 8 adult rhesus macaques (4 males, 4 females, age 4-6 yrs) inoculated with combination of intranasal (0.5ml per nostril), intratracheal, oral and ocular of a 4x10^5 TCID50/ml (3x10^6 genome copies/ml). 
- Pulmonary infiltrates visible in lung radiographs 
- High viral load in nose and throat swabs and bronchoalveolar lavages of all animals. 
- prolonged rectal shedding detected in 1 animal  
- Rhesus macaque recapitulates moderate disease with regard to virus replication, shedding, presence of pulmonary infiltrates, histological lesions and seroconversion. |
| Nat Med 12MAY2020 | A serological assay to detect SARS-CoV-2 seroconversion in humans | Amanat et al., USA [gotopaper](#) | Diagnostic | Describing a serological enzyme-linked immunosorbent assay for the screening and identification of human SARS-CoV-2 seroconverters.  
- based on reactivity to the immunogenic S protein of the virus, is relatively simple and quick in its execution and can be performed at biosafety level 2  
- there is no or only negligible cross-reactivity from human coronaviruses to SARS-CoV-2 in the tested individuals  
- strong seroconversion with ELISA AUC values in the 1:1,000 range after natural infection with SARS-CoV-2 |
| Cancer discovery 12MAY2020 | Impact of PD-1 blockade on severity of COVID-19 in patients with lung cancers | Luo, Jia et al. USA [gotopaper](#) | Therapeutic/ Clinic | Analyses on 69 consecutive patients with lung cancers who were diagnosed with COVID-19. Severity based on no or prior receipt of PD-1 blockade was examined.  
- Overall, the severity of COVID-19 in patients with lung cancer was high, including need for hospitalization in more than half of patients and death in nearly a quarter.  
- Prior PD-1 blockade was, as expected, associated with smoking status.  
- After adjustment for smoking status, PD-1 blockade exposure was not associated with increased risk of severity of COVID-19. PD-1 blockade does not appear to impact the severity of COVID-19 in patients with lung cancers.  
These initial results in patients with lung cancers support the safety of PD-1 blockade treatment to achieve optimal cancer outcomes. |
| JAMA Intern Med 12MAY2020 | Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19 | Liang W et al, China [gotopaper](#) | Clinic | Develop and validate a clinical score at admission for predicting critical illness  
Retrospective cohort (575 hospital in China)  
1590 patients with data were include for variable selection:  
- Mean age: 48,9y – 57,3% were men – 25,1% had at least 1 comorbidity  
- 72 variables entered in selection process (LASSO and logistic regression)  
10 variables were independently statistically significant predictors of critical illness:  
- CXR abnormality: OR: 3,39  
- Age OR: 1,03  
- Hemoptysis OR 4,53  
- Dyspnea OR 1,88  
- Unconsciousness OR 4,71  
- Number of comorbidities OR 1,60  
- Cancer history OR 4,07  
- Neutrophil to lymphocyte ratio OR 1,06  
- Lactate dehydrogenase OR: 1,002  
- Direct bilirubin OR: 1,15  
Validation: cohort of 710 patients  
AUC of COVID-GRAM 0,88 IC95% [0,84 – 0,93]  
Limitations: data are entirely from China  
- risk score at the admission for predicting critical illness
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| JAMA 11MAY2020   | Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State | Rosenberg, Eli S. et al. USA [gotopaper](http://gotopaper) | Therapeutic | Retrospective multicenter cohort study of 1438 hospitalized patients who received both hydroxychloroquine and azithromycin, hydroxychloroquine alone, azithromycin alone, or neither.  

=> Compared with patients receiving neither drug, there were no significant differences in mortality for patients receiving hydroxychloroquine + azithromycin (HR, 1.35 [95% CI, 0.76-2.40]), hydroxychloroquine alone (HR, 1.08 [95% CI, 0.63-1.85]), or azithromycin alone (HR, 0.56 [95% CI, 0.26-1.21]).  

=> Compared with patients receiving neither drug, cardiac arrest was significantly more likely in patients receiving hydroxychloroquine + azithromycin (adjusted OR, 2.13 [95% CI, 1.12-4.05]), but not hydroxychloroquine alone (adjusted OR, 1.91 [95% CI, 0.96-3.81]) or azithromycin alone (adjusted OR, 0.64 [95% CI, 0.27-1.56]).  

=> No significant differences in the relative likelihood of abnormal electrocardiogram findings.  

Limitations: mortality limited to in-hospital death; potential confounders such as inflammatory markers were not frequently measured; confidence intervals for some of the findings are wide, reflecting limits in study power for some analyses. |
| Bio-design and manufacturing 11MAY2020 | Development of a rapid test kit for SARS-CoV-2: an example of product design | Cui, Zhanfeng and al. China [gotopaper](http://gotopaper) | Diagnostic | The urgent need for large numbers of tests in field setting imposes constraints such as short test time and lack of access to specialist equipment, laboratories and skilled technicians to perform the test and interpret results.  

To meet these needs, an antigen test based on RT-LAMP with colorimetric readout was chosen. Direct use of swab sample with no RNA extraction was explored.  

After extensive experimental study, a rapid test kit has been fabricated to satisfy all design criteria. |
| J. Clin. Microbiol. 11MAY2020 | Open Development and Clinical Validation Of Multiple 3D-Printed Nasopharyngeal Collection Swabs: Rapid Resolution of a Critical COVID-19 Testing Bottleneck | Callahan, Cody J. and al. USA [gotopaper](http://gotopaper) | Diagnostic | To address the shortage of the nasopharyngeal swabs, we designed and executed a translational-research program to allow immediate mass production by 3D printing.  

We validated four prototypes through an institutional review board (IRB)-approved clinical trial that involved 276 outpatient volunteers.  

Each participant was swabbed with a reference swab (the control) and a prototype, and SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) results were compared.  

All prototypes displayed excellent concordance with the control. Contact information for ordering can be found at [http://printedswabs.org](http://printedswabs.org) |

-> Of 18,401 who had undergone a SARS-CoV-2 test, participants reporting loss of smell and taste was 65.03% in those with a positive test result and 21.72% in those with a negative test result (odds ratio = 6.74; 95% CI = 6.31–7.21).  

->A model combining symptoms to predict probable infection was applied to the data from all app users who reported symptoms (805,753) and predicted that 140,312 (17.42%) participants are likely to have COVID-19 |
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| **Journal of Allergy and Clinical Immunology 11MAY2020** | Safety and efficacy of early high-dose IV anakinra in severe COVID-19 lung disease | Pontali, Emanuele et al. Italy [gotopaper](#) | Therapeutic | Pilot study of early use of high IV doses of anti-IL-1 anakinra in 5 patients with severe/moderate COVID-19 with pulmonary involvement.  
- All five patients experienced rapid resolution of systemic inflammation, and remarkable improvement of respiratory parameters, with reduction of oxygen support requirement and early amelioration of chest CT scan abnormalities before discharge in 3 patients.  
- All patients were discharged 6 to 13 days after the start of anakinra.  
- No secondary infections or other adverse events were observed.  
**Limitations:** non-controlled study; small size; short-term duration of the treatment; variability of laboratory biomarkers. |
| **Clin. Infect. Dis. 11MAY2020** | Hydroxychloroquine in COVID-19 patients: what still needs to be known about the kinetics | Martin-Blondel, G. et al. France [gotopaper](#) | Therapeutic | Aim: to determine whether or not the pharmacokinetics in systemic lupus erythematosus (SLE) patients can be applied to COVID-19 patients.  
Different dosage regimens were applied based on data that emerged: regimen 1 (200 mg x 3/day), regimen 2 (400 mg x 2 on day 1 followed by 200 mg x 3/day), regimen 3 (400 mg x 2 on day 1 followed by 400 mg x 1/day) and regimen 4 (600 mg x 2 followed by 400 mg x 1/day).  
Blood samples (n=101) were collected from 57 COVID-19 patients for 7 days and concentrations were compared with simulated kinetic profiles.  
⇒ Hydroxychloroquine exposure tends to be low and in most instances lower than the values reported in SLE patients, in particular for the standard regimen of “200 mg x 3/day”.  
⇒ The pharmacokinetic behavior in COVID-19 patients cannot be predicted by the SLE population or by rheumatoid arthritis patients. |
| **European heart journal 11MAY2020** | Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019 | Shi S and al, China [gotopaper](#) | Clinic | 671 hospitalized patients COVID-19  
Median age: 63 years  
Main comorbidities: hypertension (29,7%) – diabetes (14,5%) – CHD(9%)  
Case fatality rate 9,2%  
**Death versus survivor group**  
- Older and more often male (p<0,001)  
- More comorbidities (p<0,001)  
- More myocardial injury: 75,8% vs 9,7% (p<0,001)  
**Cardiac troponin I predicting in-hospital mortality:**  
- AUC 0,92  
- Se 86% and Spe 86%  
- Single cut-off concentrations 73 μg/L  
**Predictor of myocardial injury:**  
- Older age – comorbidities  
- High level of CRP  
**Limitation:** small sample size, cause of death or myocardial injury underestimated  
⇒ CtnI and CK-MB predict risk for in hospital mortality |
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Median age: 13 years [4,2 – 16,6]  
Comorbidities (83%)  
Median PICU length of stay: 5 days  
Respiratory symptoms: 73 % ➔ 39/48 required ventilatory support: 21 non-invasively and 19 IMV  
Specific therapies (28/46): Hydroxychloroquine or hydroxy+azithro or remdesivir or tocilizumab  
Case fatality rate: 4,2% (2/48) ➔ pre-hospital comorbidities = important factor |
| Emerging Infectious Disease journal 08MAY2020 | Prolonged Persistence of SARS-CoV-2 RNA in Body Fluids | Jiufeng Sun and al. gotopaper | Virology | To estimate the frequency and duration of detectable SARS-Cov-2 RNA in human body fluids. The prolonged persistence of virus RNA in various body fluids may guide the clinical diagnosis and prevention of onward virus transmission.  
43 patients with mild cases of COVID-19 - 490 specimens collected.  
Results: through an AFT-based modeling study: persistent shedding of virus RNA in nasopharyngeal swab and feces samples. The estimated time until loss of virus RNA detection ranged from 45.6 days for nasopharyngeal swab samples to 46.3 days for feces samples in mild cases and from 48.9 days for nasopharyngeal swab samples to 49.4 days for feces samples in severe cases (longer than those for SARS-Cov and MERS-Cov).  
| Pediatric Blood Cancer 08MAY2020 | COVID-19 infection in children and adolescents with cancer in Madrid | De Roja T and al, Spain gotopaper | Clinic | 15 pediatric oncology patients  
Median age: 10,6 years [0,6 – 18,6]  
Hematological malignancy (73%) and solid tumor (27%)  
60% received chemotherapy in the 15 days before infection  
Symptoms: fever (67%) – cough (40%) – asymptomatic (13%)  
Radiological finding: 8/14 pathological findings  
2 patients received oxygen therapy  
Median hospital stays: 8 days  
All favorable outcome ➔ prevalence among children with cancer in Madrid: 1,3% ➔ mild symptomatic and better prognosis than adults |
| American Journal of Obstetrics & Gynecology MFM 08MAY2020 | Clinical course of severe and critical COVID-19 in hospitalized pregnancies: a US cohort study | Rebecca Am, and al USA gotopaper | Clinic | 64 pregnant women hospitalized: 44 severe and 20 critical – no death  
Gestational age at admission: 30 ± 6 weeks  
Admission: 7 days after onset symptoms  
Majoration of dyspnea at day 8 and MV at day 9  
Median duration of hospital stays: 6 day for severe and 12 for critical  
Delivery preterm: 75% of critical women  
- Severe: 37 ± 2  
- Critical: 32 ± 4  
Critical cases: 95% required MV - 70% ARDS - 20% prone position  
Neonate:  
- 64% need ICU  
- One tested positive at 48-h without any symptoms ➔ clinical course not different from not pregnant women ➔ pregnancy should not be considered an independent risk of factor |
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| **Cell 08MAY2020** | Host-viral infection maps reveal signatures of severe COVID-19 patients | Bost, Pierre; et al. Israel-France-China [gotopaper](#) | Fundamental research | Viral-Track, a new computational method to analyze host-viral infection maps:  
- enables transcriptional sorting of infected vs bystander cells and reveals virus-induced expression (scans unmapped scRNA-seq data for presence of viral RNA).  
- Applicable to multiple models of infection (HBV, HIV, VSV, etc)  
Applied to Bronchoalveolar-Lavage samples from severe vs mild COVID-19 patients, reveals:  
- SARS-CoV-2 infects epithelial cells and alters immune landscape in severe patients.  
- detected unexpected coinfection with hMPV (human MetaPneumoVirus) mainly in monocytes, dampening interferon response.  
-> robust technology for dissecting mechanisms of viral-infection and pathology. |
| **Lancet 08MAY2020** | Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial | Hung, Ivan Fan-Ngai et al. China [gotopaper](#) | Therapeutic | Multicentre, prospective, open-label, randomised, phase 2 trial in 127 adults with COVID-19 hospitalized in Hong Kong. Random assignment (2:1) to the combination group (lopinavir-ritonavir + ribavirin+ interferon beta-1) or to the control group (lopinavir-ritonavir).  
=> The triple combination, when given within 7 days of symptom onset, is effective in suppressing the shedding of SARS-CoV-2, not just in a nasopharyngeal swab, but in all clinical specimens, compared with lopinavir-ritonavir alone.  
=> The significant reductions in duration of RT-PCR positivity and viral load were associated with clinical improvement as shown by the significant reduction in NEWS 2 and duration of hospital stay.  
=> Subgroup comparison suggested interferon beta-1b to be a key component of the combination treatment.  
**Limitations:** open label, no placebo group, confounded by a subgroup omitting interferon beta-1b within the combination group, no critically ill patients. |
| **Science 08MAY2020** | A highly conserved cryptic epitope in the receptor-binding domains of SARS-CoV-2 and SARS-CoV | Yuan, Meng; et al. USA-China [gotopaper](#) | Fundamental research | Crystal structure of CR3022 (neutralizing antibody from convalescent SARS-CoV infected patient) in complex with the receptor-binding domain of the SARS-CoV-2 spike:  
- 3.1a resolution  
=> CR3022 targets a highly conserved epitope (conserved in SARS-CoV-2 and SARS-CoV) that is distal from the receptor binding site, and enables cross-reactive binding between SARS-CoV-2 and SARS-CoV.  
- CR3022 likely binds more tightly to SARS-CoV because its epitope contains a glycan absent in SARS-CoV-2.  
-> Modeling showed this epitope only accessible when at least 2 of the 3 spike proteins are in a conformation competent to bind the receptor. |
| **Science 08MAY2020** | Harnessing multiple models for outbreak management | Shea et al, USA [gotopaper](#) | Public Health/Epidemiology | COVID-19 pandemic has triggered the development of several valuable models that can differ in various elements and provide disparate predictions, which could ultimately hinder intervention planning and response by policymakers.  
We advocate a more systematic approach, by merging two well-established research fields.  
1. Formal expert elicitation methods applied to multiple models to deliberately generate, retain, and synthesize valuable individual model ideas and share important insights during group discussions, while minimizing various cognitive biases.  
2. Using a decision-theoretic framework to capture and account for within- and between-model uncertainty as we evaluate actions in a timely manner to achieve management objectives. |
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<tr>
<td>JAMA 08MAY2020</td>
<td>Changes in SARS-CoV-2 Positivity Rate in Outpatients in Seattle and Washington State, March 1-April 16, 2020</td>
<td>Randhawa et al, USA <a href="#">gotopaper</a></td>
<td>Public Health/Epidemio</td>
<td>Patient demographics: SARS-CoV-2 positivity rates were 8.2% in Washington State outpatient clinics, 8.4% in Seattle-area outpatient clinics, and 14.4% in Seattle EDs. The SARS-CoV-2 positivity rate was analysed by fitting penalized cubic regression splines to binomial testing data, and accounting for variation in the daily testing totals. SARS-CoV-2 positivity rate was 17.6% in the outpatient clinics and 14.3% in EDs at the peak period and 3.8% and 9.8%, respectively, at the end of the analysis period. SARS-CoV-2 infections in patients of Washington outpatient clinics and Seattle ED settings peaked in late March and have been declining. -&gt; This trajectory is aligned with local physical distancing and the &quot;Stay Home, Stay Healthy&quot; order announced March 23, 2020.</td>
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<tr>
<td>Nature structural &amp; molecular biology 07MAY2020</td>
<td>Structural basis for the inhibition of SARS-CoV-2 main protease by antineoplastic drug carmofur</td>
<td>Jin, Zhenming et al. China <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>The antineoplastic drug carmofur is shown to inhibit the SARS-CoV-2 main protease (M^pro). The X-ray crystal structure of M^pro in complex with carmofur reveals that the carbonyl reactive group of carmofur is covalently bound to catalytic Cys145, whereas its fatty acid tail occupies the hydrophobic S2 subsite. Carmofur inhibits viral replication in VeroE6 cells (EC50 = 24.30 μM). Carmofur has a favorable selectivity index (SI) of 5.36, but further optimization will be required to develop an effective drug. This study provides a basis for rational design of carmofur analogs with enhanced inhibitory efficacy to treat COVID-19.</td>
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<tr>
<td>The Lancet Rheumatology 07MAY2020</td>
<td>Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study</td>
<td>Cavalli, Giulio et al. Italy <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Retrospective cohort study in adult patients with COVID-19, moderate-to-severe ARDS, and hyperinflammation, managed with non-invasive ventilation outside of the ICU and who received standard treatment of hydroxychloroquine and lopinavir-ritonavir, with or without anakinra. 29 patients received high-dose intravenous anakinra, 16 patients comprised the comparison group for this study, and 7 patients received low-dose subcutaneous anakinra but treatment was interrupted after 7 days. At 21 days, treatment with high-dose anakinra was associated with clinical improvement in 21 (72%) of 29 patients versus 8 (50%) in the standard treatment group. At 21 days, survival was 90% in the high-dose anakinra group and 56% in the standard treatment group (p=0.009). Discontinuation of anakinra was not followed by inflammatory relapses. Limitations: retrospective nature, relatively small size of the cohorts (particularly the historical comparator group), a more extended follow-up is also needed to assess long-term outcomes of treated patients.</td>
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<tr>
<td>Journal of Clinical Virology 07MAY2020</td>
<td>SARS-CoV-2 detection by direct rRT-PCR without RNA extraction</td>
<td>Merindol, Natacha, and al. <a href="#">gotopaper</a></td>
<td>Diagnostic</td>
<td>There are many challenges associated with ramping up testing capacity, including shortage in the chain of supplies for extraction reagents. This situation called for alternatives protocols with similar sensitivity to ensure the continuity of testing in laboratories. -&gt;Comparison of sensitivity of 2 approved rRT-QPCR Assays with and without RNA extraction. Conclusion : the two tests provided the same sensitivity. Direct rRT-PCR without RNA extraction is possible if samples are in UTM or molecular water; specimens collected in water should be screened rapidly. RNA extraction is necessary if samples are in saline water or Hanks medium.</td>
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2- Framework for Distribution ➝ For flexible, trusted governance  
- take advantage of well-established international forums (e.g. G7) rather than build something new + central role of WHO in planning and coordinating the implementation of the framework  
- requires coordination of several institutions, donors, governments and pharmaceutical companies  
- COVID-19 access accelerator (ACT), recently launched and supported by the European Commission, should extend to other major contributors, members of the G20.  
- involve entities that develop vaccines, treatments and diagnostics and support group supply in LMICs (CEPI, Gavi, the Global Fund...)  

 ➝ Adequate, Predictable Financing  
Provide a funding mechanism to generate income for R&D + deployment of vaccines and therapeutic products (advance purchase commitments (APC) for COVID-19 products + profiles of target products)  
Funds ➝ mixture of national and philanthropic contributions, mobilized to raise additional funds on the capital markets  
Contribution from world leaders + subscription depending on payment capacity of countries. ➝ low-income countries highly subsidized /free.  
Transparent regulatory pathway for approval of COVID-19 products ➝ instill global confidence, reduce development costs and accelerate access to less profitable markets. |
SARS-CoV-2 isolated from COVID-19 patients:  
- infected ciliated, mucus-secreting, and club cells of bronchial epithelium, type 1 pneumocytes in the lung, and the conjunctival mucosa.  
- In bronchus: replication similar to MERS-CoV, and higher than SARS-CoV, but lower than H1N1.  
- In lung: replication similar to SARS-CoV and H1N1, but lower than MERS-CoV.  
- In conjunctiva: replication greater than SARS-CoV.  
- SARS-CoV-2 was a less potent inducer of proinflammatory cytokines than H5N1, H1N1pdm, or MERS-CoV.  

 ➝ Conjunctival epithelium and conducting airways are potential portals of infection for SARS-CoV-2. SARS-CoV-2 replicated similarly to SARS-CoV in alveolar epithelium; but more extensively in bronchus. |
| Cell 07MAY2020 | Coast-to-Coast Spread of SARS-CoV-2 during the Early Epidemic in the United States | Fauver et al, USA [gotopaper](#) | Public Health/Epidemiology | SARS-CoV-2 detected in all 50 states of USA. Data on sequencing of nine viral genomes from early reported COVID-19 patients, the majority of which from Washington State, combined with domestic and international travel patterns, showed:  
- SARS-CoV-2 transmission in Connecticut was likely driven by domestic introductions  
- the risk of domestic importation to Connecticut exceeded that of international importation by mid-March regardless of our estimated effects of federal travel restrictions  

