REACTing
research & action
targeting emerging infectious diseases

Inserm

COVID-19

Selection of peer-reviewed articles

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

UPDATE OF

07 JANUARY 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
CORD19 Publication Dashboard: https://france-science.com/en/homepage-english-2/

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

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

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

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Science 04JAN2021	Neutralizing antibody titres in SARS-CoV-2 infections	Lau E.H.Y., *et al.* USA gotopaper	Immunology	**Characterization of neutralizing antibody persistance in Infected patients.** Testing of 293 sera from an observational cohort of 195 reverse transcription polymerase chain reaction (RT-PCR) confirmed SARS-CoV-2 infections collected from 0 to 209 days after onset of symptoms. **Findings:** > Of 115 sera collected ≥61 days after onset of illness tested using plaque reduction neutralization (PRNT) assays, 99.1% remained seropositive for both 90% (PRNT90) and 50% (PRNT50) neutralization endpoints. > PRNT50 titres dropping to the detection limit of a titre of 1:10 for severe, mild and asymptomatic patients takes at least 372, 416 and 133 days > At day 90 after onset of symptoms (or initial RT-PCR detection in asymptomatic infections), it took 69, 87 and 31 days for PRNT50 antibody titres to decrease by half (T1/2) in severe, mild and asymptomatic infections, respectively. > Patients with severe disease had higher peak PRNT90 and PRNT50 antibody titres than patients with mild or asymptomatic infections. > Age did not appear to compromise antibody responses, even after accounting for severity. **SARS-CoV-2 infection elicits robust neutralizing antibody titres in most individuals.**
Nature Commun. 04JAN2021	Dose-dependent response to infection with SARS-CoV-2 in the ferret model and evidence of protective immunity	Ryan K.A., *et al.* UK gotopaper	Immunology / Preclinical model	> Understand if ferrets are a suitable species for a model of human SARS-CoV-2 infection > Dose titration study of SARS-CoV-2 in the ferret model > Animals are challenged intranasally with a range of titres of SARS-CoV-2 (5 × 102, 5 × 104 and 5 × 106 pfu) in 1 ml volume **Findings** > After a high (5×10^6 pfu) and medium (5×10^4 pfu) dose of virus is delivered, **intranasally**, viral RNA shedding in the **upper respiratory tract** (URT) is observed in 6/6 animals > Only 1/6 ferrets show similar signs after low dose (5 × 102 pfu) challenge > Ferrets re-challenged, after virus shedding ceased, are fully protected from acute lung pathology > The endpoints of URT viral RNA replication & distinct lung pathology are observed most consistently in the high dose group > This ferret model of SARS-CoV-2 infection presents a mild clinical disease

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Clin Infect Dis. 03JAN2021	Distinct disease severity between children and older adults with COVID-19: Impacts of ACE2 expression, distribution, and lung progenitor cells	Zhang Z., *et al.* China gotopaper	Epidemiology	> Examine the expression pattern of angiotensin-converting enzyme 2 (ACE2), the cell-entry receptor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the role of lung progenitor cells in children and older patients. > cohort of 299 patients with COVID-19 > Expression and distribution of ACE2 and lung progenitor cells examinations: combination of public single-cell RNA-seq datasets, lung biopsies, and ex vivo infection of lung tissues with SARS-CoV-2 pseudovirus in children and older adults **Findings** **>** Compared to children, **ACE2 positive cells are generally decreased in older adults** and **mainly presented in the lower pulmonary tract** (alveolar region) and rarely in airway regions in the older adults ($p < 0.01$). > The lung progenitor cells are also decreased. These risk factors may impact disease severity and recovery from pneumonia caused by SARS-Cov-2 infection in older patients.
NEJM 30DEC2020	Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine	Baden L.R., *et al.* USA gotopaper	Vaccine	**Phase 3 randomized, observer-blinded, placebo-controlled trial conducted at 99 centers across the United States.** **> Population:** Persons at high risk for SARS-CoV-2 infection or its complications **> Intervention:** 2 adminsitration of vaccine (100 µg each) or placebo 28 days apart. 30,420 volunteers enrolled; 15,210 participants in each group **> Primary end point:** 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. **Findings** > More than 96% of participants received both injection > 2.2% had evidence (serologic, virologic, or both) of SARS-CoV-2 infection at baseline. > 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); > Vaccine efficacy was 94.1% (95% CI, 89.3 to 96.8%; P<0.001). > 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. > Severe Covid-19 occurred in 30 participants, with one fatality; all 30 were in the placebo group. > Moderate, transient reactogenicity after vaccination occurred more frequently in the mRNA-1273 group. > Serious adverse events were rare, and the incidence was similar in the two groups. **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.

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Science 23DEC2020	Afucosylated IgG characterizes enveloped viral responses and correlates with COVID-19 severity	Larsen M.D., *et al.* Netherlands gotopaper	Immunology	Analysis of afucosylated IgGs 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:** >**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. >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.
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.**
Cell Host Microbe 23DEC2020	Intranasal vaccination with a lentiviral vector protects against SARS-CoV-2 in preclinical animal models	Ku M.W., *et al.* France gotopaper	Vaccine	**Vaccine candidate against (COVID-19) based on a lentiviral vec-tor (LV) eliciting neutralizing antibodies against the Spike glycoprotein of SARS-CoV-2.** **Findings:** **>** Systemic vaccination by this vector in trangenic 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. > Eliciting an immune response in the respiratory tract through an intranasal boost results in a >3 log10 decrease in the lung viral loads and reduces local inflammation. > 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.

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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.**
JAMA Netw. Open 22DEC2020	Assessment of Maternal and Neonatal SARS-CoV-2 Viral Load, Transplacental Antibody Transfer, and Placental Pathology in Pregnancies During the COVID-19 Pandemic	Edlow A.G., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim**: to quantify SARS-CoV-2 viral load in maternal and neonatal biofluids, transplacental passage of anti–SARS-CoV-2 antibody, and incidence of fetoplacental 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.
Science Immunol. 22DEC2020	Rapid generation of durable B cell memory to SARS-CoV-2 spike and nucleocapsid proteins in COVID-19 and convalescence	Hartley G.E., *et al.* Australia gotopaper	Immunology	Generation of fluorescently-labeled tetramers of the spike receptor binding domain (RBD) and nucleocapsid protein (NCP) to determine the **longevity and immunophenotype of SARS-CoV-2-specific memory B (Bmem) cells** in COVID-19 patients. > 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 IgG1+ 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.
Lancet Microbe 21DEC2020	Multiplex assays for the identification of serological signatures of SARS-CoV-2 infection: an antibody-based diagnostic and machine learning study	Rosado J., *et al.* France gotopaper	Diagnostics	Aim: to develop more accurate serological diagnostics exploiting the complexity of the antibody response targeting SARS-CoV-2 antigens. 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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Nature 21DEC2020	Underdetection of COVID-19 cases in France threatens epidemic control	Pullano G., *et al.* France gotopaper	Public Health / Epidemiology	**Aim**: 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. > Around 90,000 incident symptomatic infections, corresponding to 9 out 10 cases, **were not ascertained by the surveillance system** in the first 7 weeks following lockdown (May 11 - June 28 2020), although the test positivity rate did not exceed WHO recommendations (5%). > The median detection rate increased from **7% to 38% over time**, with large regional variations, owing to a strengthening of the system as well as a decrease of epidemic activity. > According to participatory surveillance data, **only 31%** of individuals with COVID-19-like symptoms consulted a doctor in the study period. **Encouraging awareness and same-day healthcare-seeking behaviour** in suspect cases is critical to improve detection. > 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. Substantially more aggressive, targeted, and efficient testing with easier access is required to act as a pandemic-fighting tool.
Clin Infect Dis. 18DEC2020	Impact of Sex and Metabolic Comorbidities on COVID-19 Mortality Risk Across Age Groups: 66,646 Inpatients Across 613 U.S. Hospitals	Goodman K.E., *et al.* USA gotopaper	Public Health / Epidemiology	**Association between common patient characteristics and mortality across age-groups among COVID-19 inpatients.** Retrospective cohort study of patients discharged from hospitals (April – June 2020). **RESULTS** 66,646 (6.5%) admissions with COVID-19, 613 U.S. hospitals: > 12,388 (18.6%) died in-hospital. > male sex was independently associated with 30% higher mortality risk (aRR, 1.30, 95% CI: 1.26 – 1.34) > Diabetes without chronic complications was not a risk factor at any age (aRR 1.01, 95% CI: 0.96 – 1.06) > Hypertension without chronic complications was only a risk factor in 20-39 year-olds (aRR, 1.68, 95% CI: 1.17 – 2.40) > Diabetes with chronic complications, hypertension with chronic complications, and obesity were risk factors in most age-groups, with highest relative risks among 20-39 year-olds (respective aRRs 1.79, 2.33, 1.92; p-values ≤ 0.002). 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.
Lancet Respir Med. 17DEC2020	Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study	Piroth L.*et al.* France gotopaper	Public Health / Epidemiology	**Aim**: comparing influenza and COVID-19 epidemiology. > 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). > 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. Patients with influenza more frequently had heart failure, chronic respiratory disease, cirrhosis, and deficiency anaemia. > **Patients admitted to hospital** 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. > **In-hospital mortality** was higher in patients with COVID-19 than in patients with influenza (16·9% vs 5·8%), with a relative risk of death of 2·9 and an age-standardised mortality ratio of 2·82. > Of the patients hospitalised, the **proportion of paediatric patients** (<18 yrs) was smaller for COVID-19 than for influenza (1·4% vs 19·5%), but a larger proportion of patients <5 yrs needed intensive care support for COVID-19 than for influenza (2·3% vs 0·9%). > In **adolescents** (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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
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 **favoured 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 (stratificatins 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 gotopaper	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** Single-blinded phase 1/2 randomized controlled trial of healthy adults aged 18–55 years, 56 d following prime vaccination > homologous full-dose (SD/SD D56; n = 20) > or half-dose (SD/LD D56; n = 32). **RESULTS** > a booster dose of ChAdOx1 nCoV-19 is safe and better tolerated than priming doses. > anti-spike neutralizing antibody titers, as well as Fc-mediated functional antibody responses, including antibody-dependent neutrophil/monocyte phagocytosis, complement activation and natural killer cell activation, are substantially enhanced by a booster dose of vaccine. > a booster dose of vaccine induced stronger antibody responses than a dose-sparing half-dose boost, although the magnitude of T cell responses did not increase with either boost dose.
NEJM 17DEC2020	REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19	Weinreich D.M., *et al.* USA gotopaper	Therapeutics	**Interim study results: effects of high viral loads with complications and death from coronavirus disease 2019 (Covid-19)-REGN-COV2 effects on outpatients** **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 log10 copies per milliliter (95% confidence interval [CI], −1.02 to −0.11) among patients who were serum antibody–negative at baseline > −0.41 log10 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 Rt (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 Rt 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 Rt to below 1 without a stay-at-home order by issuing other NPIs.
Lancet Child Adolesc. Health 15DEC2020	**Neuroimaging manifestations in children with SARS-CoV-2 infection: a multinational, multicentre collaborative study**	Lindan C.E., *et al.* UK/USA gotopaper	Clinics	**Neuroimaging manifestations of COVID-19 in the paediatric population**. 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.
Cell 15DEC2020	**COVID-19 neutralizing antibodies predict disease severity and survival**	Garcia-Beltran W.F., *et al.* USA gotopaper	Clinics	**Relationship between severity and the humoral immune response** is poorly understood. > 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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 10DEC2020	**Efficacy of Tocilizumab in Patients Hospitalized with Covid-19**	Stone J.H., *et al.* USA gotopaper	Therapeutics	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. **RESULTS** > 243 patients; 58% were men and 42% women, median age was 59.8 yrs (21.7-85.4), 45% were Hispanic or Latino. > **The hazard ratio for intubation or death** in the tocilizumab group as compared with the placebo group was **0.83**, and the **hazard ratio for disease worsening** was **1.11**. > At 14 days, **18.0%** of the patients in the tocilizumab group and **14.9%** of the patients in the placebo group had had worsening of disease. > Median time to discontinuation of supplemental oxygen was **5.0 days** in the tocilizumab group and **4.9 days** in the placebo group. At 14 days, **24.6%** of the patients in the tocilizumab group and **21.2%** of the patients in the placebo group were still receiving supplemental oxygen. > Patients who received tocilizumab had **fewer serious infections** than patients who received placebo. **Tocilizumab was not effective for preventing intubation or death in moderately ill hospitalized patients with Covid-19**. Some benefit or harm cannot be ruled out, as the confidence intervals for efficacy comparisons were wide.
JAMA Netw Open 10DEC2020	**Risk Factors Associated With In-Hospital Mortality in a US National Sample of Patients With COVID-19**	Rosenthal N., *et al.* USA gotopaper	Public Health / Epidemiology	**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. > 64 781 patients with COVID-19 (29 479 [45.5%] outpatients; 35 302 [54.5%] inpatients) analysed. > 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. > **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%). > **Older age** was the risk factor most strongly associated with death (eg, age ≥80 years vs 18-34 years: odds ratio [OR], 16.20). > 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**. > Patients with both azithromycin and hydroxychloroquine had **increased odds of death** (OR, 1.21), compared with patients with did not received 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.

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NEJM 10DEC2020	**Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine**	Polack F.P., *et al.* USA gotopaper	Vaccines	**BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 fulllength spike protein. Efficacy et ssafetu results are presented.** **METHODS:** > Multinational, randomized, placebo-controlled, observer-blinded, pivotal efficacy trial, we randomly assigned persons ≥16 yrs > 43,548 participants randomized, 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo > Two doses of 30 µg/dose de BNT162b2, 21 days apart, or placebo Primary end points: efficacy of the vaccine against laboratory-confirmed Covid-19 and safety. **RESULTS** > 8 cases of Covid-19 with onset at least 7 days after the second dose among participants assigned to receive BNT162b2 and 162 cases among those assigned to placebo; - BNT162b2 was **95% effective** in preventing Covid-19 (95% credible interval, 90.3 to 97.6). - Similar vaccine efficacy (generally 90 to 100%) observed **across subgroups** defined by age, sex, race, ethnicity, baseline body-mass index, and the presence of coexisting conditions. > Among 10 cases of severe Covid-19 with onset after the first dose, 9 occurred in placebo recipients and 1 in a BNT162b2 recipient. > Safety profile of BNT162b2: short-term, mild-to-moderate pain at the injection site, fatigue, and headache. > Incidence of serious adverse events: low and was similar in the vaccine and placebo groups. **CONCLUSIONS** A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines.
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 vs71 [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%** (95·8% 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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Lancet Infect Dis. 08DEC2020	**SARS-CoV-2 infection and transmission in educational settings: a prospective, cross-sectional analysis of infection clusters and outbreaks in England**	Ismail S.A., *et al.* UK gotopaper	Public Health / Epidemiology	**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. > Early years settings (<5-year-olds) > Primary schools (5–11-yr-olds; only yrs 1 and 6 allowed to return), > Secondary schools (11–18-year-olds; only years 10 and 12) > Mixed-age settings (spanning a combination of the above). **FINDINGS:** > 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) > Overall median daily attendance: 928 000 students (630 000–1 230 000) > 113 single cases of SARS-CoV-2 infection, nine coprimary cases, and 55 outbreaks > 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) > 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]) > 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.
Lancet Psychiatry 08DEC2020	**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**	Pan K.Y., *et al.* Netherlands gotopaper	Public Health / Epidemiology	**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. > The number and chronicity of disorders showed a **positive graded dose–response relation**, with greater perceived impact on mental health, fear, and poorer coping. > 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. > 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 prepandemic levels.
Science 08DEC2020	**Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic**	Buss L.F., *et al.* Brazil gotopaper	Public Health / Epidemiology	The SARS-CoV-2 attack rate in the **Brazilian Amazon** is an estimate of the final size of a largely **unmitigated epidemic**. > By June, 1 month after the epidemic peak in Manaus, capital of Amazonas state, **44%** of the population had detectable IgG Abs.. > Correcting for cases without a detectable antibody response and antibody waning, we **estimate a 66% attack rate** in June, **rising to 76%** in October. > 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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Ann Intern Med. 08DEC2020	**Dynamics and Correlation Among Viral Positivity, Seroconversion, and Disease Severity in COVID-19 - A Retrospective Study**	Fu Y., *et al.* China gotopaper	Immunology	**Aim**: to describe patterns of SARS-CoV-2 PCR positivity and evaluate their correlations with seroconversion and disease severity. Retrospective study on 3192 adult patients with COVID-19. > 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 r**emained 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	**Humoral responses to SARS-CoV-2** - frequency of antibody-secreting cells - presence of SARS-CoV-2-specific neutralizing antibodies in the serum, saliva and BAL - 159 patients COVID-19 + tested **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	**Characterization of IgA responses in a cohort of 149 convalescent individuals** - 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? **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**.

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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 PRVN80): 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.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 02DEC2020	**Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results**	WHO Soidarity Trial Consortium gotopaper	Therapeutics	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** > In total, 1253 deaths were reported (median day of death, day 8). > The Kaplan–Meier 28-day mortality was 11.8% (39.0% if the patient was already receiving ventilation at randomization and 9.5% otherwise). > 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). > **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.
Nature 01DEC2020	**A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate**	Sanchez-Felipe L., *et al.* Belgium gotopaper	Vaccines	**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. > Vaccine candidate YF-S0 has outstanding safety profile and induces **high levels of SARS-CoV-2 neutralizing antibodies** in hamsters, mice and cynomolgus macaques. > Concomitantly a protective **immunity against YFV**. > Humoral immunity is complemented by a **favourable Th1 cell-mediated immune response** as profiled in mice. > In a stringent hamster model and non-human primates, **YF-S0 prevents infection** with SARS-CoV-2. > 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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Neurosci. 30NOV2020	**Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19**	Meinhardt J., *et al.* Germany gotopaper	Virology	Given the neurological symptoms observed in a large majority of individuals with COVID-19, SARS-CoV-2 penetrance of the CNS is likely. > 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.
Clin Infect Dis. 30N0V2020	**Long COVID in the Faroe Islands - a longitudinal study among non-hospitalized patients**	Petersen M.S., *et al.* Faeroe Islands gotopaper	Public Health / Epidemiology	**Methods** > 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.**
BMJ 27NOV2020	**Infection fatality risk for SARS-CoV-2 in community dwelling population of Spain: nationwide seroepidemiological study**	Pastor-Barriuso R., *et al.* Spain gotopaper	Public Health / Epidemiology	**Aim:** Nationwide seroepidemiological study in Spain, to estimate the infection fatality risk for SARS-CoV-2, based on deaths with confirmed COVID-19 and excess deaths from all causes (First Wave of COVID-19). **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.**

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Clin Infect Dis. 25NOV2020	**Estimated incidence of COVID-19 illness and hospitalization — United States, February–September, 2020**	Reese H., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim**: Estimate the cumulative incidence SARS-CoV-2 infections, symptomatic illnesses, and hospitalizations in the USA (February–September, 2020) **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.
BMC Medicine 25NOV2020	**Evidence for treatment with estradiol for women with SARS-CoV-2 infection**	Seeland U., *et al.* Germany gotopaper	Public Health / Epidemiology	**Aim:** A **s**urvey of the effects of systemic hormone administration in women. Study on the incidence and outcome of COVID-19 infections by considering an age- and sex-disaggregated data analysis. **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 17ß-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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NEJM 24NOV2020	**A Cluster-Randomized Trial of Hydroxychloroquine for Prevention of Covid-19**	Mitjà O., *et al.* Spain gotopaper	Therapeutics	Study on Hydroxychloroquine (HCQ) effect as a postexposure therapy to prevent COVID19 **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 symptoms - 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.**
NEJM 24NOV2020	**A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia**	Simonovich V.A., *et al.* Argentina gotopaper	Therapeutics	Randomized, controlled clinical trial on hospitalized adult patients with severe Covid-19 pneumonia, assigned in a 2:1 ratio to receive convalescent plasma or placebo. 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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Cell 23NOV2020	**Functional SARS-CoV-2-specific immune memory persists after mild COVID-19**	Rodda L.B., *et al.* USA gotopaper	Immunology	Longitudinal assessment of individuals recovered from mild COVID-19 to study SARS-CoV-2-specific immunological memory. > 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.
Clin Infect Dis. 21NOV2020	**Comprehensive health assessment three months after recovery from acute COVID-19**	Van den Borst B., *et al.* The Netherlands gotopaper	Public Health / Epidemiology - Long COVID	**Aim**: to study the long-term health sequelae of COVID-19 (Admitted patients or patients with mild disease and >6 weeks of symptoms). > 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**.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Clin Infect Dis. 20NOV2020	**Risk Factors and Outcomes of Hospitalized Patients with Severe COVID-19 and Secondary Bloodstream Infections: A Multicenter, Case-Control Study**	Bhatt P.J., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim**: to report on microbiology, risk factors and outcomes of secondary bloodstream infections (sBSI) in patients with severe COVID-19. > Of 375 hospitalized patients included, **128 had a sBSIs** 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	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.**
Eclinical Medicine 19NOV2020	**Multi-center nationwide comparison of seven serology assays reveals a SARS-CoV-2 non-responding seronegative subpopulation**	Oved K., *et al.* Israel gotopaper	Diagnosis	Multi-center clinical and analytical validation of 7 serology assays to determine their utility and limitations for SARS-CoV-2 diagnosis. Methods: > Serology assays from Roche, Abbott, Diasorin, BioMerieux, Beckman-Coulter, Siemens, and Mt.-Sinai ELISA. >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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Lancet Microbe 19NOV2020	**SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis**	Cevik M., *et al.* UK gotopaper	Public Health / Epidemiology	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: > **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. > **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. > Pooled mean SARS-CoV-2 shedding duration is **positively associated with age** > No study detected live virus **beyond day 9 of illness**, despite persistently high viral loads. > SARS-CoV-2 viral load in the upper respiratory tract peaks in the **first week of illness**
The Lancet 18NOV2020	**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**	Ramasamy M., *et al.* UK gotopaper	Vaccines	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** > 560 participants enrolled: 160 aged 18–55 yrs; 160 aged 56–69 yrs; 240 aged ≥70 years. > **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 ≥56 years) than younger adults. > **13 serious adverse events** occurred during the study period, none of which were considered to be related to either study vaccine. > 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. > **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). > **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.**

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Lancet Infect Dis. 17NOV2020	**Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial**	Zhang Y., *et al.* China gotopaper	Vaccines	CoronaVac phase 1/2 clinical trial (inactivated vaccine candidate against COVID-19 from Cansino using Alu as adjuvant) NCT04352608. - 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 ug 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.**
J. Antimicrob. Chemother. 13NOV2020	**An observational cohort study of bacterial co-infection and implications for empirical antibiotic therapy in patients presenting with COVID-19 to hospitals in North West London**	Wang L., *et al.* UK gotopaper	Public Health / Epidemiology	**Aim**: to describe prevalence and nature of bacterial co-infections in COVID-19 patients within 48h of hospital admission, assess the appropriateness of empirical antibiotic treatment they received. > 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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Science Adv. 13NOV2020	**JAK inhibition reduces SARS-CoV-2 liver infectivity and modulates inflammatory responses to reduce morbidity and mortality**	Stebbing J., *et al.* International gotopaper	Therapeutics	**Baricitinib: anti-viral and anti-cytokine drug.** > 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 **baricinitib 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.
Lancet Respir Med. 12NOV2020	**Safety and efficacy of inhaled nebulised interferon beta-1a (SNG001) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial**	Monk P.D., *et al.* UK gotopaper	Therapeutics	**Efficacy and safety of inhaled nebulised interferon beta-1a (SNG001) for hospitalized patients with COVID-19.** **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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Clin Infect Dis. 12NOV2020	**Susceptibility to Sars-COV-2 Infection Among Children And Adults: A Seroprevalence Study of Family Households in the Barcelona Metropolitan Region, Spain**	Brotons P., *et al.* Spain gotopaper	Public Health / Epidemiology	Cross-sectional seroprevalence study on families with at least 1 first-reported adult positive to SARS-CoV-2 PCR and at least 1 child <15 years living in the same household under strict confinement. > **381 family** households including 381 first-reported PCR-positive adult cases and **1,084 contacts (672 children, 412 adults)** enrolled > Infection seroprevalence rates were **17.6% (118/672) in children and 18.7% (77/335) in adult** contacts > 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. > 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 >6 weeks post-infection, especially in mild disease cases.
Blood 12NOV2020	**Convalescent plasma therapy for B-cell–depleted patients with protracted COVID-19**	Huseo T., *et al.* France gotopaper	Therapeutics	**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) > Within 48 hours of transfusion, all but 1 patient experienced an improvement of clinical symptoms. > The inflammatory syndrome abated within a week. > Only 1 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 all 9 evaluated patients. > 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.**
Ann Intern Med. 11NOV2020	**Sixty-Day Outcomes Among Patients Hospitalized With COVID-19**	Chopra V., *et al.* USA gotopaper	Public Health / Epidemiology	**Aim**: to describe 60-day post-discharge clinical, financial, and mental health outcomes of patients with COVID-19. > 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. > By 60 days after discharge, 84 more patients (6.7% of hospital survivors and 10.4% of ICU survivors) had died. O**verall mortality** rate for the cohort was **29.2%**, **63.5% for the ICU** (405 patients). > Within 60 days of discharge, **189 patients** (15.1% of hospital survivors) were **rehospitalized**. > 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. > **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. > 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. > Nearly half of all patients (238/488) reported being **emotionally affected** by their health, and 28 sought mental health care. >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.

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BMJ 11NOV2020	**Accuracy of UK Rapid Test Consortium (UK-RTC) "AbC-19 Rapid Test" for detection of previous SARS-CoV-2 infection in key workers: test accuracy study**	Mulchandani R., et al. UK gotopaper	Diagnostics	**Aim**: to assess the accuracy of the AbC-19 Rapid Test lateral flow immunoassay for detection of past SARS-CoV-2 infection. 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.**
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.

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Science 10NOV2020	**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 10NOV2020	**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 a**ntibodies 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**.
Science Adv. 06NOV2020	**Differential effects of intervention timing on COVID-19 spread in the United States**	Pei S., *et al.* USA gotopaper	Public Health / Epidemiology	Observations of reported COVID-19 infections and deaths, human mobility data, and a metapopulation transmission model were used to quantify changes in disease transmission rates in US (March 15 - May 3, 2020). > **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. 05NOV2020	**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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NEJM 05NOV2020	**Remdesivir for the Treatment of Covid-19 — Final Report**	Beigel J.H., *et al.* USA/International gotopaper	Therapeutics	Double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults hospitalized with Covid-19 and with evidence of lower respiratory tract infection. 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 gotopaper	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 gotopaper	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.
Cell 03NOV2020	**Quick COVID-19 Healers Sustain Anti-SARS-CoV-2 Antibody Production**	Chen Y., *et al.* USA gotopaper	Immunology	**Study on longitudinal antibody responses to SARS-CoV-2 in 92 subjects after symptomatic COVID-19**. > 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 Ifect 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 gotopaper	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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Cell 03NOV2020	**Compromised humoral functional evolution tracks with SARS-CoV-2 mortality**	Zohar T., *et al.* USA gotopaper	Immunology	**Analysis of the evolution of the humoral response in 193 hospitalized individuals ranging from moderate-to severe**. > Robust IgM and IgA responses both in survivors and non-survivors with severe disease > However, non-survivors showed attenuated IgG responses and compromised Fcγ-receptor binding and Fc-effector activity --> deficient humoral development rather than disease-enhancing humoral immunity > Individuals with moderate disease exhibited delayed responses that ultimately matured. These data highlight distinct humoral trajectories associated with resolution of SARS-CoV-2 infection and the need for early functional humoral immunity.
Science Transl Med. 02NOV2020	**Prothrombotic autoantibodies in serum from patients hospitalized with COVID-19**	Zuo Y., *et al.* USA gotopaper	Immunology	**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. > **aPS/PT IgG** were detected in 24% of samples, **anticardiolipin IgM** in 23% of samples, and **aPS/PT IgM** in 18% of samples. > **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). > 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. > 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. Half of COVID-19 hospitalised patients seem to become at least transiently positive for aPL antibodies, potentially pathogenic.
Lancet Infect Dis. 02NOV2020	**SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study**	NG O.T., *et al.* Singapore gotopaper	Public Health / Epidemiology	Retrospective cohort study involving all close contacts of confirmed COVID-19 cases in Singapore (Jan 23 and April 3, 2020). **>** 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. **>** 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. **>** 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**. **>** Sharing a bedroom (odd ratio 5·38) and being spoken to by an index case for >30 min (7·86) were associated with SARS-CoV-2 transmission among **household contacts**. **> Among non-household contacts**, exposure to >1 case (OR 3·92), being spoken to by an index case for >30 min (2·67), and sharing a vehicle with an index case (3·07) were associated with SARS-CoV-2 transmission. **>** Among both household and non-household contacts, indirect contact, meal sharing, and lavatory co-usage were not independently associated with SARS-CoV-2 transmission.

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Nature 02NOV2020	**Age-specific mortality and immunity patterns of SARS-CoV-2**	O'Driscoll M., *et al.* France/UK gotopaper	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 ys) 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 gotopaper	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 of 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 **shrank 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 gotopaper	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 **detectible neutralizing antibody responses**. These titers remain relatively stable for several months after infection.

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NEJM 28OCT2020	**SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19**	Chen P., *et al.* USA gotopaper	Therapeutics	Ongoing phase 2 trial involving outpatients with recently diagnosed mild or moderate Covid-19. - 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.
Nature 26OCT2020	**Spike mutation D614G alters SARS-CoV-2 fitness**	Plante J.A., *et al.* USA gotopaper	Virology	**AIM**: to engineer the D614G mutation, that became dominant in SARS-CoV-2 during the pandemics, in the USA-WA1/2020 strain and characterize its effect. > 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.
BMJ 22OCT2020	**Convalescent plasma in the management of moderate covid-19 in adults in India: open label phase II multicentre randomised controlled trial (PLACID Trial)**	Argarwal A., *et al.* India gotopaper	Therapeutics	Open label, parallel arm, phase II, multicentre, randomised controlled trial (39 public and private hospitals across India). >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.