 ➝ Widespread transmission of SARS-CoV-2 within USA, need for critical surveillance |
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<tr>
<td>Infect. Control Hos. Epidemiol. MAY2020</td>
<td>Effect of ambient air pollutants and meteorological variables on COVID-19 incidence</td>
<td>Jiang et al, China gotopaper</td>
<td>Public Health/Epidemiology</td>
<td>The multivariate Poisson regression used to analyse correlation between COVID-19 incidence, eight air pollutants and three meteorological variables in three China’s worst COVID-19 hit provinces. Daily COVID-19 incidence was positively associated with PM2.5 and humidity in all cities. The relative risk (RR) of PM2.5 was 1.036 (95% CI, 1.032 - 1.039), 1.059 (95% CI, 1.046 - 1.072) and 1.144 (95% CI, 1.12 - 1.169) for COVID-19 incidence per day in the three provinces. The RR of humidity was lower than that of PM2.5, difference ranging from 0.027 to 0.111. PM10 and temperature exhibited a negative correlation with daily COVID-19 incidence: the RR of PM10 ranged from 0.915 (95% CI, 0.896 - 0.934) to 0.961 (95% CL, 0.95 - 0.972) while that of temperature was 0.738 (95% CI, 0.717 - 0.759) to 0.969 (95% CL, 0.966 - 0.973). Data suggest that PM2.5/humidity and PM10/temperature could substantially increase and decrease the risk of COVID-19 incidence, respectively.</td>
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<tr>
<td>Nature 07MAY2020</td>
<td>The pathogenicity of SARS-CoV-2 in hACE2 transgenic mice</td>
<td>Bao, Linlin; et al. China gotopaper</td>
<td>Animal model</td>
<td>Human ACE2 transgenic mice infected with SARS-CoV-2: - SARS-CoV-2 intranasal inoculation at 10^4 TCID50/50 μL inoculum volume per mouse. (14 days observation) - 6-11 month-old, male and female WT (n=19) and hACE2 mice (n=19). - Typical histopathology: interstitial pneumonia with infiltration of significant macrophages and lymphocytes into the alveolar interstitium, and accumulation of macrophages in alveolar cavities. - Weight loss observed in hACE2 mice (up to 8% at 5 dpi), not in WT mice. - Viral load detectable (qRT-PCR) at 1, 3, 5 and 7 dpi (peak at 3 dpi) in lungs of HACE2 mice but not in WT mice. - Infectious virus isolated from lungs of HACE2 mice at 1, 3 dpi and 5 dpi (peak titters at 3 dpi), but not WT mice. - Viral antigens detected in bronchial epithelial cells, macrophages and alveolar epithelia. -&gt; Confirmed pathogenicity of SARS-CoV-2 in HACE2 expressing mice and suggests that hACE2 was essential for infection and replication in mice.</td>
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<td>The Journal of Infectious Diseases 07MAY2020</td>
<td>T cell subset counts in peripheral blood can be used as discriminatory biomarkers for diagnosis and severity prediction of COVID-19</td>
<td>Jiang, Mei and al. China gotopaper</td>
<td>Diagnostic</td>
<td>Assessment of the significance of lymphocyte subsets detection in peripheral blood in the diagnosis and prognosis of Covid-19 disease. The counts of CD8+T and CD4+T cells can be used as diagnostic markers of COVID-19 and predictors of disease severity.</td>
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<td>The Lancet Psychiatry 07MAY2020</td>
<td>COVID-19, unemployment, and suicide</td>
<td>Kowohl And Nordt., Switzerland gotopaper</td>
<td>Psy</td>
<td>High scenario: the worldwide unemployment rate would increase from 4.936% to 5.644%, which would be associated with an increase in suicides of about 9570 per year. Low scenario: the unemployment would increase to 5.088%, associated with an increase of about 2135 suicides.</td>
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<tr>
<td>New England Journal of Medicine 07MAY2020</td>
<td>Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19</td>
<td>Geleris, Joshua et al. USA gotopaper</td>
<td>Therapeutic</td>
<td>Observational study involving consecutive patients with Covid-19 admitted to a hospital, and comparing outcomes in patients who received hydroxychloroquine with those in patients who did not. The primary end point was a composite of intubation or death in a time-to-event analysis. Of the 1376 patients, 811 (58.9%) received hydroxychloroquine and 565 (41.1%) did not. Hydroxychloroquine-treated patients were more severely ill at baseline than those who did not receive hydroxychloroquine. Overall, 346 patients (25.1%) had a primary end-point of respiratory failure. In the main analysis, there was no significant association between hydroxychloroquine use and intubation or death (hazard ratio, 1.04, 95% confidence interval, 0.82 to 1.32). Results were similar in multiple sensitivity analyses.</td>
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<td>Nat Rev Immunology 06MAY2020</td>
<td>Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages</td>
<td>Merad et al., USA <a href="#">gotopaper</a></td>
<td>Immuno</td>
<td>The delay in production of type I interferon promotes the enhanced release of monocyte chemoattractants by alveolar epithelial cells leading to sustained recruitment of blood monocytes into the lungs. · Monocytes differentiate into pro-inflammatory macrophages · Activated natural killer (NK) cells and T cells further promote the recruitment and activation of monocyte-derived macrophages through the production of granulocyte–macrophage colony-stimulating factor (GM-CSF), tumour necrosis factor (TNF) and interferon-γ (IFNγ). · Oxidized phospholipids (OxPLs) are accumulated in infected lungs and activate monocyte-derived macrophages through the Toll-like receptor 4 (TLR4)–TRAF6–NF-κB pathway. · It is possible that type I interferons induce the expression of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) entry receptors, enabling the virus to gain access to the cytoplasm of macrophages and to activate the NLRP3 inflammasome, leading to the secretion of mature IL-1βand/or IL-18. · IL-1β can amplify activation of monocyte-derived macrophages in an autocrine or paracrine way, but it can also reduce type I interferon production in infected lungs. · The engagement of Fcγ receptors (FcγRs) by anti-spike protein IgG immune complexes can contribute to increased inflammatory activation of monocyte-derived macrophages. <strong>Conclusion:</strong> Identifying the mechanisms that contribute to reduced type I interferon activity will be critical for the development of targeted immunomodulatory strategies in patients with COVID-19.</td>
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<tr>
<td>Antimicrobial agents and chemotherapy 06MAY2020</td>
<td>Inhibition of SARS-CoV-2 infection by the cyclophilin inhibitor Alisporivir (Debio 025)</td>
<td>Softic, Lauren et al. France, <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Cyclophilins play a key role in the lifecycle of coronaviruses. <strong>Alisporivir</strong> (Debio 025) is a non-immunosuppressive analogue of cyclosporin A with potent cyclophilin inhibition properties. It has been administered to more than 1,800 patients with chronic hepatitis C virus infection in Phase 2 and 3 clinical trials, alone or in combination with pegylated interferon alpha and/or ribavirin. =&gt; Alisporivir reduced SARS-CoV-2 RNA production in a dose-dependent manner in VeroE6 cell line, with an EC50 of 0.46±0.04 μM. =&gt; Anti-SARS-CoV-2 effectiveness of alisporivir was confirmed by immunofluorescence. =&gt; Alisporivir did not inhibit SARS-CoV-2 entry into VeroE6 cells. Effect of alisporivir was preserved when the compound was added 3 h post-infection. These results suggest that alisporivir inhibits a post-entry step of the SARS-CoV-2 life cycle.</td>
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<tr>
<td>Journal of the American College of Cardiology 06MAY2020</td>
<td>Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19</td>
<td>Paranjpe, Ishan et al. USA <a href="#">gotopaper</a></td>
<td>Therapeutic</td>
<td>Association between administration of in-hospital anticoagulation (AC) and survival in a large cohort of 2,773 hospitalized patients with COVID-19, among which 786 (28%) received systemic AC during their hospital course. =&gt; Systemic AC may be associated with improved outcomes among patients hospitalized with COVID-19. Potential benefits of systemic AC need to be weighed against the risk of bleeding and therefore should be individualized. The association of in-hospital AC and mechanical ventilation likely reflects reservation of AC for more severe clinical presentations. =&gt; Association with AC and improved survival after adjusting for mechanical ventilation. <strong>Limitations:</strong> observational study, unobserved confounding, unknown indication for AC, lack of metrics to further classify illness severity in the mechanically ventilated subgroup, and indication bias.</td>
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Symptoms:  
- More frequent: fever (64%) – cough (44%)  
- Less frequent: diarrhea (6%) – abdominal pain (4%) – rhinorrhea (16%)  
- Asymptomatic 12%  
Laboratory:  
- Lymphopenia (16%) – thrombocytopenia (14%)  
- Elevated CRP (20%) – anemia (12%)  
43/50 had abnormalities on CT:  
- Ground glass opacity (64%)  
29/50 >1 CT which 65% had improved CT and 28% had more lesions  
At discharge: no association between changes in CT lesions  
CT allow to detect COVID19 but do not evaluated the resolution of illness for children |
| Cell host & microbe PREPRINT | Identification of human single-domain antibodies against SARS-CoV-2 | Yanling Wu et al, China gotopaper | Therapeutic        | SARS-CoV-2 spike protein, containing the receptor-binding domain (RBD) and S1 subunit involved in receptor engagement, is a potential therapeutic target.  
- Development of a phage-displayed single-domain antibody library by grafting naïve complementarity-determining regions (CDRs) into framework regions of a human germline immunoglobulin heavy chain variable region (IGHV) allele.  
- Panning this library against SARS-CoV-2 RBD and S1 subunit identified fully human single-domain antibodies targeting five distinct epitopes on SARS-CoV-2 RBD with subnanomolar to low nanomolar affinities. Some of these antibodies neutralize SARS-CoV-2 by targeting a cryptic epitope located in the spike trimeric interface. |
| SCIENCE 06MAY2020 | Development of an inactivated vaccine candidate for SARS-CoV-2 | Qiandg Gao et al, China gotopaper | Vaccine            | Development of PiCoVacc Vaccine based on the inactivated SARS-CoV-2 virus (Sinovac vaccine currently in ph1)  
-> Isolation of 11 SARS-CoV-2 strains COVID19 patients BALF (China, Italy, Switzerland, UK, and Spain) to developed preclinical in vitro neutralization and challenge models. A strain from a Chinese patient inactivated with b-propiolactone was used for vaccine development (not causing severe disease).  
Immunogenicity in BAL/C mice:  
-> Inactivated Chinese patient virus+adjuvant (PiCoVacc) was injected at day 0 and 7 at different doses (0ug, 1.5ug, 3ug, 6ug)  
-> SARS-CoV-2 S and RBD specific IgGs were developed very quickly in mice sera  
-> The dominant immunogen was shown to be the RBD (no response to N protein)  
-> Neutralizing antibodies against all the SARS-CoV-2 strains were also produced  
Immunogenicity and protection in macaques  
-> 3 immunizations at d 0, 7 and 14 with at different doses of PiCoVacc (3 or 6ug)  
-> Specific IgG and neutralizing antibodies were induced from two weeks after vaccination  
-> macaques at day 22 after fist immunization: viral loads were shown to decrease.  
-> No detectable viral load in pharynx, crissum and lung in high dose vaccinated monkeys from 7 d after challenge. No changes on serological markers (CD3+, CD4+, CD88+, TNF-a, IFN-g, IL2, IL4...) nor pathologies in heart, spleen kidney or lung were observed suggesting that PiCoVacc do not induce exacerbated T cell response nor organ pathology. |
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| **Pediatr Infect Dis J 6MAY2020** | The risk of children Hospitalized with severe COVID-19 in Wuhan | Wang Y and al China [link](https://doi.org/10.1097/INF.0000000000002739) | Clinic | Retrospective case-control study – 8 severe children matched with 35 - Median age of severe cases: 5,06 years 2/8 had comorbidities  
Symptoms in both groups: fever – cough – dyspnea – diarrhea/vomiting  
Laboratory:  
-WBC higher in severe group  
-No difference for lymphocytes counts p>0,05  
-IL6 – IL10, D-dimer higher in severe group  
Hospital stay: 13,5 (severe) versus 11 days (non severe)  
Time for PCR turning negative: 10,5 (severe) versus 7,1 (p<0,05)  
More lung segment involves in severe children → unique risk factor for severe  
mild symptomatic (8 severe cases on 260 COVID-19) → rare mortality  
some factors associated with severity: CT scan lesions – immune response (IL-6) – intravascular coragulation (D-dimer) |
| **Science 05MAY2020** | Rapid implementation of mobile technology for real-time epidemiology of COVID-19 | Drew et al, USA [link](https://doi.org/10.1126/science.abc0473) | Public Health/Epidemiology | The Coronavirus Pandemic Epidemiology (COPE) consortium developed a Symptom Tracker mobile application, launched in the UK on March 24, 2020 and the US on March 29, 2020 garnering more than 2.8 million users as of May 2, 2020.  
This mobile application offers data on risk factors, herald symptoms, clinical outcomes, and geographical hot spots.  
This initiative offers critical proof-of-concept for the repurposing of existing approaches to enable rapidly scalable epidemiologic data collection and analysis which is critical for a data-driven response to this public health challenge. |
| **Autoimmunity reviews 05MAY2020** | Continuous hydroxychloroquine or colchicine therapy does not prevent infection with SARS-CoV-2: Insights from a large healthcare database analysis | Gendelman, Omer et al, Israel [link](https://doi.org/10.1016/j.autrev.2020.102566) | Therapeutic | Retrospective study based on a large healthcare computerized database including all patients that were screened for the SARS-CoV-2 in the study period from February 23rd 2020 to March 31st 2020.  
Comparison between subjects tested positive for SARS-CoV-2 and those found negative in terms of rate of administration of hydroxychloroquine/ colchicine therapy.  
- An overall sample of 14,520 subjects were screened for SARS-CoV-2 infection and 1317 resulted positive.  
- No significant difference was found in terms of rates of usage of hydroxychloroquine or colchicine between those who were found positive for SARS-CoV-2 and those who were found negative (0.23% versus 0.25% for hydroxychloroquine, and 0.53% versus 0.48% for colchicine, respectively).  
Isolation of single-domain antibodies (VHHs) from a llama immunized with prefusion-stabilized coronavirus spikes.  
These VHHs neutralize MERS-CoV or SARS-CoV-1 S pseudotyped viruses, respectively. Crystal structures of these VHHs bound to their respective viral targets reveal two distinct epitopes, but both VHHs interfere with receptor binding. Cross-reactivity between the SARS-CoV-1 S-directed VHH and SARS-CoV-2 S.  
Cross-reactive VHH neutralizes SARS-CoV-2 S pseudotyped viruses as a bivalent human IgG Fc-fusion.  
These data provide a molecular basis for the neutralization of pathogenic betacoronaviruses by VHHs and suggest that these molecules may serve as useful therapeutics during coronavirus outbreaks. |
| **Cell 05MAY2020** | Structural Basis for Potent Neutralization of Beta-coronaviruses by Single-domain Camelid Antibodies | DanielWrapp and al, [link](https://doi.org/10.1016/j.cell.2020.04.031) | Therapeutic | Structural Basis for Potent Neutralization of Beta-coronaviruses by Single-domain Camelid Antibodies  
These data provide a molecular basis for the neutralization of pathogenic betacoronaviruses by VHHs and suggest that these molecules may serve as useful therapeutics during coronavirus outbreaks. |
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<tr>
<td>Nature Communications 04MAY2020</td>
<td>A human monoclonal antibody blocking SARS-CoV-2 infection</td>
<td>Wang, Chunyan et al, <a href="https://www.nature.com/articles/s41467-020-18206-y">link</a></td>
<td>Therapeutic</td>
<td>First report of a (human) monoclonal antibody that neutralizes SARS-CoV-2 (and SARS-CoV) in cell culture. 47D11 binds a conserved epitope on the spike RBD explaining its ability to cross-neutralize SARS-CoV and SARS-CoV-2, using a mechanism that is independent of receptor-binding inhibition.</td>
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<tr>
<td>Intensive Care Med 04MAY2020</td>
<td>High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study</td>
<td>Helms J, and al France <a href="https://doi.org/10.1016/j.iccm.2020.04.017">link</a></td>
<td>Clinic</td>
<td>Multicentric study – 4 ICU in France – 150 patients with ARDS Historical prospective cohort → comparison of COVID to non-COVID by propensity score matching At baseline: &gt;95% patients elevated had D-dimer and fibrinogen Median age = 63 years 64/150 thrombotic complications and 16.7% pulmonary embolisms COVID19 (=77) vs non-COVID19 (=145): - More thrombotic complication in COVID19 (11.7 vs 2.1%, p&lt;0.008) Thrombotic complications despite prophylactic or therapeutic anticoagulation → large number of patients still intubated → under-estimated → monitoring anticoagulant treatment/ higher targets than usual?</td>
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<tr>
<td>Nature 04MAY2020</td>
<td>Effect of non-pharmaceutical interventions to contain COVID-19 in China</td>
<td>Lai, Shengjie et al, <a href="https://www.nature.com/articles/s41567-020-10256-y">link</a></td>
<td>Public Health/Epidemiology</td>
<td>Modelling framework that uses daily travel networks to simulate different outbreak and intervention scenarios across China, using epidemiological and anonymised human movement data. -&gt; Total of 114,325 COVID-19 cases (interquartile range 76,776 - 164,576) estimated in mainland China as of February 29, 2020. -&gt; Without non-pharmaceutical interventions (NPIs), the COVID-19 cases would likely have shown a 67-fold increase (interquartile range 44 - 94) by February 29, 2020, with the effectiveness of different interventions varying. -&gt; The early detection and isolation of cases was estimated to have prevented more infections than travel restrictions and contact reductions, but combined NPIs achieved the strongest and most rapid effect. -&gt; The lifting of travel restrictions since February 17, 2020 does not appear to lead to an increase in cases across China if the social distancing interventions can be maintained, even at a limited level of 25% reduction on average through late April.</td>
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<tr>
<td>Cell host &amp; microbe 04MAY2020</td>
<td>Heightened innate immune responses in the respiratory tract of COVID-19 patients</td>
<td>Zhou, Zhuo; et al. China <a href="https://doi.org/10.1016/j.chom.2020.04.017">link</a></td>
<td>Immunology</td>
<td>Metatranscriptomic seq. to profile immune signatures in bronchoalveolar lavage fluid of 8 COVID-19, 146 community-acquired pneumonia patients, and 20 healthy controls : - Proinflammatory gene expression, especially chemokines, markedly elevated in COVID-19 vs community-acquired pneumonia patients and healthy controls, suggesting SARS-CoV-2 causes hypercytokinemia. - SARS-CoV-2 triggered robust expression of IFN-inducible genes (ISGs) with immunopathogenic potential (overrepresentation of genes involved in inflammation), unlike SARS-CoV which is thought to induce inadequate IFN. - Estimations of cell immune populations, show increased activated dendritic cells and neutrophils. Revealing the glycan structures on a recombinant SARS-CoV-2 spike (S) glycoprotein immunogen by site-specific mass spectrometry. -SARS-CoV-2 S gene encodes 22 N-linked glycan sequons per protomer, which likely play a role in protein folding and immune evasion. -&gt; Glycosylation analysis enables detailed mapping of the glycan-processing states and signatures across the trimeric viral spike. Glycan profiling have implications in viral pathobiology as well as vaccine design for comparing immunogen integrity and monitoring manufacturing processes.</td>
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<td>Science 04MAY2020</td>
<td>Site-specific glycan analysis of the SARS-CoV-2 spike</td>
<td>Watanabe, Yasunori, et al. UK - USA <a href="https://doi.org/10.1126/science.abc9198">link</a></td>
<td>Structural biology</td>
<td>-&gt;</td>
</tr>
</tbody>
</table>
### Journal and date
- **Autoimmunity reviews**
  - **03MAY2020**

### Title
- **Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform**
- **Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy**
- **Detection of SARS-CoV-2 specific humoral and cellular immunity in COVID-19 convalescent individuals**
- **Evidence for and against vertical transmission for SARS-CoV-2 (COVID-19)**

### Authors and link
- Thao, Tran Thi Nhu, et al. Switzerland - Germany - Russia
- Toniati, Paola et al., Italy
- Ling et al., China
- A, Amouroux; et al. France

### Field of expertise
- Fundamental research
- Therapeutic
- Diagnostic
- Clinic

### Key facts
- Accelerated yeast-based reverse genetics pipeline can genetically reconstruct diverse long RNA viruses, including Coronaviridae, Flaviviridae and Paramyxoviridae families:
  - Viral subgenomic fragments (from viral isolates, cloned viral DNA, clinical samples, or synthetic DNA) are reassembled in one step in S. cerevisiae using transformation associated recombination (TAR) cloning to maintain the genome as a yeast artificial chromosome (YAC). T7-RNA polymerase then used to generate infectious RNA and viable virus.
  - Approach to generate SARS-CoV-2 is rapid (1 week after receipt of synthetic DNA fragments) and applicable to other emerging RNA viruses, and can provide infectious virus to health authorities and diagnostic labs without the need of access to clinical samples.
  - Also possible to rapidly introduce sequence variations to functionally characterize phenotypic consequences of SARS-CoV-2 evolution in real-time.
- A prospective series of 100 consecutive patients admitted to a Hospital in Brescia (Italy) between March 9th and March 20th with confirmed COVID-19 pneumonia and ARDS requiring ventilatory support were administered Tocilizumab (TCZ, monoclonal antibody that targets the interleukin 6 receptor).
  - The outcome measure was an improvement in ARDS assessed by means of the Brescia COVID Respiratory Severity Score.
  - Out of 100 treated patients (88 M, 12 F; median age: 62 years), the respiratory condition was improved or stabilized in 77 (77%) patients, of whom 61 showed a significant clearing of diffuse bilateral opacities on chest x-ray and 15 were discharged from the hospital. Respiratory condition worsened in 23 (23%) patients, of whom 20 (20%) died.
  - All the patients presented with lymphopenia and high levels of C-reactive protein (CRP), fibrinogen, ferritin and interleukin 6 (IL-6) indicating a HIS. During the 10-day follow-up, three cases of severe adverse events were recorded.
    - 1. SARS-CoV-2-specific antibodies are detected in COVID-19 convalescent subjects.
    - 2. Most COVID-19 convalescent individuals have detectable neutralizing antibodies.
    - 3. Cellular immune responses to SARS-CoV-2 are found in COVID-19 convalescent subjects.
    - 4. Neutralization antibody titers correlate with the numbers of virus-specific T cells.
- Observations from 12 articles published from 10 February to 4 April 2020 reporting on 68 deliveries and 71 neonates with maternal infection in the third trimester of pregnancy:
  - SARS-CoV-2 recovered (RT-PCR) from nasal and throat swabs, sputum and feces of symptomatic patients including neonates but not from vaginal swabs, amniotic fluid, placenta, cord blood, neonatal blood or breast milk.
  - Neonatal infection was diagnosed within 48 hours of life in 4 cases.
  - More complete evidence and reliable serological studies needed before counselling pregnant women on the risk of congenital infection with SARS-CoV-2.
<table>
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<tr>
<th>Journal and date</th>
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<th>Field of expertise</th>
<th>Key facts</th>
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</table>
| Int. J. Infect. Dis. 03MAY2020 | Viral kinetics of SARS-CoV-2 in asymptomatic carriers and presymptomatic patients | Kim, Seong Eun; et al. South Korea [https://doi.org/10.1016/j.jid.2020.04.083](https://doi.org/10.1016/j.jid.2020.04.083) | Virology | 71 laboratory-confirmed SARS-CoV-2 cases, identified 3 presymptomatic patients and 10 entirely asymptomatic infections:  
- 2 out of 3 incubation period patients (presymptomatic) had very high viral titer (Ct value <20).  
- In entirely asymptomatic carriers: median days to first negative RT-PCR was 4.5 (2.5–9) days and all reached a first Ct>35 RT-PCR within 14 days after diagnosis.  
> COVID-19 patients may already be infectious before symptoms manifestation, and 14 days isolation after diagnosis may be sufficient in entirely asymptomatic cases. |
| Gastroenterology 01MAY2020 | Gastrointestinal and Hepatic Manifestations of 2019 Novel Coronavirus Disease in a Large Cohort of Infected Patients From New York: Clinical Implications | Kaveh H and al USA [https://doi.org/10.1038/j.gastro.2020.05.010](https://doi.org/10.1038/j.gastro.2020.05.010) | Clinic | 1059 patients COVID-19 - 33% at least one gastrointestinal symptom  
GI symptom: diarrhea (22%) – abdominal pain (7%) – nausea (16%)  
62% had biochemical liver injury  
GI manifestation and liver injury were associated with higher admission rate  
Multivariate analysis ➔ independent predictor of death or ICU admission  
- Liver injury at presentation OR:2,53  
- Older age OR:1,03  
- Tachypnea OR:1,73  
- Severe hypoxemia OR:1,47  
GI manifestation ➔ no effect on the outcome  
COVID-19 patients had commonly GI manifestation |
Among 90 patients given hydroxychloroquine, 53 received concomitant azithromycin. Those receiving concomitant azithromycin had a greater median change in QT interval compared with those receiving hydroxychloroquine.  
Seven patients (19%) who received hydroxychloroquine monotherapy developed prolonged QTc of 500 milliseconds or more, and 3 patients (3%) had a change in QTc of 60 milliseconds or more. Of those who received concomitant azithromycin, 11 of 53 (21%) had prolonged QTc of 500 milliseconds or more and 7 of 53 (13 %) had a change in QTc of 60 milliseconds or more. Ten patients had hydroxychloroquine discontinued early because of potential adverse drug events, including intractable nausea, hypoglycemia, and 1 case of torsades de pointes. |
| Molecular Cell 01MAY2020 | A Multibasic Cleavage Site in the Spike Protein of SARS-CoV-2 Is Essential for Infection of Human Lung Cells | Hoffmann, Markus; et al. Germany [https://doi.org/10.1016/j.molcel.2020.04.022](https://doi.org/10.1016/j.molcel.2020.04.022) | Fundamental research | The spike protein of SARS-CoV-2 harbors a multiple arginine residues (multibasic) S1/S2 site.  
- The host cell protease furin cleaves the SARS-CoV-2 spike protein at the S1/S2 site.  
- Cleavage at the S1/S2 site is essential for spike-driven cell-cell fusion and viral entry entry into lung cells.  
> Suggests that acquisition of a S1/S2 multibasic cleavage site was essential for SARS-CoV-2 infection of humans and identify furin as a potential target for therapeutic intervention. |
<p>| New England Journal of Medicine 01MAY2020 | Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19 | Mehrha M, and al USA <a href="https://doi.org/10.1056/NEJMc2007821">https://doi.org/10.1056/NEJMc2007821</a> | Clinic | RETRACTED |</p>
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- Persons enrolled online and were sent kits, by rapid-delivery services, for home collection of a midnasal swab; samples were returned by mail.
- Persons reporting symptoms of respiratory illness provided informed consent for testing to identify influenza and other respiratory pathogens.
- The first Covid-19 case detected through the Seattle Flu Study, in a specimen collected on February 24, 2020, was the first documented U.S. case of community transmission at the time. |
| Clin. Infect. Dis 01MAY2020 | Early detection of SARS-CoV-2 antibodies in COVID-19 patients as a serologic marker of infection | Zhao, Rongqing and al. [https://doi.org/10.1093/cid/ciaa523](https://doi.org/10.1093/cid/ciaa523) | Diagnostic | A COVID-19/SARS-CoV-2 S1 serology ELISA kit was developed. The overall accuracy rate reached 97.3%. The assay was able to detect SARS-CoV-2 antibody on day one after the onset of COVID-19 disease. SARS-CoV-2 antibodies were detected in 28 out of 276 asymptomatic medical staff and one out of five nucleic acid test-negative “Close contacts” of COVID-19 patient. |
| Science 01MAY2020 | SARS-CoV-2 productively infects human gut enterocytes | Lamers, Mart M.; et al. Netherlands [https://doi.org/10.1126/science.abc1669](https://doi.org/10.1126/science.abc1669) | Fundamental research | Infection of human small intestinal organoids (hSIOs) grown from primary gut epithelial stem cells to investigate intestine as another viral target organ:
- hSIOs enterocytes were readily infected by SARS-CoV and SARS-CoV-2 (confluent- and electron-microscopy) and significant titers of infectious viral particles detected.
- SARS-CoV-2 infected airway and gut organoids.
- mRNA expression analysis revealed strong induction of a generic viral response program. SARS-CoV-2 induced a stronger interferon response than SARS-CoV in HIOs.
- Intestinal epithelium supports SARS-CoV-2 replication, and data imply that human organoids represent faithful experimental models to study of coronavirus infection and biology. |
Kinetics of SARS-CoV-2 specific IgM and IgG responses in COVID-19 patients

Sun et al., China

Immuno

- Kinetic steps:
  - A total of 130 blood samples from 38 COVID-19 patients were analyzed.
  - Study showed that the seropositive rates of N-IgM, N-IgG, S-IgM and S-IgG antibody responses in non-ICU (intensive care unit) patients gradually increased within 1-3 weeks after the onset.
  - N-IgM and S-IgM reached a peak in the second week, while N-IgG and S-IgG antibodies continued to increase in the third week.
  - The joint detection of N-IgM, N-IgG, S-IgM, and S-IgG antibodies, could detect up to 75% of infections in the first week and the joint detection of N-IgM+N-IgG, or N-IgG+S-IgG could detect up to 94.7% of infections in the second week. Finally, in the third weeks after symptom onset, seropositive rates for N-IgG and S-IgG reached 100%.

- Comparison between ICU and non-ICU patients
  - Most ICU patients had higher N-IgG than S-IgG after the symptom onset.
  - ICU patients had SARS-CoV-2 nucleic acid positive days of 31.0, whereas non-ICU patients had SARS-CoV-2 nucleic acid positive days of 13. Therefore, a continuous increase of N-IgG may indicate disease progression towards more severe illness.
  - S-IgG in ICU patients was significantly lower than non-ICU patients by 2 weeks after the onset

Conclusion: Intensive care unit monitoring the kinetics of S-IgG should help to predict prognosis.

Structural basis for inhibition of the RNA-dependent RNA polymerase from SARS-CoV-2 by remdesivir

Yin, Wanchao; et al.
China
https://doi.org/10.1126/science.abc1560

Structural biology

- Cryo-EM structure of the SARS-CoV-2 RNA-dependent RNA polymerase (RdRp) in the apo from (unbound) (2.8 Å) or in complex with a 50-base template-primer RNA and the active form of Remdesivir (2.5 Å).

- Structure comparison and sequence alignment suggest that mode of substrate RNA recognition and Remdesivir inhibition of RdRp is highly conserved in diverse RNA viruses
  - Providing a basis for designing broad spectrum antiviral drugs based on nucleotide analogs and a template structure for modeling/modifying existing nucleotide drugs (ex. EIDD-2801).
  - Complex structure reveals the partial double-stranded RNA template is inserted into the central channel of the RdRp where Remdesivir is covalently incorporated into the primer strand at the first replicated base pair and terminates chain elongation.

Systematic review (case series/case-control/ cohort studies) (January 1st - April 21st, 2020) reporting on ageusia/dysgeusia:
- 4 single-nation studies, 1 multinational study from Europe at total of 817 patients included.
- Prevalence: almost half of patients (49.8%) with COVID-19 have altered taste sensation across the five studies.

Limitations: lack of data comparing ageusia/dysgeusia in COVID-19 +ve vs -ve patients, or severe COVID-19.

In contexts of lack of diagnostic tests (ex. developing world), distinctive clinical features like ageusia/dysgeusia can be useful in identifying suspected COVID-19 patients.

Relation between previous treatment that act on the RAAS and the likelihood of a positive test or the likelihood of severe illness?

Five class of antihypertensive medication examined.
Estimated a propensity score for the likelihood of treatment with each medication class
- 12594 patients were tested
- 5894 patients positive COVID19 which 17% had severe illness
- 2573(5894) had HTA which 24.6% had severe illness

No association between medication examined and increased likelihood of a positive test or in the risk of severe Covid19.
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<td><a href="https://doi.org/10.1056/NEJMo2007621">Mehra MR, et al.</a></td>
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<td>- Mehra et al. database study, 8910 hospitalised Covid-19 patients, 11 countries: ACE inhibitors nor ARBs associated with increased risk in-hospital death. Secondary analysis restricted to hypertension patients (for whom ACE inhibitor or ARB would be indicated) also did not show harm.</td>
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<td><a href="https://doi.org/10.1056/NEJMo2001023">Mancia, Giuseppe; et al.</a></td>
<td></td>
<td>- Mancia et al. case-control study, 6272 confirmed SARS-CoV-2 patients in Lombardy (Italy) vs 30,759 matched controls: ACE inhibitors nor ARBs associated with likelihood of SARS-CoV-2 infection. In severe/fatal infections vs matched controls, no association between these drugs and severe Covid-19.</td>
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<td><a href="https://doi.org/10.1056/NEJMo2003975">Reynolds HR, et al.</a></td>
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<td>- Reynolds et al. electronic health records, 12,594 people in New York University: &gt;5894 tested +ve, of which 1002 had severe illness (admission to ICU/mechanical ventilation/death): no +ve association for drug classes, ACE inhibitors and ARBs, for a +ve test result or severe illness.</td>
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<td>- &gt; none of the 3 studies showed evidence of harm with continued use of ACE inhibitors and ARBs.</td>
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<td>JAMA Cardiology 30APR2020</td>
<td>Assessment of QT Intervals in a Case Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated With Hydroxychloroquine Alone or in Combination With Azithromycin in an Intensive Care Unit</td>
<td><a href="https://jamanetwork.com/journals/jamacardiology/fullarticle/2705633">Bessiere, Francis et al.</a></td>
<td>Therapeutic</td>
<td>40 consecutive patients with COVID-19 confirmed by positive RT-PCR results on respiratory samples admitted to the ICU who received hydroxychloroquine with or without were included.</td>
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<td>- 30 patients (75%) required invasive mechanical ventilation and 25 (63%) received vasoactive drugs.</td>
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<td>- Hydroxychloroquine with or without azithromycin was given to 18 (45%) and 22 patients (55%), respectively. 20 patients (50%) also received other treatments favoring QT prolongation in the ICU.</td>
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<td>- Most patients (37 [93%]): increase in QTC. Prolonged QTC was observed in 14 patients (36%) after a duration of antiviral treatment of 2 to 5 days. No ventricular arrhythmia, including torsades de pointes.</td>
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<td>- Among patients treated with hydroxychloroquine and azithromycin, 6 of 18 (33%) developed an increase in QTC of 500 milliseconds or greater vs 1 of 22 (5%) of those treated with hydroxychloroquine alone (P = .03).</td>
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<td>- The antiviral treatment ceased before completion for 7 patients (17.5%) following ECG abnormalities and in 10 (25%) for acute renal failure.</td>
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<td>Nature 30APR2020</td>
<td>A SARS-CoV-2 protein interaction map reveals targets for drug repurposing</td>
<td><a href="https://www.nature.com/articles/s41586-020-2286-9#Abs1">Gordon, David E et al.</a></td>
<td>Therapeutic</td>
<td>26 of the 29 SARS-CoV-2 proteins in human cells were cloned, tagged and expressed, and the human proteins physically associated with each were identified using affinity-purification mass spectrometry (AP-MS)</td>
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<td>- Identification of 332 high-confidence SARS-CoV-2-human protein-protein interactions (PPIs).</td>
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<td>- Among these, 66 druggable human proteins or host factors targeted by 69 compounds (29 FDA-approved drugs, 12 drugs in clinical trials, and 28 preclinical compounds).</td>
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<td>- Screening a subset of these in multiple viral assays identified two sets of pharmacological agents that displayed antiviral activity: inhibitors of mRNA translation and predicted regulators of the Sigma1 and Sigma2 receptors. Further studies of these host factor targeting agents, including their combination with drugs that directly target viral enzymes, could lead to a therapeutic regimen to treat COVID-19.</td>
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| Jama Psychiatry 30APR2020 | Mental Health in the Coronavirus Disease 2019 Emergency—The Italian Response | De Girolamo et al., Italy | Psy | Experience of mental health services and the lessons learned in Italy  
> During epidemic: challenges have occurred in the management of health services  
> Psychiatric wards have been reorganized to admit patients with COVID-19, and many physicians and nurses have been diverted to wards managing patients with COVID-19  
> Facilities for patients with psychiatric needs have been temporarily closed  
> Patient confined in the facilities with very limited or no leave  
Considerable stresses  
Need for a leadership position in the psychosocial management of disasterlike situations. |
| Lancet 30APR2020 | Obesity could shift severe COVID-19 disease to younger ages | Kass, David A.; et al. USA | Clinic | Correlation of body-mass index (BMI) vs age in COVID-19 patients admitted to ICU at 5 US university hospitals, 265 patients (58% male):  
- significant inverse correlation between age and BMI -> younger individuals admitted to hospital more likely obese.  
- no difference by sex  
-> In populations with high prevalence of obesity, COVID-19 will affect younger populations more than previously reported. |
| Viruses 30APR2020 | The SARS-CoV-2 Exerts a Distinctive Strategy for Interacting with the ACE2 Human Receptor | Brielle, Esther S.; et al. Israel | Computational Structural Biology | Using molecular dynamics simulations to compare interaction between human ACE2 receptor and spike protein (SARS-CoV, SARS-CoV-2, and HCoV-NL63):  
- SARS-CoV and SARS-CoV-2 have comparable binding affinities achieved by balancing energetics and dynamics.  
-> SARS-CoV–2–ACE2 complex -> higher number of interacting residues larger, larger interface area, decreased interface residue fluctuations relative to the SARS-CoV–ACE2 complex.  
-> Data implies therapeutic challenge attributed to the enhanced rigidity of the COVID-19 RBD relative to that of SARS-2002. |
| Cell 30APR2020 | Genomic Epidemiology of SARS-CoV-2 in Guangdong Province, China | Lu, Jing; et al. China | Phylogenetic analysis | Extensive early surveillance in densely populated Guangdong, China’s, 1.6 million tests from 30 Jan - 19 March, resulted in 1,388 reported RNA-positive SARS-CoV-2.  
53 genomes generated from infected individuals (combination of metagenomic sequencing and tiling amplicon approaches) indicated:  
- most infections were due to virus importation to Guangdong, and chains of local transmission limited in size and duration, (clustering uncertain due to low virus genetic variation early in the pandemic).  
-> national travel restrictions and province’s large-scale intensive surveillance and intervention measures helped reduce/ eliminate transmission chains.  
- vigilance still required following recent increase in COVID-19 cases imported to China from other countries. |
| Nature 29APR2020 | Massively multiplexed nucleic acid detection using Cas13 | Ackerman, Cheri M. and al. USA | Diagnostic | Combinatorial Arrayed Reactions for Multiplexed Evaluation of Nucleic acids (CARMEN), a platform for scalable, multiplexed pathogen detection.  
The combination of CARMEN and Cas13 detection allowed to develop a multiplexed assay that simultaneously differentiates all 169 human-associated viruses with ≥10 published genome sequences and rapidly incorporated an additional crRNA to detect the causative agent of the 2020 COVID-19 pandemic.  
CARMEN-Cas13 further enables comprehensive subtyping of influenza A strains and multiplexed identification of dozens of HIV drug-resistance mutations.  
**Conclusion:** Scalable, highly-multiplexed CRISPR-based nucleic acid detection shifts diagnostic and surveillance efforts from targeted testing of high-priority samples to comprehensive testing of large sample sets. |
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<tr>
<td>Science 29APR2020</td>
<td>Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China</td>
<td>Zhang J, and al China <a href="https://doi.org/10.1126/science.abb8001">https://doi.org/10.1126/science.abb8001</a></td>
<td>Public Health/Epidemio</td>
<td>Analysis of contact surveys data in Wuhan and Shanghai before and during the outbreak ➔ construction of a model Social distancing ➔ 7-8-fold daily contact / most interaction restricted to household</td>
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<td>The Lancet 29APR2020</td>
<td>Remdesivir in adults with severe COVID-19: a randomised, doubleblind, placebo-controlled, multicentre trial</td>
<td>Wang et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30222-8/fulltext?utm_campaign=coronavirus2019&amp;utm_source=">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30222-8/fulltext?utm_campaign=coronavirus2019&amp;utm_source=</a> twitter&amp;utm_medium=social</td>
<td>Therapeutic</td>
<td>Clinical data showed that the symptoms, hypoxegenemia, and CT opacity changes were improved immediately after the treatment with tocilizumab in most of the patients, suggesting that tocilizumab could be an efficient therapeutic for the treatment of COVID-19. No obvious adverse reactions were observed. Limitations: limited number of patients, single observation study.</td>
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Higher level of healthcare performance is associated with higher incidence ➔ ability to detect?