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JCM 22OCT2020	**Comparison of upper respiratory viral load distributions in asymptomatic and symptomatic children diagnosed with SARS-CoV-2 infection in pediatric hospital testing programs**	Kociolek L.K., *et al.* USA gotopaper	Public Health / Epidemiology	**AIM:** 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. **METHODS:** 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.** **RESULTS:** > **Ct values were significantly higher in asymptomatic children of all ages** compared to symptomatic children matched by age bracket and test collection date range. > **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. > 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**. > 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.
Lancet Infect Dis. 22OCT2020	**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**	Li Y., *et al.* UK gotopaper	Public Health / Epidemiology	**Modelling study,** 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. **AIM:** 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). **METHODS:** 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, …). **RESULTS** > Effect of introducing and lifting NPIs was **not immediate** and that the time required to reach certain levels of effect differed by NPI. > **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). > 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. > **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

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NEJM 21OCT2020	Efficacy of Tocilizumab in Patients Hospitalized with Covid-19	Stone J.H., *et al.* USA gotopaper	Therapeutics	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. Primary outcome: intubation or death. **>** 243 patients; 58% men, 42% women. The median age: 59.8 years, 45% of the patients were Hispanic or Latino. **>** 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. **>** 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. **>** Patients who received TCZ had **fewer serious infections** than patients who received placebo. **TCZ was not effective for preventing intubation or death** 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.
JAMA Intern Med. 20OCT2020	Effect of Tocilizumab vs Usual Care in Adults Hospitalized With COVID-19 and Moderate or Severe PneumoniaA Randomized Clinical Trial	Hermine O., *et al.* France gotopaper	Therapeutics	**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). Primary outcomes: scores >5 on the WHO 10-point Clinical Progression Scale (WHO-CPS) on D4 and survival without need of ventilation at D14. Secondary outcomes: clinical status at D7 and D14, overall survival, time to discharge, time to oxygen supply independency, biological factors, adverse events. **> 130 patients** analysed - 63 in TCZ group, 67 in UC group. 32% were women, median age was 64 years. **>** In the **TCZ group, 12 patients had a WHO-CPS score >5 at D4 vs 19 in the UC group**, with a posterior probability of negative absolute risk difference of 89.0% not achieving the 95% predefined efficacy threshold. **>** At day 14, **12% fewer patients needed noninvasive ventilation (NIV) or mechanical ventilation (MV) or died in the TCZ group** than in the UC group (24% vs 36%) with a posterior probability of haward ratio (HR) less than 1 of 95.0%, achieving the predefined efficacy threshold. The HR for MV or death was 0.58. **>** 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. In this clinical trial, **TCZ did not reduce WHO-CPS scores <5 at D4 but might have reduced the risk of NIV, MV, or death by D14**. No difference on D28 mortality was found.

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JAMA Intern Med. 20OCT2020	Effect of Tocilizumab vs Standard Care on Clinical Worsening in Patients Hospitalized With COVID-19 PneumoniaA Randomized Clinical Trial	Salvarani C., *et al.* Italy gotopaper	Therapeutics	**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). **>** 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). **>** 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. **>** 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. **>** 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.
JAMA Intern Med. 20OCT2020	Association Between Early Treatment With Tocilizumab and Mortality Among Critically Ill Patients With COVID-19	Gupta S., *et al.* USA gotopaper	Therapeutics	**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. **>** 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 aterial pO2 to fraction of inspired oxygen of <200 mm Hg) than the control group. **>** 1544 patients **(39.3%) died**, including 125 **(28.9%) treated with TCZ** and 1419 **(40.6%) of control group**. **>** 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.
Clin Infect Dis. 20OCT2020	Clinical Characteristics and Outcomes of COVID-19 Patients Receiving Compassionate Use Leronlimab	Yang B., *et al.* USA gotopaper	Therapeutics	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 > 700mg leronlimab subcutaneously, repeated after 7 days in 17/23 patients still hospitalized. > 18/23 received other experimental treatments (convalescent plasma, hydroxychloroquine, steroids, and/or tocilizumab). > 5/23 received leronlimab after blinded placebo-controlled trials of remdesivir, sarilumab, selinexor, or tocilizumab. **RESULTS** **>** Mean age: 69.5±14.9 years. 20/23 had significant co-morbidities. 22/23 receiving supplemental oxygen **>** Blood showed markedly elevated inflammatory markers and elevated neutrophil:lymphocyte ratio. **>** 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** > Leronlimab appeared **safe and well tolerated**. **High recovery rate** suggesting benefit.

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Clin Infect Dis. 17OCT2020	Hydroxychloroquine as pre-exposure prophylaxis for COVID-19 in healthcare workers: a randomized trial	Rajasingham R., *et al.* USA gotopaper	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 hydroxychloroquin**e (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.
THE LANCET Infectious diseases 15OCT2020	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 gotopaper	Vaccines	> **Safety and immunogenicity** in human of an **inactivated** SARS-CoV-2 vaccine candidate, **BBIBP-CorV** (Sinopharm and IBP Beijing). **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 170·87 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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NEJM 15OCT2020	Evaluation of the mRNA-1273 Vaccine against SARS-CoV-2 in Nonhuman Primates	Corbett K.S., *et al.* USA gotopaper	Vaccines	> Effect of mRNA 1273 on viral replication in upper and lower airways (nonhuman primates model, NHP). **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 trimerized 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. 12OCT2020	**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. 12OCT2020	**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. 12OCT2020	**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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Clin Infect Dis. 10OCT2020	**Convalescent plasma for patients with severe COVID-19: a matched cohort study**	Rogers R., *et al.* USA gotopaper	Therapeutics	**METHODS**: Impact of convalescent plasma (CP) on: > 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 sequalae** 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.
Lancet Respir Med. 08OCT2020	**Clinical impact of molecular point-of-care testing for suspected COVID-19 in hospital (COV-19POC): a prospective, interventional, non-randomised, controlled study**	Brendish N.J., *et al.* UK gotopaper	Public Health / Epidemiology	Interventional, non-randomised, controlled study of molecular point-of-care testing for Covid-19. Nose and throat swab samples were tested with the **QIAstat-Dx Respiratory SARS-CoV-2 Panel** (March 20 – April 29, 2020). - 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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NEJM 08OCT2020	**Remdesivir for the Treatment of Covid-19 — Final Report**	Beigel J.H., *et al.*, ACTT-1 Study Group International gotopaper	Therapeutics	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. - 541 patients assigned to remdesivir and 521 to placebo. - Patients who received remdesivir had a **median recovery time of 10 days as compared with 15 days** among those who received placebo. - 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 day 15 and 11.4% with remdesivir and 15.2% with placebo by day 29. - **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%). **Remdesivir was superior to placebo in shortening the time to recovery in this cohort.**
NEJM 08OCT2020	**Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19**	The RECOVERY Collaborative Group gotopaper	Therapeutics	**METHODS** RCT, open-label platform trial comparing a range of possible treatments with usual care in patients hospitalized with Covid-19. > 1561 patients received hydroxychloroquine > 3155 to receive usual care. Primary outcome: 28-day mortality. **RESULTS** > **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. > 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%). > 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%). > **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. **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.

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Nature Commun. 06OCT2020	**Deep phenotyping of 34,128 adult patients hospitalised with COVID-19 in an international network study**	Burn E., *et al.* International gotopaper	Public Health / Epidemiology	AIM: to describe the characteristics of adults hospitalised with COVID-19 and compare them with influenza patients. - 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.
Lancet Neurol. 05OCT2020	**Neuropathology of patients with COVID-19 in Germany: a post-mortem case series**	Matschke J., *et al.* Germany gotopaper	Public Health / Epidemiology	Post-mortem investigation of brain tissue of 43 Covid-19 patients (aged 51-94) for glial responses, inflammatory changes, and presence of SARS-CoV-2 in the CNS. - **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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BMJ Open Respir Res. 05OCT2020	**Association of smoking status with outcomes in hospitalised patients with COVID-19**	Adrish M., *et al.* USA gotopaper	Public Health / Epidemiology	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.
Clin Infect Dis. 03OCT2020	**Survival of SARS-CoV-2 and influenza virus on the human skin: Importance of hand hygiene in COVID-19**	Hirose R., *et al.* Japan gotopaper	Virology	The stability of the severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) on human skin remains unknown. > 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. **Results**: > SARS-CoV-2 and IAV were inactivated more rapidly on skin surfaces than on other surfaces (stainless steel/glass/plastic); > 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)]. > Both SARS-CoV-2 and IAV in the mucus/medium on human skin were completely inactivated within 15 s by ethanol treatment. **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.

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Clin Infect Dis. 03OCT2020	**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**	Jespersen S., *et al.* Denmark gotopaper	Public Health / Epidemiology	Seroprevalence survey on SARS-CoV-2 among Danish healthcare workers (HCW) to identify high-risk groups. **Methods** 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 **Results** 25,950 participants > 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. > Overall seroprevalence: 3.4% (CI: 2.5%-3.8%). > Higher seroprevalence in the western part of the region than in the eastern part (11.9% vs 1.2%). > 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%). **Conclusions** 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.
Blood 01OCT2020	**Waning of SARS-CoV-2 RBD antibodies in longitudinal convalescent plasma samples within four months after symptom onset**	Perreault J., *et al.* Canada gotopaper	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 > One of the main hypotheses to explain the potential clinical benefits of CCP is the presence of SARS-CoV-2 neutralizing antibodies (nAb) > Analysis of SARS-CoV-2 spike RBD antibodies using ELISA represents a valuable tool for the initial characterization of CCP. **Methods**: > Potential donors were recruited after at least 14 days of resolution of COVID-19 symptoms (Hema-Quebec; CONCOR-1 study) > presence of antibodies against SARS-CoV-2 RBD was determined using a semi-quantitative ELISA **Results**: > 262 patients; **6.9% seronegative** at recruitment, **up to 15%** when considering only donors who had waited >11-12 weeks after symptom onset before donating > level of **anti-RBD antibodies at the first donation varies greatly** between donors. > 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) > anti-RBD response is **relatively stable during the first 10 weeks** after disease onset

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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 reactiogenicity 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 anti–S-2P** specific IgGs 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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The Lancet 25SEP2020	**Prevalence of SARS-CoV-2 antibodies in a large nationwide sample of patients on dialysis in the USA: a cross-sectional study**	Anand S., *et al.* USA gotopaper	Public Health / Epidemiology	Cross-sectional study on plasma of 28 503 randomly selected adult patients receiving dialysis in July 2020, to determine SARS-CoV-2 seroprevalence. - The sampled population had similar age, sex, and race and ethnicity distribution to the US dialysis population. - **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. - Comparing seroprevalent and case counts per 100 000 population, **9·2% of seropositive patients were diagnosed**. - 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. - County mobility restrictions of >5% in March 2020 were associated with lower odds of seropositivity in July 2020, compared with mobility reduction of <5%. During the first wave of the COVID-19 pandemic, <10% of the US adult population formed antibodies against SARS-CoV-2, and <10% of those with antibodies were diagnosed.
The Lancet 25SEP2020	**Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry**	Barbaro R.P., *et al.* International gotopaper	Public Health / Epidemiology	First large, international cohort study of ECMO for COVID-19: 1035 patients aged >16 yrs with confirmed COVID-19 who required ECMO at 213 hospitals in 36 countries. - 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**. - 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**. - 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%. These data provide a generalisable estimate of ECMO mortality in the setting of COVID-19.
Clin Infect Dis. 25SEP2020	**Mass screening of asymptomatic persons for SARS-CoV-2 using saliva**	Yokota I., *et al.* Japan gotopaper	Diagnostics	The utility of saliva as an alternative specimen for SARS-CoV-2 detection in asymptomatic persons is yet to be determined. **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) **RESULTS** Sensitivity of nucleic acid amplification testing with nasopharyngeal and saliva specimens were 86% and 92%, respectively, with specificities greater than 99.9%. 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. **CONCLUSION** Self-collected saliva is a valuable specimen to detect SARS-CoV-2 in mass screening of asymptomatic persons.

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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 outcome**s: 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.
Science 24SEP2020	**Auto-antibodies against type I IFNs in patients with life-threatening COVID-19**	Bastard P., *et al.* France / International gotopaper	Immunology	Reported findings: - 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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Science 24SEP2020	**Inborn errors of type I IFN immunity in patients with life-threatening COVID-19**	Zang Q., *et al.* International gotopaper	Immunology	Repoted findings: - 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 534 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 gotopaper	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.
Clin Infect Dis. 23SEP2020	**High Frequency of SARS-CoV-2 RNAemia and Association With Severe Disease**	Hogan C.A., *et al.* USA gotopaper	Diagnostics	**AIM** Determine the frequency of SARS-CoV-2 RNA in plasma and its association with coronavirus disease 2019 (COVID-19) clinical severity. **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. **CONSLUSIONS** 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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Science 21SEP2020	**Immune life story, vaccination, and the dynamics of SARS-CoV-2**	Saad Roy C.M., *et al.* USA gotopaper	Public Health / Epidemiology	**Epidemiological model to estimate the magnitude and timing of future Covid19** assuming: > different protective efficacy and duration of the adaptive immune response and a potential >interaction with vaccines and non-pharmaceutical interventions 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 SARSCoV 2 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.
Clin Infect Dis. 21SEP2020	**Treatment of COVID-19 Patients with Prolonged Post-Symptomatic Viral Shedding with Leflunomide -- a Single-Center, Randomized, Controlled Clinical Trial**	Wang M., *et al.* China gotopaper	Therapeutics	**Aim**: to evaluate efficacy and safety of leflunomide (approved dihydroorotate dehydrogenase inhibitor) to treat COVID-19 patients with prolonged post-symptomatic viral shedding. **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.
Blood 21SEP2020	**Convalescent plasma therapy for B-cell depleted patients with protracted COVID-19 disease**	Hueso T., *et al.* France gotopaper	Therapeutics	Report of a series of 17 consecutive patients with profound B-cell lymphopenia and prolonged COVID-19 symptoms, negative IgG-IgM SARS-CoV-2 serology and a positive RNAemia, **treated with 4 units of COVID-19 convalescent plasma**. - 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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Lancet Microbe 17SEP2020	**Assessing a novel, lab-free, point-of-care test for SARS-CoV-2 (CovidNudge): a diagnostic accuracy study**	Gibani M.M., *et al.* UK gotopaper	Diagnostic	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.
JAMA Otolaryngol. Head Neck Surg. 17SEP2020	**In Vitro Efficacy of a Povidone-Iodine Nasal Antiseptic for Rapid Inactivation of SARS-CoV-2**	Frank S., *et al.* USA gotopaper	Therapeutics	**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.
Cell 16SEP2020	**Antigen-specific adaptive immunity to SARS-CoV-2 in acute COVID-19 and associations with age and disease severity**	Rydyznski Moderbacher C., *et al.* USA gotopaper	Immunology	**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 > 65** years old. Scarcity of naive 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.

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Nature Med 15SEP2020	**Convalescent plasma treatment of severe COVID-19: a propensity score–matched control study**	Liu S.T.H., *et al.* US gotopaper	Therapeutic	Retrospective, propensity score–matched case–control study to assess the effectiveness of convalescent plasma therapy in 39 patients with severe or life-threatening COVID-19 at The Mount Sinai Hospital (NYC). - 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.
JAMA Intern. Med. 10SEP2020	**Effect of Recombinant Human Granulocyte Colony–Stimulating Factor for Patients with Coronavirus Disease 2019 (COVID-19) and Lymphopenia. A Randomized Clinical Trial**	Cheng L.L., *et al.* China gotopaper	Therapeutic	**AIM**: Lymphopenia correlates with poor clinical outcomes in patients with COVID-19. Does increased peripheral blood leukocytes and lymphocyte cell count lead to clinical improvement in patients with COVID-19? 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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 09SEP2020	**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 SARSCoV2 Infection - Young adults with more than 1 of these conditions faced risks comparable with those observed in middle-aged adults without them
JAMA Netw Open 08SEP2020	**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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Ann Intern Med 04SEP2020	**Attitudes Toward a Potential SARS-CoV-2 Vaccine: A Survey of U.S. Adults**	Fisher K.A., *et al.* USA gotopaper	Public Health/Epidemio	**AIM:** to assess intent to be vaccinated against COVID-19 among a representative sample of 991 adults in the United States and identify predictors of and reasons for vaccine hesitancy (Cross-sectional survey, April 2020). - **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 gotopaper	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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JEM 04SEP2020	**Phenotypical and functional alteration of unconventional T cells in severe COVID-19 patients**	Jouan Y., *et al.*, France gotopaper	Immunology	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. - **Circulating unconventional T cells** of COVID-19 patients presented with a profound and persistent **phenotypic alteration**. - **In the airways, highly activated unconventional T cells** were detected, potentially contributing to the regulation of local inflammation. - **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. Thus, COVID-19 patients present with an altered unconventional T cell biology.
The Lancet 04SEP2020	**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**	Logunov *et al.*, Russia gotopaper	Vaccine	-> 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**). -> 2 formulations (**frozen and lyophilised**) ->76 participants enrolled in two non-randomised phase 1/2 studies (38 in each study) -> 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 **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.
JAMA 02SEP2020	**Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19. The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial**	Angus D.C. *et al.*, USA gotopaper	Therapeutic	**AIM**: To determine whether hydrocortisone improves outcome for patients with severe COVID-19. Bayesian randomized clinical trial – open-label intervention – **384 adults admitted to an ICU**. 3 arms: - A fixed 7-days course of intravenous hydrocortisone (n=137) - A shock-dependent course (n=146) - No hydrocortisone (n=101). Primary endpoint: organ support-free days (days alive and free of ICU-based respiratory or cardiovascular support) within 21 days. **RESULTS**: **For the fixed-dose, shock-dependent, and no hydrocortisone groups, respectively:** - 30%, 26% and 33% mortality rates - and 11.5, 9.5, and 6 median organ support–free days among survivors. **Compared with no hydrocortisone**, treatment with a 7-day fixed-dose course of hydrocortisone or shock-dependent dosing of hydrocortisone: - 93% and 80% probabilities of superiority with regard to the odds of improvement in organ support-free days within 21 days. - Few serious adverse events were reported in the 3 arms: 3%, 3% and 1% respectively. Following a press release from the RECOVERY trial on June 16, 2020 **--> stop enrollment of patients with COVID-19 in the corticosteroid domain due to a loss of equipoise.** --> **the trial was stopped** early and no treatment strategy met prespecified criteria for statistical superiority, precluding definitive conclusions. --> No strategy was determined to be optimal.

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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 of 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 trial. 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 event**s – 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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Nature 26AUG2020	**Sex differences in immune responses that underlie COVID-19 disease outcomes**	Takahashi et al., USA gotopaper	Immunology	**Focusing the analysis on patients with moderate disease who had not received immunomodulatory medications;** ->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. ->female patients mounted significantly more robust T cell activation than male patients during SARS-CoV-2 infection, which was sustained in old age. -> 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. -> 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
Clin Infect Dis 25AUG2020	**COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing**	Kai-Wang To K., et al., China gotopaper	Public Health/Epidemio	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**.
LANCET GLOBAL HEALTH 25AUG2020	**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**	Hamadani J D et al., Bangladesh gotopaper	Public Health/Epidemio	AIM: The immediate impact of COVID-19 lockdown orders on women and their families in rural Bangladesh -> 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:** - 96% reported a reduction in paid work for the family: median monthly family income fell from US$212 at baseline to $59 during lockdown. - Proportion of families earning less than $1,90/days rose from 0,2% (5) to 47,3% (992). - The number of families experiencing any level of food insecurity increased by 51,7% (p<0,0001). - Mother's depression and anxiety symptoms increased during the lockdown. - Over half women reported that emotional or moderate physical violence had increase during the lockdown. -> 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.
Clin Infect Dis 24AUG2020	**BCG vaccination in infancy does not protect against COVID-19. Evidence from a natural experiment in Sweden**	Chaisemartin and Chaisemartin, Sweden gotopaper	Vaccine	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. -> 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.

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Nat Com 21AUG2020	**An adenovirus-vectored COVID-19 vaccine confers protection from SARS-COV-2 challenge in rhesus macaques**	Feng et al., China gotopaper	Vaccines	Generation of a replication-incompetent recombinant serotype 5 adenovirus, Ad5-S-nb2, carrying a codon-optimized gene encoding Spike protein (S). -> In mice and rhesus macaques, intramuscular injection with Ad5-S-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-S-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 × 1010 viral particles) are also protected, demonstrating the effectiveness of Ad5-S-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 ?
Clin Infect Dis 21AUG2020	**Empiric Antibacterial Therapy and Community-onset Bacterial Co-infection in Patients Hospitalized with COVID-19: A Multi-Hospital Cohort Study**	Vaughn V.M., et al. USA gotopaper	Public Health / Epidemiology	AIM: to determine prevalence and predictors of empiric antibacterial therapy and community-onset bacterial co-infections in hospitalized patients with COVID-19. - 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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JAMA 21AUG2020	**Epidemiology of COVID-19 Among Incarcerated Individuals and Staff in Massachusetts Jails and Prisons**	Jiménez M.C. et al. USA gotopaper	Public Health / Epidemiology	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.
Lancet Rheumatology 21AUG2020	**Risk of hydroxychloroquine alone and in combination with azithromycin in the treatment of rheumatoid arthritis: a multinational, retrospective study**	Lane J C E et al USA gotopaper	Therapeutic	AIM : Hydroxychloroquine is commonly used in the treatment of rheumatoid arthritis. Studied the safety of HCQ alone and in combinaition 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 counfoundig. - 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 -> addition of AZT increase the risk of heart failure and cardiovascular mortality even in the short term.
Cell 20AUG2020	**Longitudinal Isolation of Potent Near-Germline SARS-CoV-2-Neutralizing Antibodies from COVID-19 Patients**	Kreer et al., Germany gotopaper	Immuno/Therapeutic	- 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 -> 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.

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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 placentas 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 placentas 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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Cell 14AUG2020	**A single-dose intranasal ChAd vaccine protects upper and lower respiratory tracts against SARS-CoV-2**	Hassan et al., USA gotopaper	Vaccines	Evaluation of protective activity of a chimpanzee adenovirus-vectored 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. ->Intramuscular dosing of ChAd-SARS-CoV-2-S induces robust systemic humoral and cell-mediated immune responses and protects against lung infection, inflammation, and pathology but does not confer sterilizing immunity, as evidenced by detection of viral RNA and induction of anti-nucleoprotein antibodies after SARS-CoV-2 challenge ->In contrast, a single intranasal dose of ChAd-SARS-CoV-2-S induces high levels of neutralizing antibodies, promotes systemic and mucosal IgA and T cell responses, and virtually completely prevents SARS-CoV-2 infection in both the upper and lower respiratory tracts. Intranasal administration of ChAd-SARS-CoV-2-S is a candidate for preventing SARS-CoV-2 infection and transmission, and curtailing pandemic spread.
JAMA 14AUG2020	**Association Between Number of In-Person Health Care Visits and SARS-CoV-2 Infection in Obstetrical Patients**	Reale S.C., et al., USA gotopaper	Public Health / Epidemio	**AIM:** 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. - 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. - 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. 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.
Cell 14AUG2020	**Robust T cell immunity in convalescent individuals with asymptomatic or mild COVID-19**	Sekine et al., Sweden gotopaper	Immuno	SARS-CoV-2-specific memory T cells will likely prove critical for long-term immune protection against COVID-19. Method: 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. **Results:** - Acute phase SARS-CoV-2-specific T cells display an activated cytotoxic phenotype - Broad and polyfunctional SARS-CoV-2-specific T cell responses in convalescent phase - Detection of SARS-CoV-2-specific T cell responses also in seronegative individuals **Conclusions:** 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.

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JAMA 13AUG2020	**Effect of an Inactivated Vaccine Against SARS-CoV-2 on Safety and Immunogenicity OutcomesInterim 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 angioedeman 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-Hodgin lymphoma - Aggressive non-Hodgkin lymphoma - Plasma cell neoplasms - Severe or critical COVID-19

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Clin Inf Dis 12AUG2020	**Methylprednisolone as Adjunctive Therapy for Patients Hospitalized With COVID-19 (Metcovid): A Randomised, Double-Blind, Phase IIb, Placebo-Controlled Tria**	Prado Jeronimo CM et al., Brazil gotopaper	Therapeutic	**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 & 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 >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 > 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).
Nature 12AUG2020	**Phase 1/2 study of COVID-19 RNA vaccine BNT162b1 in adults**	Mulligan M J et al., USA gotopaper	Vaccine	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 & 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.

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Lancet Global Health 10AUG2020	**Effect of the COVID-19 pandemic response on intrapartum care, stillbirth, and neonatal mortality outcomes in Nepal: a prospective observational study**	Ashish KC et al., Nepal/Sweden/… gotopaper	Epidemiology	**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 < 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 lockdoxn 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**
Clinical Infectious Disease 09AUG2020	**Clinical Outcomes Associated with Methylprednisolone in Mechanically Ventilated Patients with COVID-19**	Nelson B C et al., USA gotopaper	Clinic	**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

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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 / Epidemio	**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 04AUG2020	**Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans**	Mateus et al., USA and Australia gotopaper	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 4AUG2020	**Engineering human ACE2 to optimize binding to the spike protein of SARS coronavirus 2**	Chan et al., USA gotopaper	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 04AUG2020	**SeroTracker: a global SARS-CoV-2 seroprevalence dashboard**	Arora, R.K. et al., Canada gotopaper	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. **https://serotracker.com/Dashboard**
Nature Medicine 03AUG2020	**Immune complement and coagulation dysfunction in adverse outcomes of SARS-CoV-2 infection**	Ramlall, V. et al., USA, gotopaper	Public Health / Epidemiology	Aim: retrospective observational study to determine whether conditions associated with dysregulated complement or coagulation systems impact Covid-19 disease. - **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. 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.

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Clinical infectious diseases 03AUG2020	**Longitudinal dynamics of the neutralizing antibody response to SARS-CoV-2 infection**	Wang, K. et al., China gotopaper	Public Health / Epidemiology	**AIM: studying the longitudinal dynamics of SARS-CoV-2-specific neutralizing antibodies (NAbs) and he levels of 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** d after symptom onset and **increased after 2-3 weeks**. The median peak time for NAbs was 33 d 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.
Journal of Inf Dis 01AUG2020	**Prospective study comparing deep-throat saliva with other respiratory tract specimens in the diagnosis of novel coronavirus disease (COVID-19)**	Lai et al., China gotopaper	Diagnostic	**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.**
The Lancet Public Health 31JUL2020	**Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study**	Nguyen, L.H. et al., USA / UK, gotopaper	Public Health / Epidemiology	**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.

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Nature 30JUL2020	**Single-shot Ad26 vaccine protects against SARS-CoV-2 in rhesus macaques**	Mercadi N B et al., USA gotopaper	Vaccine	**A vaccine that requires only a single immunization would be optimal.** 52 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. **-> Robust single-shot vaccine protection against SARS-CoV-2 in rhesus macaques.** **-> Being evaluated in clinical trials**
SCIENCE 30JUL2020	**Adaptation of SARS-CoV-2 in BALB/c mice for testing vaccine efficacy**	Gu et al., China gotopaper	Vaccine	**Clinical isolate of SARS-CoV-2 by serial passaging in the respiratory tract of aged BALB/c mice.** -> 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. -> Deep sequencing revealed a panel of adaptive mutations potentially associated with the increased virulence. In particular, the N501Y mutation is located at the receptor binding domain (RBD) of the spike protein. -> 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.**
EBioMedicine 30JUL2020	**Serologic responses to SARS-CoV-2 infection among hospital staff with mild disease in eastern France**	Fafi-Kremer, S. et al., France, gotopaper	Public Health / Epidemiology	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.

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JAMA 29JUL2020	**Association Between Statewide School Closure and COVID-19 Incidence and Mortality in the US**	Auger et al., USA gotopaper	Public Health/Epidemio	**Analysis conducted between March 9, 2020, and May 7, 2020.** -> 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.**
Nature 29JUL2020	**SARS-CoV-2-reactive T cells in healthy donors and patients with COVID-19**	Braun, J. et al, Germany, gotopaper	Public Health / Epidemiology	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.
Nature 29JUL2020	**Association of COVID-19 inflammation with activation of the C5a–C5aR1 axis**	Carvelli, J. et al, France, gotopaper	Public Health / Epidemiology	Aim: longitudinal analysis of immune responses linked to soluble factor C5a and cells expressing its receptor C5aR1 (CD88) in the blood and broncho-alveolar lavage fluid of patients at various stages of COVID-19 severity. - An **increase in soluble C5a levels proportional to COVID-19 severity and high levels of C5aR1 expression in blood and pulmonary myeloid cells** is reported, supporting a role for the C5a-C5aR1 axis in the pathophysiology of acute respiratory distress syndrome (ARDS). - **Anti-C5aR1 therapeutic monoclonal antibodies prevented C5a-mediated human myeloid cell recruitment and activation**, and inhibited acute lung injury in human C5aR1 knockin mice. These results suggest that C5a-C5aR1 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.

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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 gotopaper	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 gotopaper	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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Communications 24JUL2020	**Structural basis of RNA cap modification by SARS-CoV-2**	Viswanathan, Thiruselvam et al., USA gotopaper	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.
Clinical infectious diseases 24JUL2020	**Remdesivir for Severe COVID-19 versus a Cohort Receiving Standard of Care**	Olender, Susan A. et al., gotopaper	Therapeutics	**Comparison of the efficacy of remdesivir versus standard-of-care** treatment in adults with **severe COVID-19** using data from a phase 3 remdesivir trial (GS-US-540-5773) and a **retrospective cohort** of patients with severe COVID-19 **treated with standard-of-care** (GS-US-540-5807), using the stabilized inverse probability of treatment weighting (IPTW) method. 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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NEJM 23JUL2020	**Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19**	Cavalcanti, Alexandre B. et al., Brazil gotopaper	Therapeutics	**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. **Primary outcome**: 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 **not affected by 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. **=> 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.**
Science 23JUL2020	**Evolution and epidemic spread of SARS-CoV-2 in Brazil**	Candido, Darlan S. et al., UK-Brazil gotopaper	Public Health/ Epidemio	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 >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 e**arly epidemic phase, SARS-CoV-2 spread mostly locally** and within-state borders. A**fter 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.** -> 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**.

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Nature structural & molecular biology 22JUL2020	**Controlling the SARS-CoV-2 spike glycoprotein conformation**	Henderson, Rory et al. USA gotopaper	Vaccine	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. => 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.
Nature 22JUL2020	**Hydroxychloroquine use against SARS-CoV-2 infection in non-human primates**	Maisonnasse, Pauline et al. France gotopaper	Therapeutics	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**. **=> 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.**

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Nature 22JUL2020	**Potent neutralizing antibodies directed to multiple epitopes on SARS-CoV-2 spike**	Liu, Lihong et al., USA/China gotopaper	Therapeutics	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**. => 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 S 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 S trimer remain to be discovered.**
Nature 22JUL2020	**Chloroquine does not inhibit infection of human lung cells with SARS-CoV-2**	Hoffmann, Markus et al., Germany gotopaper	Therapeutics	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. => 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**. => 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**.