- Reduction of DCI:
  - slow the increasing number of COVID19
  - improve outcome in COVID-19 patients

Model to study the impact of social distancing and school closures:

- social distancing alone is sufficient to control the outbreak
- School closures ➔ reduce peak incidence (40-60%) and delay the epidemic / impact on the disease dynamic and hospital surge capacity

- Refining age-specific estimates of susceptibility to infection ➔ to evaluating the impact of interventions put in place.
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<tr>
<td>J Infect Dis</td>
<td>Effect of Convalescent Plasma Therapy on Viral Shedding and Survival in COVID-19 Patients</td>
<td>Zeng, Qing-Lei et al, China <a href="https://doi.org/10.1093/infdis/jia228">https://doi.org/10.1093/infdis/jia228</a></td>
<td>Therapeutic</td>
<td>6 COVID-19 subjects with respiratory failure received convalescent plasma at a median of 21.5 days after first detection of viral shedding. All tested negative for SARS-CoV-2 RNA by 3 days after infusion, and 5 died eventually. In conclusion, convalescent plasma treatment can discontinue SARS-CoV-2 shedding but cannot reduce mortality in critically end-stage COVID-19 patients, and treatment should be initiated earlier.</td>
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<tr>
<td>Cancer discovery</td>
<td>Patients with cancer appear more vulnerable to SARS-COV-2: a multi-center study during the COVID-19 outbreak</td>
<td>Dai M, and al USA <a href="https://doi.org/10.1198/2155-8256.20200422">https://doi.org/10.1198/2155-8256.20200422</a></td>
<td>Clinic</td>
<td>Patients with cancer are more vulnerable to infections 195 and 536 patients with and without cancer respectively matched. More in-hospital infection and smoking history in cancer group patients with cancer had higher: - ICU admission [OR:2.84 (1.15 – 5.08)] - Death rate [OR:2.34 (1.15 – 4.77)] - Having one or more severe/critical symptom [OR:2.79 (1.74 – 4.41)] - Changes of needing MV Hematological, lung, metastatic cancer → higher rates of severe events patients with cancer tend to have more severe outcomes</td>
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<td>Public Health</td>
<td>Examining the Effect of Social Distancing on the Compound Growth Rate of SARS-CoV-2 at the County Level (United States) Using Statistical Analyses and a Random Forest Machine Learning Model</td>
<td>Cobb J and al, USA <a href="https://doi.org/10.1093/nsr/nsaa086">https://doi.org/10.1093/nsr/nsaa086</a></td>
<td>Public Health/Epidemi</td>
<td>Trends among US counties and COVID 19 growth rate in relation to existence of shelter in place (SIP) orders Machin learning Limiting gatherings to &lt; 10 people reduced growth rate by 6,6% SIP → reduction of 7,8% versus counties with no SIP SIP orders and limitation gathering were additive Features predicting the effect of SIP: - Population / Longitude / Population per square SIP was effective Counties with large population or high population density: benefit the most from a SIP</td>
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<td>Cell PreProof</td>
<td>Clinically Applicable AI System for Accurate Diagnosis, Quantitative Measurements and Prognosis of COVID-19 Pneumonia Using Computed Tomography</td>
<td>Zhang et al., China <a href="https://doi.org/10.1126/science.aaz5466">https://doi.org/10.1126/science.aaz5466</a></td>
<td>Diagnostic</td>
<td>Using a large computed Tomography (CT) database from 4,154 patients, we developed an AI system that can diagnose NCP and differentiate it from other common pneumonia and normal controls.</td>
</tr>
<tr>
<td>Science Advances 27APR2020</td>
<td>Squalene-based multdrug nanoparticles for improved mitigation of uncontrolled inflammation</td>
<td>Dormont, Flavio et al, France <a href="https://doi.org/10.1126/sciadv.aaz5466">https://doi.org/10.1126/sciadv.aaz5466</a></td>
<td>Therapeutic</td>
<td>Development of multdrug nanoparticles for the mitigation of uncontrolled inflammation.</td>
</tr>
<tr>
<td>European Journal of Clinical Microbiology &amp; Infectious Diseases 27APR2020</td>
<td>Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards</td>
<td>La Scola, Bernard and al. France <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC722834/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC722834/</a></td>
<td>Virology</td>
<td>It is of paramount importance to define when a treated patient can be considered as no longer contagious.</td>
</tr>
</tbody>
</table>

--> Epitopes were selected from known SARS-CoV-2 antigenic proteins (Nucleocapside, membrane, Spike) by using *in silico* prediction tools. |
--> Identification of 6 high immunogenic epitopes targeting HTL, 18 targeting CTL, 9 targeting B-cells. |
--> Epitopes were linked together to build a S66 aa subunit vaccine - Human b-defensine 1 (68aa): as adjuvant |

Extensive bioinformatics analysis suggest that the vaccine is immunogenic, non-toxic, non-allergic, thermostable, with the capability to elicit a humoral and cell-mediated immune response. The binding modes, dynamics, and stability of the vaccine-TLR3 complex were validated by using molecular dynamics simulation studies. Estimation of the half-life of the vaccine:

- 30 h in mammalian reticulocytes (in vitro) |
- > 20 h in yeast (in vivo) |
- > 10 h in E. coli (in vivo), suggesting that the construct is stable in vivo |
--> Probability of showing good protective efficacy and safety against SARS-CoV-2 infection in humans |
## COVID-19 Impact on Vaccine Preventable Diseases

**Journal and date**: Eurosurveillance 27APR2020  
**Title**: Coronavirus disease (COVID-19) – impact on vaccine preventable diseases  
**Authors and link**: Hungerdord et al., UK  
**Field of expertise**: HSS/Politic  
**Key facts**: COVID-19 has caused an unintentional drop of the European’s delivery of routine immunisations of 2020 birth cohorts + catch up campaigns + immunisation of at risk groups because of:  
1. Isolation + COVID-19 illness in families with newborn children  
2. Disruption of vaccine supplies  
3. Healthcare staffing issues  
4. Difficulty to launch a prevention campaign for adults at risk  

**Impact**:  
- Increase in number of sensitive children facing winter illnesses  
- The poorest populations are disproportionately affected  
- Risk of outbreaks of diseases such as measles...  

**To deal with this impact,**  
- ensure consideration + resources for delivery of routine vaccination  
- Vaccination rates should be monitored by analysts and immunization teams to identify hotspots + vaccine coverage surveillance + modeling. This will help face and not allow the Covid to increase the disability and mortality from vaccine preventable diseases.

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## Epidemiology and Transmission of COVID-19 in 391 Cases and 1286 of Their Close Contacts in Shenzhen, China: A Retrospective Cohort Study

**Journal and date**: The Lancet Infectious Diseases 27APR2020  
**Title**: Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study  
**Authors and link**: Qifang B and al, China/USA  
**Field of expertise**: Public Health/Epidemiology  
**Key facts**:  
- 391 cases and 1286 close contact cases were older - Most case mild or moderate and 9% severe  
- Median incubation period: 4.8 days  
- All those develop symptoms will do within 14 days  
- Median time recovery: 20.8 days  
- Contact tracing reduced isolation period by 1.9 days  
- Higher risk of infection:  
  - Household contact (OR:6.27)  
  - Contact travelling with a case (OR:7.06)  
- Secondary attack = 11.2%  
- Children likely to be infected (7.4%) than adults (6.6%)  
- Isolation and contact tracing reduce the R and time during which cases are infectious  
- Children similar risk analyses for transmission and control  

---

## Coronavirus Disease 2019 in Pregnancy

**Journal and date**: Inter J Infectious Disease 27APR2020  
**Title**: Coronavirus disease 2019 in pregnancy  
**Authors and link**: Xu Q and al, China  
**Field of expertise**: Clinic  
**Key facts**:  
- Pregnant woman (28) compared to non-pregnant woman (54)  
- Time from illness to admission: shorter pregnant women  
- Laboratory: significantly  
  - Higher leukocyte in pregnant women (10 vs 2 x 10^3/L)  
  - Higher CRP (17 vs 14 mg/dl)  
- 75% pregnant received antiviral vs 100% non-pregnant  
- No association between  
  - pregnancy and virus clearance time  
  - pregnancy and LOS  
  - pregnancy and severity of disease  
- Median gestational age: 38 [IQR:36.5 – 39]  

**None of neonates had a positive result for SARS-CoV-2**  

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## Emergence of Drift Variants That May Affect COVID-19 Vaccine Development and Antibody Treatment

**Journal and date**: Pathogens 26APR2020  
**Title**: Emergence of Drift Variants That May Affect COVID-19 Vaccine Development and Antibody Treatment  
**Authors and link**: Takahiko Koyama et al., USA  
**Field of expertise**: Vaccines  
**Key facts**:  
- A variant replacing 23403A>G in the S protein B-cell epitope has been frequently observed in European countries (Netherlands, Switzerland, and France) although it is not yet known if it is the predominant sub-strain.  
- This change involves a substitution of a large acidic residue D (aspartic acid) into small hydrophobic residue G (glycine), meaning differences in both size and hydrophobicity in the middle of the epitope and compromising the action of vaccines against wt S protein  
- Genetic drift
<table>
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<tr>
<td>The Lancet. Infectious diseases 27APR2020</td>
<td>Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study</td>
<td>Qifang B and al., China/USA [<a href="http://www.sciencedirect.com/science/article/pii/S1473309920302875">http://www.sciencedirect.com/science/article/pii/S1473309920302875</a>]</td>
<td>Public Health/Epidemi</td>
<td>391 cases and 1286 close contact Cases were older - Most case mild or moderate and 9% severe Median incubation period: 4,8 days All those develop symptoms will do within 14 days Median time recovery: 20,8 days Contact tracing reduced isolation period by 1,9 days Higher risk of infection: - Household contact (OR:6,27) - Contact travelling with a case (OR:7,06) Secondary attack = 11,2% Children likely to be infected (7,4%) than adults (6,6%) → Isolation and contact tracing reduce the R and time during which cases are infectious → Children similar risk → analyses for transmission and control</td>
</tr>
<tr>
<td>An International Journal of Obstetrics &amp; Gynaecology 27APR2020</td>
<td>Vaginal delivery in SARS-CoV-2 infected pregnant women in Northern Italy: a retrospective analysis</td>
<td>Ferrazzi E and al., Italy [<a href="https://doi.org/10.1111/j.1470-0238.2011.02342">https://doi.org/10.1111/j.1470-0238.2011.02342</a>]</td>
<td>Clinic</td>
<td>42-woman COVID-19 who delivered during study period Diagnosis COVID: 10 before delivered / 27 in delivery room / 5 within 36h after 19 woman diagnosed pneumonia which 4 admitted ICU 24 cases vaginal delivery – 10 cesareans related to COVID19 Cesareans related to pneumonia (p=0,024) 3 neonates positive for SARS-CoV: - 2 newborns of women diagnosed after delivery - 1 newborn after vaginal delivery: gastrointestinal and respiratory symptoms → ICU with 24h of MV → vaginal delivery is inappropriate → cesarean: women with sever symptoms</td>
</tr>
<tr>
<td>Clinical microbiology and infection 25APR2020</td>
<td>Umifenovir treatment is not associated with improved outcomes in patients with coronavirus disease 2019: A retrospective study</td>
<td>Lian, Ningfang et al., China [<a href="http://www.sciencedirect.com/science/article/pii/S1187643220302342">http://www.sciencedirect.com/science/article/pii/S1187643220302342</a>]</td>
<td>Therapeutic</td>
<td>Retrospective study, 81 COVID-19 patients included, with 45 in umifenovir group and 36 in control group. Baseline clinical, laboratory characteristics were comparable between two groups. Umifenovir treatment did not shorten the negativity time of SARS-CoV-2, or the length of hospital stay in non-ICU hospitalized patients with COVID-19. No severe side effect was found in umifenovir treatment. Limitations: single center, retrospective study with a small sample size; pharyngeal swabs were not collected every day due to the limited medical resources, and pathogenic nucleic acids were not quantified as well; only included patients with moderate and severe COVID-19, so the effectiveness of umifenovir in mild and critical patients cannot be confirmed in this study</td>
</tr>
<tr>
<td>Cell 24APR2020</td>
<td>SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues</td>
<td>Ziegler et al., USA [<a href="https://www.cell.com/wellfed/fulltext/S1097-4177(20)30006-6">https://www.cell.com/wellfed/fulltext/S1097-4177(20)30006-6</a>]</td>
<td>Fundamental research</td>
<td>→ Meta-analysis of human, primate &amp; mouse scRNA-seq for putative SARS-CoV-2 targets → Type II pneumocytes, nasal secretory cells &amp; absorptive enterocytes are ACE2+TMPRSS2+ → Interferon &amp; influenza increase ACE2 in human nasal epithelia and lung tissue → Mouse Ace2 is not upregulated by interferon, raising implications for disease models</td>
</tr>
<tr>
<td>Infection, Genetics and Evolution 24APR2020</td>
<td>Emerging genetic diversity among clinical isolates of SARS-CoV-2: Lessons for today</td>
<td>Sheikh, Javaid Ahmad; et al., India-Germany-UK [<a href="https://doi.org/10.1053/j.med.2020.104930">https://doi.org/10.1053/j.med.2020.104930</a>]</td>
<td>Phylogenetics</td>
<td>Machine learning approaches to analyse genome sequences of 257 available SARS-CoV-2 clinical isolates: - At least 5 different clades of SARS-CoV-2, great deal of genetic diversity emerging among clinical isolates. - Every continent appears to have multiple introductions of different viral strains (no geographical clustering unlike previous pandemics). - 5’ terminal of viral genome more prone to mutations compared to 3’ end. - ORF3a, spike, ORF3a and E proteins most prone to mutations. - RBD of spike protein is a mutational hotspot (major driver of diversity). - Greater transmission/mortality in the Lombardy region (Italy), compared to other European countries or African continent or China, could not be correlated to any specific molecular divergence pattern.</td>
</tr>
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</table>
Clinical course of coronavirus disease 2019 (COVID-19) in a series of 17 patients with systemic lupus erythematosus under long-term treatment with hydroxychloroquine

Mathian, Alexis et al., France
https://ars.elsevier.com/content/emb/2020/04/23/a mmheumdis-2020-217566.long

Observational study with the aim to follow the clinical course of COVID-19 in patients with systemic lupus erythematosus (SLE) who received long-term treatment with HCQ (17 patients).

-> Main comorbidities were obesity and chronic kidney disease. The duration of HCQ treatment prior to COVID-19 was relatively long, with a median (range) of 7.5 (0.5–29.8) years. Twelve (71%) patients were also treated with prednisone, and seven (41%) with an immunosuppressant.

-> This case series does not allow to draw conclusions on the incidence rate and severity of COVID-19 in SLE. However, it gives a first clinical picture of the course of this infection in patients with SLE treated with HCQ.

Based on the observation that most of the patients with SLE in this study received long-term treatment with HCQ, having blood concentrations of the drug within therapeutic range, is that HCQ does not seem to prevent COVID-19, at least its severe forms, in patients with SLE.

Clinical course of coronavirus disease 2019 (COVID-19) in a series of 17 patients with systemic lupus erythematosus under long-term treatment with hydroxychloroquine

Mathian, Alexis et al., France
https://ars.elsevier.com/content/emb/2020/04/23/a mmheumdis-2020-217566.long

Many COVID-19 patients develop pneumonia called novel coronavirus pneumonia (NCP) and rapidly progress to respiratory failure. However, rapid diagnosis and identification of high-risk patients for early intervention are challenging.

Development of an AI system that can diagnose NCP and differentiate it from other common pneumonia and normal controls.

The AI system can assist radiologists and physicians in performing a quick diagnosis and is able to identify important clinical markers that correlated with the NCP lesion properties.

It provides accurate clinical prognosis that can aid clinicians to consider appropriate early clinical management and allocate resources appropriately.

This AI system has been made available globally to assist the clinicians to combat COVID-19.

SARS-CoV-2 RNA was present in all 4 specimen types, though not all specimen types were positive simultaneously.

C*: SARS-CoV-2 can infect multiple systems, including the urinary tract. Testing different specimen types may be useful for monitoring disease changes and progression, and for establishing a prognosis.

Effect of High vs Low Doses of Chloroquine Diphosphate as Adjunctive Therapy for Patients Hospitalized With Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection: A Randomized Clinical Trial

Borba, Mayla Gabriela Silva et al., Brazil
https://doi.org/10.1001/jama networkopen.2020.8827

Parallel, double-masked, randomized, phase IIb clinical trial 81 adult patients with severe acute respiratory syndrome SARS-CoV-2 infection

High-dosage CQ (ie, 600 mg CQ twice daily for 10 days) versus low-dosage CQ (ie, 450 mg twice daily on day 1 and once daily for 4 days)

At Day 13, 6 of 40 patients (15.0%) in the low-dose group had died, compared with 16 of 41 patients (39.0%) in the high-dose group. Prolongation of QTc interval was observed in 4 of 36 patients (11.1%) in the low-dose group and 7 of 37 patients (18.9%) in the high-dose group. In addition, 2 patients in the high-dose group (2.7%) experienced ventricular tachycardia. The trial was stopped.

The preliminary findings of this study suggest that the higher CQ dosage should not be recommended for critically ill patients with COVID-19.

SARS-CoV-2 can be detected in urine, blood, anal swabs and oropharyngeal swabs specimens

Peng, Liang and al. China

To assess the presence of the SARS-CoV-2 ribonucleic acid (RNA) in urine and blood specimens, and anal and oropharyngeal swabs.

SARS-CoV-2 RNA was present in all 4 specimen types, though not all specimen types were positive simultaneously.

S*: SARS-CoV-2 can infect multiple systems, including the urinary tract. Testing different specimen types may be useful for monitoring disease changes and progression, and for establishing a prognosis.
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| Nature Medicine 24APR2020 | The QT interval in patients with COVID-19 treated with hydroxychloroquine and azithromycin | Chorin, Ehud et al, USA [link](https://doi.org/10.1038/s41395-020-0838-2) | Therapeutic | Charts review and corrected QT (QTc) interval follow-up in a consecutive cohort of 84 patients receiving HY (400mg daily on D1, then 200mg daily from D2 to D5)/AZ (500mg per day for 5 days).  
• QTc significantly prolonged.  
• In a subset of nine (11%) of those patients, the QTc was severely prolonged to >500 ms, a known marker of high risk of malignant arrhythmia and sudden cardiac death. Five of the nine patients had a normal QTc at baseline.  
• No torsades de pointes events recorded for any patients, including those with a severely prolonged QTc.  
⇒ Suggest that the QTc should be followed repeatedly in patients with COVID-19 who are treated with HY/AZ, particularly in those with co-morbidities and in those who are treated with other QT-prolonging medications. |
| JAMA Pediatrics 24APR2020 | Mental Health Status Among Children in Home Confinement During the Coronavirus Disease 2019 Outbreak in Hubei Province, China | Xinyan Xie et al., China [link](https://jamanetwork.com/journals/jamapediatrics/fullarticle/2755130) | Psy | Investigation of depressive and anxiety symptoms among students in Hubei province, China.  
Restricted to home for a mean (SD) of 33.7 days  
⇒ A total of 403 students (22.6%) and 337 students (18.9%) reported depressive and anxiety symptoms, respectively.  
⇒ Students in Wuhan: significantly higher CDI-S scores than those in Huangshi + greater risk of depressive symptoms  
⇒ Students who were slightly or not worried about being affected by COVID-19 had significantly lower CDI-S scores than those who were quite worried, with a decreased risk of depressive symptoms.  
Those who were not optimistic about the epidemic, compared with those who were quite optimistic, had significantly higher CDI-S scores, with an increased risk of depressive symptoms.  
There was no significant association between demographic characteristics and anxiety symptoms. |
| Nat Com 24APR2020 | Neutralization of SARS-CoV-2 spike pseudotyped virus by recombinant ACE2-Ig | Lei, Changhai et al, China [link](https://doi.org/10.1038/s41591-020-0046-4) | Therapeutic | A recombinant protein was generated by connecting the extracellular domain of human ACE2 to the Fc region of the human immunoglobulin IgG1. A fusion protein containing an ACE2 mutant with low catalytic activity is also used in this study. The fusion proteins are then characterized.  
• Both fusion proteins have a high binding affinity for the receptor-binding domains of SARS-CoV and SARS-CoV-2 and exhibit desirable pharmacological properties in mice.  
• Moreover, the fusion proteins neutralize virus pseudotyped with SARS-CoV or SARS-CoV-2 spike proteins in vitro.  
⇒ As these fusion proteins exhibit cross-reactivity against coronaviruses, they have potential applications in the diagnosis, prophylaxis, and treatment of SARS-CoV-2. |
CI*: The proposed multiplex rRT-PCR methodology enable highly sensitive detection of SARS-CoV-2 RNA, reducing reagent use and cost, and time required by clinical laboratory technicians.  
32 patients with COVID 19 and direct oral anticoagulants (DOACs) eligible for antiviral therapy (lopinavir, ritonavir or darunavir)  
DOAC stopped in 20, and continued in 12.  
On average, C-trough DOAC levels were 6.14 times higher during hospitalization than in pre-hospitalization period  
Physicians should consider withholding DOACs from patients with SARS-CoV-2 and replacing them with alternative parenteral antithrombotic strategies for as long as antiviral agents are deemed necessary and until discharge. |
| Journal of Thrombosis and Haemostasis 23APR2020 | Direct oral anticoagulant plasma levels striking increase in severe COVID-19 respiratory syndrome patients treated with antiviral agents. The Cremona experience | Testa, Sophie et al, Italy [link](https://doi.org/10.1111/jh.14871) | Therapeutic |  
⇒ Suggest that the QTc should be followed repeatedly in patients with COVID-19 who are treated with HY/AZ, particularly in those with co-morbidities and in those who are treated with other QT-prolonging medications. |

*CI*: The proposed multiplex rRT-PCR methodology enable highly sensitive detection of SARS-CoV-2 RNA, reducing reagent use and cost, and time required by clinical laboratory technicians.
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<td>BMJ 23APR2020</td>
<td>Covid-19: Two thirds of healthcare workers who have died were from ethnic minorities</td>
<td>Rimmer et al., UK [<a href="https://doi.org/10.1136/bmj">https://doi.org/10.1136/bmj</a>. m1525]</td>
<td>HSS/Politic</td>
<td><code>- Two thirds of healthcare workers who have died from covid-19 were from an ethnic minority background, and at least half were not born in the UK: causes could be biological, medical, or sociological =&gt; need for a concerted effort to seek explanations and solutions. Notable absence of deaths occurred among certain staff groups: </code>- Deaths notably in surgery (five cases), general practice (four), emergency medicine (two). No anaesthetists or intensivists. =&gt; Better use of PPE? Need for a central registry of deaths among health and social care workers</td>
</tr>
<tr>
<td>Canadian Journal of Political Science 23APR2020</td>
<td>Sociodemographic and psychological correlates of compliance with the Covid-19 public health measures in France</td>
<td>Bouraurd et al., France [<a href="https://doi.org/10.1037/50008423920000335">https://doi.org/10.1037/50008423920000335</a>]</td>
<td>HSS/Politic</td>
<td>In order to face the Covid-19 pandemic, the French government adopted health measures at an unprecedented scale to slow the spread of the virus. However, compliance by citizens cannot be taken for granted. Individual panel data =&gt; personality and demographic characteristics are relevant predictors of compliance, more than ideology, trust (towards the government and scientists), and emotional reactions. Main characteristics that lead to complying with the measures are: - Age (older people) - Sex (women) - Conscientiousness Characteristics with no impact on behavior: - Education - Extraversion - Neuroticism - Ideological extremity</td>
</tr>
<tr>
<td>Nature Medicine 23APR2020</td>
<td>SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes</td>
<td>Sungnak, Waradon; et al. UK-France-Netherlands-Germany-USA [<a href="https://doi.org/10.1038/s41585-020-0668-6">https://doi.org/10.1038/s41585-020-0668-6</a>]</td>
<td>Fundamental research</td>
<td>Tropism analysis from single cell RNA-seq datasets from multiple tissues from healthy human donors (Human Cell Atlas tissue consortium): - ACE2 expressed in cells from multiple tissues at generally low levels. - TMPRSS2 highly expressed with a broader distribution, suggesting that ACE2, rather than TMPRSS2, may be a limiting factor for viral entry stage. - ACE2 and TMPRSS2 highest co-expression in nasal secretory epithelial cells (nasal goblet and ciliated cells), co-expressed with genes involved in innate immunity. Expression of viral receptor genes used by other coronaviruses and influenza viruses (ANPEP used by HCoV-22944, DPP4 used by MERS-CoV45, ST6GAL1, ST3GAL4 important for influenza viruses) show: - expression distribution coincided with viral transmissibility based on a comparison to R0 =&gt; upper airway in viruses with higher R0/infertility (SARS-CoV-2, influenza) vs lower airway/lung parenchyma for MERS-CoV =&gt; All data provided as a user-friendly open resource: <a href="http://www.covid19cellatlas.org">www.covid19cellatlas.org</a></td>
</tr>
<tr>
<td>Radiology 23APR2020</td>
<td>Acute Pulmonary Embolism in COVID-19 Patients on CT Angiography and Relationship to D-Dimer Levels</td>
<td>Leonard-Lorant I and al, France [<a href="https://doi.org/10.1148/">https://doi.org/10.1148/</a> radiol.2020205583]</td>
<td>Clinic/Radiology</td>
<td>106 patients COVID19+ and CT angiograms 32 (30%) positive for pulmonary embolus: - Higher D-dimer levels (6110 vs 1920, p&lt;0.01) - More in ICU (75% vs 32u, p&lt;0.01) - Treated more often with LWMH (78% vs 23%) D-dimer levels &gt;2660µg/L: - Sensitivity 100% - Specificity 67%</td>
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| Emerging Infectious Disease 23APR2020 | Population-Based Estimates of Chronic Conditions Affecting Risk for Complications from Coronavirus Disease, United States | Mary L. Adams; USA https://doi.org/10.3201/eid2608.200679 | Demographic / Risk assessment | USA demographic analysis to infer risk for complications from COVID-19 due to chronic conditions: (Based on publicly available 2017 Behavioral Risk Factor Surveillance System (BRFSS) data from telephone surveys of 444,649 randomly selected adults (>18 years of age) in the 50 states and District of Columbia). 

-> 45.4% of US adults are potentially at increased risk of complications because of cardiovascular disease, diabetes, respiratory disease, hypertension, or cancer.  

- Rates increased by age: 19.8% for 18–29 years of age, 80.7% for persons >80 years of age, and varied by state, race/ethnicity, health insurance status, and employment.  |

The results of the validation experiment met the requirements for clinical diagnostic reagents.  

Conclusion: this new assay can achieve rapid and sensitive detection of anti-SARS-CoV-2 IgG in human serum and allow positive identification in suspicious cases; it can also be useful for monitoring the progression COVID-19 and evaluating patients’ response to treatment.  |
| Science of the Total Environment journal 22APR2020 | COVID-19 outbreak: Migration, effects on society, global environment and prevention | Chakraborty et al., India https://doi.org/10.1016/j.scitotenv.2020.138882 | HSS/Politic | Economic impact:  

- Threat of high inflation and high unemployment as a result of lack of productivity and increased expenditures  

- For each month there will be an approximate loss of 2% points in annual GDP growth  

- The tourism sector alone faces an output decrease as high as 50% to 70%  

Global environment:  

-> Non-functioning of industries: decrease of industrial waste emission, recovery of ecosystems and revival of ozone layer.  

->Deforestation linked to disease outbreaks.  

->Population growth: increasing sources of pollution + deforestation = exposing populations to new pathogens  

The global strategy for COVID-19 prevention and control:  

• Global threat that requires a global response involving all countries – in the short term: Restricting mass gatherings + research for new drugs/vaccines/prevention  

• In the long run:  

  o Forestation/Respecting wildlife habitats.  

  o Control of population growth  

  o Global ban on wildlife trade  |
| Science 22APR2020 | Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease | Dai, Wenhao et al, China https://doi.org/10.1126/science.abb4489 | Therapeutic | The main protease (Mpro) of SARS-CoV-2 is a key enzyme that plays a pivotal role in mediating viral replication and transcription.  

Two lead compounds (11a and 11b) targeting Mpro were designed and synthesized.  

Both exhibited excellent inhibitory activity and potent anti-SARS-CoV-2 infection activity.  

The X-ray crystal structures of SARS-CoV-2 Mpro in complex with 11a or 11b, both determined at 1.5 Å resolution, showed that the aldehyde groups of 11a and 11b are covalently bound to Cys145 of Mpro.  