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Cell Reports Medicine 21JUL2020	**Characterization and Treatment of SARS-CoV-2 in Nasal and Bronchial Human Airway Epithelia**	Pizzorno, Andrés et al., France gotopaper	Therapeutics	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. => 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**. => 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.
Science 21JUL2020	**Serial interval of SARS-CoV-2 was shortened over time by nonpharmaceutical interventions**	Ali, Sheikh Taslim et al., UK-France-USA-China gotopaper	Public Health/ Epidemio	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. -> Findings could improve assessment of transmission dynamics, forecasting future incidence, and estimating the impact of control measures.

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PLoS Med 21JUL2020	**Impact of self-imposed prevention measures and short-term government-imposed social distancing on mitigating and delaying a COVID-19 epidemic: A modelling study**	Teslya, Alexandra et al., Netherlands-Portugal gotopaper	Public Health/ Epidemio	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.
Science Translational Medicine 20JUL2020	**An alphavirus-derived replicon RNA vaccine induces SARS-CoV-2 neutralizing antibody and T cell responses in mice and nonhuman primates**	Erasmus, Jesse H et al., USA gotopaper	Vaccine	Development of an alphavirus-derived replicon RNA vaccine candidate, repRNA-CoV2S, 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. **Results:** - A single intramuscular injection of the LION/repRNA-CoV2S 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. **Conclusion:** Potential for LION/repRNA-CoV2S, which will enter clinical development under the name HDT-301, to induce rapid immune protection from SARS-CoV-2 infection. **Limitations:** Absence of challenge data ; limited number of animals ; time points after vaccination where observed responses, especially T-cell responses, exhibited great variability

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Gut 20JUL2020	**Depicting SARS-CoV-2 faecal viral activity in association with gut microbiota composition in patients with COVID-19**	Zuo, Tao et al., China gotopaper	Gut Microbiota	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 -> higher abundances of** bacterial species ***Collinsella aerofaciens*, *Collinsella tanakaei*, *Streptococcus infantis*, *Morganella morganii*, and higher capacity for nucleotide *de novo* biosynthesis**, amino acid biosynthesis and glycolysis. - Faecal samples with **low-to-no SARS-CoV-2 infectivity signature -> higher abundances of short-chain fatty acid producing bacteria**, *Parabacteroides merdae*, *Bacteroides stercoris*, *Alistipes onderdonkii* and *Lachnospiraceae bacterium*. **-> 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.

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LANCET 20JUL2020	**Immunogenicity and safety of a recombinant adenovirus type-5-vectored 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-vectored COVID 19 vaccine from CanSino > Phase 2 clinical trial; randomized, double blinded, 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**: > Geometric mean titers of specific ELISA antibody responses to the receptor binding domain (RBD) > Neutralising 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 93–98) > 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-vectored COVID 19 vaccine from Oxford/AstraZeneca > Phase 1/2 clinical trial; randomized, single blinded, -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

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Cell host & microbe 18JUL2020	**Retrospective Multicenter Cohort Study Shows that Early Interferon Therapy is Associated with Favorable Clinical Responses in COVID-19 Patients**	Wang, Nan et al., China/USA gotopaper	Therapeutics	**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.
N. Engl. J. Med. 17JUL2020	**Dexamethasone in Hospitalized Patients with Covid-19 - Preliminary Report**	Horby, Peter et al., UK gotopaper	Therapeutics	**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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Eurosurveillance 16JUL2020	**Convalescent plasma treatment for SARS-CoV-2 infection: analysis of the first 436 donors in England, 22 April to 12 May 2020**	Harvala, Heli et al., UK gotopaper	Therapeutics	**Serological reactivity** was analysed in **plasma from 436 individuals with a history of disease compatible with COVID-19**, including 256 who had been l**aboratory-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 stream-lined and rapid way to guide convalescent plasma donor selection.
Ann Intern Med. 16JUL2020	**Hydroxychloroquine in Nonhospitalized Adults With Early COVID-19: A Randomized Trial**	Skipper, Caleb P. et al., USA/Canada gotopaper	Therapeutics	**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 < 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). **=> 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.
Clin. Infect. Dis. 16JUL2020	**Hydroxychloroquine for Early Treatment of Adults with Mild Covid-19: A Randomized Controlled Trial**	Mitja, Oriol et al., Spain gotopaper	Therapeutics	**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.

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

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BMJ 15JUL2020	**Physical distancing interventions and incidence of coronavirus disease 2019: natural experiment in 149 countries**	Islam, N et al., UK/USA gotopaper	Public Health / Epidemio	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.
Journal of clinical medicine 14JUL2020	**Epidemiology and Clinical Presentation of Children Hospitalized with SARS-CoV-2 Infection in Suburbs of Paris**	Gaborieau, L et al., France gotopaper	Public Health / Epidemio	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 rhinorrhoea (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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Nature 15JUL2020	**Potently neutralizing and protective human antibodies against SARS-CoV-2**	Zost, Seth J. et al., USA gotopaper	Therapeutics	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.
JAMA 14JUL2020	**Rapid implementation of SARS-CoV-2 sequencing to investigate cases of health-care associated COVID-19: a prospective genomic surveillance study**	Meredith et al., UK gotopaper	Public Health/Epidemio	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 pu blic health policy as they enable rapid tracking and investigation of infections in hospital and community settings.

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JAMA 14JUL2020	**Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers**	Wang et al., USA gotopaper	Public Health/Epidemio	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 -> 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 < .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 multipronged infection reduction strategy in health care settings.
Nature Comm 14JUL2020	**Transplacental transmission of SARS-CoV-2 infection**	Vivanti A J. et al, France gotopaper	Clinic Case study	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 & 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 -> Description of an actual neonatal infection -> A case of congenital infection associated with neurological manifestations following neonatal viremia -> Demonstration that the transplacental transmission of SARS-CoV-2 infection is possible

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Nature Communications 14JUL2020	**Exploring the SARS-CoV-2 virus-host-drug interactome for drug repurposing**	Sadegh, Sepideh et al., Germany gotopaper	Therapeutics	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.
NEJM 14JUL2020	**An mRNA Vaccine against SARS-CoV-2 — Preliminary Report**	Jackson LA et al., USA gotopaper	Vaccine	> Phase 1 clinical Trial with mRNA-1273 vaccine from Moderna - dose-escalation, open-label trial including - 45 healthy adults, 18 to 55 years of age - two vaccinations, 28 days apart - Doses: 25 µg, 100 µg, or 250 µg. **RESULTS:** > After the first vaccination, antibody responses were higher with higher dose. GMTs (measured by ELISA d29): - 40,227 in the 25-µg group, - 109,209 in the 100-µg group - 213,526 in the 250-µg group. > After the second vaccination, the titers increased. GMT(measured by ELISA d57): - 299,751 in the 25-µg group, - 782,719 in the 100-µg group - 1,192,154 in the 250-µg group. - Serum neutralizing activity was detected in all participants evaluated > Solicited AE occurred in more than half the participants (fatigue, chills, headache, myalgia, and pain at the injection site) > Systemic AE adverse events were more common after the second vaccination, particularly with the highest dose. > 3 participants in the 250-µg dose group reported one or more severe AE **CONCLUSIONS** The mRNA-1273 vaccine induces anti–SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified.
Nature structural & molecular biology 13JUL2020	**Neutralizing nanobodies bind SARS-CoV-2 spike RBD and block interaction with ACE2**	Huo, Jiangdong et al., UK gotopaper	Therapeutics	Using a naive 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. - 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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Science 13JUL2020	**Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients**	Hadjadj J et al, France gotopaper	Therapeutic	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-kB pathway SARS-CoV-2 infection à an absence of circulating IFN-b in COVID-19 patients with all disease-severity grade > Suggested that infected patients had no detectable circulating IFN-b and that an impaired IFN-a production characterized the most severeCOVID-19 cases. > Impaired type I IFN response in severe and critical COVID-19 patients, accompanied by high blood viral load and an excessive NF-kB driven inflammatory response associated with increase TNFa and IL-6. > Type I IFN deficiency is a hallmark of severe COVID-19 à combined therapeutic approaches
Cell 13JUL2020	**Longitudinal isolation of potent near-germline SARS-CoV-2-neutralizing antibodies from COVID-19 patients**	Kreer, Christoph et al., Germany gotopaper	Vaccines	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-reactiveB 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.
Clin. Infect. Dis. 11JUL2020	**Tocilizumab for treatment of mechanically ventilated patients with COVID-19**	Somers, Emily C. et al., USA gotopaper	Therapeutics	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<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.

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Nature Med 10JUL2020	**Rapid isolation and profiling of a diverse panel of human monoclonal antibodies targeting the SARS-CoV-2 spike protein**	Zost SJ et al., USA gotopaper	Therapeutic	Use a rapid antibody discovery platform to isolate hundreds of human monoclonal antibodies (mAbs) against SARS-CoV-2 s protein à obtain human mAbs from the B cells of some patients in North America (4 patients) à used different workflows in parallel The antibodies cold be grouped into five binding patterns on the basis of domain recognition and cross-reactivity. à Most neutralizing mAbs recognizing the receptor-binding domain (RBD) of S à the RBD= the principal site of vulnerability for SARS-CoV-2 neutralization à RBD of SARS-CoV-2 for vaccine design and therapeutic-antibody development
PNAS 9 JULY2020	**BCG vaccine protection from severe coronavirus disease 2019 (COVID-19)**	Escobar LE et al., USA gotopaper	Vaccine/Public Health	> Epidemiological explorations suggest a negative association between national BCG vaccination policy and the prevalence and mortality of COVID-19 > But comparisons are difficult due to broad differences between countries: - socioeconomic status, - demographic structure - rural vs. urban settings - number of diagnostic tests - national control strategies RESULTS: 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 (r 2 = 0.88; P = 8 × 10−7) - every 10% increase in the BCG index was associated with a 10.4% reduction in COVID-19 mortality 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 3. Nevertheless, the analyses should be considered with caution. BCG vaccination clinical trials are required to corroborate the patterns detected
Eurosurveillance 09JULY2020	**International external quality assessment for SARS-CoV-2 molecular detection and survey on clinical laboratory preparedness during the COVID-19 pandemic, April/May 2020**	Matheeussen, V et al., International gotopaper	Public Health/Epidemio	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.

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Nature 08JULY2020	**OpenSAFELY: factors associated with COVID-19 death in 17 million patients**	Williamson, EJ et al., gotopaper	Public Health/Epidemio	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	Rendesivir (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 µ M) 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/Epidemio	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.
The Lancet 06JULY2020	**Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study**	Pollan et al., Spain and USA gotopaper	Public Health/Epidemio	- 35 883 households were selected From April 27 to May 11, 2020, 61 075 participants anwered a qustionnaire 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 19·5% (16·3–23·2) of symptomatic participants who were seropositive by both the point-of-care test and immunoassay reported a previous PCR test.
The Lancet ID 03JULY2020	**Asymptomatic SARS-CoV-2 infection in Belgian long-term care facilities**	Hoxha et al., Sweden and Belgium gotopaper	Public Health/Epidemio	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

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Ann Rheum Dis 03JUL2020	**Interleukin-6 blockade with sarilumab in severe COVID-19 pneumonia with systemic hyperinflammation: an open-label cohort study**	Della-Tore E et al Italy gotopaper	Therapeutic	Open label study of sarilumab (IL-6 blockade) in severe COVID-19 patients with hyperinflammation 2 groups: 28 patients sarilumab + standard of care matched with 28 patients standard of care At day 28 of follow-up - Survival rate: 93% (sarilumab) vs 82% (control): HR: 0,36 IC95%[0,08 – 1,68] - Median time to death: 19 days (sarilumab) vs 4 (control), p= 0,006 - Death: 7% (sarilumab) vs 18% (control), p=0,42 - Clinical improvement: 60% (sarilumab) vs 64% (control), p=0,99 - Adverse events: similar in both group, 43% (sarilumab) vs 36% (control) Independent factors of clinical improvement: - Baseline PaO2/FiO2 > 100mmHg - Lung consolidation <17% at CT scan No difference for clinical improvement and mortality between two group Sarilumab was associated with faster recovery in a subset of patient showing minor lung consolidation at baseline
Lancet Child Adolesc Healt 02JUL2020	**Emergence of Kawasaki disease related to SARS-CoV-2 infection in an epicenter of the French COVID-19 epidemic: a time-series analysis**	Ouldali N et al France gotopaper	Clinic	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) 230 patients with KD (dec 2005 to may 2020) à 1,2 case/month (quasi-Poisson model) 2 peak of hospital admission due to KD April 2020: - Increase of KD (497% increase): 6 cases per month - Starting 2 weeks after the peak of COVID-19 - 10 cases between April 15 and May 20 - 80% of the cases were positive for SARS-CoV-2 (PCR or serology) - 6 cases required intensive care - Similar characteristics to the patients with KD in Bergamo **December 2009:** - Concomitant with the influenza A H1N1 pandemic – 1 – 3 weeks after the peak in Paris - 6 cases per month (365% increase) Characteristics of patients with KD in April 2020 appeared to be different from those diagnosed during the H1N1 epidemics: - Older (11,8 years vs 2,1 years, p=0,034) - Less inflammatory: CRP à 23,6 mg/dL vs 8,4 mg/dL, p=0,042 SARS-CoV-2 : only respiratory virus with intense circulation in April 2020 - Viral respiratory infections could be triggers for KD
Eurosurveillance 02JULY2020	**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**	Eurosurveillance editorial team, Europe gotopaper	Public Health/Epidemio	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). 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 explaning apparent increase of resurgence vary (changes in case ascertainment, genuine increases in transmission, importation of cases). 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.

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Eurosurveillance 02JULY2020	**Introductions and early spread of SARS-CoV-2 in France, 24 January to 23 March 2020**	Gámbaro, F. et al., France gotopaper	Public Health/Epidemio	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 01JUL2020	**Identification of druggable inhibitory immune checkpoints on Natural Killer cells in COVID-19**	Demaria, Olivier et al. France gotopaper	Therapeutic	Analysis of NK cells in blood from a cohort of 82 individuals: 10 healthy controls (HC), 10 paucisymptomatic COVID-19 patients (pauci), 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 monalizumab 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-(L)1, 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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J Intern Med 01JUL2020	**Treatment with proton pump inhibitors increases the risk of secondary infections and ARDS in hospitalized patients with COVID-19: coincidence or underestimated risk factor?**	Luxenburger, H. et al. Germany gotopaper	Therapeutic	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. ð 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.
MICROBIOLOGY AND INFECTION 26JUN2020	**Childhood COVID-19: a multi-center retrospective study**	Chen Z et al- CHINA gotopaper	Public Health/Epidemio	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
LANCET PHSYCHIATRY 25JUN2020	**Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study**	Varatharaj A et al UK and USA gotopaper	Public Health/Epidemio	The aim of this study was to investigate the breadth of complications of COVID-19 across the UK that affected the brain **METHODS** > development of a rapid case report notifications portal across UK neurosciences bodies > 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) > 77 (62%) of 125 patients presented with a cerebrovascular event, > 39 (31%) of 125 patients presented with altered mental status, > 9 (23%) with unspecified encephalopathy > 7 (18%) with encephalitis. > 23 (59%) fulfilled the clinical case definitions for psychiatric diagnoses (mostly new onset disorders)

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JAMA network open 24JUN2020	**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**	Deftereos, Spyridon G. et al. Greece gotopaper	Therapeutic	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.
THE LANCET CHILD & ADOLESCENT HEALTH 25JUN2020	**COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study**	Götzinger Florian et al- 25 European countries. gotopaper	Public Health/Epidemio	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 SARSCoV2 Infection (PCR). 82 participating health-care institutions; 25 European countries (Paediatric Tuberculosis Network European Trials Group) RESULTS : Four children died. > 145 (25%) had pre-existing medical conditions. > 363 (62%) individuals were admitted to hospital. > 48 (8%) individuals required ICU admission, > 25 (4%) mechanical ventilation > 19 (3%) inotropic support, > 1 (<1%) extracorporeal membrane oxygenation Significant risk factors for requiring ICU admission were: > being younger than 1 month > male sex > pre-existing medical conditions > presence of lower respiratory tract infection signs > symptoms at presentation
Cell Metabolism 24JUN2020	**In-hospital Use of Statins is Associated with a Reduced Risk of Mortality among Individuals with COVID-19**	Zhang, Xiao-Jing et al. China gotopaper	Therapeutic	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

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American Journal of Obstetrics and Gynecology 23JUN2020	**Exposure and Seroconversion to SARS-CoV-2 Among Obstetric Healthcare Providers Following a Contained Outbreak**	KIEFER MK et al, USA gotopaper	Public Health/Epidemio	Key question: Exposure and seroconversion to SARS-CoV-2 among obstetric HCWs (in a tertiary care center) > 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 STUDY DESIGN - Prospective cohort of HCW: study of SARS-CoV-2 antibody levels Collection of Blood samples at two time points four weeks apart (IgM and IgG levels) RESULTS - 110 HCW recruited (females, median age 34). 68,2% nurses, 24,5% physicians > 90 participants (82%) reported a SARS-CoV-2 exposure > 66 (60%) reported one or more COVID-19 symptoms; > 52 (47%) had nasopharyngeal PCR testing, of which 15 (29%) tested positive for the virus, 14 seroconverted > at baseline, 3 participants (2,7%) had positive antibodies > 5 participants (4.5%) who reported being asymptomatic, seroconverted
Blood 23JUN2020	**Improved Clinical Symptoms and Mortality on Severe/Critical COVID-19 Patients Utilizing Convalescent Plasma Transfusion**	Xia, Xinyi et al. China gotopaper	Therapeutic	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. - 2.2% and 4.1% of cases died in the CPT group and in the standard-treatment group, respectively. - 2.4% and 5.1% of patients in the CPT and the standard-treatment group have been admitted to ICU eventually. - 70% of the patients who had severe respiratory symptoms got improved and removed oxygen supports within 7 days after CPT. - The viral loads and C-reactive protein (CRP) concentration significantly decreased (P<0.001), and the percentage of lymphocytes increased (P=0.006), 76.8% of cases received radiological improvements within 14 days after CPT. - Patients with a higher percentage of lymphocytes and a lower percentage of neutrophils and CRP concentration respond better to CPT (P<0.05). - 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. **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.** 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.

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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 SARSCoV2 vaccine candidate > Selected sequences: from R319 to K537 > Dimerization and binding to hACE was demonstrated > Immunization of BABL/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 compare to monomer > No differnces 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/Epidemio	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 stimates should be interpreted as an illustration of how population heterogeneity affects herd immunity, rather than an exact value or even a best estimate.
J Infect Dis 19JUN2020	**Interferon-beta 1a inhibits SARS-CoV-2 in vitro when administered after virus infection**	Clementi, Nicola et al. Italy gotopaper	Therapeutic	Evaluation of anti-SARS-CoV-2 in vitro activity of Interferon-beta 1a. 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 el 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/Epidemio	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 (14d 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 ?
New England Journal of Medicine 17JUN2020	**Genomewide Association Study of Severe Covid-19 with Respiratory Failure**	Ellinghaus, D., et al. Multicentre gotopaper	Public Health/Epidemio	AIM: performing a Genomewide association analysis on patients with severe disease and controls (Italy/Spain) to identify potential genetic factors involved in the development of 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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Lancet Rheumatol 16JUN2020	**GM-CSF blockade with mavrilimumab in severe COVID-19 pneumonia and systemic hyperinflammation: a single-centre, prospective cohort study**	De Lucas G et al Italy gotopaper	Therapeutic	Single center prospective cohort study, open label – Adults patients with severe COVID-19, hypoxemia & 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
Nature Medicine 16JUN2020	**Age-dependent effects in the transmission and control of COVID-19 epidemics**	Davies et al., UK gotopaper	Public Helath/Epidemio	Age-structured mathematical model to epidemic data from China, Italy, Japan, Singapore, Canada and South Korea. **Estimation:** - 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 -> 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 **Conclusion:** -> 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. ->Without effective control measures, regions with relatively older populations could see disproportionally more cases of COVID-19, particularly in the later stages of an unmitigated epidemic.

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CELL 15JUIN2020	**Structures of human antibodies bound to SARS-CoV-2 spike reveal common epitopes and recurrent features of antibodies**	Christopher O et al, USA/SWITZERLAND gotopaper	Vaccine/Therapeutics	Characterization of polyclonal IgGs and Fabs from COVID-19 convalescent individuals for recognition of coronavirus spikes. Analysis of purified IgG and Fabs from the plasmas of 10 COVID-19 convalescent individuals showed > binding to trimeric S and monomeric RBD/S1B domains of six human coronaviruses > neutralizing activity against SARS-CoV-2 pseudoviruses By using EM approaches it was shown that: > Fabs recognize both S1A and RBD epitopes on SARS-CoV-2 S protein > the monoclonal Fab-spike neutralizing complex passes thought an specific epitope that blocks ACE2 receptor binding Overall, these studies structurally define a recurrent anti-SARSCoV-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.
Science 15JUN2020	**Antibody cocktail to SARS-CoV-2 spike protein prevents rapid mutational escape seen with individual antibodies**	Baum, Alina et al. USA gotopaper	Therapeutic	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 => **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 => **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 => **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

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Science 15JUN2020	**Potent neutralizing antibodies from COVID-19 patients define multiple targets of vulnerability**	Brouwer, Philip J. M. et al. Netherlands/USA gotopaper	Therapeutic	**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. - 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.
Science 15JUN2020	**Studies in humanized mice and convalescent humans yield a SARS-CoV-2 antibody cocktail**	Hansen, Johanna et al. USA gotopaper	Therapeutic	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**. - screened for binding affinity to RBD monomer and dimer, epitope diversity, ability to block ACE2 receptor binding to RBD, and neutralize VSV-based SARS-CoV-2 spike pseudoparticles (pVSV-SARS-CoV-2-S(mNeon)). => Screening yielded over 200 neutralizing mAbs with broad potency ranges, dozens of which displayed neutralization potency in the pM range. - 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).
Science 15JUN2020	**Broad neutralization of SARS-related viruses by human monoclonal antibodies**	Wec, Anna Z. et al. USA gotopaper	Therapeutic	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 spike (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 Helath/Epidemio	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**.
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	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).

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SCIENCE 12JUN2020	**The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries**	Walker et al., UK, USA gotopaper	Public Helath/Epidemio	Combining data on demography, contact patterns, disease severity, and health care capacity and quality to understand its impact and inform strategies for its control -> Younger populations in lower income countries may reduce overall risk ->Limited health system capacity coupled with closer inter-generational contact largely negates this benefit. -> Mitigation strategies that slow but do not interrupt transmission will still lead to COVID-19 epidemics rapidly overwhelming health systems, with substantial excess deaths in lower income countries due to the poorer health care available.
The Lancet 11JUN2020	**Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study**	Stringhini, S. et al. Switzerland gotopaper	Public Health/Epidemio	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. - In the first week, we estimated a seroprevalence of 4·8%. The estimate increased to 8·5% in the second week, to 10·9% in the third week, 6·6% in the fourth week, and 10·8% in the fifth week. - Individuals aged 5–9 years and those older than 65 years had a significantly lower risk of being seropositive than those aged 20–49 years. We estimated that for every reported confirmed case, there were 11·6 infections in the community. These results suggest that most of the population of Geneva remained uninfected during this wave of the pandemic. Assuming that the presence of IgG antibodies is associated with immunity, these results highlight that the epidemic is far from coming to an end by means of fewer susceptible people in the population.
The Journal of clinical investigation 11JUN2020	**Early safety indicators of COVID-19 convalescent plasma in 5,000 patients**	Joyner, Michael J et al. USA gotopaper	Therapeutic	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. - **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 subjet 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, > positive relationship between COVID-19 conspiracy beliefs and use of social media as a source of information about COVID-19. **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 <u>Animal treated with remdesivir → 12 hours after inoculation:</u> - **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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Intensive Care Medicine 08JUN2020	**Hydroxychloroquine pharmacokinetic in COVID-19 critically ill patients: an observational cohort study**	Painvin B et al France gotopaper	Therapeutic	HCQ pharmacokinetic in COVID-19 critically ill patients 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 <u>After tocilizumab</u> - 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 Medecine 8JUN2020	**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 paly 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 pubic heath 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	**Retractation:** **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
NEJM 04JUN2020	**Retraction:** **Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. N Engl J Med. DOI: 10.1056/NEJMoa2007621**	Mehra MR et al USA gotopaper	Clinic	**Unable to validate the primary data source underlying the article "**Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19" The raw data could not be made available to a third-party auditor Withdrawal of the article at the request of the authors

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Nature 8JUN2020	**Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe**	Flaxman, Seth et al. UK gotopaper	Therapeutic	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< 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**. => 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.
Blood 08JUN2020	**COVID and Coagulation: Bleeding and Thrombotic Manifestations of SARS-CoV2 Infection**	Al-Samkari H et al USA gotopaper	Clinic	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 > $450x10^9$/L / CRP > 100mg/L / Erythrocyte sedimentation rate >40mm/h → **Randomized trials are needed to determine any potential benefit of intensified anticoagulation prophylaxis**
JAMA 08JUN2020	**Clinical Characteristics of 58 Children with a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2**	Whittaker E et al UK gotopaper	Clinic	**58 children** in 8 hospitals in England with PIMS-TS → 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 & 45% conjunctival injection / 22% children met definition of KD (AHA) Biology - PCR SARS-CoV-2 positive 15/58 & 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 →**the comparison suggests this disorder differ from other pediatric inflammatory entities**

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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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J Med Virol 5JUN2020	**Identification of nsp1 gene as the target of SARS-CoV-2 real-time RT-PCR using nanopore whole genome sequencing**	Chan, Wan-Mui et al. Hong Kong gotopaper	Virology	There is an **increasing number of SARS-CoV-2 viruses with mutations** at the primer or probe binding sites. T**hese mutations may affect the sensitivity** of RT-PCR) assays targeting the N, E, and ORF1a/b genes. => 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. => we have developed **a novel nsp1 real-time RT-PCR assay**. The primers and probes are highly specific for SARS-CoV-2. **Results:** 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%) **Conclusion**: 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. **Limitations**: 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.
Med 5JUN2020	**Outcomes of hydroxychloroquine usage in United States veterans hospitalized with COVID-19**	Magagnoli, Joseph et al. USA gotopaper	Therapeutic	**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. **Limitations**: non-randomization of treatments; demographic composition of patients (US veterans) with a majority of men and majority of black.
HEART FAILURE JUN2020	**Incidence of New-Onset and Worsening Heart Failure Before and After the COVID-19 Epidemic Lockdown in Denmark**	Andersson C et al, DENMARK gotopaper	Public Health/Epidemio	Consequences of the lockdown for patients with heart failure (Cohort Study in Denmark) > Incidence of new onset HF and and hospitalizations for worsening HF before and after the lockdown (2019 vs 2020, same period) **Results:** **1. Before lockdown:** > 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:** > 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. **Conclusions:** > These data raise concerns for a potential undertreatment of HF currently that may impact prognosis in the longer term

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JOURNAL OF MEDICAL INTERNET RESEARCH 05JUN2020	**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	SHS/SciPo	**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 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.
Sci. Total Environ. 5JUN2020	**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	Public Health	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 method**s: (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 gotopaper	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-CoV-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-Irland gotopaper	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 gotopaper	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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 3JUN2020	**Effect of Convalescent Plasma Therapy on Time to Clinical Improvement in Patients With Severe and Life-threatening COVID-19: A Randomized Clinical Trial**	Li, Ling et al. China gotopaper	Therapeutic	**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, 11.39 [95% CI, 3.91-33.18]; P < .001). - Two patients in the convalescent plasma group experienced adverse events within hours after transfusion that improved with supportive care. => **Among patients with severe or life-threatening COVID-19, convalescent plasma therapy added to standard treatment, compared with standard treatment alone, did not result in a statistically significant improvement in time to clinical improvement within 28 days.** **Interpretation is limited by early termination** of the trial, which may have been underpowered to detect a clinically important difference.
Biosensors and Bioelectronics JUN2020	**Homogeneous circle-to-circle amplification for real-time optomagnetic detection of SARS-CoV-2 RdRp coding sequence**	Tian, Bo et al. Denmark gotopaper	Diagnostic	**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**. -> 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. -> 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.

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J. Infect. 3JUN2020	**Detection of SARS-CoV-2 antibodies using commercial assays and seroconversion patterns in hospitalized patients**	Tuaillon, E. et al. France gotopaper	Diagnostic	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**. => 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. **Cl°: 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 -> the estimation of sensitivity and specificity values are relatively imprecise. Patients with moderate to severe COVID-19 -> intensity of the humoral response to SARS-CoV-2 N or S proteins may be lower in asymptomatic or paucity symptomatic cases.
NEJM 03JUN2020	**A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19**	David R. Boulware et al. USA/Canada gotopaper	Therapeutic	**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.

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The Lancet Public Health 02JUN2020	**Effects of non-pharmaceutical interventions on COVID-19 cases, deaths, and demand for hospital services in the UK: a modelling study**	Davies, N.G., et al. UK gotopaper	Public Health/Epidemio	Assessment of the potential impact of control measures for COVID-19 in the UK, using a stochastic age-structured transmission model tracking 66·4 million people. Interventions modelled were school closures, physical distancing, shielding of people aged >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**
European journal of heart failure 2JUN2020	**ACE-inhibitors and Angiotensin-2 Receptor Blockers are not associated with severe SARS-COVID19 infection in a multi-site UK acute Hospital Trust**	Bean, Daniel M. *et al.* UK gotopaper	Clinic	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 < 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.
Cell Systems 02JUN2020	**Ultra-high-throughput clinical proteomics reveals classifiers of COVID-19 infection**	Messner et al., UK,Germany,Sweden gotopaper	Diagnostic	-A standardized, ultra-highthroughput 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
The Lancet Psy 2JUN2020	**Global mental health and COVID-19**	Lola Kola, Nigeria gotopaper	Psy	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) -> to increase access and coverage in hard-to-reach areas calls for more research on their e!ectiveness in LMICs - - >the *Lancet* Commission on global mental health recommended adoption of digital interventions alongside traditional treatments/ -> Efforts to respond to mental health needs present researchers with an important opportunity to build on what we know and advance progress in achieving the mental health objectives of universal health coverage.