Both compounds showed good PK properties in vivo, and 11a also exhibited low toxicity, suggesting that these compounds are promising drug candidates.  |
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<tr>
<td>European Journal of Epidemiology 22APR2020</td>
<td>Vaccine confidence in the time of COVID-19</td>
<td>Harrison et al., US <a href="https://doi.org/10.1007/s10632-021-04564-3">link</a></td>
<td>HSS/Politic</td>
<td>Rushing for a vaccine in the Covid19 epidemic will not solve the problem of vaccine hesitation among the population. Need to re-imagine the culture of public health more broadly than the delivery of vaccine /technology. <strong>4 points to consider:</strong> 1- Vaccination technologies presented as a technical/ objective solution to the problem of prevention and health of the population. The broader view of public health (social/political equality…) has been eroded: idea that vaccines could obviate need for broader social and environmental policies kept prevention in clinical hands. 2- The success, in the first years, of preventive mass vaccination programs ≠ a timeless public acceptance of vaccination as a preventive strategy. Result of a complex set of circumstances. 3- Reluctance to vaccinate: symptom of a greater desire to ignore threats because they are not bothersome or do not constitute an emergency (yet). 4- Essential ethical dilemma of public health: tension between autonomy and state power. Oppose a logic of &quot;care&quot;: capacity of the States to provide the biomedical resources but also the economic and social resources making it possible to fairly protect the life of the citizens against health disasters. ➞ A broader confidence in vaccines or any pre-emptive measure depends on widespread public trust in preventive health directives and involves strong care and social solidarity structures.</td>
</tr>
<tr>
<td>The Lancet Infectious diseases 22APR2020</td>
<td>No SARS-CoV-2 detected in amniotic fluid in mid-pregnancy</td>
<td>Yu, Nan; et al. China <a href="https://doi.org/10.1016/S1473-3099(20)30520-0">link</a></td>
<td>Clinic</td>
<td>2 pregnant women diagnosed with COVID-19 at first trimester : - In the second trimester, both positive for SARS-CoV-2 total antibodies in serum and negative for SARS-CoV-2 RNA in throat swabs. - Amniotic fluid : negative (RT-PCR) and SARS-CoV-2 IgM and IgG negative in both patients. - In serum : both IgG positive, and only case 1 tested positive for IgM. ➞ No SARS-CoV-2 detected in the amniotic fluid of both women diagnosed with COVID-19 in early stage of pregnancy. - Limit : Only 2 patients, sensitivity (RNA is much less stable in amniotic fluid than is DNA), lack of cord blood.</td>
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<td>Eur J Neurol 22APR2020</td>
<td>Acute-onset smell and taste disorders in the context of Covid-19: a pilot multicenter PCR-based case-control study</td>
<td>Beltran-Corbellini A and al, Spain <a href="https://doi.org/10.1111/ene.14273">link</a></td>
<td>Clinic</td>
<td>Multicenter study – cases (79) controls (40) study Controls: historical group of season influenza patients Basal characteristics: no difference between group Cases: 31(39%) with new onset smell or taste disorders (STD): for 35.5% initial symptoms Now-set of STD more frequent in cases than controls: - Adjusted OR: 21.4 [2.77 – 165.4] No difference for gender/smoking habits/severity between STD or not in case group. Increased frequency of STD in young patients STD more frequent among COVID-19 patients Limitations: historical controls – lack of comparison with others virus – self reported questionnaire.</td>
</tr>
<tr>
<td>Radiology 22APR2020</td>
<td>Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected by Pulmonary CT Angiography</td>
<td>Grillet F and al, France <a href="https://doi.org/10.1148/radiol.2020021544">link</a></td>
<td>Clinic/Radiology</td>
<td>100 patients COVID19+ and severely ill Mean age: 66 years and 70% males 23% had acute pulmonary embolus: - More frequent in critical care unit (p&lt;0.01) - Longer delay from symptoms onset to CT (12 d) Requirement of mechanical ventilation was associated with pulmonary embolus (OR=3.8, p=0.049) Extent of lesions was not associated with pulmonary embolus. <strong>Contrast enhanced CT rather for these patients</strong></td>
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- Threat of high Inflation and high unemployment as a result of lack of productivity and increased expenditures  
- For each month there will be an approximate loss of 2% points in annual GDP growth  
- The tourism sector alone faces an output decrease as high as 50% to 70%  
Global environment:  
- Non-functioning of industries: decrease of industrial waste emission, recovery of ecosystems and revival of ozone layer.  
- Deforestation linked to disease outbreaks.  
- Population growth: increasing sources of pollution + deforestation = exposing populations to new pathogens  
The global strategy for COVID-19 prevention and control:  
- Global threat that requires a global response involving all countries – in the short term: Restricting mass gatherings + research for new drugs/vaccines/prevention  
- In the long run:  
  o Forestation/Respecting wildlife habitats.  
  o Control of population growth  
  o Global ban on wildlife trade |
| Gastroenterology, 21APR2020 | Characteristics and prognosis of patients with inflammatory bowel disease during the SARS-CoV-2 pandemic in the Basque Country (Spain) | Rodríguez-Lago, Iago et al, Espagne, https://doi.org/10.1053/j.gastro.2020.04.043 | Clinic Gastroenterology | Patients (N=40) with inflammatory bowel disease (IBD) and a positive test for SARS-CoV-2 from 5 sites as for the 8th April 2020. Mean age: 59 (range 18 – 90)  
28% under immunomodulator (28%) and 18% under biologic monotherapy.  
Most frequent symptoms: fever (77%) and cough (67%), with 21% reporting diarrhea  
No patient was admitted to the ICU  
Two deaths were reported (5%):  
  a 86-year-old male with diabetes, prostate adenocarcinoma and ulcerative proctitis on mesalamine  
  a 77-year-old male with dementia and left-sided ulcerative colitis under mesalamine and methotrexate.  
patients with IBD and COVID have a good overall prognosis |
SARS-CoV-2 RNA could be detected in the conjunctival swabs of 2.5% (3/121) patients.  
->Eight patients (6.6%) had ocular symptoms: itching, redness, tearing, discharge, and foreign body sensation.  
->Two patients without ocular symptoms tested positive for conjunctival SARS-CoV-2.  
The appearance of ocular symptoms or the result of conjunctival SARS-CoV-2 detection was not significantly correlated with the duration of disease. The proportion with a positive result for SARS-CoV-2 RNA was significantly different between the conjunctival and nasopharyngeal specimens. These findings may help to improve precaution practices during the COVID-19 pandemic. |
61.3% reported at least 1 gastrointestinal symptom:  
anorexia (34,8%), diarrhea (33,7%) and nausea (26,4%)  
Lost of smell/taste more frequent in gastrointestinal symptoms group (p<0,05)  
No difference in patients with gastrointestinal symptom and those without for:  
  - Laboratory results  
  - Rates of clinical deterioration  
  - ICU admission, mechanical ventilation, mortality |
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<th>Field of expertise</th>
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| The Lancet Psychiatry 21APR2020 | Suicide risk and prevention during the COVID-19 pandemic | Gunnel et al., UK [https://doi.org/10.1016/j.lyps.2020.03.017](https://doi.org/10.1016/j.lyps.2020.03.017) | Psy | - Suggestions that suicide rates will rise  
  - Many people vulnerable to mental health problems and suicidal behaviour  
  - Need for timely public health responses: list of actions presented in the publication |
| Emerging Infectious Disease journal 21APR2020 | Possible Bat Origin of Severe Acute Respiratory Syndrome Coronavirus 2 | Susanna K.P. Lau; et al, Hong Kong, China [https://www.ncbi.nlm.nih.gov/pubmed/32070092](https://www.ncbi.nlm.nih.gov/pubmed/32070092) | Virology | Phyllogenetic analysis:  
  - SARS-CoV-2 genome closest to that of SARS-related coronaviruses (SARSr-CoVs) from horseshoe bats, and receptor-binding domain (RBD) closest to that of pangolin viruses.  
  - Potential recombination sites identified around the RBD region - none of existing SARSr-CoVs represents its immediate ancestor.  
  - SARS-CoV-2 probably a novel recombinant virus (genome backbone evolved from Yunnan bat virus–like SARSr-CoVs and RBD from pangolin virus—like SARSr-CoVs).  
  - Its origin and direct ancestral viruses not identified. |
| BMJ 21APR2020 | Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January–March 2020: retrospective cohort study | Zheng S and al, China [https://doi.org/10.1136/bmj.m3449](https://doi.org/10.1136/bmj.m3449) | Clinic/Virology | Retrospective study – hospitalized patients only  
  - 3497 samples collected from 96 patients COVID-19  
  - Samples: serum/respiratory/stool/urine  
  - Duration of virus significantly longer in stool samples:  
    - median duration of virus in severe disease was significantly longer than in mild disease (14 days, 10-21 days; P<0.04)  
    - patients with severe disease: significantly higher viral loads.  
    - Letter shedding peak in severe group  
  - Other samples: no difference  
  - No effect of the antiviral treatment on viral load/duration  
  - Factors associated significantly with duration of virus:  
    - glucocorticoid > 10 days in severe group  
    - men  
    - > 60 years  
  - Limitations: small sample size / viral load influenced by many factors |
  - Cases showed significantly higher fibrinogen and D-dimer plasma levels versus healthy controls  
  - Markedly hypercoagulable thromboelastometry profiles in COVID-19 patients,  
  - COVID-19 patients with acute respiratory failure present a severe hypercoagulability rather than consumptive coagulopathy |
| CDC Morbidity and Mortality Weekly Report 20APR2020 | Cleaning and Disinfectant Chemical Exposures and Temporal Associations with COVID-19 — National Poisdo Data System, United States, January 1, 2020–March 31, 2020 | Chang et al., USA [https://www.cdc.gov/mmwr/volumes/69/wr/mm6916e1.htm](https://www.cdc.gov/mmwr/volumes/69/wr/mm6916e1.htm) | Public Health/Epidemiology | - To assess whether there might be a possible association between COVID-19 cleaning recommendations from public health agencies and the media and the number of chemical exposures reported to the National Poison Data System (NPDS)  
  - During January–March 2020, poison centers received 45,550 exposure calls related to cleaners (28,158) and disinfectants (17,392), representing overall increases of 20.4% and 16.4% from January–March 2019 (37,822) and January–March 2018 (39,122), respectively.  
  - Although NPDS data do not provide information showing a definite link between exposures and COVID-19 cleaning efforts, there appears to be a clear temporal association with increased use of these products. |
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<tr>
<td>Antimicrobials and chemotherapy 20APR2020</td>
<td>Nafamostat mesylate blocks activation of SARS-CoV-2: New treatment option for COVID-19</td>
<td>Hoffmann, Markus et al, Germany</td>
<td>Therapeutic</td>
<td>The SARS-24 CoV-2 spike protein (S) is inserted into the viral envelope and mediates viral entry into cells. For this, the S protein depends on the cellular enzyme transmembrane protease serine 2 (TMPRSS2), which cleaves and thereby activates the S protein. Serine protease inhibitors gabexate mesylate (F0Y), nafamostat mesylate (Futhan) along with camostat mesylate were tested for inhibition of SARS-CoV-2 infection of lung cells. All compounds are approved for human use in Japan.</td>
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<td>J of Emerg Microb and Inf 20APR2020</td>
<td>Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients</td>
<td>Yongchen et al., China</td>
<td>Diagnostic</td>
<td>-&gt; Detailed timeline of nucleic acid testing results for throat or anal samples along with the anti-SARS-CoV-2 IgM and IgG responses in 21 individuals infected with SARS-CoV-2, including 11 non-severe COVID-19 patients, 5 severe COVID-19 patients and 5 asymptomatic carriers.</td>
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<td>Metabolism: clinical and experimental 19APR2020</td>
<td>Obesity as a risk factor for greater severity of COVID-19 in patients with metabolic associated fatty liver disease</td>
<td>Zheng, Kenneth I and al China</td>
<td>Clinic</td>
<td>Sixty six COVID-19 patients with metabolic associated fatty liver disease (MAFLD)</td>
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<td>Clin Inf Dis 19APR2020</td>
<td>Profile of RT-PCR for SARS-CoV-2: a preliminary study from 56 COVID-19 patients</td>
<td>Xiao et al., China</td>
<td>Diagnostic</td>
<td>Dynamic profile of SARS-CoV-2 from 56 recovered COVID-19 patients</td>
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<td>Clinical Therapeutic 19APR2020</td>
<td>Association between clinical manifestations and prognosis in patients with COVID-19</td>
<td>Yu T and al, China</td>
<td>Clinic</td>
<td>Multicenter study – 95 patients COVID-19+ 73 had pneumonia (CT findings), significantly: - Older - Higher BMI, ASAT and LDH levels - Lower lymphocyte and platelet count ARDS (n=24) and non-ARDS (n=71) Independent risk factors associated with ARDS: - High systolic blood pressure (OR:1.04, p=0.025) - High LDH level (OR:1.01, p=0.021) Association with pneumonia exacerbation (n=19): - High BMI (OR: 1.28, p=0.017) - Tobacco smoking (OR: 16.13, p=0.032) Limitations: exacerbation based on CT scan findings</td>
</tr>
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</table>
### Antibody Detection and Dynamic Characteristics in Patients with COVID-19

**Authors and link:** Xiang et al., China

**Field of expertise:** Diagnostic

**Key facts:** ELISA based on the recombinant nucleocapsid protein of SARS-CoV-2.

- Seroconversion of specific IgM and IgG antibodies were observed as early as the 4th day after symptom onset.

- In confirmed patient:
  - **IgM:** Sensitivity, 77.3% Specificity, 100% PPV, 100% NPV, 80.0% Consistency rate: 88.1%
  - **IgG:** Sensitivity, 83.3% Specificity, 95.0% PPV, 94.8% NPV, 83.8% Consistency rate: 88.9%

- In patients with suspected COVID-19, sensitivity, specificity, PPV, NPV, and consistency rate of IgM were 87.5% (21/24), 100%, 100%, 95.2%, and 96.4%, and those of IgG were 70.8% (17/24), 96.6%, 85.0%, 89.1%, and 88.1%.

  -> Both antibodies performed well in serodiagnosis for COVID-19 rely on great specificity.

### Efficacy and safety of lopinavir/ritonavir or arbidol in adult patients with mild/moderate COVID-19: an exploratory randomized controlled trial

**Authors and link:** Li, Y et al, China

**Field of expertise:** Therapeutics

**Key facts:** Exploratory randomized (2:2:1) controlled trial assessing the efficacy and safety of lopinavir/ritonavir (LPV/r) or arbidol monotherapy for treating patients with mild/moderate COVID-19.

- 86 patients with mild/moderate COVID-19 enrolled.

- LPV/r and arbidol did not shorten the time of positive-to-negative conversion of COVID-19 nucleic acid in respiratory specimens (9.0 vs. 9.1 vs. 9.3 days), nor did they improve the symptoms of COVID-19 or pneumonia on lung CT imaging at 7 days and 14 days. More patients treated with LPV/r progressed from mild/moderate to severe/critical status than patients from the other two groups. Adverse events occurred in the treatment groups.

- Limitations: small sample size, no severely or critically ill patients, or patients at increased risk of poor outcome with many comorbidities, not completely blinded.

### Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China

**Authors and link:** Zhu L and al, China

**Field of expertise:** Clinic

**Key facts:** 10 kidney transplant patients + COVID-19 pneumonia:

- Classical symptoms: fever, cough, shortness of breath, dyspnea
- 100% lymphopenia and elevated CRP
- 50% had temporally increase of serum creatinine
- Abnormalities on chest CT scan
- 8/10 were severe or critical cases and 1 died

**Versus controls:**

- Transplants patients more severe
- Much longer time to become negative for SARS-CoV-2 (median time: 28.4 d)
- Reduce fatal severe pneumonia: suppressing the hyperimmune response

### Comparative pathogenesis of COVID-19, MERS, and SARS in a nonhuman primate model

**Authors and link:** Rockx, Barry; et al. Netherlands

**Field of expertise:** Fundamental research

**Key facts:** Cynomolgus macaques inoculated with SARS-CoV-2 or MERS-CoV.

- SARS-CoV-2 causes COVID-19-like disease in macaques: virus excreted from nose and throat in the absence of clinical signs, detected in type I and II pneumocytes in foci of diffuse alveolar damage and in ciliated epithelial cells of nasal, bronchial, and bronchiolar mucosa.
- Lung lesions typically more severe with SARS-CoV-2 than in MERS-CoV infection, where virus was detected mainly in type II pneumocytes.
- Cynomolgus macaques provide a new infection model to test preventive and therapeutic strategies.
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<tr>
<td>J Thromb Haemost 17APR2020</td>
<td>The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome</td>
<td>Ranucci M and al, Italy <a href="https://doi.org/10.1111/jh.14854">link</a></td>
<td>Clinic</td>
<td>16 patients COVID-19 pneumonia and ARDS in ICU 94% were male and 31% were obese D-Dimer, IL-6 and fibrinogen = higher than upper limit Association between IL-6 and fibrinogen levels Clot firmness higher than normal Follow-up: - Significant decrease of D-dimere and fibrinogen - Significant prolongation of the aPTT Pro-coagulant profile of COVID-19 ARDS patients and its normalization after an increased thromboprophylaxis. Limitation: lack of data on thrombin generation and fibrinolysis. Further studies: best prophylaxis and treatment?</td>
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<td>Circulation research 17APR2020</td>
<td>Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19</td>
<td>Zhang, Peng et al, China <a href="https://doi.org/10.1161/CIRCRESAHA.120.317134">link</a></td>
<td>Therapeutics</td>
<td>Retrospective, multi-center study including 1128 adult patients with hypertension diagnosed with COVID-19, including 188 taking ACEI/ARB (ACEI/ARB group; median age 64 [IQR 55–68] years; 53.2% men) and 940 without using ACEI/ARB (non-ACEI/ARB group; median age 64 [IQR 57–69]; 53.5% men). Among hospitalized COVID-19 patients with hypertension, inpatient use of ACEI/ARB was associated with lower risk of all-cause mortality compared with ACEI/ARB non-users. Limitations: hospital only, modest sample size, retrospective study.</td>
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<td>Gut 17APR2020</td>
<td>Covid-19 and immunomodulation in IBD</td>
<td>Neurath, Germany <a href="https://gut.bmj.com/content/early/2020/04/20/gutjnl-2020-323159">link</a></td>
<td>Immunology</td>
<td>Results/recommendations: - No evidence for an increased risk or aggravated outcomes in patients with IBD in the context of covid-19 - However, covid-19 risks situation comprise older patients with IBD with comorbidities as well as patients suffering from malnutrition - Experimental covid-19 treatment with hydroxychloroquine or remdesivir may increase the risks for drug-drug interactions with established IBD medications. - Currently available recommendations for patients with IBD are: o Continue current treatment if disease is stable and discuss suitable medicine if disease has flared o Use of mesalamine should be continued and should not increase the risk of infection. o Corticosteroid use can be continued, but be cautious of possible side effects. o A new prescription of immunosuppressant or increase in dose of an ongoing immunosuppressant is not recommended in epidemic areas. o Use of biologics such as the antitumour necrosis factors infliximab or adalimumab should be continued. o If infliximab infusion is not accessible, switching to adalimumab injection at home should be considered. o Vedolizumab use can be continued due to the specificity of the drug for the intestine. o Ustekinumab use can be continued, but starting ustekinumab requires infusion centre visits and therefore should be discussed before initiation of therapy. o Enteral nutrition might be used if biologics are not accessible o Tofacitinib should not be newly prescribed in epidemic areas unless there are no other alternatives.</td>
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<td>Nature Biotechnology 16APR2020</td>
<td>CRISPR–Cas12-based detection of SARS-CoV-2</td>
<td>Broughton, James P. and al. USA <a href="https://doi.org/10.1038/s41598-020-0515-4">link</a></td>
<td>Diagnostic</td>
<td>Development of a rapid (&lt;40 min), easy-to-implement and accurate CRISPR–Cas12-based lateral flow assay for detection of SARS-CoV-2 from respiratory swab RNA extracts. Validation using contrived reference samples and clinical samples, including 36 patients with COVID-19 infection and 42 patients with other viral respiratory infections. The CRISPR-based DETECTR assay provides a visual and faster alternative to SARS-CoV-2 real-time RT–PCR assay, with 95% positive predictive agreement and 100% negative predictive agreement.</td>
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<td>NEJM 16APR2020</td>
<td>Not a Perfect Storm — Covid-19 and the Importance of Language</td>
<td>Brandt M. et al., USA <a href="https://doi.org/10.1056/NEJMmp2009312">link</a></td>
<td>HSS/Politic</td>
<td>Metaphors we use to describe disease shape our experience of illness: has an impact on the approach taken against the Covid =&gt; misleading our approach. Covid characterized as a “perfect storm”=“fierce storm arising from a rare combination of adverse meteorological factors” (randomness/volatility =&gt; reactive, disempowering). Vs developing and implementing preventive strategies to prepare for pandemics What is the impact of the language facing Pandemics? - The use of language eludes important conversation about our responsibility for emerging zoonoses + effects on the most vulnerable people. - The force of language minimizes our capacity to anticipate and prevent the next epidemics: long term investments in disease tracking and surveillance, scientific research and public health infrastructure <strong>Conclusion:</strong> Covid is not a simple natural event. It is also the result of human actions. =&gt; Be conscientious about our language and its implications as a first step for reforms and preventive measures to strengthen our health infrastructure to face future disease outbreaks.</td>
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<tr>
<td>Cell 16APR2020</td>
<td>Development of CRISPR as an antiviral strategy to combat SARS-CoV-2 and influenza</td>
<td>Abbott, T et al, USA <a href="https://www.cell.com/press/assets/products/coronavirus/C111_CELL-O-20-00736.pdf">link</a></td>
<td>Therapeutics</td>
<td>A CRISPR-Cas13-based strategy, PAC-MAN (Prophylactic Antiviral CRISPR in huMAN cells), for viral inhibition can <strong>effectively degrade RNA from SARS-CoV-2 sequences</strong> and live influenza A virus (IAV) in human lung epithelial cells. CRISPR RNAs (crRNAs) targeting conserved viral regions were designed and screened, and <strong>functional crRNAs targeting SARS-CoV-2 were identified.</strong> The bioinformatic analysis showed a group of only six crRNAs can target more than 90% of all coronaviruses. With the development of a safe and effective system for respiratory tract delivery, PAC-MAN has the potential to become an important pan-coronavirus inhibition strategy.</td>
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<td>Plos One 16APR2020</td>
<td>Mental health problems and social media exposure during COVID-19 outbreak</td>
<td>Gao et al., China <a href="https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0231924">link</a></td>
<td>Psy</td>
<td>Social media exposure (SME) +++ during Covid-19. Study on 4872 participants from 31 provinces and autonomous region -&gt; High prevalence of mental health problems -&gt;frequently SME was positively associated with high odds of anxiety (OR = 1.72, 95%CI: 1.31–2.26) and combination of depression and anxiety (CDA) (OR = 1.91, 95%CI: 1.52–2.41) compared with less SME. -&gt; Need to combat with “infodemic” while combating public health emergency</td>
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<td>International journal of antimicrobial agents 16APR2020</td>
<td>Can post-exposure prophylaxis for COVID-19 be considered as one of outbreak response strategies in long-term care hospitals?</td>
<td>Lee, Sun Hee et al, Republic of Korea <a href="https://doi.org/10.1016/j.jamiaog.2020.105988">link</a></td>
<td>Therapeutics</td>
<td>After a large COVID-19 exposure event in a long-term care hospital (LTCH) in Korea, PEP using hydroxychloroquine (HCQ) was conducted to 211 persons including 189 patients and 22 careworkers, with baseline negative PCR tests for COVID-19 (oral, dose of 400mg daily until the completion of 14 days of quarantine). =&gt; PEP was completed in 184 (97.4%) patients and 21 (95.5%) careworkers without serious adverse events. =&gt; At the end of 14 days of quarantine, follow-up PCR tests were all negative. <strong>Limitations:</strong> - no control group. - 92 hospital staff showed negative results by RT-PCR after 14-day quarantine even though they did not receive PEP, however this group was considered at low risk exposure.</td>
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<td>ACS nano 15APR2020</td>
<td>Rapid Detection of COVID-19 Causative Virus (SARS-CoV-2) in Human Nasopharyngeal Swab Specimens Using Field-Effect Transistor-Based Biosensor</td>
<td>Seo, Giwan and al Rep of Korea <a href="https://doi.org/10.1021/acsnano.0c02823">https://doi.org/10.1021/acsnano.0c02823</a></td>
<td>Diagnostic</td>
<td>Technology based on a field-effect transistor (FET)-based biosensing device for detecting SARS-CoV-2 in clinical samples. The sensor was produced by coating graphene sheets of the FET with a specific antibody against SARS-CoV-2 spike protein. The performance of the sensor was determined using antigen protein, cultured virus, and nasopharyngeal swab specimens from COVID-19 patients. CI*: the device is a highly sensitive immunological diagnostic method for COVID-19 that requires no sample pretreatment or labeling.</td>
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<tr>
<td>Nature Medicine 15APR2020</td>
<td>Temporal dynamics in viral shedding and transmissibility of COVID-19</td>
<td>He, Xi; et al. China <a href="https://doi.org/10.1038/s41591-020-0869-5">https://doi.org/10.1038/s41591-020-0869-5</a></td>
<td>Virology</td>
<td>Temporal viral shedding (94 patients with lab-confirmed COVID-19) and modeling of COVID-19 infectiousness profiles (separate 77 infector–infectee transmission pairs): - highest viral load in throat swabs was at the time of symptom onset. - 44% of secondary cases were infected during the infectors’ presymptomatic stage, in settings with substantial household clustering, active case finding and quarantine outside the home. - Control measures should be adjusted to account for substantial presymptomatic transmission.</td>
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<td>Journal of Biomolecular Structure and Dynamics 15APR2020</td>
<td>Reverse vaccinology approach to design a novel multi-epitope vaccine candidate against COVID-19: an in silico study</td>
<td>Maryam Enayatkhani et al. Iran <a href="https://doi.org/10.1088/0305-4470/53/11/1156411">https://doi.org/10.1088/0305-4470/53/11/1156411</a></td>
<td>Vaccine</td>
<td>3 known antigenic proteins of SARS-CoV-2 (Nucleocapsid, ORF3a, and Membrane protein) -&gt; used to predict in silico the potential immunogenic B and T-cell epitopes. -&gt; Prediction of best tertiary structure of selected epitopes docking TLR4 and HLA-A - Evaluation of the end the stability of complex of these receptors with the selected epitopes , by molecular Dynamic simulation methods. Antigenicity of the designed antigenic sequence -&gt; predicted by bioinformatic methods. The designed protein sequences without adjuvant were sufficient to produce an immune response. The allergenicity of the sequence was also predicted and this vaccine was not recognized as an allergen. As a conclusion, the engineered epitope could be considered as a possible vaccine candidate against COVID-19</td>
</tr>
<tr>
<td>Nat Med 15APR2020</td>
<td>Temporal dynamics in viral shedding and transmissibility of COVID-19</td>
<td>He et al., China <a href="https://www.nature.com/articles/s41591-020-0869-5">https://www.nature.com/articles/s41591-020-0869-5</a></td>
<td>Public Health/Epidemio</td>
<td>94 COVID-19 patients: - Highest Viral loads in Throat swabs at time of symptom onset - Estimation: 44% (95% confidence interval, 25–69%) of secondary cases were infected during the index cases’ presymptomatic stage -&gt; Infectiousness started from 2.3 days (95% CI, 0.8–3.0 days) before symptom onset and peaked at 0.7 days (95% CI, −0.2–2.0 days) before symptom onset</td>
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<tr>
<td>ACS nano 14APR2020</td>
<td>Computational Design of ACE2-Based Peptide Inhibitors of SARS-CoV-2</td>
<td>Han, Yaxiao et al., USA <a href="https://doi.org/10.1021/acsnano.0c02857">https://doi.org/10.1021/acsnano.0c02857</a></td>
<td>Therapeutics</td>
<td>Design of peptide inhibitors against the SARS-CoV-2, mostly formed by two sequential self-supporting alpha-helices (bundle) extracted from the protease domain (PD) of angiotensin-converting enzyme 2 (ACE2), which bind to the SARS-CoV-2 receptor binding domains. Molecular dynamics simulations revealed that the alpha-helical peptides maintain their secondary structure and provide a highly specific and stable binding (blocking) to SARS-CoV-2. To provide a multivalent binding to the SARS-CoV-2 receptors, many such peptides could be attached to the surfaces of nanoparticle carriers. The proposed peptide inhibitors could provide simple and efficient therapeutics against the COVID-19 disease.</td>
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<td>Kidney International 14APR2020</td>
<td>Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China</td>
<td>Su et al., China <a href="https://www.kidneyinternational.org/article/S1004-142X(20)30369-0/fulltext">https://www.kidneyinternational.org/article/S1004-142X(20)30369-0/fulltext</a></td>
<td>Clinic</td>
<td>Analyzing kidney abnormalities in 26 autopsies: Patients: respiratory failure associated with multiple organ dysfunction syndrome as the cause of death. 9/26: clinical signs of kidney injury that included increased serum creatinine and/or new-onset proteinuria. Light microscopy: diffuse proximal tubule injury with loss of brush border, non-isometric vacuolar degeneration, and even frank necrosis. + Occasional hemosiderin granules and pigmented casts. + Prominent erythrocyte aggregates obstructing the lumen of capillaries without platelet or fibrinoid material. + Absence of evidence of vasculitis, interstitial inflammation or hemorrhage. Electron microscopic: clusters of coronavirus particles with distinctive spikes in the tubular epithelium and podocytes. ACE2 was found to be upregulated in patients with COVID-19, and immunostaining with SARS-CoV nucleoprotein antibody was positive in tubules.</td>
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<tr>
<td>Journal of Autoimmunity 14APR2020</td>
<td>Assessing ACE2 expression patterns in lung tissues in the pathogenesis of COVID-19</td>
<td>Li, Guoping; et al. China <a href="https://doi.org/10.1016/j.jaut.2020.102463">https://doi.org/10.1016/j.jaut.2020.102463</a></td>
<td>Fundamental research</td>
<td>Data mining analysis (6 independent studies) of ACE2 expression in healthy population compared to patients with underlying diseases (chronic obstructive pulmonary diseases, asthma patients, smokers): - no difference in ACE2 lung expression in healthy vs patients with chronic airway disease, suggesting no difference in susceptibility to SARS-CoV-2 infection. - long-term smokers have significantly greater ACE2 expression than healthy non-smokers (smal airway epithelium), suggesting a risk factor for COVID-19. - ACE2 expression dramatically increased between 12-24h post SARS-CoV infection (airway epithelial cells), suggesting a role of ACE2 in post-infectious regulation. - In SARS-CoV infected cells, ACE2 expression significantly correlated with activation of neutrophils, NK cells, Th17 cells, Th2 cells, Th1 cells, dendritic cells and production of IL-1, IL-10, IL-6 and IL-8 (healthy non-smokers). Protein-protein regulation networks before and after infection indentify: - ribosomal protein RPS3 plays a key role in viral replication. - non-receptor protein kinase SRC has a role in macrophage mediated innate immunity and cytokine release. Working hypothesis: SARS-CoV-2 infection increases ACE2 expression, which affects RPS3 and SRC activity, two key hub genes involved in viral replication and inflammatory responses.</td>
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<td>Disaster medicine and public health preparedness 14APR2020</td>
<td>Public Education and Electronic Awareness of the New Coronavirus (COVID-19): Experiences from Iran</td>
<td>Peyravi, M. et al, Iran <a href="https://doi.org/10.1017/dmp.2020.94">https://doi.org/10.1017/dmp.2020.94</a></td>
<td>HSS/Polic</td>
<td>When WHO declared a global health emergency, the Iranian Red Crescent Society and Ministry of Health took measures for public awareness (13 measures).</td>
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<tr>
<td>BMJ 14APR2020</td>
<td>COVID-19: why we need a national health and social care service</td>
<td>Pollock, A. et al, UK <a href="https://doi.org/10.1136/bmj.m1465">https://doi.org/10.1136/bmj.m1465</a></td>
<td>HSS/Polic</td>
<td>Social services in the UK: most privatized and fragmented in Western world.</td>
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<td>High proportion of NHS workforce currently off work+pay very low. Sector short 120 000 workers. Emergency legislation in the UK curtailed rights to social care services of elderly, ill and disabled people in community/residential settings contrary to international law and common sense.</td>
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<td>Lack of access to, i.e., support after hospital discharge or mental health services: =&gt; more health crises &amp; hospital admissions + essential care workers taking time off to care for family members.</td>
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<td>Conclusion: Universal integrated health and social care service =&gt; bring all services and staff under government control.</td>
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<td>=&gt; social care delivered by a trained and properly equipped workforce with decent terms of service.</td>
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<td>+ mandate collection of data quantifying effect of COVID on social care sector.</td>
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<td>Ear, nose, &amp; throat journal 13APR2020</td>
<td>Clinical Presentation of COVID-19: A Systematic Review Focusing on Upper Airway Symptoms</td>
<td>Lovato A and al, Italy <a href="https://doi.org/10.1177/0145561320920762">https://doi.org/10.1177/0145561320920762</a></td>
<td>Clinic</td>
<td>5 retrospective studies and cohort studies</td>
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<td>Quality of evidence = level 4 (low)</td>
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<td>1556 patients: 57.5% males</td>
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<td>Mortality: 2.4% - ICU admission: 7.3%</td>
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<td>Upper airways symptoms:</td>
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<td>- Pharyngodynia: 12,4%</td>
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<td>- Nasal congestion: 3.7%</td>
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<td>- Rhinorrhea: 4% (1 study)</td>
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<td>None of the studies reported olfactory or gustative dysfunction</td>
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<td>Rest symptoms: same other study (fever, cough, fatigue)</td>
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<td>Alteration chest CT: 83% → bilateral++++</td>
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<td>Severe cases: older, lymphopenia, radiologic abnormalities</td>
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<td>Limits: only hospitalized patients → not full clinical spectrum of COVID-19 / olfactory disorders could have been underestimated</td>
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<td>Mayo Clinic Proceedings 13APR2020</td>
<td>ST-segment Elevation, Myocardial Injury, and Suspected or Confirmed COVID-19 Patients: Diagnostic and Treatment Uncertainties</td>
<td>Bennett et al., USA <a href="https://doi.org/10.1001/jamacardio.2020.04005">https://doi.org/10.1001/jamacardio.2020.04005</a></td>
<td>Diagnostic</td>
<td>-&gt; For patients with COVID-19, the evaluation can be challenging due to reports of STE without obstructive coronary disease, which creates diagnostic and management challenges</td>
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<tr>
<td>Travel Med. Infect. Dis. 11APR2020</td>
<td>Clinical and microbiological effect of a combination of hydroxychloroquine and azithromycin in 80 COVID-19 patients with at least a six-day follow up: A pilot observational study</td>
<td>Gautret, Philippe et al, France <a href="https://doi.org/10.1016/j.jtma.2020.101663">https://doi.org/10.1016/j.jtma.2020.101663</a></td>
<td>Therapeutic</td>
<td>Uncontrolled non-comparative observational study in a cohort of 80 relatively mildly infected inpatients treated with a combination of hydroxychloroquine and azithromycin over a period of at least three days. All patients improved clinically except one 86 year-old patient who died, and one 74 year-old patient still in intensive care. A rapid fall of nasopharyngeal viral load was noted, with 83% negative at Day7, and 93% at Day8. Virus cultures from patient respiratory samples were negative in 97.5% of patients at Day5. Limitations: descriptive pilot study in only 80 patients with relatively mild clinical presentation. No analytic approach to account for possible confounds including notably the severity of illness.</td>
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<tr>
<td>The Lancet 11APR2020</td>
<td>Centring sexual and reproductive health and justice in the global COVID-19 response</td>
<td>Matthew J Harris et al., UK <a href="https://doi.org/10.1016/S0140-6736(20)38015-5">https://doi.org/10.1016/S0140-6736(20)38015-5</a></td>
<td>HSS/Politic</td>
<td>COVID-19 + existing sexual &amp; reproductive health inequities =&gt; women, girls and vulnerable populations’ health, wellbeing and economic stability disproportionately impacted. 1) COVID-19 =&gt; Increased risks for women - Women’s risk factors of contracting COVID-19 may be higher = 70% of the global health and social care workforce worldwide, - Potential pregnancy-related complications 2) Impact on sexual/reproductive health care - Disruption/Diversion of resources away from essential sexual/reproductive health care for COVID - Restrictive global policies that target vulnerable populations (Protecting Life in Global Health Assistance + migration policies of deterrence) Solutions: - Additional resources for sexual/reproductive health care + increase of telemedicine - Sex-disaggregated mortality and morbidity surveillance for COVID-19 research - Community driven efforts: recognize inequitable power structures + collaborative response - Eliminate legal/policy restrictions to sexual/reproductive health care.</td>
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<td>Journal of Clinical Virology 11APR2020</td>
<td>Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: a descriptive study</td>
<td>Xiao et al., China <a href="https://www.sciencedirect.com/science/article/pii/S1879627520308857">https://www.sciencedirect.com/science/article/pii/S1879627520308857</a></td>
<td>Diagnostic</td>
<td>301 patients: -&gt; median period between symptoms presence and positive SARS-CoV-2 RT-PCR results was 16 days -&gt; median period between symptoms presence and an effective negative SARS-CoV-2 RT-PCR result was 20 days Although two consecutive negative results were confirmed in 70 patients, 30% of them had positive viral test results for the third time. Using specimens from nasal swabs to run the RT-PCR test showed a higher positive rate than using specimens from throat swabs.</td>
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<tr>
<td>Science 10APR2020</td>
<td>Structure of the RNA-dependent RNA polymerase from COVID-19 virus</td>
<td>Gao, Yan; et al., China - Australia <a href="https://doi.org/10.1126/science.aaz7488">https://doi.org/10.1126/science.aaz7488</a></td>
<td>Structural biology</td>
<td>Cryo-EM structure of SARS-CoV-2 full-length RNA-dependent RNA polymerase (RdRp, also named nsp12) in complex with cofactors nsp7 and nsp8 (2.9 Å resolution) reveal: -&gt; Conserved architecture of nsp12 with polymerase core of SARS-CoV, and resolution of a newly identified β-hairpin domain at its N terminus. -&gt; Comparative modeling reveals how remdesivir binds to nsp12 polymerase, its primary antiviral drug target. -&gt; provides basis for design of new antiviral therapeutics /cocktails targeting viral RdRp (nsp12).</td>
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<td>Emerg. Infect. Dis. 10APR2020</td>
<td>Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020</td>
<td>Zhen-Dong Guo; et al., China <a href="https://doi.org/10.3201/eid2607.200885">https://doi.org/10.3201/eid2607.200885</a></td>
<td>Virology</td>
<td>Samples taken from potentially contaminated objects and air from an ICU (housed 15 patients with severe COVID-19) and a general ward (housed 24 patients with milder COVID-19): - SARS-CoV-2 contamination greater in ICU than general ward. - Almost all positive samples concentrated in the contaminated areas. - Virus widely distributed on floors, computer mice, trash cans, sickbed handrails in both the ICU and general wards. - Virus-laden aerosols mainly concentrated near and downstream from patients, up to 4 m. -&gt; Atricter protective measures should be taken by medical staff working in the ICUs then general wards. -&gt; Aerosol distribution in the general ward indicate transmission distance of SARS-CoV-2 might be 4 m</td>
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<td>NEJM 10APR2020</td>
<td>Compassionate Use of Remdesivir for Patients with Severe Covid-19</td>
<td>Grein, Jonathan et al, USA <a href="https://doi.org/10.1056/NEJMoa2007016">https://doi.org/10.1056/NEJMoa2007016</a></td>
<td>Therapeutic</td>
<td>63 compassionate use of remdesivir for COVID patients with either an oxygen saturation of 94% or less while breathing ambient air or need for oxygen support: 40 patients (75%) received the full 10-day course of remdesivir, 10 (19%) received 5 to 9 days of treatment, and 3 (6%) fewer than 5 days of treatment. During a median follow-up of 18 days, 36 patients (68%) had an improvement in oxygen-support class, including 17 of 30 patients (57%) receiving mechanical ventilation who were extubated. A total of 25 patients (47%) were discharged, and 7 patients (13%) died Point of attention : Measurement of efficacy will require ongoing randomized, placebo-controlled trials</td>
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<td>Journal of Clinical Virology 10APR2020</td>
<td>Clinical characteristics and risk assessment of newborns born to mothers with COVID-19</td>
<td>Yang, Pu et al, China <a href="https://doi.org/10.1016/j.jcv.2020.104356">https://doi.org/10.1016/j.jcv.2020.104356</a></td>
<td>Clinic</td>
<td>Case report of 7 newborns delivered by SARS-CoV-2 infected pregnant women The current data show that the infection of SARS-CoV-2 in late pregnant women does not cause adverse outcomes in their newborns</td>
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<td>Euro Surv 9APR2020</td>
<td>Excess cases of influenza-like illnesses synchronous with coronavirus disease (COVID-19) epidemic, France, March 2020</td>
<td>Boëlle, Pierre-Yves et al, France <a href="https://doi.org/10.5832/ie.2560-7017.3.2020.25.14.2000126">https://doi.org/10.5832/ie.2560-7017.3.2020.25.14.2000126</a></td>
<td>HSS/Politic</td>
<td>Comparison of data from the Sentinelles network monitors influenza-like illnesses (ILI) and acute respiratory infections (ARI) in general practice in France and official COVID 19 reported cases in early March 2020 from the Santé Publique France It is estimated that 760 (95% CrI: 219–1,706) of acute respiratory infections consultations in those older than 65 years in two regions of France (BFC and GRE) could have been caused by COVID-19 during week 10.</td>
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| Clinical infectious disease 9APR2020 | Factors associated with prolonged viral RNA shedding in patients with COVID-19 | Xu K and al, China [link](https://doi.org/10.1093/clinmicrobiol/213) | Clinic | Retrospective study – Two hospital – 113 patients  
Median age: 52 years – 58,4% were male  
28,3% were diagnosed as severe illness  
Median hospital stays: 15 days  
74,3% had viral RNA clearance within 21 days after illness onset (median: 15 days)  
Prolonged RNA shedding:  
- Male (p=0.009)  
- Old age (p=0.033)  
- Concomitant hypertension (p=0.009)  
- Invasive mechanical ventilation (p=0.006)  
- Use of corticosteroid (p=0.025)  
- Delay recovery on radiological image (p<0.001)  
→ Multivariate analysis:  
- Male (OR: 3.24)  
- Delay hospital admission (OR: 1.30)  
- Invasive mechanical support  
Limitations:  
- Viral RNA shedding ≠ viral shedding  
- Didn’t not evaluated the effect of the treatment |
| Obesity 9APR2020 | High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation | Simonnet A and al, France [link](https://doi.org/10.1002/oby.22831) | Clinic | Retrospective study – 124 patients in ICU  
Control group: non-SARS-CoV2 in ICU  
Median age: 60 years – 73% male -15% died  
68,6% required invasive mechanical ventilation (IMV)  
Obesity and severe obesity were significantly more frequent in SARS-CoV2 patients (p<0.001)  
Median BMI in SARS-CoV2 patients higher than in non-SARS-CoV2: 29,6 vs 24,0 (p<0.001)  
IMV vs non IMV:  
- BMI higher in IMV group: 31,1 vs 27,0 (p<0.001)  
Need for IMV gradually increase with BMI category.  
Patients with obesity should take extra measure to avoid COVID19 contamination. |
| F1000 Research 9APR2020 | In silico identification of vaccine targets for 2019-nCoV | Chloe H. Lee and Hashem Koohy UK [link](https://doi.org/10.12688/f1000research.22507.1) | Vaccine | The authors define computationally identified immunogenic and/or cross-reactive peptides from 2019-nCoV, based on comparison with immunogenic peptides deposited in the Immune Epitope Database and Analysis Resource (IEDB). They found:  
i) 28 SARS-derived peptides having exact matches in 2019-nCoV proteome previously characterized to be immunogenic by in vitro T cell assays (high affinity to HLA-A class I and II and targeted by CD8+ and CD4+ T cells)  
ii) 22 nCoV peptides having a high sequence similarity with immunogenic peptides but with a greater predicted immunogenicity score  
iii) 44 nCoV peptides predicted to be immunogenic by the iPred algorithm and 1G4 TCR positional weight matrices respectively (de novo in silico search of immunogenic peptides against the 2019-nCoV proteome sequence) |
| Psychotherapy and psychosomatics 9APR2020 | Mental Health and Psychosocial Problems of Medical Health Workers during the COVID-19 Epidemic in China | Hong-xing Wang et al., China [link](https://doi.org/10.1093/psycho/bax158) | Psy | Method : online survey (2182 participants from China)  
Result :  
- higher prevalence rates of psychological symptoms among medical health workers = insomnia, anxiety, depression, somatization, and obsessive-compulsive symptoms  
- risk factors : having organic disease, living in rural areas, being female, and being at risk of contact with COVID-19 patients  
Main reasons :  
- insufficient understanding of the virus initially  
- lack of prevention and control knowledge  
- long-term workload  
- high risk of exposure to patients with COVID-19  
- shortage of medical protective equipment, lack of rest  
- exposure to critical life events, such as death.  
Need for :  
- health protection and adequate working conditions: lowering job demands and workload / increasing job control and reward, medical protective equipment, adequate rest...  
- recovery programs focused on resilience and psychological well-being |
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| **Clinical infectious diseases 9APR2020** | Comparative replication and immune activation profiles of SARS-CoV-2 and SARS-CoV in human lungs: an ex vivo study with implications for the pathogenesis of COVID-19 | Chu, Hin; et al. China https://doi.org/10.1093/cid/ciaa410 | Virology | Ex vivo human lung tissues infected with SARS-CoV-2 compared to SARS-CoV:  
- SARS-CoV-2 infected and replicated in human lung tissues more efficiently, generating 3.20 folds more infectious virus particles within 48hrs.  
- Both viruses were similar in cell tropism: both targeting types I and II pneumocytes, and alveolar macrophages.  
- Despite a more efficient virus replication in the infected human lung tissue, SARS-CoV-2 did not significantly induce types I, II, or III interferons, and only upregulated 38 % (= IL6, MCP1, CXCL1, CXCL3, and CXCL10) of the 13 key inflammatory mediators tested (in contrast to 85 % for SARS-CoV). |
- Substandard drugs driven by cost reduction  
- Falsified agents thrive on shortages, especially when buyers depart from regulated supply chains (masks, diagnostic tests, false claim of treatments…).  
When proven efficacious treatment, robust policies need to ensure prompt affordable, access for all people in need + quality assured, not diverted from other treatments:  
- Coordinated information-sharing among medicine regulators on authorizations for clinical trials  
- Ensure global manufacture + investigational interventions for unregistered + off label use  
- Comprehensive/rapid reporting of shortages of active ingredients and finished products  
- Robust evaluation of diagnostic tests  
- Innovative regional mechanisms (e.g. African Vaccine Regulatory Forum) for nations without robust regulatory systems |
| **NEJM 9APR2020** | Disease Control, Civil Liberties, and Mass Testing — Calibrating Restrictions during the Covid-19 Pandemic | David M. Studdert et al., US https://doi.org/10.1056/NEJMa2007557 | HSS/Politic | Civil liberties: courts insist coercive restrictions must be 1) necessary, 2) crafted as narrowly as possible, 3) not used to target ostracized groups.  
Clear criteria for quarantine for other diseases don't apply to social restrictions for COVID-19:  
1) Quarantine is community-wide and applies to government and private actors;  
2) Transmission dynamics make it difficult to identify / target risk groups.  
3) Stay-at-home restrictions unlikely to be a one-shot deal  
=> Need for a graduated approach to restrictive measures.  
Curfew laws most adapted: courts give leeway to government to adapt + see COVID-19 restrictions as more of a public policy than a legal issue.  
Tailor restrictions with credible person-level information => identify people most likely to transmit infection through population wide program of testing and surveillance.  
Aggregate test results at community+state level to dial up or down.  
=>Federal, state and local governments to finance & oversee + rely on hospitals, pharmacies, private labs, mobile health services for implementation + civil organizations to foster compliance. |
| **Life Sciences 9APR2020** | In silico studies on therapeutic agents for COVID-19: Drug repurposing approach | Shah, Bhumi et al, India https://doi.org/10.1016/j.jinf.2020.117612 | Therapeutic | 61 molecules that are already being used in clinics or under clinical scrutiny as antiviral agents are surveyed via docking study.  
37 molecules were found to interact with >2 protein structures of COVID-19. Among them, HIV protease inhibitors and RNA-dependent RNA polymerase inhibitors showed promising features of binding to COVID-19 enzyme. Along with these, Methisazone an inhibitor of protein synthesis, CGP42112A an angiotensin AT2 receptor agonist and ABT450 an inhibitor of the non-structural protein 3-4A might become convenient treatment option as well against COVID-19. |
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<tr>
<td>EuroSur 9APR2020</td>
<td>An alternative workflow for molecular detection of SARS-CoV-2 – escape from the NA extraction kit shortage, Copenhagen, Denmark, March 2020</td>
<td>Fomsgaard et al., Denmark <a href="https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.14.2000398">https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.14.2000398</a></td>
<td>Diagnostics</td>
<td>Development of an alternative simple and fast workflow for molecular detection of SARS-CoV-2 that does not require NA extraction and could serve as an alternative in diagnostic laboratories to overcome chemical-based kit shortages. Approach consists of heating samples at 98°C for 5 min. This simplified heat-approach should not be for general use but only if the gold standard approaches are not available. Simply heating the samples could serve as an easy, fast and inexpensive alternative to chemical extraction kits, which would detect 97.4% of the COVID-19-positive patients with no false positives; however, there might be a small risk of false negatives, which could be minimised by performing the assay in duplicates.</td>
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<td>Clin Inf Dis 9APR2020</td>
<td>Prediction for Progression Risk in Patients with COVID-19 Pneumonia: the CALL Score</td>
<td>Ji, Dong and al., China <a href="https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa398">https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa398</a></td>
<td>Diagnostics</td>
<td>Overall, 208 patients were divided into stable group (n=168, 80.8%) and progressive group (n=40,19.2%) based on whether their conditions worsened during the hospitalization. Comorbidity, older age, lower lymphocyte and higher lactate dehydrogenase were shown to be independent high-risk factors for COVID-19 progression. By incorporating these 4 factors a novel scoring model, named as CALL, was established and tested. Conclusion: using the CALL score model can help the clinicians to improve the therapeutic effect and reduce the mortality of COVID-19 with more accurate and reasonable resolutions on medical resources.</td>
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<tr>
<td>Clin Inf Dis 8APR2020</td>
<td>PCR Assays Turned Positive in 25 Discharged COVID-19 Patient</td>
<td>Yuan, Jing and al., China <a href="https://doi.org/10.1093/cid/ciaa398">https://doi.org/10.1093/cid/ciaa398</a></td>
<td>Clinic</td>
<td>172 COVID-19 infected patients discharged from Hospital: (1) Normal body temperature for more than 3 consecutive days. (2) Significant reduction of respiratory symptoms evaluated by following indicators: cough and expectoration disappeared, normal ranges for inflammatory markers IL-6 and CRP, as well as oxygenation index ≥50. (3) Substantial improvement over conventional chest radiography detection. (4) At least two consecutively negative results of RT-PCR testing separated by at least 24-hour interval. All discharged patients were required another 14 days of self-segregating at home for further observation. -&gt; 25 discharged patients sent to hospital again because of the positive RT-PCR results. They experienced an average of 7.3±3.86 days from their last negative RT-PCR result to turning positive again. Some immunological parameters such as D-dimer and absolute lymphocyte count, and even antibody test should be combined with RT-PCR negative test as additional measures to assure that infected patients have completely recovered and can be released from quarantine.</td>
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<tr>
<td>Clinical Immunology 8APR2020</td>
<td>Epigenetic dysregulation of ACE2 and interferon-regulated genes might suggest increased COVID-19 susceptibility and severity in lupus patients</td>
<td>Sawalha, Amr H. et al., USA-China <a href="https://doi.org/10.1016/j.cit.2020.10410">https://doi.org/10.1016/j.cit.2020.10410</a></td>
<td>Virology</td>
<td>Patients with systemic lupus erythematosus might be especially prone to severe COVID-19, independent of their immunosuppressed state. - ACE2 is hypomethylated and overexpressed in lupus T cells suggesting an increased susceptibility to SARS-CoV-2 infection. - Increased oxidative stress induced by viral infection exacerbates ACE2 demethylation defect in lupus and may enhance viremia. &gt; Maintaining disease remission in lupus patients is critical to prevent DNA demethylation and increased oxidative stress, which may exacerbate susceptibility to SARS-CoV-2 infection and likelihood of cytokine storm.</td>
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<td>JAMA pediatric 8APR2020</td>
<td>Screening and Severity of Coronavirus Disease 2019 (COVID-19) in Children in Madrid, Spain</td>
<td>Tagarro A and al, Spain <a href="https://doi.org/10.1001/jamanetw.2020.134">https://doi.org/10.1001/jamanetw.2020.134</a></td>
<td>Clinic.</td>
<td>365 screened children and 41 were positive = 11% Median age = 1 year 34% had upper respiratory tract infection – 127 % fever without source - 5% viral like pneumonia 60% were hospitalized and 9.7% were admitted to PICU and needed respiratory support No one died Limitations: probably more hospitalisation because of an increase awareness of COVID-19.</td>
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<tr>
<td>The Lancet 8APR2020</td>
<td>First-wave COVID-19 transmissibility and severity in China outside Hubei after control measures, and second-wave scenario planning: a modelling impact assessment</td>
<td>Leung et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30746-7/fulltext?utm_source=twitter&amp;utm_medium=social">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30746-7/fulltext?utm_source=twitter&amp;utm_medium=social</a></td>
<td>Public Health/Epidemio</td>
<td>➔ The first wave of COVID-19 outside of Hubei has abated because of aggressive non-pharmaceutical interventions. ➔ the R, decreased substantially since Jan 23, when control measures were implemented, and have since remained below 1. ➔ Relaxing the interventions (resulting in R, &gt;1) when the epidemic size was still small would increase the cumulative case count exponentially as a function of relaxation duration, even if aggressive interventions could subsequently push disease prevalence back to the baseline level. Given the substantial risk of viral reintroduction, particularly from overseas importation, close monitoring of R, and cCWR is needed to inform strategies against a potential second wave to achieve an optimal balance between health and economic protection.</td>
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<td>The European respiratory journal, 8APR2020</td>
<td>Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China</td>
<td>Wen-hua Liang et al, China <a href="https://doi.org/10.1183/13993003.00562-2020">https://doi.org/10.1183/13993003.00562-2020</a></td>
<td>Clinic</td>
<td>1590 cases from 575 hospitals in 31 provincial administrative regions were collected (core cohort). The overall rate of severe cases and mortality was 16.0% and 3.2%, respectively, but Potential risk factors analysed using proportional hazard (PH) Cox regression models Patients in Hubei [severe event rate 23.0% versus 11.1%, death rate 7.3% versus 0.3%, hazards ratio (HR) for critical illness 1.59, 95%CI 1.05–2.41] have a poorer prognosis compared with patients outside of Hubei after adjusting for age and comorbidity This might be attributed to the prolonged duration of symptom onset to hospitalization in the epicenter.</td>
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<td>Journal of biomolecular structure &amp; dynamics, 8APR2020</td>
<td>In-silico homology assisted identification of inhibitor of RNA binding against 2019-nCoV N-protein (N terminal domain)</td>
<td>Sarma, Phulen et al, India [<a href="https://journal.kew.co">https://journal.kew.co</a> m/pmcjournal/abstract/crinef/Coronavirus_Disease_2019_in_CritIc ally_Ill.08057.aspx](<a href="https://journal.kew.co">https://journal.kew.co</a> m/pmcjournal/abstract/crinef/Coronavirus_Disease_2019_in_CritIc ally_Ill.08057.aspx)</td>
<td>Therapeutic</td>
<td>Two NTD structures of N proteins were selected (2OFZ and 1SSK, 92% homology) for virtual screening of 56,079 compounds from Asinex and Maybridge library to identify top 15 hits for each of the targets based on “docking score” This study suggests two important class of compounds, theophylline and pyrimidine derivatives as possible inhibitors of RNA binding to the N terminal domain of N protein of coronavirus, thus opening new avenues for in vitro validations</td>
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<td>Pediatric Critical Care 7APR2020</td>
<td>Coronavirus Disease 2019 in Critically Ill Children: A Narrative Review of the Literature</td>
<td>Ong J and al, Singapore/Italy /Canada [<a href="https://journals.lww.co">https://journals.lww.co</a> m/jpccjournal/Abstract/onlinefirst/Coronavirus_Disease_2019_in_CritIc ally_Ill.08057.aspx](<a href="https://journals.lww.com/jpccjournal/Abstract/onlinefirst/Coronavirus_Disease_2019_in_CritIc">https://journals.lww.com/jpccjournal/Abstract/onlinefirst/Coronavirus_Disease_2019_in_CritIc</a> ally_Ill.08057.aspx)</td>
<td>Clinic</td>
<td>Children account for a few proportions of COVID19 diseases Not severely III: asymptomatic++++ or mild Infant under 1 year appear to have an increased risk of severe disease. Spared from severe disease: - Less lymphopenia: 9.5% ≠ 70% in adults, - Appear to be less pro-inflammatory than adults, - Variation of expression of ACE2 and activity with age could protect against lung injury. Management: - Noninvasive ventilation or hight-flow nasal canula would be preferred, - Intubation should be performed by experienced practitioner with PPE and rapid sequence induction - Used cuffed tubes (minimized air leak), - Avoided disruption to the ventilator circuit - Creation of a family liaison contact</td>
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<td>The Lancet Public Health 07APR2020</td>
<td>The French response to COVID-19: intrinsic difficulties at the interface of science, public health, and policy</td>
<td>Moatti, Jean-P. et al., France <a href="https://doi.org/10.1016/S2468-2667(20)30067-4">https://doi.org/10.1016/S2468-2667(20)30067-4</a></td>
<td>HSS/Politic</td>
<td>French authorities appointed an advisory board of 11 scientists to help manage the crisis: evidence-based policy: 1) France did not have logistic capacity to promote mass testing. Rather than setting goal of scaling up, authorities argued systematic testing was not needed; 2) Maintaining second round of elections # social science literature established disaster communication should avoid dissonant incentives/double binds. 3) Referring to clinical trials to prove efficacy of hydroxychloroquine without considering alternative evaluation methods for quicker evidence =&gt; reduced ability of authorities to mitigate effects or rumors and regulate prescription practices. Setting up second experts' committee: implicit recognition of the intrinsic difficulties of directly using science in political management of a health crisis.</td>
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<td>J Mol Diag PRE-PROOF 7MAR2020</td>
<td>Development of Reverse Transcription Loop-mediated Isothermal Amplification (RT-LAMP) Assays Targeting SARS-CoV-2</td>
<td>Park et al., Republic of Korea <a href="https://www.leaven.org/content/10.1101/2020.03.19.38304v1">https://www.leaven.org/content/10.1101/2020.03.19.38304v1</a></td>
<td>Diagnostic</td>
<td>Development of highly specific RT-LAMP assays for detection of SARS-CoV-2. Results of these RT-LAMP assays can be detected within 30 minutes after amplification reaction begin. Optimization of reaction conditions where LCV colorimetric detection method is applied that can be used for point-of-care tests.</td>
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<td>Clinical infectious diseases 7APR2020</td>
<td>Towards Optimization of Hydroxychloroquine Dosing in Intensive Care Unit COVID-19 Patients</td>
<td>Perinel, Sophie et al, France <a href="https://doi.org/10.1111/j.1651-0018.2013.00394">https://doi.org/10.1111/j.1651-0018.2013.00394</a></td>
<td>Therapeutic</td>
<td>Prospective pharmacokinetic study: 13 patients in intensive care unit received 200 mg x 3 of oral HCQ daily, mean age 68 y, 46% obese, 31% with moderate or severe renal failure. HCQ levels &gt;1 mg/L and &lt;2 mg/L were considered to be therapeutic. 161 blood levels recorded. Simulations performed based on data from patients with rheumatoid arthritis. PK studies are needed to define the optimal dosing regimen. Based on simulations, a loading dose of 800 mg once daily on day 1, followed by 200 mg twice daily for 7 days is proposed.</td>
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<td>Science Translational Medicine 6APR2020</td>
<td>An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 in human airway epithelial cell cultures and multiple coronaviruses in mice</td>
<td>Sheahan, Timothy P. et al. USA <a href="https://doi.org/10.1212/actn.000000000000583">https://doi.org/10.1212/actn.000000000000583</a></td>
<td>Therapeutic</td>
<td>In human airway epithelial cell cultures: - Orally bioavailable ribonucleoside analog (NHC, EIDD-1931) has broad spectrum antiviral activity against SARS-CoV-2, MERS-CoV, SARS-CoV, and related zoonotic group 2b or 2c Bat-CoVs, and a coronavirus bearing resistance mutations to remdesivir. In mice: - Prophylactic and therapeutic administration improved pulmonary function, reduced virus titer and weight loss (mice infected with SARS-CoV or MERS-CoV) =&gt; potency of NHC/EIDD-2801 against multiple coronaviruses and oral bioavailability makes it a potential effective antiviral against SARS-CoV-2.</td>
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<td>Journal of Medical Virology 6APR2020</td>
<td>Tocilizumab treatment in COVID-19: a single center experience</td>
<td>Luo, Pan et al, China <a href="https://doi.org/10.1016/j.jmv.25801">https://doi.org/10.1016/j.jmv.25801</a></td>
<td>Therapeutic</td>
<td>15 COVID-19 patients under Tocilizumab (TCZ) therapy were retrospectively assessed. TCZ treatment ameliorated the increased CRP in all patients rapidly, - 4 critically ill patients who received an only single dose of TCZ =&gt; 3 died and the CRP level in the rest one patient failed to return to normal range with a clinical outcome of disease aggravation. - Serum IL-6 level tended to further spiked firstly and then decreased after TCZ therapy in 10 patients. - Persistent and dramatic increase of IL-6 was observed in these 4 patients who failed treatment. =&gt; A single dose of TCZ seems to fail to improve the disease activity in critically ill patients although it was used in combination with glucocorticoid. However, repeated doses of TCZ might improve the condition of critically ill patients. Limitations: small number of cases reported; use of laboratory parameters to define the disease activity is still challenging; treatment duration observed may not be sufficient to make a final conclusion.</td>
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Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy

Authors and link: Grasselli G et al, Italy

Field of expertise: Clinic

Key facts: Retrospective - 1591 patients COVID-19 – multicentric

Demographic:
- 82% male - median age: 63 years
- 68% had at least 1 comorbidity (HTA+++)

Clinical data:
- 1150 patients required mechanical ventilation (higher than reported for other ICU patients)
- Median PEEP: 14 cmH$_2$O
- Median $P_{aO2}/F_{IO2}$ = 166 (IQR:114-220), higher in young patients (< 63 years)
- Mortality: 26%, higher in older patients (15% vs 36%, p<0.001)
- Median length of stay: 9 days in ICU

Limitation:
- Short follow up → mortality rate could change?
- Missing data for some patients

Potential false-negative nucleic acid testing results for Severe Acute Respiratory Syndrome Coronavirus 2 from thermal inactivation of samples with low viral loads

Authors and link: Pan et al., China

Field of expertise: Diagnostic

Key facts: -> Ct values are increased (higher threshold for detection) in specimens from diagnosed COVID-19 patients in RT-PCR tests after thermal incubation.