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Lancet 01JUN2020	**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**	Chu et al, Canada gotopaper	Public Health/Epidemio	Aim: to investigate the effects of physical distance, face masks, and eye protection on virus transmission in health-care 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. 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.
Eur. Respir. J. 01JUN2020	**Estimates of the ongoing need for social distancing and control measures post-"lockdown" from trajectories of COVID-19 cases and mortality**	Lonergan, M., Chalmers, J.D. UK gotopaper	Public Health/Epidemio	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.
Nature Communications 01JUN2020	**Two linear epitopes on the SARS-CoV-2 spike protein that elicit neutralizing antibodies in COVID-19 patients**	Poh, Chek Meng et al; Singapore gotopaper	Immuno	**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.

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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	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	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 RNAsnap™ 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. **CI°**: 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	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. **CI°**: **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.

REACTing research & action targeting emerging infectious diseases

Inserm

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J. Clin. Virol. 30MAY2020	**Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19**	Gombar, Saurabh et al. USA gotopaper	Diagnostic	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. **Objective**: to better understand the appropriate length of symptom-based return to work and contact precaution strategies. 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. **CL°**: the fixed length of time before returning to work or ceasing contract precautions be revised **to over one-month**. Note: our analysis could be overestimating the length of infectious spreading by detecting non-infectious viral shedding. Large trials that rely on methods that detect the infective virus (ie viral culture) have not yet been reported in the literature.
Brain, Behavior and Immunity 30MAY2020	**COVID-19 pandemic and mental health consequences: systematic review of the current evidence**	Vindegaard and Eriksen Benros, Denmark gotopaper	Psy	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 health care workers. •A decrease in psychological well-being was observed in the general public. •However, well conducted large-scale studies are highly needed.
Clin. Infect. Dis. 30MAY2020	**Maximum Daily Temperature, Precipitation, Ultra-Violet Light and Rates of Transmission of SARS-Cov-2 in the United States**	Shera T et al., USA gotopaper	Public Health/Epidemio	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.
Cell Reports 30MAY2020	**Structural and biochemical characterization of nsp12-nsp7-nsp8 core polymerase complex from SARS-CoV-2**	Peng, Qi et al. China gotopaper	Structural biology	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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Clin. Infect. Dis. 30MAY2020	**Surgical mask partition reduces the risk of non-contact transmission in a golden Syrian hamster model for Coronavirus Disease 2019 (COVID-19)**	Chan, Jasper Fuk-Woo *et al.* China gotopaper	Transmission - Animal model	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.**
J Med Virol 29MAY2020	**Serum KL-6 concentrations as a novel biomarker of severe COVID19**	d'Alessandro, Miriana et al. Italy gotopaper	Virology	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**. **Cl°: 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.
BMJ 29MAY2020	**Covid-19: the ethics of clinical research in quarantine**	Nicholas G Evans, USA gotopaper	SHS/Sciences Po	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).
Journal of Allergy and Clinical Immunology 29MAY2020	**Successful use of methylprednisolone for treating severe COVID-19**	Liu, Jing et al. China gotopaper	Therapeutic	**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. -> **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. -> Single-dose pulse methylprednisolone (40-500mg methylprednisolone) had **no apparent negative impact on SARS-CoV-2 removal and production of specific IgG**.

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Nature Communications 29MAY2020	**Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients**	Chia, PY et al., Singapore gotopaper	Public Health/Epidemio	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 ward detected SARS-CoV-2 PCR-positive particles of sizes >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.
Science 29MAY2020	**Introductions and early spread of SARS-CoV-2 in the New York City area**	Gonzalez-Reiche et al, USA gotopaper	Public Health/Epidemio	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.
Science Advances 29MAY2020	**Emergence of SARS-CoV-2 through recombination and strong purifying selection**	Li, Xiaojun *et al.* USA - China gotopaper	Phylogenetic	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. **Note:** 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. **-> 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.**
Lancet 29MAY2020	**Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study**	COVIDSurg Collaborative UK gotopaper	Clinic	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%** **Pulmonary complications= 51,2% with 38% of mortality** Association with mortality (adjusted analysis): - Male sex OR: 1,75 [1,28 – 2,40] - > 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] → pulmonary complication in more than half of patients with perioperative SARS-CoV-2 infection → **postponing non urgent procedure and promoting non operative treatment**

Journal and date	Title	Authors and link	Field of expertise	Key facts
The Journal of clinical investigation 28MAY2020	**Impaired immune cell cytotoxicity in severe COVID-19 is IL-6 dependent**	Mazzoni, Alessio et a, Italy gotopaper	Immuno	**Characterization of the immune response in SARS-CoV-2 infected patients hospitalized at the Careggi University Hospital, Florence, Italy** • 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.
Natl Sci Rev 28MAY2020	**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	**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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Lancet HIV 28MAY2020	**Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort**	Vizcarra P et al Spain gotopaper	Clinic	Observational & prospective study: 51 HIV-infected COVID-19+ & 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 comorbity 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
Lancet 28MAY2020	**Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study**	Kuderer NM et al USA gotopaper	Clinic	Cohort study from the USA, Canada & Spain from the COVID-19 & cancer consortium (CCC19) Patients with active or previous malignancy & 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**
The Lancet ID 28MAY2020	**Implication of SARS-CoV-2 evolution in the sensitivity of RT-qPCR diagnostic assays**	Sampaio Osorio and Correia-Neves, Portugal gotopaper	Diagnostic	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.

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BMJ 28MAY2020	**Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study**	Toubiana J et al France gotopaper	Clinic	**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 (>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 & results of test for SARS-CoV-2 in children with Kawasaki-like disease suggest a causal link → **further study is needed**
BMJ 27MAY2020	**Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study**	Knight M et al UK gotopaper	Clinic	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 & 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**

REACTing research & action targeting emerging infectious diseases

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Gene Reports 2020	**COVID-19 target: A specific target for novel coronavirus detection**	Kakhki, Reza Kamali et al. Iran gotopaper	Diagnostic	**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
Critical care medicine 27MAY2020	**Routine Venous Thromboembolism Prophylaxis May Be Inadequate in the Hypercoagulable State of Severe Coronavirus Disease 2019**	Maatman, Thomas K. et al.USA gotopaper	Therapeutic/ Clinic	**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 ($p < 0.05$). - 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; $p < 0.0001$), 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.
NEJM 27MAY2020	**Remdesivir for 5 or 10 Days in Patients with Severe Covid-19**	Jason D. Goldman et al. gotopaper	Therapeutic	**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. => **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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
SCIENCE 27MAY2020	**Reducing transmission of SARS-CoV-2**	Prather et al., USA-China gotopaper	Public Health/Epidemio	**PERSPECTIVE** - 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 infected individuals with no symptoms.** **-> It is essential that control measures be introduced to reduce aerosol transmission (face masks +++)**
Nature reviews Immunology 26MAY2020	**Dysregulation of type I interferon responses in COVID-19**	Dhiraj Acharya et al, USA gotopaper	Immuno	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 cells10. 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 gotopaper	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 gotopaper	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?
The Lancet 25MAY2020	**Assistance Publique–Hôpitaux de Paris' response to the COVID-19 pandemic**	The COVID19-APHP Group, France gotopaper	Public Health/Epidemio	**Key points of an effective AP-HP response to the Covid-19 crisis:** - 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 porposed (69 countries, 50 US states and 30 Chinese provinces; 85% of global population; 87% of global emissions) **Results** > Estimated decrease in daily fossil CO2 emissions from the severe and forced confinement of world populations: –17% (–11 to –25%) > Annual associated decrease: –4.2 to –7.5% (rates needed over the next decades to limit climate change to 1.5 °C warming) > However observed changes are likely to be temporary as they do not reflect structural changes in the economic, transport or energy systems.
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. Cl°: a CRISPR-based fluorescent application has potential to improve current COVID-19 screening efforts.
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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Circulation 22MAY2020	**Cardiovascular Toxicities Associated with Hydroxychloroquine and Azithromycin: An Analysis of the World Health Organization Pharmacovigilance Database**	Nguyen, Lee S. et al. France/USA gotopaper	Therapeutic	**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<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.
Annals of Translational Medicine MAY2020	**Preliminary study to identify severe from moderate cases of COVID-19 using combined hematology parameters**	Wang, Changzheng et al. China gotopaper	Diagnostic	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. Cl°: **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

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Gastroenterology 22MAY2020	**Famotidine Use is Associated with Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study**	Freedberg, Daniel E. et al. USA gotopaper	Therapeutic	**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. **Primary outcome** was a composite of death or endotracheal intubatio n. 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. **Limitations**: observational; no samples were gathered, and mechanism cannot be directly assessed; single center study.
Clinical infectious diseases 22MAY2020	**Association of renin-angiotensin-aldosterone system inhibitors with COVID-19-related outcomes in Korea: a nationwide population-based cohort study**	Jung, Sun-Young et al. Korea gotopaper	Therapeutic/ Clinic	**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. **Limitations**: accuracy of diagnostic codes may be limited; retrospective observational design.
Clinical infectious diseases 22MAY2020	**Thymosin alpha 1 (Talpha1) reduces the mortality of severe COVID-19 by restoration of lymphocytopenia and reversion of exhausted T cells**	Liu, Yueping et al. China gotopaper	Therapeutic	**Retrospective cohort study** to evaluate the clinical outcomes of **severe or critical** COVID 19 hospitalized patients receiving **Thymosin alpha 1** (Tα1) supplement. A total of **76 patients** were enrolled (36 in the treatment group and 40 in the non treatment group) Compared with untreated group, **Tα1 treatment significantly reduces mortality** of severe COVID-19 patients (11% vs. 30%, p=0.044). **Tα1 timely enhances blood T cell numbers** in COVID-19 patients with **severe lymphocytopenia**. Under such conditions, Tα1 also successfully **restores CD8+ and CD4+ T cell numbers in aged patients**. Meanwhile, Tα1 **reduces PD-1 and Tim-3 expression on CD8+ T cells** from severe COVID-19 patients in comparison with untreated cases. **Limitations**: issue with the normalization of TREC levels among individuals; retrospective study and small sample size; mortality as primary clinical outcome and not clinical improvement.

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 22MAY2020	**Remdesivir for the Treatment of Covid-19 — Preliminary Report**	Beigel, John H. et al. , USA gotopaper	Therapeutic	**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. Awaiting final visits, data entry, monitoring, and data lock for the last of the 1063 patients enrolled, to provide an update of the results.
The Lancet 22MAY2020	**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	**RETRACTED**
mBio 22MAY2020	**Antiviral Efficacies of FDA-Approved Drugs against SARS-CoV-2 Infection in Ferrets**	Park, Su-Jin et al. Korea gotopaper	Therapeutic	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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
BMJ 22MAY2020	**Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study**	Petrilli CM, et al., USA gotopaper	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 age 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, gotopaper	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 evaluted (because of low number of particiapnts) > 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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Neurology 22MAY2020	**Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy**	Benussi A et al Italy gotopaper	Clinic	Outcomes of patients admitted with neurological disorders with and without COVID-19 173 patients included: **56 COVID-19 pos & 117 COVID-19 neg** No difference for comorbitities 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*<0,001) -Wider use of high flow oxygenation: 76,8% versus 9,4% (*p*<0,001) -Prolonged length of stay Potential risk factor of poor prognosis: high qSOFA score – thrombocytopenia – increase lactate deshydrogenase level
Clinical infectious diseases 22MAY2020	**Predicting infectious SARS-CoV-2 from diagnostic samples**	Bullard, Jared and al. Canada gotopaper	Diagnostic	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. => SARS-CoV-2 Vero cell infectivity was only observed for RT-PCR Ct < 24 and STT < 8 days. Infectivity of patients with Ct >24 and duration of symptoms >8 days may be low. Cl°: this information can inform public health policy and guide clinical, infection control and occupational health decisions.However, further studies of larger size are needed.
Analytical chemistry 22MAY2020	**A novel one-step single-tube nested quantitative Real-Time PCR assay for highly sensitive detection of SARS-CoV-2**	Wang, Ji and al. China gotopaper	Diagnostic	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). Cl° : 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.
New England Journal of Medicine 21MAY2020	**Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19**	Ackermann, Maximilian, *et al.* Germany-Belgium-UK-USA gotopaper	Clinic	Lungs (autopsy) form patients: 7 who died from Covid-19 vs 7 who died from acute respiratory distress syndrome secondary to influenza A (H1N1) infection vs 10 age-matched, uninfected control lungs. Common to both Covid-19 and influenza-associated respiratory failure : - diffuse alveolar damage with perivascular T-cell infiltration **In Covid-19 patients :** **- severe endothelial injury** (associated to intracellular virus and disrupted cell membranes) **- widespread thrombosis with microangiopathy** **- capillary microthrombi 9x more prevalent** compared to influenza patients **- new vessel growth 2.7x** higher than in lungs from influenza patients **-> Vascular angiogenesis distinguished pulmonary pathobiology of Covid-19 from that of equally severe influenza virus infection**

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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.** - **Predominant histopathologic findings: acute and organizing diffuse alveolar damage and SARS-CoV-2 persistence in the respiratory tract, constituting the leading cause of death in patients with and without invasive ventilation.** - Periportal liver lymphocyte infiltration considered unspecific inflammation. - Whether myoepicardial alterations represented systemic inflammation or early myocarditis is unclear (criteria for true myocarditis not met). - **Central nervous system involvement by COVID-19 could not be detected** Limitations: small number of cases from a single center and missing proof of direct viral organ infection
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 t**his 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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Nature 20MAY2020	**Viral and host factors related to the clinical outcome of COVID-19**	Zhang, Xiaonan, *et al.* China gotopaper	Clinic	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.**
Eur. Respir. J. MAY2020	**A Fully Automatic Deep Learning System for COVID-19 Diagnostic and Prognostic Analysis**	Wang et al., China gotopaper	Diagnostic	**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**
Science 20MAY2020	**SARS-CoV-2 infection protects against rechallenge in rhesus macaques**	Chandrashekar A et al. USA gotopaper	Vaccine	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 naïve 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 naïve animals > All animals developed anamnestic antibody responses following re-challenge→ protection mediated by immunologic control
Cell 20MAY2020	**Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals**	Grifoni et al., USA gotopaper	Immuno	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

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The Lancet Infectious Diseases 20MAY2020	**Individual quarantine versus active monitoring of contacts for the mitigation of COVID-19: a modelling study**	Peak, C. et al, USA gotopaper	Public Health/Epidemio	**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 20MAY2020	**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 20MAY2020	**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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NEJM 19MAY2020	**Respecting disability rights – towards improved crisis standards of care**	Mello M. et al, US gotopaper	HSS/Politic	Policymakers and hospitals can take key steps to honor commitments to antidiscrimination principles while appropriately stewarding scarce resources during a public health emergency. **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. **2- Do not use perceived quality of life** = biases in how the public/physicians evaluate the quality of life of persons with disabilities. **3- Use hospital survival and near-term prognosis but not long-term life expectancy**. Predictions of long-term life expectancy are much more uncertain + 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. **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.
Clinical Infectious Diseases 19MAY2020	**Early Short Course Corticosteroids in Hospitalized Patients with COVID-19**	Fadel, Raef et al. USA gotopaper	Therapeutic	**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. - 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. - Significant reduction in median hospital length of stay was also observed in the early corticosteroid group (8 vs. 5 days, p < 0.001). - 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]). Conclusion: **An early short course of methylprednisolone in patients with moderate to severe COVID-19 reduced escalation of care and improved clinical outcomes**. **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.