- About half of the weak-positive samples (7 of 15 samples, 46.7%) were RT-PCR negative after heat inactivation in at least one parallel testing

Thermal inactivation adversely affected the efficiency of RT-PCR for SARS-CoV-2 detection. Given the limited applicability associated with chemical inactivators, other approaches to ensure the overall protection of laboratory personnel need consideration.

A first Case of Meningitis/Encephalitis associated with SARS-CoV-2

Authors and link: Moriguchi, Takeishi et al, Japan

Field of expertise: Clinic

Key facts: Case report : 23-year old male, with seizure accompanied by unconsciousness. The specific SARS-CoV-2 RNA was not detected in the nasopharyngeal swab but was detected in a CSF brain MRI: hyperintensity along the wall of right lateral ventricle and hypertensive signal changes in the right mesial temporal lobe and hippocampus, suggesting the possibility of SARS-CoV-2 meningitis

Chest CT small ground glass opacities
At D15 : still ventilated and with impaired consciousness

This case warns the physicians of patients who have CNS symptoms.

Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19

Authors and link: Liu et al., China

Field of expertise: Clinic

Key facts: 245 COVID-19 patients :
- Multivariate analysis demonstrated that there was 8% higher risk of in-hospital mortality for each unit increase in NLR.
- Compared with patients in the lowest tertile, the NLR of patients in the highest tertile had a 15.04-fold higher risk of death after adjustment for potential confounders
- Fully adjusted OR for mortality was 1.10 in males for each unit increase of NLR

NLR is an independent risk factor of the in-hospital mortality for COVID-19 patients especially for male.

Arbidol Monotherapy is Superior to Lopinavir/ritonavir in Treating COVID-19

Authors and link: Zhu, Zhen et al, China

Field of expertise: Therapeutic

Key facts: 50 patients into 2 groups
- lopinavir/ritonavir group (34 cases)
- arbidol group (16 cases).

Data from these patients were retrospectively analyzed.
At D14 post admission: no viral load was detected in arbidol group.

44.1% of patients in lopinavir/ritonavir group had positive RNA test on day 14.

Patients in the arbidol group had a shorter duration of positive RNA test.
No apparent side effects were found in both groups.

Arbidol monotherapy may be superior to lopinavir/ritonavir in treating COVID-19.
The sample size is the major limitation of this study.
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<tr>
<td>CELL preproof</td>
<td>Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2</td>
<td>Monteil, Kwon et al,</td>
<td>Therapeutic</td>
<td>ACE2 has now also been identified as a key receptor for SARS-CoV-2 infections and it has been proposed that inhibiting this interaction might be used in treating patients with COVID-19. Clinical grade human recombinant soluble ACE2 (hrsACE2) reduced SARS-CoV-2 recovery from Vero cells by a factor of 1,000-5,000. An equivalent mouse rsACE2 had no effect. SARS-CoV-2 can also directly infect engineered human blood vessel organoids and human kidney organoids, which can be inhibited by hrsACE2. These data demonstrate that hrsACE2 can significantly block early stages of SARS-CoV-2 infections.</td>
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<td>Nature Medicine 3APR2020</td>
<td>Respiratory virus shedding in exhaled breath and efficacy of face masks</td>
<td>Leung, Nancy H. L. et al., <a href="https://doi.org/10.1038/s41586-020-02843-2">https://doi.org/10.1038/s41586-020-02843-2</a> China - USA</td>
<td>Virology</td>
<td>Detection of virus RNA shedding in exhaled breath: and coughs of children and adults with acute respiratory illness (influenza (n=23-28 infected individuals), coronavirus (n=10-11) and rhinoviruses (n=36-32)). 5 μm particle size fractionation. Without face mask: - Viral RNA identified in 30%, 26% and 28% of respiratory droplets and 40%, 35% and 56% of aerosols collected while not wearing a face mask (coronavirus, influenza virus and rhinovirus-infected participants, respectively) Surgical face masks significantly reduced detection of viral RNA for: - Influenza virus in respiratory droplets, but not in aerosol. - Coronavirus in aerosols (≤5 μm particles), and non-significant reduction in respiratory droplets. Limitation: infectivity of detected virus not tested. → Surgical face masks could prevent transmission of human coronaviruses and influenza viruses from symptomatic individuals.</td>
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<td>Antiviral Research 3APR2020</td>
<td>Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro</td>
<td>Choy, Yin-Lam Wong et al, Hong Kong <a href="https://doi.org/10.1016/j.antiviral.2020.104786">https://doi.org/10.1016/j.antiviral.2020.104786</a></td>
<td>Therapeutic</td>
<td>Evaluation of the in vitro antiviral effect of compounds that were previously reported to inhibit coronavirus replication and compounds that are currently under evaluation in clinical trials for SARS-CoV-2 patients. ⇒ Antiviral effect of remdesivir, lopinavir, homorringtonine, and emetine against SARS-CoV-2 virus in Vero E6 cells with the estimated 50% effective concentration at 23.15 μM, 26.63 μM, 2.55 μM and 0.46 μM, respectively. ⇒ Ribavirin or favipiravir that are currently evaluated under clinical trials showed no inhibition at 100 μM. ⇒ Synergy between remdesivir and emetine was observed, and remdesivir at 6.25 μM in combination with emetine at 0.195 μM may achieve 64.9% inhibition in viral yield. Combinational therapy may help to reduce the effective concentration of compounds below the therapeutic plasma concentrations and provide better clinical benefits.</td>
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<td>International Journal of Antimicrobials Agents 3APR2020</td>
<td>Structural and molecular modeling studies reveal a new mechanism of action of chloroquine and hydroxychloroquine against SARS-CoV-2 infection</td>
<td>Fantini, Di Scala et al, France <a href="https://doi.org/10.1016/j.ijantimicag.2020.105960">https://doi.org/10.1016/j.ijantimicag.2020.105960</a></td>
<td>Therapeutic</td>
<td>Identification of a new mechanism of action of CLQ and CLQ-OH supporting the use of these repositioned drugs to cure SARS-CoV-2 infected patients. Using a combination of structural and molecular modeling approaches: ⇒ chloroquine (CLQ) binds sialic acids and gangliosides with high affinity. ⇒ New type of ganglioside-binding domain at the tip of the N-terminal domain of the SARS-CoV-2 spike (S) protein identified. This domain (aa 111-158), which is fully conserved among clinical isolates worldwide, may improve the attachment of the virus to lipid rafts and facilitate the contact with the ACE-2 receptor. ⇒ In presence of CLQ (or of the more active derivative hydroxychloroquine, CLQ-OH), the viral spike is no longer able to bind gangliosides.</td>
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| Journal of Thrombosis and Thrombolysis 3APR2020 | Difference of coagulation features between severe pneumonia induced by SARS-CoV2 and non-SARS-CoV2 | Shiyu Y et al, China [https://doi.org/10.18038/jtj.2020.02105-3](https://doi.org/10.18038/jtj.2020.02105-3) | Clinic            | Retrospective – 2 groups 449 patients COVID-19 and 104 severe pneumonia non-COVID 28 days mortality → higher in COVID group (29.8% vs 15.4%, p<0.005)  
Heparin treatment: 22% in COVID and 21% non-COVID  
Platelet count: higher in COVID group significantly Elevated D-Dimer (sixfold of upper limit of normal) was associated with poor prognosis only in COVID group  
Anticoagulant therapy may benefit to selected COVID patients (elevated D-Dimer)?  
Limits:  
- Retrospective  
- Influence of others therapies? |
| Circulation 3APR2020 | The Variety of Cardiovascular Presentations of COVID-19 | Fried J et al, USA [https://doi.org/10.1161/CIRCULATIONAHA.120.047164](https://doi.org/10.1161/CIRCULATIONAHA.120.047164) | Clinic            | 4 cases reports  
- SARS-CoV2 infection should be in the differential of typical cardiac syndrome during pandemic event without infection signs  
- Myocarditis like presentations with COVID-19 → further study  
- Direct cardiac injury = result of viral invasion OR cytokine storm induced by SARS-CoV2 → toxic effect on myocardium  
- COVID-19 can cause decompensation of heart failure → mixed shock |
| JAMA 3APR2020 | Personal Risk and Societal Obligation Amidst COVID-19 | Tsai et al., USA, [https://doi.org/10.1001/jama.2020.5450](https://doi.org/10.1001/jama.2020.5450) | HSS/Polit         | Health workers with pre-existing medical conditions/in older age groups are at greater risk of severe illness and death if exposed to COVID-19. → Telemedicine  
Issue : guilt – putting other colleagues at risk; what risk acceptable as a necessary part of a path in medicine?  
Assessment takes an inherently individual path: no single rule can guide a physician’s involvement in high-risk scenarios  
Comforted by:  
1) High need for virtual-based care  
2) Sense of purpose in the community  
How much risk in the career of medicine should be acceptable to physicians? → Need for medical profession to balance the obligations and duties of this profession with physicians’ fundamentally human limitations and fears |
Two sets of X-Ray images from patients were used as follow:  
- 1st set: a collection of 1427 X-ray images including 224 images with confirmed Covid-19 disease, 700 images with confirmed common bacterial pneumonia, and 504 images of normal conditions.  
- 2nd set: 224 images with confirmed Covid-19 disease, 714 images with confirmed bacterial and viral pneumonia, and 504 images of normal conditions.  
Deep Learning with X-ray imaging would extract significant biomarkers related to the Covid-19 disease, while the best accuracy, sensitivity, and specificity obtained is 96.78%, 98.66%, and 96.46% respectively. Further research are needed to confirm the efficiency of this type of technology for automatic detection of Covid-19 cases; moreover, it is necessary to develop models capable of distinguishing Covid-19 cases from other similar viral cases, but also from a greater variety of common pneumonia or even physiological X-rays |
| Antiviral Research, 3APR2020 | The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro | Caly, Leon et al, Australia [https://doi.org/10.1016/j.antiviral.2020.104787](https://doi.org/10.1016/j.antiviral.2020.104787) | Therapeutic       | Ivermectin is an inhibitor of the COVID-19 causative virus (SARS-CoV-2) on Vero/hSLAM cells.  
A single treatment able to effect ~5000-fold reduction in virus at 48h in cell culture compared to control sample.  
Ivermectin is FDA-approved for parasitic infections, Ivermectin is widely available, due to its inclusion on the WHO model list of essential medicines |
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| The Lancet Microbe 2APR2020 | Stability of SARS-CoV-2 in different environmental conditions | Chin, Alex W. H. et al., China [Link](https://doi.org/10.1016/S2666-5247(20)30003-3) | Virology | Infectious SARS-CoV-2 Stability at different temperatures (in virus transport medium):  
-  highly stable at 4°C (only ~ 0·7 log-unit reduction of infectious titre on day 14)  
-  at 70°C, virus inactivation reduced to 5 mins  
-  On a surgical mask, infectious virus detectable on day 7 (~0-1% of the original inoculum).  
-  Except from hand soap, no infectious virus detected after 5-min incubation at RT (22°C) with virucidal disinfectants (Household bleach (1:49), Ethanol (70%), Povidone-iodine (7.5%), …).  

--> SARS-CoV-2 can be highly stable in a favourable environment, but also susceptible to standard disinfection methods. |
| Liver Int 2APR2020 | Clinical characteristics of Non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: A Retrospective study | Xie et al., China [Link](https://doi.org/10.1111/liv.14449) | Clinic | Retrospective study of 79 patients, median age 60 years and 55.7% male.  
29 had liver injury (elevated ALT, AST and/or bilirubin)  
Multivariate analysis suggested that CT scores was an independent predictor for liver injury. Patients with liver injury stayed longer in the hospital. |
Median age: 54y and 58% male  
40% severe pneumonia and 9% were ARDS  
4.3% had CKD with long-term hemodialysis  
None patient meet criteria for AKI during or after treatment  
12 patients without CKD showed mild increase of BUN or serum creatinine (≥ criteria of AKI).  
Temporary abnormal renal function → injury due to hypoxemia?  
SARS-CoV2 RNA in urine sediment was positive in 4 patients  
Mortality: 6%  
Results are similar with study on SARS-CoV infection in 2003  
Be careful because ACE2 expression is high in kidney. |
Controls significantly older – no other difference  
No difference between group in the level of ALT or AST  
Majority of COVID19 had mild abnormalities  
COVID-19 had reduction of albumin  
Liver is not the main target organ  
Relationship with the disease progression:  
-  Higher level of ALT or AST in severe cases than mild cases,  
-  Higher total bilirubin in severe cases,  
-  Lower level of albumin in severe cases,  
Liver function did not show an independent association with severe COVID19 |
<p>| CDC 1APR2020 | Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020 | Wei et al., China [Link](<a href="https://www.cdc.gov/mmwr/">https://www.cdc.gov/mmwr/</a> volumes/69/wr/mm6914e1.htm#summary) | Public Health/Epidemiology | -&gt; Identification of 7 clusters of COVID-19 in Singapore in which presymptomatic transmission likely occurred and which may explain the occurrence of secondary cases |</p>
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| The Lancet Neurology 1APR2020 | Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? | Zhao, Hua; et al. China [https://www.thelancet.com/journals/lannee/article/PIIS1474-4422(20)30109-5/fulltext](https://www.thelancet.com/journals/lannee/article/PIIS1474-4422(20)30109-5/fulltext) | Clinic | Patient was diagnosed with Guillain-Barré syndrome (autoimmune disorder damaging the peripheral nervous system resulting in aggravating muscle weakness) with lymphocytopenia and thrombocytopenia upon hospitalization. 
Patient then developed symptoms of SARS-CoV-2 on day 8 and tested +ve by RT-PCR. 
Given the temporal overlap, authors speculate that SARS-CoV-2 infection might have been responsible for the development of Guillain-Barré syndrome with a possible parainfectious profile. 
Limitations: patient was not tested for SARS-CoV-2 upon admission, so causality is not clear. 
->This is the first, and single case report. It only suggests a possible association and more cases are necessary to support a causal relationship. |
-> Pharyngeal virus shedding: very high during 1st week of symptoms. 
-> Infectious virus was readily isolated from throat- and lung-derived samples, but not from stool samples (in spite of high virus RNA concentration). 
-> Blood and urine never yielded virus. 
Active replication in the throat is confirmed by viral replicative RNA intermediates in throat samples. 
Sequence-distinct virus populations were consistently detected in throat and lung samples from the same patient, proving independent replication. 
Shedding of viral RNA from sputum outlasted the end of symptoms. 
Serocconversion occurred after 7 days in 50% of patients (14 days in all), but was not followed by a rapid decline in viral load. 
COVID-19 can present as a mild upper respiratory tract illness. 
Active virus replication in the upper respiratory tract puts the prospects of COVID-19 containment in perspective. |
| NEJM 01APR2020 | Ten Weeks to Crush the Curve | Fineberg, Harvey v.et al. USA [https://doi.org/10.1056/NEJMhie2007265](https://doi.org/10.1056/NEJMhie2007265) | HSS/Politic | 1. Appoint a commander who reports to the President with powers and authority of the President to mobilize all civil and military means (same at the level of the state) + redeploy limited national supplies where most needed. 
2. Perform millions of diagnostic tests over the next 2 weeks. Organize dedicated clinical trial sites, physically separate from other health centers. 
3. Provide all health workers with personal protective equipment. 
4. Act on the basis of symptoms, examinations, viral RNA detection tests and exposures to differentiate the population into 5 groups to be treated accordingly: 1 / infected; 2 / presumed infected; 3 / exposed; 4 / unknown exposure/infection; 5 / recovered & sufficiently immune. 
Hospitalize severely affected or high-risk individuals+ create quarantine centers. 
Identify the fifth group by tests to enable economy to restart quickly and safely. 
5. Mobilize the entire population. With PPE for all health workers, deliver surgical masks and hand sanitizer to every American household. If everyone is wearing a mask, no stigma. 
6. Learn through real-time, fundamental research. 
Over the long-term: Reinvigorate the public health infrastructure for future threats. |
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<tr>
<td>The Lancet 01APR2020</td>
<td>Racism and discrimination in COVID-19 responses</td>
<td>Devakumar, D. et al., UK [10.1016/S0140-6736(20)30792-]</td>
<td>HSS/Politic</td>
<td>COVID 19 engenders fear ➞ social, political racism and xenophobia with racialised/ discriminatory responses to fear + disproportionately affecting marginalised groups. Social dimension: COVID could have been an equalizer but disproportionately affects people of color + migrants 1) Microaggression/Violence towards different ethnic groups (i.e.: Chinese) 2) lower socio-economic groups (limited access to healthcare + precarious jobs) 3) Ethnic minority groups at greater risk (comorbidities) 4) Migrants avoid hospitals for fear of identification/reporting Political dimension: Misappropriation of Covid-19 crisis for political purpose (racial discrimination, conflating public health restrictions and border policies + trade policies). Health protection relies on a well functioning health system with universal coverage, + social inclusion, justice, and solidarity</td>
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<td>Virol Sin 31MAR2020</td>
<td>Inefficiency of Sera from Mice Treated with Pseudotyped SARS-CoV to Neutralize 2019-nCoV Infection</td>
<td>Zehong Liu et al., China [10.1011/02250-020-00214-5]</td>
<td>Therapeutic</td>
<td>S proteins: - 76% homology SARS CoV / SARS CoV-2 - 29% homology SARS CoV / MERS-CoV. RBS: - Significantly different, even if the bind to the same receptor (ACE2). Cross-reaction of sera? SARS-CoV and MERCoV pseudovirus expression S protein: produced and injected into BALBc mice. -&gt; Sera tested on ACE2 expressing 293T cells. -&gt; Effective neutralization for SARS-PsV-treated mice but not MERS-PsV treated mice. When SARS-PsV-treated mice was exposed to a SARS-CoV-2 pseudovirus -&gt; no neutralization effect was evidenced. It may not be practical to treat SARS-CoV-2 patients.</td>
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<td>Emerging microbes &amp; infections 31MAR2020</td>
<td>Renin-angiotensin system inhibitors improve the clinical outcomes of COVID-19 patients with hypertension</td>
<td>Meng, Juan et al., China, [10.1080/22221751.2020.1846200]</td>
<td>Therapeutic</td>
<td>Retrospective study of 42 patients with treated hypertension admitted in hospitalization for COVID 19. Before hospitalization, 17 were on angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II type 1 receptor blockers (ARBs), 25 were on other drugs. Results: in patients from the ACEI/ARB group: - Less severe cases - Trend toward lower IL-6 levels - Increased CD3 and CD8 T cell counts - Peak viral load during hospitalization significantly lower ACEI/ARB therapy may attenuate the inflammatory response, potentially through the inhibition of IL-6 levels. Point of attention: retrospective study, small sample.</td>
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<td>Annals of internal medicine 30MAR2020</td>
<td>A Rush to Judgment? Rapid Reporting and Dissemination of Results and Its Consequences Regarding the Use of Hydroxychloroquine for COVID-19</td>
<td>Kim, Alfred H.J et al., USA [10.7326/M20-1223]</td>
<td>HSS/Politic</td>
<td>Urgency: certain limits of this study are acceptable (small sample size, use of an unvalidated surrogate end point, lack of randomization or blinding, ...). But methodological flaws that may affect the validity of the results: Conclusion: -&gt; Sufficient justification to continue investigation of the efficacy and safety of HCQ in patients hospitalized with COVID-19. -&gt; No data currently to recommend the use of HCQ as a prophylaxis for COVID-19. -&gt; Lack of recommendation of its use outside of marketing authorization until it is justified and offer is reinforced. -&gt; Risk of penury to patients with rheumatic diseases who depend on HCQ for their survival. -&gt; HCQ shortage will limit availability to patients with COVID-19 if efficacy truly established.</td>
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| Medicine in Drug Discovery – pre-Proof 22MAR2020 | Novel decoy cellular vaccine strategy utilizing transgenic antigen-expressing cells as immune presenter and adjuvant in vaccine prototype against SARS-CoV-2 virus | Henry Ji et al., China [link](https://doi.org/10.1016/j.medidd.2020.100026) | Vaccine | S1 SARS-CoV-2 protein is expressed on the surface of K562 human myelogenous leukemia cells (HLA negative - highly sensitive to NK mediating kills):  
-> Provides a means of targeting and activating an innate driver of the host adaptive immune response.  
-> Stable clones are selected and irradiated to be formulated as vaccine product and administered via intramuscular or subcutaneous injection. This kind of cell vaccine can drive the host cellular immune response toward Th1, generating both potent cytotoxic T cell immunity against the major determinant of SARS-CoV-2 cellular entry and pathogenesis.  
This approach has already being used for cancer vaccine treatments inducing robust cellular and humoral anti-tumor immune responses. |
| Journal of infectious Disease 31MAR2020 | Characteristics of peripheral lymphocyte subset alteration in COVID-19 pneumonia | Fan W et al, China [link](https://doi.org/10.1093/infdis/jiaa150) | Immunology | 60 patients – monocentric – total lymphocytes in COVID-19 were compared to healthy controls (HC)  
Median age 60 y  
32% were serious illness  
Compared to HCs, COVID-19 had a decrease in:  
- Total lymphocytes  
- CD4+ - CD8+ - NK cells and B cells  
Serious compared to mild patient:  
- Decrease total lymphocytes, CD4+, CD8+ and B cells in serious patients  
Post-treatment:  
- Total lymphocytes, CD8+ and B cells increased significantly in responders  
- No significant change in non responder’s  
CD8+ cells potential predictor for disease severity and poor clinical efficacy |
- Mean duration from onset of symptoms to death : 17,8 days  
- Mean duration from onset to hospital discharge: 24,7 days  
- Crude case fatality ratio: 3,67%  
After further adjusting for demography and under-ascertainment:  
- Case fatality ratio: 1,38% / <60 y : 0,32% / >60y: 6,4% / >80y: 13,4%  
Estimates of case fatality ratio from international cases stratified by age were consistent with those from China (see paper for data)  
Estimated overall infection fatality ratio for China: 0·66%, with an increasing profile with age.  
Estimates of the proportion of infected individuals likely to be hospitalised increased with age up to a maximum of 18·4% in those aged 80 years or older.  
Diarrhoea (2 to 10%) and nausea/vomiting (1 to 10%) are the most frequent gastrointestinal symptoms.  
Early in the disease course: earlier than pyrexia  
Liver injury: abnormal level of ALAT and ASAT in 15 to 53 % of patients – mild and transient  
-> microvesicular steatosis and mild lobular activity  
-> direct viral infection of hepatocytes (ACE2 receptor) or drug toxicity or immune-related injury  
Possible tropism of SARS-CoV-2 for gastrointestinal tract: ACE2 receptor  
Faecal source: viral transmission ? |
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<td>The Lancet ID 27MAR2020</td>
<td>Clinical and virological data of the first cases of COVID-19 in Europe: a case series</td>
<td>Leszure et al., France <a href="https://doi.org/10.1016/S1473-3099(20)30302-0">https://doi.org/10.1016/S1473-3099(20)30302-0</a></td>
<td>Clinic</td>
<td>5 Patients: 3 men: aged 31 years, 48 years, and 80 years – 2 women: aged 30 years and 46 years 3 different clinical evolutions: - 2 paucysymptomatic women diagnosed within a day of exhibiting symptoms, with high nasopharyngeal titres of SARS-CoV-2 within the first 24 h of the illness onset and viral RNA detection in stools - A two-step disease progression in 2 young men, with a secondary worsening around 10 days after disease onset despite a decreasing viral load in nasopharyngeal samples - an 80-year-old man with a rapid evolution towards multiple organ failure and a persistent high viral load in lower and upper respiratory tract with systemic virus dissemination and virus detection in plasma. The 80-year-old patient died on day 14 of illness. All other patients had recovered and been discharged by Feb 19, 2020.</td>
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<td>Clinical Infectious Disease 27MAR2020</td>
<td>Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China</td>
<td>Mo P et al, China <a href="https://doi.org/10.1093/cid/ciaa270">https://doi.org/10.1093/cid/ciaa270</a></td>
<td>Clinic</td>
<td>155 patients with median age of 54 years – 85 refractory COVID-19: - Older and more male (p &lt; 0.05) - More comorbidities: diabetes, cardiovascular disease, cerebrovascular disease (p&lt;0,05) - Higher incidence of breath shortness and anorexia (p&lt;0,05) - Bilateral pneumonia - Higher CRP, LDH, ASAT and neutrophil Risk factors: - Male (OR: 2.3 [1.0,4.8]) and anorexia admission (OR:3.9 [1.1,13.4]) Received more oxygen (OR: 3.0), corticosteroid (OR:2.32) Protective factor: fever on admission (OR: 0.33 [0.1 – 0.9])</td>
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<td>JAMA 27MAR2020</td>
<td>Treatment of 5 critically ill patients with COVID-19 with convalescent plasma</td>
<td>Shen C et al, China <a href="https://jamanetwork.com.proxy.inserm.fr/journals/jama/fullarticle/2762883">https://jamanetwork.com.proxy.inserm.fr/journals/jama/fullarticle/2762883</a></td>
<td>Therapeutic</td>
<td>5 patients: severe pneumonia + ( P_{A02} / F_{O2} ) &lt; 300 mmHg + currently or has been supported by mechanical ventilation All received antiviral agents and steroids Administered between 10 and 22 days after admission After transfusion: - Ct value and viral load declined - Value of inflammatory biomarkers decreased - Clinical improvement: improved ( P_{A02} / F_{O2} ), reduced body temperature, improved chest imaging - No longer required respiratory support by 9 days after transfusion Limitations: - No control group and small cases - Improved without transfusion? / Improvement related to transfusion or other therapies? - Late administration of transfusion: different timing would be associated with different outcomes?</td>
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<td>The Lancet 27MAR2020</td>
<td>Historical linkages: epidemic threat, economic risk, and xenophobia</td>
<td>White, A. et al., USA <a href="https://doi.org/10.1016/S0140-6736(20)30797-6">https://doi.org/10.1016/S0140-6736(20)30797-6</a></td>
<td>HSS/Politic</td>
<td>Global management of pandemic disease threats and global commerce historically linked: - History of international infectious disease control shaped by a distinctly European/US perspective prioritizing epidemic threats from colonial/post-colonial sites potentially affecting trade ( =&gt; aggressive control in sites of epidemic outbreak and aggressive scrutiny of those deemed responsible. - Importance of colonial trade from Asia led to bias against people of Asian descent. “Chinese virus” connected to a long legacy of associating epidemic disease threat and trade with movement of Asian peoples. Aggressive racist and xenophobic responses in the name of health controls. - Concern for trading relationships central to US economic growth pivotal for US Congress to endorse creation of WHO. - Nations have recently aligned infectious disease control policy alongside concerns for national security.</td>
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-> High false negative rate of RT-PCR testing  
-> RT-PCR results from several tests at different points were variable from the same patients during the course of diagnosis and treatment of these patients  
Clinical indicators such as CT images should also be used not only for diagnosis and treatment but also for isolation, recovery/discharge and transferring for hospitalized patients clinically diagnosed with COVID-19 during the current epidemic. |
| JAMA 26MAR2020 | Antibodies in Infants Born to Mothers With COVID-19 Pneumonia | Zeng et al., China [https://jamanetwork.com/journals/jama/fullarticle/2763854](https://jamanetwork.com/journals/jama/fullarticle/2763854) | Clinic | A novel study on 6 pregnant women and their infants confirm no maternal-infant transmission of SARS-CoV-2 based on reverse transcriptase–polymerase chain reaction (RT-PCR) and reveals the presence of antibodies in all newborns:  
- 6 mothers had mild clinical manifestations and had cesarean deliveries in their third trimester  
- Neonatal throat swabs and blood samples are negative by RT-PCR test  
- All 6 infants had IgG and IgM virus-specific antibodies in their serum and their mothers also had elevated levels of IgG and IgM  
- Inflammatory cytokine IL-6 was significantly increased in all infants.  
Point of care/conclusion  
The detection of high level of IgM in 2 infants, is not usually. Whether the placetas of women were damaged and abnormal or whether IgM could have been produced by the infant if the virus crossed the placenta need to be confirm in a larger cohort. |
| BMJ 26MARS2020 | The world's largest refugee camp prepares for covid-19 | Gaia Vince, UK [https://doi.org/10.1136/bmj.m2125](https://doi.org/10.1136/bmj.m2125) | HSS/Politic | Biggest camp in Cox’s Bazar (Bangladesh):  
- Nearly 1 million people live in overcrowded conditions.  
- Particularly vulnerable (physical distanciation impossible).  
United Nations Refugee Agency coordinate efforts to increase hand washing, using community leaders to inform (imams and women group leaders).  
Other initiative for preparedness : creation of isolation unit in the camp. Aid workers are credible after experience of managing other crisis (malaria, dengue, cholera...) in the camp since 2 years and a half. |
| The Lancet Public Health 25MAR2020 | The Italian health system and the COVID-19 challenge | Armocida et al., Italy [https://doi.org/10.1016/S2468-2667(20)30074-8](https://doi.org/10.1016/S2468-2667(20)30074-8) | HSS/Politic | In Italy, National Healthcare Service is regionally based, with local authorities responsible for the organisation and delivery of health services. Due to progressive privatisation and finance cuts, system close to collapse. 4 lessons to be learned:  
- Decentralisation and fragmentation of health services seems to have restricted timely interventions and effectiveness  
- Health-care systems capacity and financing need to be more flexible in case of emergencies  
- Solid partnerships between the private and public sector should be institutionalised  
- Recruitment of HR must be planned and financed with a long-term vision |
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Mean age gestational: 39 + 1 - All caesarean section  
Fever (6) - Cough (1) - Shortness of breath (1) - Diarrhea (1)  
Laboratory tests:  
- Elevated CRP (7)  
- Lymphopenia (5) – thrombopenia (2)  
- Elevated IL-6 (4)  
Chest CT: all pneumonia → bilateral (6), unilateral (1)  
Treatment: oxygen + antiviral + antibiotic (single or combination) + traditional medicine.  
Methylprednisolone for 5 after caesarean section.  
Neonatal: 3 stays in observation and 1 was positive for SARS-CoV2 with mild shortness of breath.  
At 28 days after birth: all child was healthy  
No arguments for vertical transmission |
| SCIENCE 25MAR2020 | The effect of human mobility and control measures on the COVID-19 epidemic in China | Kraemer et al., [UK](https://science.sciencemag.org/content/368/6495/2469) | Public Health/Epidemi | Use of real-time mobility data from Wuhan and detailed case data including travel history  
-> Early: spatial distribution of COVID-19 cases in China was explained well by human mobility data  
-> After implementation of control measures: this correlation dropped and growth rates became negative in most locations  
Travel restrictions are particularly useful in the early stage of an outbreak when it is confined to a certain area that acts as a major source. However, travel restrictions may be less effective once the outbreak is more widespread. |
| Inter J of Infectious Diseases 25MAR2020 | Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings | Zhang X et al, China [Link](https://www.journalofinfection.com/article/S1201-9712(20)30997-2/fulltext) | Clinic | 645 patients with 72 no-pneumonia and 573 pneumonia  
Bilateral lung disease: 432 (67%)  
Group with pneumonia:  
- Older: 46,6 vs 34,9 years  
- One coexisting underlying: 28,8% vs 16%  
- Less exposure to Wuhan or confirmed patient  
- Time from onset to COVID-19 was longer: 5 days vs 2 days  
- Symptoms: fever and cough  
- Lower lymphocyte, albumin and NaCl  
- Higher LDH and CRP  
Predictive factor of severe pneumonia:  
- Lymphopenia and higher creatinine  
- Shortness of breath |
| Disaster medicine and public health preparedness 24MAR2020 | Chronology of COVID-19 cases on the Diamond Princess cruise ship and ethical considerations: a report from Japan | Nakazawa, et al, Japan [Link](http://www.ncbi.nlm.nih.gov/pubmed/32207674) | HSS/Polit | Ship = virus incubator + "international miniature company"  
- Difficulty in testing such a large number of people of various origins and faiths  
Recommendations of the article:  
Politically:  
- Alert political decision-makers to the impact of multiple, contradictory, false or unconfirmed information on the health of confined passengers  
- Mobilize collective intelligence / academic consensus by involving a large number of experts  
In terms of ethics and public health:  
- When is the principle of confinement at sea justified: human rights dilemma (ensuring minimum well-being for passengers and crew) / health security (preventing the spread of the virus on land)  
- Two criteria for authorizing a ship to dock or not = "1) the nation’s geopolitical status + 2) the nation’s ability to provide adequate health care ».  
- Optimizing the material and psychological conditions of confinement on a ship: access to medication; psychological support ; means of communication with the outside world ; transparency and consistency of media information + take into account cultural differences  
Legally:  
- Design and implement international regulations because an epidemic on board a ship should not be dealt with solely with regard to local policies (territory in which the ship is at anchor)  
- Strengthen international cooperation. |
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<td>The Lancet Global Health 24MAR2020</td>
<td>Early in the epidemic: impact of preprints on global discourse about COVID-19 transmissibility COMMENT</td>
<td>Maimuna et al., USA <a href="https://doi.org/10.1016/S2214-109X(20)30113-3">link</a></td>
<td>HSS/Politic</td>
<td>Novelty of SARS-CoV-2, so scientists rushed to fill epidemiological, virological, and clinical knowledge gap - &gt; 50 new studies about the virus between January 10 and January 30 alone. Use of a simple method to plot the ten $R_0$ estimations posted as preprints before publication of the first peer-reviewed study on Jan 29. Result of the peer review $R_0$ estimations are very similar to those in the peer-reviewed studies published on and after Jan 29. <strong>Conclusions</strong>: - Powerful role preprints can have during public health crises because of the timeliness with which they can disseminate new information. - Use of preprint does not jeopardise future peer-reviewed publication (first step: preprint and then peer reviewed) - Impact of preprints on discourse and decision making to the ongoing COVID-19 outbreak (even if in some cases the preprints have conveyed erroneous ideas)</td>
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<td>Emerging microbes and Infections 24MAR2020</td>
<td>Establishment and validation of a pseudovirus neutralization assay for SARS-CoV-2</td>
<td>Jianhui Nie et al., China <a href="http://www.ncbi.nlm.nih.gov/pubmed/32207377">link</a></td>
<td>Therapeutic</td>
<td>Necessity of handling SARS-CoV-2 in BSL-3 facilities and accessibility to virus strains - &gt; barriers to develop candidate vaccines and therapeutics. - &gt; Hence, development of a SARS-CoV-2 pseudovirus based in neutralization assays using 5 viral genes cloned into pcDNA3.1 plasmids. - &gt; Expressed in a VSV pseudoviral platform. - &gt; Huh7 cells plated at 5x10^4/well were identified as the best cell system for SARS-CoV2 pseudovirus infection (inocula of 650 TCID50/well). When tested against the SARS-CoV-2 pseudovirus, SARS-CoV-2 convalescent patient sera showed high neutralizing potency, which underscore its potential as therapeutics. <strong>at home</strong> = stress can be eased <strong>in local hospitals/ collective medical observation centers</strong> = separated from caregivers (children infected/suspected of being infected or caregivers infected/dead) Potential consequences: 1) grief and fear + 2) potential mood disorders and psychosis/death by suicide in adulthood 30% = post-traumatic stress disorder <strong>Chinese gov. strategies to prevent risks</strong>: 1. nurses 24 h per day 2. guidance by nutritionists for children’s diets 3. communication with parents any time 4. citizens volunteering as temporary mothers 5. 24 h free psychological counselling hotlines <strong>Guidelines issued</strong>: more communication time with parents; access to disease information via comic books and videos; regular activity schedule; night lights and gifts for children; referrals for psychiatrists <strong>Need for</strong>: 1. formal training for paediatric health-care workers 2. evidence-based guidelines 3. national collaborative networks (psychiatrists, psychotherapists, researchers, community volunteers) 4. post-pandemic surveillance of children</td>
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<td>The Lancet Child &amp; Adolescent Health 24MAR2020</td>
<td>Mental health considerations for children quarantined because of COVID-19</td>
<td>Liu, Jia Jia; Bao, Yanping et al., China <a href="https://doi.org/10.1016/S2352-4642(20)30096-1">link</a></td>
<td>HSS/Politic</td>
<td><strong>• at home</strong> = stress can be eased <strong>in local hospitals/ collective medical observation centers</strong> = separated from caregivers (children infected/suspected of being infected or caregivers infected/dead) Potential consequences: 1) grief and fear + 2) potential mood disorders and psychosis/death by suicide in adulthood 30% = post-traumatic stress disorder <strong>Chinese gov. strategies to prevent risks</strong>: 1. nurses 24 h per day 2. guidance by nutritionists for children’s diets 3. communication with parents any time 4. citizens volunteering as temporary mothers 5. 24 h free psychological counselling hotlines <strong>Guidelines issued</strong>: more communication time with parents; access to disease information via comic books and videos; regular activity schedule; night lights and gifts for children; referrals for psychiatrists <strong>Need for</strong>: 1. formal training for paediatric health-care workers 2. evidence-based guidelines 3. national collaborative networks (psychiatrists, psychotherapists, researchers, community volunteers) 4. post-pandemic surveillance of children</td>
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| The Lancet 23MAR2020 | Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study | Kai-Wang et al., China [link](https://www.thelancet.com/journals/lanres/article/PIIS1473-3099(20)30196-6/fulltext) | Virology | 23 persons were included  
- Median viral load in posterior oropharyngeal saliva or other respiratory specimens at presentation was 5.2 log_{10} copies per mL  
- Salivary viral load: highest during the first week after symptom onset and subsequently declined with time  
- In one patient, viral RNA was detected 25 days after symptom onset.  
- Older age was correlated with higher viral load  
- For 16 patients with serum samples available 14 days or longer after symptom onset, rates of seropositivity were 94% for anti-NP IgG, 88% for anti-NP IgM, 100% for anti-RBD IgG, and 94% for anti-RBD IgM.  
- Anti-SARS-CoV-2-NP or anti-SARS-CoV-2-RBD IgG levels correlated with virus neutralisation titre. |
| JAMA 23MAR2020 | Ethics Committee Reviews of Applications for Research Studies at 1 Hospital in China During the 2019 Novel Coronavirus Epidemic | Zhang H et al.- China [link](https://doi.org/10.1001/jama.2020.4362) | HSS/Politic | - Henan hospital: designated to provide care to COVID-19 patients.  
- Hospital ethics committee organized 4 emergency video conference in 35 days.  
- Projects evaluated within 2,13 days after submission: more quickly that other previous boards organized in an outbreak context.  
- 41 applications were reviewed; 6 were approved; 4 rejected; and 31 referred for modification because of lack statistical basis for sample size calculation, deficiencies in inclusion/exclusion criteria or issues related to consent form. Although the rush, review standards were not lowered during the outbreak. |
| Open Forum Infect Dis 21MAR2020 | High-dose intravenous immunoglobulin as a therapeutic option for deteriorating patients with Coronavirus Disease 2019 | Wei Cao and al, China [link](https://doi.org/10.1093/ofid/ofaa102) | Therapeutic | 3 adults (56, 34 and 35 y)  
- treated by 25 grams per day for five days of immunoglobulins at the time of respiratory distress initiation + antibiotic  
- temperature back to normal in one to two days, and breathing difficulties alleviating in 3-5 days  
Point of attention: other treatments were given, antiviral for 2/3 patients, corticoid for 1.  
The first few days of deterioration may present a critical point when potent suppression of inflammatory cascade could save the patients from fatal immune-mediated injuries Hospitalized patients : i) age >12 years and ii) PCR documented SARS-CoV-2 carriage in nasopharyngeal sample at admission  
- Treatment: oral hydroxychloroquine sulfate 200 mg, 3/day during 10 days.  
- 26 treated among them, six patients received additional azithromycin.  
- Control group : 16 patients from another centre or refusal to participate  
- 6 patients treated were excluded from the analysis Primary endpoint : virological clearance at day 6 post-inclusion  
70% of hydroxychloroquine-treated patients (N=20) were virologically cured comparing with 12.5% in the control group (N=16) (p= 0.001) |

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| Journal Travel Medecine and Infectious Disease 20MAR2020 | COVID-19: Active measures to support community-dwelling older adults | K, Kuwahara et al., Japan [2] | HSS/Politic | • With no proven drug and vaccine treatments, non-pharmaceutical measures, especially social distancing, are an essential to slow the spread of the epidemic.  
• Given the higher risk associated with older adults, practical information should be provided to community-dwelling adults to help maintain appropriate community activity levels.  
• Issue of social isolation: efforts are needed to mitigate the negative psychological impact. recent technological advances may help detect and provide care for groups at high risk of social isolation. plans and measures to maintain social ties should be prepared at the individual level (family, friends, neighborhood, etc.), organizational or community levels, and societal level. |
| Travel Med Infect Dis 20MAR2020 | Rapid viral diagnosis and ambulatory management of suspected COVID-19 cases presenting at the infectious diseases referral hospital in Marseille, France, - January 31st to March 1st, 2020: A respiratory virus snapshot | Amrane et al, France [3] | Public Health/Epidemio | Rapid viral detection performed on sputum and nasopharyngeal samples from the first 280 patients suspected to have COVID-19. No SARS-CoV-2 was detected. Other viral infections were identified in 49% of the patients, with most common pathogens being influenza A and B viruses, rhinovirus, metapneumovirus and common coronaviruses, notably HKU1 and NL63. |
- RBD in SARS-CoV-2 S protein was identified  
- RBD protein bound strongly to human and bat angiotensin-converting enzyme 2 (ACE2) receptors.  
- SARS-CoV RBD-specific antibodies could crossreact with SARS-CoV-2 RBD protein  
- SARS-CoV RBD-induced antiserum could cross-neutralize SARS-CoV-2  
> potential to develop SARS-CoV RBD-based vaccines for prevention of SARS-CoV-2 and SARS-CoV infection.  
Randomized, controlled trial, open-label trial  
- 199 patients included: 99 received lopinavir-ritonavir and 100 standard care alone:  
  - Lopinavir-ritonavir was not associated with clinical improvement or mortality: median time to clinical improvement 16 days vs 16 days, HR = 1.31 [0.95 – 1.85]  
Others outcomes:  
  - 28-days mortality lower in the lopinavir-ritonavir group: 19.2% vs 25%, difference = -5.8 % [-17.3 – 5.7]  
  - Detectable viral RNA for SARS-CoV2 was similar between two groups: 40.7 % of the patients of lopinavir-ritonavir group at the end of trial (28d)  
  - Serious adverse events: 19 in the lopinavir-ritonavir group (4 serious gastrointestinal adverse events related to the trial medication) and 32 in the standard care alone.  
  - No difference on duration of oxygen therapy and duration hospitalization.  
  - Post hoc finding that early initiation of lopinavir-ritonavir might accelerate clinical recovery and reduced mortality  
Overall mortality at 22.1%  
No benefit was observed with lopinavir-ritonavir treatment |
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<td>NEJM 19MAR2020</td>
<td>SARS-CoV2 Infection in children</td>
<td>Lu X. et al, China <a href="https://www.nejm.org/dotnet/journals/journalarticle.aspx?journalid=NEJMc2005073&amp;articleType=true">https://www.nejm.org/dotnet/journals/journalarticle.aspx?journalid=NEJMc2005073&amp;amp;articleType=true</a></td>
<td>Clinic</td>
<td>On the 1391 children tested at Wuhan Children’s Hospital, 171 (12.3%) were positive for SARS-CoV2 infection. Median age: 6.7 years - Male: 60.8% Fever: 41.5% - Cough: 48.5% 3 patients (with coexisting conditions) require intensive care and 1 death Most children appear to be mild symptomatic.</td>
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<td>World Journal of Pediatrics 19MAR2020</td>
<td>Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center’s observational study</td>
<td>Sun D et al, China <a href="https://link.springer.com/article/10.1007/s41423-020-00354-4">https://link.springer.com/article/10.1007/s41423-020-00354-4</a></td>
<td>Clinic</td>
<td>8 children included: 5 severely ill and 3 critically ill 2 months to 15 years Symptoms: - Polypnea 100% - Fever (6/8) - Cough (6/8) - Expectoration (4/8) Abnormalities in chest scanning 100% patients: - multiple patch-like shadows - ground glass opacity Biological: - increase CRP, PCT and LDH - elevated ALAT - increase IL6 (2/8), IL10 (5/8), IFN-γ (2/8) Level of IL6 and IL10 were significantly increase in 2 critically ill patient who remained in ICU for 20 days. Specific laboratory abnormalities and excessive immune responses may lead to long-term lung damage and severe health complication</td>
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<td>Cell and Mol Biol 17MAR2020</td>
<td>Elevated exhaustion levels and reduced functional diversity of T cells in peripheral blood may predict severe progression in COVID-19 patients</td>
<td>Zheng et al., <a href="https://www.nature.com/articles/s41423-020-00401-3">https://www.nature.com/articles/s41423-020-00401-3</a></td>
<td>Immunology</td>
<td>Immunological characteristics of peripheral blood leukocytes from 16 patients: Compared to healthy group (n=6): - Frequency of multi-functional CD4+ T cells (positive for at least two cytokines) decreased significantly in the severe group - The proportion of non-functional (IFN-γ−TNF-α−IL-2−) subsets increased significantly. - No increase in neutrophils or decrease in lymphocytes. - No statistical differences in interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) plasma concentrations were found among the three groups - Levels of interferon-γ (IFN-γ) and TNF-α in CD4+ T cells were lower in the severe group than in the mild group, whereas the levels of granzyme B and perforin in CD8+ T cells were higher in the severe group than in the mild group. - Frequency of multi-functional CD4+ T cells decreased significantly in the severe group and proportion of non-functional subsets increased significantly -&gt; Identification of potential immunological risk factors for COVID-19 pneumonia and provided clues for its clinical treatment.</td>
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<td>The NEJM 17MAR2020</td>
<td>Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1</td>
<td>Doremalen et al., USA <a href="https://www.nejm.org/doi/pdf/10.1056/NEJMc2004973?articleTools=true">https://www.nejm.org/doi/pdf/10.1056/NEJMc2004973?articleTools=true</a></td>
<td>Virology</td>
<td>-&gt; Stability of SARS-CoV-2 was similar to that of SARS-CoV-1 under the experimental circumstances tested. -&gt; Detectable in aerosols for up to three hours, up to four hours on copper, up to 24 hours on cardboard and up to two to three days on plastic and stainless steel. Aerosol and fomite transmission of SARS-CoV-2 is plausible</td>
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<td>The Lancet 17MAR2020</td>
<td>Prevention of SARS-CoV-2 infection in patients with decompensated cirrhosis</td>
<td>Xiao et al., China <a href="https://www.thelancet.com/journals/lantrans/article/PIIS1246-1253(20)30080-7/fulltext">link</a></td>
<td>Clinic</td>
<td>Previously known: Patients with decompensated cirrhosis have a higher risk of, and mortality from, infection. - 111 patients with decompensated cirrhosis were included - New precautionary procedures were implemented (see paper) - Incidence of COVID19 was lower than in other groups. The simple approach (see paper) could be an effective means of preventing COVID-19 in patients with decompensated cirrhosis.</td>
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<tr>
<td>International journal of infectious diseases 17MAR2020</td>
<td>Transmission potential and severity of COVID-19 in South Korea</td>
<td>Shim et al., Rep of Korea <a href="https://www.jidonline.com/article/S1201-879X(20)30150-4/fulltext">link</a></td>
<td>Public Health/Epidemiology</td>
<td>- COVID-19 caused 6,284 cases and 42 deaths in South Korea as of March 8, 2020. - The mean reproduction number R Bowling of COVID-19 in Korea was estimated at 1.5 (95% CI: 1.4-1.6) - The intrinsic growth rate was estimated at 0.6 (95% CI: 0.6, 0.7) and the scaling of growth parameter was estimated at 0.8 (95% CI: 0.7, 0.8), indicating sub-exponential growth dynamics of COVID-19 - The crude case fatality rate is higher among males (1.1%) compared to females (0.4%) and increases with older age, from 0.1% among those 30-39 yrs to 6% among those &gt; = 80 yrs as of March 6, 2020. - Results indicate early sustained transmission of COVID-19 in South Korea and support the implementation of social distancing measures to rapidly control the outbreak.</td>
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<tr>
<td>J Inf Dis 17MAR2020</td>
<td>Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China.</td>
<td>Wang et al., China <a href="https://academic.oup.com/jid/article/doi/10.1093/infdis/jiaa119/5807958">link</a></td>
<td>Clinic</td>
<td>55 asymptomatic carriers Conclusion: - Asymptomatic carriers occurred more often in middle aged people who had close contact with infected family members - Majority of the cases developed to be mild and ordinary COVID-19 during hospital</td>
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<td>Am J Transplant. 17MAR2020</td>
<td>Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression.</td>
<td>Zhu et al., China <a href="https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.15869">link</a></td>
<td>Clinic</td>
<td>52-year-old man who received kidney transplantation 12 years ago - Clinical characteristics (symptoms, laboratory examinations, and chest CT) were similar to those of non-transplanted COVID-19 patients - Following a treatment regimen: reduced immunosuppressant use and low dose methylprednisolone-based therapy Effectively treated case has reference value for the future treatment of other transplant patients with COVID-19 pneumonia. Analysis of additional cases is necessary to determine if this remains true.</td>
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| The Lancet 17MAR2020 | Prisons and custodial settings are part of a comprehensive response to COVID-19 | Kinnet et al., Australia [link](https://www.thelancet.com/journals/lancet/article/PII/S0140-6736(20)30358-3/fulltext) | Public Health/Epidemiology | Prisons are epicentres for infectious diseases:  
- higher background prevalence of infection  
- higher levels of risk factors for infection  
- unavoidable close contact in often overcrowded, poorly ventilated, and unsanitary facilities,  
- poor access to health-care services relative to that in community settings  
-> The public health importance of prison responses to influenza outbreaks has been recognised in the USA, where the Centers for Disease Control and Prevention have developed a checklist for pandemic influenza preparedness in correctional settings. WHO has also issued prison-specific guidance for responding to COVID-19. |
-> Unlike coronavirus infections of pregnant women caused by SARS and MERS, COVID-19 did not lead to maternal deaths  
-> Similar to pregnancies with SARS and MERS: no confirmed cases of intrauterine transmission of SARS-CoV-2  
There is no evidence that SARS-CoV-2 undergoes intrauterine or transplacental transmission from infected pregnant women to their fetuses. |
| Gynecologie, obstetrique, fertilite & senologie 16MAR2020 | Infection with SARS-CoV-2 in pregnancy. Information and proposed care. CNGOF | Peyronnet et al, France [link](https://www.sciencedirect.com/science/article/pii/S2468718920301100?via%3Dihub) | Clinic | Few pregnant women have been described  
Same symptoms as rest of adult’s patients  
Some cases of ARDS or pneumonia  
2 pregnant women with invasive ventilation have been described  
Risk: cesarian and prematurity  
No miscarriage described  
Neonatal:  
- no case of vertical transmission  
- milder symptomatic  
- symptoms probably due to maternal hypoxemia |
The emergence and rapid increase in activated CD38+HLA-DR+ T cells, especially CD8+ T cells, at days 7–9 preceded the resolution of symptoms:  
-> ASCs appeared in the blood at the time of viral clearance (day 7; 1.48%) and peaked on day 8 (6.91%).  
-> Emergence of cTFH cells in blood at day 7 (1.98%), increasing on day 8 (3.25%) and day 9 (4.46%).  
-> The frequency of co-expression of CD38 and HLA-DR on CD8+ T cells increased in this patient from day 7 (3.57%) to day 8 (5.32%) and day 9 (11.8%) as well as the frequency of co-expression of CD38 and HLA-DR on CD4+ T cells between day 7 (0.55%) and day 9 (3.33%) although at lower levels than that of CD8+ T cells.  
-> CD38+HLA-DR+CD8+ T cells, produced larger amounts of granzymes A and B and perforin (+34–54% higher) than did their parent cells (CD8+or CD4+ populations).  
-> Interestingly, minimal pro-inflammatory cytokines and chemokines were found in this patient with COVID-19, even at days 7–9. |
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| SCIENCE 16MAR2020 | Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV2). | Li et al., UK [https://science.sciencemag.org/content/early/2020/03/13/science.abb2213] | Public Health/Epidemiology | From observations of reported infection within China + mobility data + a networked dynamic metapopulation model and Bayesian inference  
-> 86% of all infections were undocumented (95% CI: [82%–90%]) prior to 23 January 2020 travel restrictions.  
-> Undocumented infections were the infection source for 79% of documented cases  
It explain the rapid geographic spread of SARS-CoV2 and indicate containment of this virus will be particularly challenging |
-> Much like Ebola, the early symptoms of COVID-19, including fever, myalgia, and fatigue, might be confused with malaria and lead to challenges in early clinical diagnosis |
| The Lancet 16MAR2020 | Screening of faecal microbiota transplant donors during the COVID-19 outbreak: suggestions for urgent updates from an international expert panel | Ianiro et al., Italy [https://www.thelancet.com/journals/lancet/article/PIIS2468-2263(20)30083-0/fulltext] | Public Health/Epidemiology | -> Before each donation, physicians should screen for two main items: the presence of typical COVID-19 symptoms  
-> In endemic countries, the RT-PCR assay should be considered in all donors  
-> Stool banks should retrospectively check the health status of the donor before using frozen faeces, according to local epidemiology, to avoid further potential spreading of SARS-CoV2 |
| JAMA 13MAR2020 | Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China | Wu et al., China [https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2763184?resultClick=1] | Clinic | -> 201 patients included in the study  
Risk factors to develop ARDS:  
• Older age, neutrophilia, and organ and coagulation dysfunction (eg, higher LDH and D-dimer)  
• Associated with ARDS but not death: Comorbidities, lymphocyte counts, CD3 and CD4 T-cell counts, AST, prealbumin, creatinine, glucose, low-density lipoprotein, serum ferritin, PT  
• Although high fever was positively associated with development of ARDS, it was negatively related to death  
• Higher CD3 and CD4 T-cell counts might protect patients from developing ARDS  
• Persistent and gradual increases in lymphocyte responses might be required for effective immunity against SARS-CoV-2 infection. |
| Euro Surv 12MAR2020 | Retrospective analysis of the possibility of predicting the COVID-19 outbreak from Internet searches and social media data, China, 2020 | Li et al., China [https://www.merscorona.net/news组织/content/10.2807/1000-9999.2020.10.200015] | Public Health/Epidemiology | To predict the development of this outbreak as early and as reliably as possible  
-> Data obtained from Google Trends, Baidu Index and Sina Weibo Index on searches for the keywords ‘coronavirus’ and ‘pneumonia’ correlated with the published NHC data on daily incidence of laboratory-confirmed and suspected cases of COVID-19, with the maximum r > 0.89.  
-> Peak interest for these keywords in Internet search engines and social media data was 10–14 days earlier than the incidence peak of COVID-19 published by the NHC.  
-> The lag correlation showed a maximum correlation at 8–12 days for laboratory-confirmed cases and 6–8 days for suspected cases |
| The Lancet 12MAR2020 | SARS-CoV-2 RNA more readily detected in induced sputum than in throat swabs of convalescent COVID-19 patients | Han et al., China [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30174-Z/fulltext] | Diagnostic | -> 2 cases in convalescence  
-> Both negative with throat swab and anal swabs  
-> Positive in induced sputum  
To reduce the risk of disease spread, viral RNA tests of induced sputum, not throat swabs, should be assessed as a criterion for releasing COVID-19 patients. |
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<tr>
<td>The Lancet 12MAR2020</td>
<td>Real estimates of mortality following COVID-19 infection</td>
<td>Baud et al., Switzerland <a href="https://www.thelancet.com/journals/lanres/article/PIIS22132600(20)30019-4/fulltext">link</a></td>
<td>Public Health/Epidemiology</td>
<td>Mortality rate estimates are based on the number of deaths relative to number of confirmed cases of infection - not representative of actual death rate. <strong>Real rates:</strong> 5-6% for China - 15% 2% outside China Current figures might underestimate the potential threat of COVID-19 in symptomatic patients.</td>
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<td>The Lancet 11MAR2020</td>
<td>Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?</td>
<td>Fang et al., Switzerland <a href="https://www.thelancet.com/journals/lancet/article/PIIS01406736(20)30566-5/fulltext">link</a></td>
<td>Clinic</td>
<td>Patients with cardiac diseases, hypertension, or diabetes, who are treated with ACE2-increasing drugs, may be at higher risk for severe COVID-19 infection. - They should be monitored for ACE2-modulating medications, such as ACE inhibitors or ARBs. - No evidence to suggest that antihypertensive calcium channel blockers increased ACE2 expression or activity: these could be a suitable alternative treatment in these patients.</td>
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<tr>
<td>The Lancet 11MAR2020</td>
<td>Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.</td>
<td>Zhou et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS01406736(20)30566-5/fulltext">link</a></td>
<td>Clinic</td>
<td>Calculation the probability that newly introduced cases might generate outbreaks in other areas. - Estimations: The median daily reproduction number (Rₚ) in Wuhan declined from 2.35 (95% CI 1.15–4.77) 1 week before travel restrictions were introduced on Jan 23, 2020, to 1.05 (0.41–2.39) 1 week after. - In locations with similar transmission potential to Wuhan in early January, once there are at least four independently introduced cases, there is a more than 50% chance the infection will establish within that population.</td>
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<td>The Lancet 11MAR2020</td>
<td>Early dynamics of transmission and control of COVID-19: a mathematical modelling study</td>
<td>Kucharski et al., UK <a href="https://www.thelancet.com/journals/lancet/article/PIIS01406736(20)30144-8/fulltext">link</a></td>
<td>Public Health/Epidemiology</td>
<td>Calculation the probability that newly introduced cases might generate outbreaks in other areas. - Estimations: The median daily reproduction number (Rₚ) in Wuhan declined from 2.35 (95% CI 1.15–4.77) 1 week before travel restrictions were introduced on Jan 23, 2020, to 1.05 (0.41–2.39) 1 week after. - In locations with similar transmission potential to Wuhan in early January, once there are at least four independently introduced cases, there is a more than 50% chance the infection will establish within that population.</td>
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<td>JAMA 11MAR2020</td>
<td>Detection of SARS-CoV-2 in Different Types of Clinical Specimens</td>
<td>Wang et al., China <a href="https://jamanetwork.com/journals/jama/fullarticle/2762997">link</a></td>
<td>Diagnostic</td>
<td>-&gt; 1070 specimens collected from 205 patients. <strong>POSITIVITY</strong> by RT-PCR: Bronchoalveolar lavage fluid (93%) Sputum (72%) Nasal Swabs (63%) Fibrobronchoscope brush biopsy (46%) Pharyngeal swabs (32%) Feces (29%) Blood (1%) Urine (3%)</td>
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<td>Sci Rep 11MAR2020</td>
<td>A high ATP concentration enhances the cooperative translocation of the SARS coronavirus helicase nsP13 in the unwinding of duplex RNA</td>
<td>Jang et al., Republic of Korea <a href="https://www.nature.com/articles/s41598-020-61432-1">link</a></td>
<td>Fundamental Research</td>
<td>To know: RNA Helicase nsP13 is essential for the viral RNA replication of the SARS coronavirus. Here: - RNA helicase nsP13 would have higher binding affinity to RNA than to DNA, at same ATP concentrations. - The open state of nsP13 binding with a higher affinity to RNA than to DNA, is a considerably energy-consuming reaction. - Unwinding of duplex RNA by nsP13 is a considerably energy-consuming reaction. SARS coronavirus nsP13 may require more ATPs to promote stable helicase translocation necessary for delicate RNA replication.</td>
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<td>Emerge Inf Dis 09MAR2020</td>
<td>Detection of Novel Coronavirus by RT-PCR in Stool Specimen from Asymptomatic Child, China</td>
<td>Tang et al., China <a href="https://wwwnc.cdc.gov/eid/article/26/6/200810_article">https://wwwnc.cdc.gov/eid/article/26/6/200810_article</a></td>
<td>Public Health/Epidemi</td>
<td>↓&gt; Asymptomatic child positive for COVID-19 by RT-PCR in stool, 17 days after the last virus exposure ↓&gt; Still positive 9 days after that (in stool) ↓&gt; Never positive in respiratory tracts specimens ↓&gt; no data on urine and blood ↓&gt; The child might have transmitted the virus to numerous persons. Stool from COVID-19 patients might serve as another vehicle for virus transmission</td>
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<td>Clin Inf Dis 09MAR2020</td>
<td>In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)</td>
<td>Yao et al., China <a href="https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa237/5801998">https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa237/5801998</a></td>
<td>Therapeutic</td>
<td>↓&gt; Vero cells were treated by Chloroquine and Hydroxychloroquine before (prophylaxy) and after (anti-viral) infection by SARS-CoV-2. ↓&gt; EC50 are calculated ↓&gt;Hydroxychloroquine has superior antiviral and prophylactic activity than chloroquine ↓&gt; Physiologically-based pharmacokinetic (PBPK) -&gt; to predict (in silico) drug concentrations in lung, plasma and blood. -PBPK model has acceptable prediction accuracy. -Kinetics were simulated with different scenari of dose regimens -Dose regiment was optimized (recommendations).</td>
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<td>Science 06MAR2020</td>
<td>The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak.</td>
<td>Chinazzi et al., USA <a href="https://science.sciencemag.org/content/early/2020/03/05/science.abc7571">https://science.sciencemag.org/content/early/2020/03/05/science.abc7571</a></td>
<td>Public Health/Epidemi</td>
<td>↓&gt; Global metapopulation disease transmission model to project the impact of travel limitations on the national and international spread of the epidemic. ↓&gt;Travel quarantine of Wuhan delayed the overall epidemic progression by only 3 to 5 days in Mainland China ↓&gt; More marked effect at the international scale, where case importations were reduced by nearly 80% until mid February ↓&gt; Sustained 90% travel restrictions to and from Mainland China only modestly affect the epidemic trajectory unless combined with a 50% or higher reduction of transmission in the community ↓&gt; Potential uses for the definition of optimized containment schemes and mitigation policies that includes the local and international dimension of the COVID-19 epidemic</td>
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<td>EuroSurveillance 05MAR2020</td>
<td>Evaluation of a quantitative RT-PCR assay for the detection of the emerging coronavirus SARS-CoV-2 using a high throughput system</td>
<td>Pfefferle et al.</td>
<td>Diagnostic</td>
<td>Assessment of a molecular assay for the detection of SARS-CoV-2 on a high-throughput platform, the cobas 6800, using the ‘open channel’ for integration of a laboratory-developed assay. Evaluated samples are swab samples. Good analytical performance in clinical specimens. The fully automated workflow enables high-throughput testing with minimal hands-on time, while offering fast and reliable results. Special notes : by its nature as a screening test targeting only a single viral gene, positive results should always be confirmed with an independent PCR as recommended). Importance of closely coordinating with local reference centres and public health authorities for determining clinical indications for testing</td>
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<td>Cell 04MAR2020</td>
<td>SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor</td>
<td>Hoffman et al., Germany <a href="https://www.cell.com/cell/">https://www.cell.com/cell/</a> fulltext/S0092-8674(20)30229-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.co m%2Fretrieve%2Fpii%2F S0092867420302294%3Fsh owfull%3Dtrue</td>
<td>Therapeutic</td>
<td>↓&gt; Priming of 5 proteins by host cell proteases (TMPRSS2) is essential for viral entry into cells. ↓&gt; ACE 2 can be blocked by a clinically proven inhibitor of TMPRSS2 ↓&gt; The study suggests that antibody responses raised against SARS-CoV could at least partially protect against SARS-CoV-2 infection</td>
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<td>Science 04MAR2020</td>
<td>Structural basis for the recognition of the SARS-CoV-2 by full-length human ACE2</td>
<td>Yan et al., China <a href="https://science.sciencemag.org/content/early/2020/03/10/science.abd7152/ab.pdf">link</a></td>
<td>Fundamental Research</td>
<td>-&gt; Cryo-EM structures of human ACE2, in the presence of a neutral amino acid transporter B0AT1, with or without the receptor binding domain (RBD) of the surface spike glycoprotein (S protein) of SARS-CoV-2.</td>
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<td>J Clin Microbiol 04MAR2020</td>
<td>Multicenter Evaluation of the QIAstat-Dx Respiratory Panel for the Detection of Viruses and Bacteria in Nasopharyngeal Swab Specimens</td>
<td>Leber et al., USA <a href="https://jcm.asm.org/content/early/2020/02/28/JCM.00155-20.long">link</a></td>
<td>Diagnostic</td>
<td>-&gt; Multiplex <em>in vitro</em> diagnostic test for the qualitative detection of 20 pathogens directly from nasopharyngeal swab specimens.</td>
</tr>
<tr>
<td>JAMA 04MAR2020</td>
<td>Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient</td>
<td>Ong et al., Singapore <a href="https://jamanetwork.com/journals/jama/fullarticle/2762069?resultClick=1">link</a></td>
<td>Public Health/Epidemiology</td>
<td>-&gt; Extensive environmental contamination by 1 SARS-CoV-2 patient with mild upper respiratory tract involvement.</td>
</tr>
</tbody>
</table>

**Limit of the study:** viral culture was not done to demonstrate viability.

> The L type is predominant (70% against 30% for S type).

> This article suggests that the L type is more aggressive.
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<tr>
<th>Journal and date</th>
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<th>Authors and link</th>
<th>Field of expertise</th>
<th>Key facts</th>
</tr>
</thead>
<tbody>
<tr>
<td>JAMA 03MAR2020</td>
<td>Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore</td>
<td>Young et al., Singapore <a href="https://jamanetwork.com/journals/jama/fullarticle/272688">link</a></td>
<td>Clinic</td>
<td>- 18 patients diagnosed with SARS-CoV-2 infection in Singapore between January 23 and February 3, 2020</td>
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<td>- Respiratory tract infection with prolonged viral shedding from the nasopharynx of 7 days or longer in 15 patients (83%)</td>
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<td>- Supplemental oxygen was required in 6 patients (33%), 5 of whom were treated with lopinavir-ritonavir, with variable clinical outcomes following treatment.</td>
</tr>
<tr>
<td>Int J Infect Dis 02MAR2020</td>
<td>Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report</td>
<td>Chen et al., China <a href="https://journals.jib.org.cn/article/S0163-7258(20)30122-9.pdf">link</a></td>
<td>Virology</td>
<td>- 46-year-old woman with multiple patchy ground glass opacities in bilateral subpleural areas by CT</td>
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<td>- Oropharyngeal swab test was positive by RT-PCR.</td>
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<td>- Received symptomatic treatment and antimicrobial therapy including oseltamivir, arbidol, Lopinavir/ritonavir and moxifloxacin</td>
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<td>- 6 testing from 28 Jan to 17FEB, all negative but one the 2FEB Discharged on 9FEB and testing remained negative during follow-up.</td>
</tr>
<tr>
<td>Jour of Infect 29FEB2020</td>
<td>Identification of the hyper-variable genomic hotspot for the novel coronavirus SARS-CoV-2</td>
<td>Wen et al., China [link](<a href="https://www.journalinfec">https://www.journalinfec</a> tion.com/article/32163-400/3/2030128-0j.pdf)</td>
<td>Genomic</td>
<td>- Confirmation of the relationship of SARS-CoV-2 with other beta coronaviruses on the amino acid level.</td>
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<td>- Hyper-variable genomic hotspot established in SARS-CoV-2 population at the nucleotide but not the amino acid level -&gt; no beneficial mutations.</td>
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<td>- Mutations in nsp1, nsp3, nsp15, and gene S would be associated with the SARS-CoV-2 epidemic (compared with RaTG13) / required for human adaptation?</td>
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<td></td>
<td>2-&gt; Immunoinformatic analysis of 13 MHC I and 3 MHC II epitopes which have antigenic properties</td>
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<td>3-&gt; These identified epitopes are candidate to formulate a multi-epitopic peptide vaccine.</td>
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<td>Need for in vitro and in vivo validations</td>
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<tr>
<td>The NEJM 28FEB2020</td>
<td>Clinical Characteristics of Coronavirus Disease 2019 in China</td>
<td>Ni et al., China <a href="https://www.nejm.org/doi/pdfplus/10.1056/NEJMoa2002302?articleTools=true&amp;toolId=showPdf&amp;articleId=10.1056/NEJMoa2002302">link</a></td>
<td>Clinic</td>
<td>Median age: 47 years / Female: 41.9%</td>
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<td>Primary composite end point (admission in ICU, use of mechanical ventilation and death) in 6.1%, with 5.0% in ICU, 2.3% with invasive mechanical ventilation, and 1.4% who died.</td>
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<td>History of direct contact with wildlife: 1.9% Among nonresidents of Wuhan, 72.3% had contact with residents of Wuhan, including 31.3% who had visited the city.</td>
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<td>Most common symptoms: fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%). Diarrhea was uncommon (3.8%).</td>
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<td>Median incubation period: 4 days (interquartile range, 2 to 7).</td>
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<td>CT: ground-glass opacity was the most common radiologic: 56.4%.</td>
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<td>No radiographic or CT abnormality: 17.9% with nonsevere disease and 2.9% with severe disease.</td>
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<td>Lymphocytopenia: 83.2%</td>
</tr>
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</table>
Early transmission patterns of coronavirus disease 2019 (COVID-19) in travellers from Wuhan to Thailand, January 2020

Authors and link:
Okada et al., Thailand
https://www.euroursurveillance.org/content/10.2807/1757-4636.ES.2020.25.8.200009

Field of expertise: Public Health/Epidemiology

Key facts:
- 2 woman arriving in Thailand at different times (8 and 13 January)
- The two viral genomes are identical to four sequences from Wuhan, while no direct link to the Huanan Seafood Market.
- Identical genomes of up to 30 kb are rare and a strong sign of recent transmission linkage
- Data suggest that transmission within Wuhan beyond the Huanan Seafood Market is likely to have occurred in the first week of January or earlier.

Epidemiological Identification of A Novel Pathogen in Real Time: Analysis of the Atypical Pneumonia Outbreak in Wuhan, China, 2019—2020

Authors and link:
Jung et al., Japan
https://www.mdpi.com/2079-7848/10/1/3

Field of expertise: Public Health/Epidemiology

Key facts:
- Non-virological descriptive characteristics could have determined that the outbreak is caused by a novel pathogen in advance of virological testing.
- Characteristics of the outbreak were collected in real time and compared with characteristics of eleven pathogens that have previously caused cases of atypical pneumonia.
- The probability that a new virus was driving the outbreak was assessed as over 29% on 31 December 2019, one week before virus identification.

Secondary attack rate and superspreading events for SARS-CoV-2

Authors and link:
Liu et al., UK
https://www.thelancet.com/journals/lancet/article/PII/S0140-6736(20)30462-4/fulltext

Field of expertise: Public Health/Epidemiology

Key facts:
The Ro value only captures the average dynamics of transmission.
The secondary attack rate (SAR) is the probability that an infection occurs among susceptible people within a specific group.
SAR among close contacts would be of 35% (95% CI 27–44).
An infection with a high household SAR but a modest Ro suggests transmission is driven by a relatively small number of high-risk contacts.
A large household SAR further suggests that between-household transmission risk is lower; otherwise the observed Ro would be larger.
More data are needed.

COVID-19: combining antiviral and anti-inflammatory treatments

Authors and link:
Stebbing et al., UK
https://www.thelancet.com/journals/lancet/article/PII/S0140-6736(20)30132-4/fulltext

Field of expertise: Therapeutic

Key facts:
- COVID-19 characterised by an overexuberant inflammatory response
- SARS > viral load is not correlated with the worsening of symptoms
- Inhibition of numb-associated kinase (NAK) family would reduce viral infection in vitro (inhibit clathrin-mediated endocytosis and thereby inhibit viral infection of cells)
- JAK–STAT signalling inhibitors, could be effective against the consequences of the elevated levels of cytokines (including interferon) typically observed in people with COVID-19
- Baricitinib is a NAK inhibitor (anti-viral)
- Baricitinib, fedratinib, and ruxolitinib are JAK inhibitors (anti-inflammatory)
- Baricitinib is the best of the group

Positive RT-PCR Test Results in Patients Recovered From COVID-19

Authors and link:
Lan et al., China
https://jamanetwork.com/journals/jama/fullarticle/2762452

Field of expertise: Public Health/Epidemiology

Key facts:
Little attention has been paid to the follow-up of recovered patients so far.
4 patients with COVID-19 who met criteria for hospital discharge or discontinuation of quarantine in China (absence of clinical symptoms and radiological abnormalities and 2 negative RT-PCR test results) had positive RT-PCR test results 5 to 13 days later, while they were still asymptomatic.
<table>
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<tbody>
<tr>
<td>The Lancet, 27FEB2020</td>
<td>Convalescent plasma as a potential therapy for COVID-19 COMMENT</td>
<td>Chen et al., China <a href="https://www.thelancet.com/pdfs/journals/lancet/Pdfs/1473-3099%2820%2930541-0.pdf">Link</a></td>
<td>Therapeutic</td>
<td>- In 2014, the use of convalescent plasma collected from patients who had recovered from <em>Ebola virus disease</em> was recommended by WHO as an empirical treatment during outbreaks. - A protocol for the use of convalescent plasma in the treatment of MERS coronavirus was established in 2015. - H1N1: significant reduction of relative risk of mortality / no adverse event. - and other studies. Antibodies from convalescent plasma might suppress viraemia.</td>
</tr>
<tr>
<td>Emerg Microb Infects, 26FEB2020</td>
<td>Detectable 2019-nCoV viral RNA in blood is a strong indicator for the further clinical severity</td>
<td>Chen et al., China <a href="https://www.tandfonline.com/doi/full/10.1080/22221763.2020.1752387">Link</a></td>
<td>Clinic</td>
<td>- All patients (n=6 / 57) with detectable viral RNA in the blood progressed to severe symptom stage, indicating a strong correlation of serum viral RNA with the disease severity (p-value = 0.0001). - 8 of the 11 patients with annal swab virus-positive was in severe clinical stage. - Concentration of viral RNA in the anal swab was higher than in the blood: virus might replicate in the digestive tract.</td>
</tr>
<tr>
<td>The Lancet, 26FEB2020</td>
<td>The psychological impact of quarantine and how to reduce it: rapid review of the evidence</td>
<td>Brooks et al., UK <a href="https://www.thelancet.com/journals/lancet/article/PiIS0140-6736%2820%2930650-8/fulltext">Link</a></td>
<td>HSS/Politic</td>
<td>- Information is key: people who are quarantined need to understand the situation. - The quarantine period should be short and the duration should not be changed unless in extreme circumstances. - Most of the adverse effects come from the imposition of a restriction of liberty; voluntary quarantine is associated with less distress and fewer long-term complications. - Public health officials should emphasise the altruistic choice of self-isolating.</td>
</tr>
<tr>
<td>Viruses, 25FEB2020</td>
<td>Preliminary Identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies</td>
<td>Ahmed et al., China <a href="https://www.mdpi.com/1999-4915/12/3/254">Link</a></td>
<td>Vaccine</td>
<td>- High genetic similarity between SARS-CoV-2 and SARS-CoV. - Identification of a set of B cell and T cell epitopes derived from the spike (S) and nucleocapsid (N) proteins that map identically to SARS-CoV-2 proteins. - No mutation has been observed in these epitopes (as of 21 February 2020). - Immune targeting of these epitopes may offer protection against this novel virus.</td>
</tr>
<tr>
<td>EuroSurv, 25FEV2020</td>
<td>Differential diagnosis of illness in patients under investigation for the novel coronavirus (SARS-CoV-2), Italy, February 2020.</td>
<td>Bordi et al., Italy <a href="https://www.eurosurveillance.org/content/10.2807/1369-5986.2020.25.8.200017">Link</a></td>
<td>Public Health/Epidemi</td>
<td>- Similarity of symptoms shared with more common respiratory infections. - Broad screening requested. - Influenza virus infections: 28.5% of all suspected cases of SARS-CoV-2 infection. - Alternative diagnoses may clarify an individual patient’s risk and may allow adjusting public health containment measures.</td>
</tr>
<tr>
<td>The Lancet, 25FEB2020</td>
<td>Potential association between COVID-19 mortality and healthcare resource availability</td>
<td>Ji et al., China <a href="https://www.thelancet.com/journals/langlo/article/PiIS1473-3099%2820%2930546-9/fulltext">Link</a></td>
<td>Public Health/Epidemi</td>
<td>Plotting mortality against the incidence of COVID-19 (cumulative number of confirmed cases since the start of the outbreak, per 10 000 population) showed a significant positive correlation, suggesting that mortality is correlated with healthcare burden.</td>
</tr>
<tr>
<td>The Lancet, 24FEB2020</td>
<td>COVID-19 control in China during mass population movements at New Year</td>
<td>Chen et al., China <a href="https://www.thelancet.com/journals/lancet/article/PiIS0140-6736%2820%2930651-9/fulltext">Link</a></td>
<td>Public Health/Epidemi</td>
<td>Several lessons that can be drawn from China’s extension of the Lunar New Year holiday: 1-&gt; Countries should consider periods of recommended or mandatory closure of non-essential workplaces and public institutions— to slow the rate of transmission. 2-&gt; To tailor the design of these actions according to specific epidemic characteristics (incubation period and transmission routes). 3-&gt; This is to prevent people with asymptomatic infections from spreading the disease. As such, governments should use the closure period for information and education campaigns, community screening, active contact tracing, and isolation and quarantine to maximise impact.</td>
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<td>Journal and date</td>
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| J Clin Med 24FEB2020 | Assessing the Impact of Reduced Travel on Exportation Dynamics of Novel Coronavirus Infection (COVID-19) | Anzai et al., Japan [https://www.mdpi.com/2077-0383/6/1/901](https://www.mdpi.com/2077-0383/6/1/901) | Public Health/Epidemiology | -> From 28 January to 7 February 2020, around 226 exported cases were prevented (=70.4% reduction in incidence)  
-> Reduced probability of a major epidemic in Japan: from 7% to 20% (=median time delay: of 2 days)  
-> Depending on the scenario, the estimated delay may be less than one day. As the delay is small, the decision to control travel volume through restrictions on freedom of movement should be balanced between the resulting estimated epidemiological impact and predicted economic fallout. |
| Cell Discov 24FEB2020 | Comparative genetic analysis of the novel coronavirus (2019-nCoV/SARS-CoV-2) receptor ACE2 in different populations | Cao et al., China [https://jcm.asm.org/content/early/2020/02/28/JCM.00155-20.long](https://jcm.asm.org/content/early/2020/02/28/JCM.00155-20.long) | Fundamental Research     | -> Previous studies demonstrated the positive correlation of ACE2 expression and the infection of SARS-CoV in vitro  
-> Here: Systematic analysis of coding-region variants in ACE2 and the eQTL variants (may affect the expression of ACE2) among different populations (GTEx database)/  
-> The East Asian populations have much higher AFs in the eQTL variants associated with higher ACE2 expression in tissues which may suggest different susceptibility or response to 2019-nCoV/SARS-CoV-2 from different populations under the similar conditions.  
-> No direct evidence supporting the existence of coronavirus S-protein binding-resistant ACE2 mutants in different populations. |
| The Lancet 24FEB2020 | Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study | Xiaobo Yang et al., China [https://www.thelancet.com/journals/laninf/article/PIIS2213-2600(20)30079-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS2213-2600(20)30079-3/fulltext) | Clinic                   | - Mortality is high. The survival term of the non-survivors is likely to be within 1–2 weeks after ICU admission.  
- Older patients (>65 years) with comorbidities and ARDS are at increased risk of death. |
| The Lancet 24FEB2020 | Viral load of SARS-CoV-2 in clinical samples | Pan et al., China [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30113-4/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30113-4/fulltext) | Virology                 | - The viral loads in throat swab and sputum samples peaked at around 5–6 days after symptom onset, ranging from around 104 to 107 copies per mL during this time  
- Sputum samples generally showed higher viral loads than throat swab samples. |
- More research is needed to correlate of CT findings with clinical severity and progression, the predictive value of baseline CT or temporal changes for disease outcome, and the sequelae of acute lung injury induced by COVID-19. |
Which are the probably most common sites undergoing to an aminoacidic change?  
-> Insight of some important proteins of the COVID-2019 that are involved in the mechanism of viral entry and viral replication  
Results: Both nsp2 and nsp3 are under selective pressure. nsp2 -> could explain why this virus is more contagious than SARS  
nsp 3 -> could suggest a potential mechanism differentiating COVID-2019 from SARS |
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<tbody>
<tr>
<td><strong>The Lancet 19FEB2020</strong></td>
<td>Asymptomatic cases in a family cluster with SARS-CoV-2 infection</td>
<td>Pan et al., China <a href="https://www.thelancet.com/journals/lancet/article/PiIs0147-379X(20)30146-0/fulltext">https://www.thelancet.com/journals/lancet/article/PiIs0147-379X(20)30146-0/fulltext</a></td>
<td>Public Health/Epidemiology</td>
<td>- in this family cluster, although all individuals tested positive for SARS-CoV-2 infection on qRT-PCR, only patient 1 showed clinical symptoms, decreased lymphocyte count, and abnormal chest CT images. - However, any of the three individuals could have been the first one to become infected and thus transmitted the virus to the other two family members.</td>
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<tr>
<td><strong>The Lancet 19FEB2020</strong></td>
<td>Enteric involvement of coronaviruses: is faecal–oral transmission of SARS-CoV-2 possible?</td>
<td>Yeo et al., Singapore <a href="https://www.thelancet.com/journals/lancet/article/PiIs1253-300487(20)30145-0/fulltext">https://www.thelancet.com/journals/lancet/article/PiIs1253-300487(20)30145-0/fulltext</a></td>
<td>Virology</td>
<td>- Considering the evidence of faecal excretion for both SARS-CoV and MERS-CoV, and their ability to remain viable in conditions that could facilitate faecal–oral transmission, it is possible that SARS-CoV-2 could also be transmitted via this route. - When SARS-CoV was seeded into sewage water obtained from the hospitals in a separate experiment, the virus was found to remain infectious for 14 days at 4°C, but for only 2 days at 20°C. SARS-CoV can survive for up to 2 weeks after drying, remaining viable for up to 5 days at temperatures of 22–25°C and 40–50% relative humidity, with a gradual decline in virus infectivity thereafter. Viability of the SARS-CoV virus decreased after 24 h at 38°C and 80–90% relative humidity. - MERS-CoV is viable in low temperature, low humidity conditions. The virus was viable on different surfaces for 48 h at 20°C and 40% relative humidity, although viability decreased to 8 h at 30°C and 80% relative humidity conditions.</td>
</tr>
<tr>
<td><strong>THE NEJM, 19FEB2020</strong></td>
<td>SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients</td>
<td>Zou et al, China <a href="https://www.nejm.org/doi/10.1056/NEJM20200125">https://www.nejm.org/doi/10.1056/NEJM20200125</a></td>
<td>Virology</td>
<td>- The higher viral loads were detected soon after symptom onset. - Higher viral loads detected in the nose than in the throat. - Our analysis suggests that the viral nucleic acid shedding pattern of patients infected with SARS-CoV-2 resembles that of patients with influenza and appears different from that seen in patients infected with SARS-CoV. - The viral load that was detected in the asymptomatic patient was similar to that in the symptomatic patients, which suggests the transmission potential of asymptomatic or minimally symptomatic patients.</td>
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</table>
**Journal and date** | **Title** | **Authors and link** | **Field of expertise** | **Key facts**
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J Infect Dis. 18FEB2020 | A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period. | Yu et al., China [1] | Public Health/Epidemiology | Familial cluster of four patients in Shanghai. One was 88 years old man with moving difficulties and was only exposed to his asymptomatic family members who developed symptoms later. The epidemiological evidence has shown a potential transmission of the 2019-nCoV during the incubation period.

*Note:* The potential person-to-person transmission of 2019-nCoV during the incubation period is an important finding that has implications for public health strategies and control measures during the ongoing COVID-19 pandemic.

**The Lancet** 18FEB2020 | Tracking online heroisation and blame in epidemics | Atlani Dusault et al., France [2] | HSS/Politic | -> Gathering online data on local perceptions has the potential to help public authorities mount more robust responses and better targeted health communications.

- It is important to track the evolving dynamics of blame in real time, both to correct inaccurate information and to respond to online scapegoating.

- Trust is a crucial support to public health systems.

Public health authorities need to be aware of complex geographies of hope and blame while planning responses to the epidemic.

**Biochem Biophy Res Comm** 17 FEB 2020 | Structure analysis of the receptor binding domain of 2019-nCoV | Chen et al., China and USA [3] | Fundamental Research | Structural analysis of the receptor binding domain (RBD) → 72% identity with SARS CoV / Higher affinity with ACE 2.

- ACE2 is widely expressed with conserved primary structures throughout the animal kingdom (possible hosts?)

- Since ACE2 is predominately expressed in intestines, testis, and kidney, fecal-oral and other routes of transmission are also possible.

- Finally, antibodies and small molecular inhibitors that can block the interaction of ACE2 with RBD should be developed to combat the virus.

**J Clin Med** 17 FEB 2020 | Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data. | Linton et al., Japan [4] | Public Health/Epidemiology | Incubation period falls within the range of 2–14 days with 95% confidence and has a mean of around 5 days.

- The mean time from illness onset to hospital admission (for treatment and/or isolation) was estimated at 3–4 days without truncation and at 5–9 days.

**PNAS, 13FEB2020** | Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection | De Wit et al., USA [5] | Therapeutic | - 24 h prior to inoculation -> completely prevented MERS-CoV-induced clinical disease, strongly inhibited MERS-CoV replication in respiratory tissues, and prevented the formation of lung lesions.

- 12 h postinoculation -> clear clinical benefit, with a reduction in clinical signs, reduced virus replication in the lungs, and decreased presence and severity of lung lesions.

- Remdesivir may be considered for SARS-CoV-2

**The Lancet** 12 FEB 2020 | What are the risks of COVID-19 infection in pregnant women? | Qiao et al., China [6] | Clinic | The clinical characteristics reported in pregnant women with confirmed COVID-19 infection are similar to those reported for non-pregnant adults with confirmed COVID-19 infection in the general population and are indicative of a relatively optimistic clinical course and outcomes for COVID-19 infection compared with SARS-CoV-1 infection.

**The Lancet** 12FEB2020 | Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records | Chen et al., China [7] | Clinic | Evidence of intrauterine vertical transmission was assessed by testing for the presence of SARS-CoV-2 in amniotic fluid, cord blood, and neonatal throat swab samples.

- All samples tested negative

- None of the 9 patients developed severe COVID-19 pneumonia or died.


- These compounds have been used in human patients with a safety track record and shown to be effective against various ailments.

- They should be assessed in human patients suffering from the novel coronavirus disease.
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<tr>
<td>Euro Surveill 6FEB2020</td>
<td>Effectiveness of airport screening at detecting travellers infected with novel coronavirus (2019-nCoV).</td>
<td>Quilty et al., UK <a href="https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.5.200008">link</a></td>
<td>Public Health/Epidemiology</td>
<td>Estimation: 46% of infected travellers would not be detected, depending on incubation period, sensitivity of exit and entry screening, and proportion of asymptomatic cases.</td>
</tr>
<tr>
<td>The Lancet 03FEB2020</td>
<td>Baricitinib as potential treatment for 2019-nCoV acute respiratory disease</td>
<td>Richardson et al., UK <a href="https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736%2820%2930304-4.pdf">link</a></td>
<td>Therapeutic</td>
<td>The receptor that 2019-nCoV uses to infect lung cells might be ACE2, a cell-surface protein on cells in the kidney, blood vessels, heart, and, importantly, lung AT2 alveolar epithelial cells. One of the known regulators of endocytosis is the AP2-associated protein kinase 1 (AAK1). The plasma concentration of Baricitinib on therapeutic dosing (either as 2 mg or 4 mg once daily) is sufficient to inhibit AAK1, we suggest it could be trialled.</td>
</tr>
<tr>
<td>Emerge Microbes Infect 03FEB2020</td>
<td>Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody.</td>
<td>Tian et al., China <a href="https://www.biorxiv.org/content/10.1101/2020.01.28.923011v1">link</a></td>
<td>Fondamental Research</td>
<td>A SARS-CoV-specific human monoclonal antibody, CR3022, could bind potently with 2019-nCoV RBD.</td>
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