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J Infect Dis 19MAY2020	**Influence of storage conditions on SARS-CoV-2 nucleic acid detection in throat swabs**	Li, Lin and al. China gotopaper	Virology	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.
Lancet 19MAY2020	**Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study**	Cummings MJ et al USA gotopaper	Clinic	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 & in hospital mortality**
Nature Medicine 19MAY2020	**Artificial intelligence–enabled rapid diagnosis of patients with COVID-19**	Mei et al., USA gotopaper	Diagnostic	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.**

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Circulation 19MAY2020	**Deep Vein Thrombosis in Hospitalized Patients with Coronavirus Disease 2019 (COVID-19) in Wuhan, China: Prevalence, Risk Factors, and Outcome**	Zang L et al, China gotopaper	Clinic	Investigation of deep vein thrombosis (DVT) in hospitalized patient with COVID-19 143 patients from Jan 29 and Feb 29 Demographic: 51,7% man – median age= 63 46,1% (66) lower extremity DVT= 23 proximal DVT and 43 distal DVT DVT vs no DVT: - Older - Lower oxygenation index - Higher rate of cardiac injury - Increase death (23 vs 9, p=0,001) Multivariate analysis, DVT associated with - CURB-65 score3-5, OR:6,12 - Padua prediction ≥ 4, OR: 4,01 - D-dimer>1µg/ml OR :5,81 Predicting DVT **CURB-65 score3-5, Padua prediction score ≥ 4 + D-dimer>1 had Se 88% and Spe 61,4%** → prevalence of DVT is high → importance of prophylaxis for venous thromboembolism (Padua prediction score ≥ 4)
Science 18MAY2020	**Susceptible supply limits the role of climate in the early SARS-CoV-2 pandemic**	Baker, Rachel E. et al. USA gotopaper	Climate	Climate-dependent model to simulate SARS-CoV-2 pandemic, probing different scenarios based on known coronavirus biology. Results suggest: • **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.**
Cell 18MAY2020	**Potent neutralizing antibodies against SARS-CoV-2 identified by high-throughput single-cell sequencing of convalescent patients' B cells**	Yunlong Cao et al., Chine, gotopaper	Immunology	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. => among of which,14 potent neutralizing mAbs were identified => 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. => 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 Conclusion: The potent neutralizing antibodies we identified may provide an effective therapeutic and prophylactic solution Limitation: 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.
Ann. Intern. Med. 18MAY2020	**Tocilizumab for Hemophagocytic Syndrome in a Kidney Transplant Recipient With COVID-19**	Faguer, Stanislas et al. France, gotopaper	Therapeutic	**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.

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The Lancet Diabetes & Endocrinology 18MAY2020	**Prevalence of obesity among adult inpatients with COVID-19 in France**	Caussy, Cyrielle et al. France gotopaper	Population studies	**Lyon University Hospital admissions** with BMI values: 340 patients with confirmed severe COVID-19 (68% non-critical and 32% critical COVID-19 patients) vs 1210 retrospective non-COVID-19 ICU patients admitted each year between 2007 - 2019. Results : - 25% of severe COVID-19 patients had obesity, vs 15·3% in French adult population in 2014. **-> Obesity prevalence 1·35 times higher in severe COVID-19 patients vs general French population.** **-> In ICU, obesity prevalence 1.89 times higher vs general population.** **-> Obesity prevalence higher in critical vs non-critical COVID-19 patients.** In agreement with preliminary data from 124 patients with critical COVID-19 and 306 ICU patients without COVID-19 from **Lille University Hospital (Simonnet A *et al.* 2020)** : **-> obesity prevalence 2·88 times higher in critical COVID-19 vs French general population** **-> Obesity prevalence higher in critical COVID-19 vs Lille ICU patients without COVID-19 (n=306).** **=> Report significant association in obesity prevalence and severe COVID-19, including critical COVID-19, and suggests obesity => risk factor of pejorative evolution of COVID-19, increasing risk of ICU admission.**
Circulation 17MAY2020	**Acute heart failure in multisystem inflammatory syndrome in children (MIS-C) in the context of global SARS-CoV-2 pandemic**	Belhadjer S et al, France gotopaper	Clinic	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 < 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**
The Journal of Antimicrobial Chemotherapy 17MAY2020	**COVID-19 infection also occurs in patients taking hydroxychloroquine**	Lahouati, M et al. France gotopaper	Therapeutic	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.

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Water research 16MAY2020	**SARS-CoV-2 RNA in wastewater anticipated COVID-19 occurrence in a low prevalence area**	Randazzo et al, Spain gotopaper	Public Health/Epidemio	**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). -> The estimated quantification of SARS-CoV-2 RNA titers in untreated wastewater waters of 5.4 ± 0.2 log10 genomic copies/L on average. -> 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.**
Developmental Cell 16MAY2020	**Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract**	Smith, Joan C. *et al.* USA gotopaper	Fundamental research	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. -> May partially explain why smokers are particularly susceptible to severe SARS-CoV-2 infections **-> identifies ACE2 as interferon-stimulated gene in lung cells -> possible positive-feedback loops increasing ACE2 levels and facilitating viral dissemination.**
J. Clin. Virol. 16MAY 2020	**A combined oropharyngeal/nares swab is a suitable alternative to nasopharyngeal swabs for the detection of SARS-CoV-2**	LeBlanc, Jason J. and al., Canada gotopaper	Diagnostic	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.
The Lancet Infectious Diseases 15MAY2020	**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**	Lusignan, Simon de et al. UK-South Africa gotopaper	Clinic	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) -> +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. -> Provides evidence of potential sociodemographic factors associated with a +ve test : deprivation, population density, ethnicity and chronic kidney disease.

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Journal and date	Title	Authors and link	Field of expertise	Key facts
Gastroenterology 15MAY2020	**Associations between Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blocker Use, Gastrointestinal Symptoms, and Mortality among Patients with COVID-19**	Tan, Nian-Di et al. China gotopaper	Therapeutic/ Clinic	**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.
Science 15MAY2020	**Serology assays to manage COVID-19**	Krammer F., Simon V., USA gotopaper	Public Health/Epidemiol	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.**
Clinical microbiology and infection 15MAY2020	**A multiple center clinical evaluation of an ultra-fast single-tube assay for SARS-CoV-2 RNA**	Wang, Ji and al. China gotopaper	Diagnostic	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 15minutes 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. Cl°: 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.
Science 15MAY2020	**Inferring change points in the spread of COVID-19 reveals the effectiveness of interventions**	Dehning et al., Germany gotopaper	PublicHealth/Epidemio	**By combining an established epidemiological model with Bayesian inference -> 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 -> 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.
Nature 14MAY2020	**Proteomics of SARS-CoV-2-infected host cells reveals therapy targets**	Bojkova, Denisa et al. Germany gotopaper	Therapeutic	**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**.

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Lancet 14MAY2020	**Use of renin–angiotensin–aldosterone system inhibitors and risk of COVID-19 requiring admission to hospital: a case-population study**	Abajo, Francisco J. De, et al. Spain gotopaper	Therapeutic/ Clinic	**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. **1139 cases** and **11 390 population controls**. 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. **Limitations**: 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.
BMJ 14MAY2020	**Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial**	Tang, Wei et al. China gotopaper	Therapeutic	**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**. **Limitations**: 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.
American journal of obstetrics and gynecology 14MAY2020	**Clinical Characteristics of 46 Pregnant Women with a SARS-CoV-2 Infection in Washington State**	Lokken EM et al, USA gotopaper	Clinic	Description of maternal disease and obstetrical outcomes – 6 hospital in Washington state **46 pregnant women** Demographic: median age: 29y – 6,5% in first & 43,4% second & 50% in third trimester 26,1% had at least one comorbidity: asthma – hypertension – diabetes - …. **28,6% were overweight and 35,7% obese** Symptoms: 93,5% had one – cought (70%) – fever (51%) – dyspnea – headache …. Outcomes: - 15% categorized has severe disease: overweight/obese/comorbidity - 16% hospitalized & 1 to ICU (all severe disease) - 8 delivered during the study period (median: 38,4 week) - 1 stillbirth: unknown etiology **→ higher risk group: chronic comorbidity / obese / overweight**

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Clinica Chimica Acta 14MAY2020	**The underlying changes and predicting role of peripheral blood inflammatory cells in severe COVID-19 patients: a sentinel?**	Sun, Da-wei and al. China gotopaper	Virology	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. This retrospective study includes two cohorts: the main cohort enrolling 45 patients of severe type serving as study group, and the secondary cohort enrolling 12 patients of no-severe type serving as control group. The PBICs analysis was based on blood routine and lymphocyte subsets. The inflammatory cell levels were compared among patients according to clinical classifications, disease-associated phases, as well as one-month outcomes. Results: the patients of severe type suffered from significantly decreased counts of lymphocytes, eosinophils, basophils, but increased counts of neutrophils. These PBICs alterations got improved in recovery phase, but persisted or got worse in aggravated phase. CI°: lymphopenia and eosinopenia may serve as predictors of disease severity and disease progression in COVID-19 patients, and enhancing the cellular immunity may contribute to COVID-19 treatment. Thus, PBICs might become a sentinel of COVID-19, and it deserves attention during COVID-19 treatment
Journal of Allergy and Clinical Immunology 14MAY2020	**Complement activation in patients with COVID-19: a novel therapeutic target**	Cugno, Massimo et al. Italy gotopaper	Therapeutic	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. - **Plasma levels of sC5b-9** were **significantly higher** in the patients with moderate disease and those with severe disease **than in the 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 **than in the healthy** (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**. 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.
BMJ 14MAY2020	**Clinical efficacy of hydroxychloroquine in patients with covid-19 pneumonia who require oxygen: observational comparative study using routine care data**	Mahévas, Matthieu et al. France gotopaper	Therapeutic	**Comparative study** that uses **real world data** collected from routine care to assess the **efficacy and safety of hydroxychloroquine** in a population of **181 patients** admitted to hospital with covid-19 hypoxaemic pneumonia. - Hydroxychloroquine treatment at 600 mg/day added to standard care was **not associated with a reduction of admissions to the intensive care unit or death** 21 days after hospital admission compared with standard care alone. - The **rate of survival without acute respiratory distress syndrome did not increase**. - Eight patients in the treatment group (10%) experienced **electrocardiographic modifications that required discontinuation of treatment**. 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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Clinical Infectious Disease 14MAY2020	**Risk Factors of Severe Disease and Efficacy of Treatment in Patients Infected with COVID-19: A Systematic Review, Meta-Analysis and Meta-Regression Analysis**	Zhang, John J. Y et al. Singapore gotopaper	Therapeutic/ Clinic	**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<0.0001), **raised alanine aminotransferase** (p=0.024), **raised aspartate transaminase** (p=0.0040), **elevated lactate dehydrogenase** (LDH) (p<0.0001) and **increased procalcitonin** (p<0.0001). - **ARDS** was **predicted by elevated LDH** (p<0.0001), while **mortality** was **predicted by raised leukocyte count** (p=0.0005) and **elevated LDH** (p<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=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.
Nature 14MAY2020	**Infection of dogs with SARS-CoV-2**	Sit, Thomas H. C Hong Kong gotopaper	Fundamental research	**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 2.5yr-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.** **-> 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.
Nature 14MAY2020	**Pathogenesis and transmission of SARS-CoV-2 in golden hamsters**	Sia, Sin Fun et al. Hong Kong gotopaper	Animal model	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. -> **Efficient SARS-CoV-2 transmission from inoculated hamsters to naïve by direct contact and via aerosols**. Transmission via fomites less efficient. **-> Communicable period was short and correlated with detection of infectious virus but not viral RNA.** **-> Inoculated and naturally-infected hamsters showed apparent weight loss, and all animals recovered with detection of neutralizing antibodies.**
Proc. Natl. Acad. Sci. U. S. A. 13MAY2020	**The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission**	Stadnytskyi et al. USA gotopaper	Public Health/Epidemio	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. -> 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**.

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Science 13MAY2020	**Estimating the burden of SARS-CoV-2 in France**	Salje et al., France gotopaper	Public Health/Epidemio	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 <20 years of age (ya), 10.1% in >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
Ann. Intern. Med. 13MAY2020	**Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure**	Kucirka, Lauren M. and al. USA gotopaper	Virology	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. Cl°: 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.
N. Engl. J. Med. 13MAY2020	**Multiorgan and Renal Tropism of SARS-CoV-2**	Puelles, Victor G. et al Germany gotopaper	Cellular tropism	**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**. **-> 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**
The Journal of Molecular Diagnostics 13MAY2020	**Detection of SARS-CoV-2 is comparable in clinical samples preserved in saline or viral transport media**	Radbel, Jared and al. USA gotopaper	Virology	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. Cl°: 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

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Lancet 13MAY2020	**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 13MAY2020	**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 13MAY2020	**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 new-borns 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.**
Annals of Internal Medicine 12MAY2020	**Pharmacokinetics of Lopinavir and Ritonavir in Patients Hospitalized With Coronavirus Disease 2019 (COVID-19)**	Schoergenhofer, Christian et al. Austria gotopaper	Therapeutic	**First pharmacokinetic data of lopinavir and ritonavir** in patients **hospitalized** with COVID-19. Series of 8 patients. - 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 ($3x10^8$ 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** 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 $IC_{95\%}$ [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	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	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	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
Nature Medicine 11MAY2020	**Real-time tracking of self-reported symptoms to predict potential COVID-19**	Menni et al, UK gotopaper	Public Health/Epidemio	A total of 2,618,862 participants reported their potential symptoms of COVID-19 on a smartphone-based app. -> 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 cormorbidities: hypertension (29,7%) –diabetes (14,5%) – CHD(9%) Case fatality rate 9,2% <u>Death versus survivor group</u> - Older and more often male (p<0,001) - More comorbidities (p<0,001) - More myocardial injury: 75,8% vs 9,7% (p<0,001) <u>Cardiac troponin I predicting in-hospital mortality:</u> - AUC 0,92 - Se 86% and Spe 86% - Single cut-off concentrations 73 µg/L <u>Predictor of myocardial injury:</u> - 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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JAMA ped 11MAY2020	**Characteristics and Outcomes of Children with Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units**	Shekerdemian LS and al, USA gotopaper	Clinic	46 PICU (March 14 and April 3) → 48 children (40 in US & 6 in Canada) Median age: 13 years [4,2 – 16,6] Comorbidities (83%) Median PICU lenght 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+azythro 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 fo SARS-Cov and MERS-Cov). **Cl°:** results show prolonged persistence of SARS-CoV-2 RNA in hospitalized patients with COVID-19. Health professionals should consider these findings in diagnostic recommendations and prevention measures for COVID-19.
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 Bronchoalveloar-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 assignement (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/Epidemio	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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JAMA 08MAY2020	**Changes in SARS-CoV-2 Positivity Rate in Outpatients in Seattle and Washington State, March 1-April 16, 2020**	Randhawa et al, USA gotopaper	Public Health/Epidemio	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. -> This trajectory is aligned with local physical distancing and the "Stay Home, Stay Healthy" order announced March 23, 2020.
Nature structural & molecular biology 07MAY2020	**Structural basis for the inhibition of SARS-CoV-2 main protease by antineoplastic drug carmofur**	Jin, Zhenming et al. China gotopaper	Therapeutic	The antineoplastic drug **carmofur is shown to inhibit the SARS-CoV-2 main protease (M^{pro})**.Tthe 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**.
The Lancet Rheumatology 07MAY2020	**Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study**	Cavalli, Giulio et al. Italy gotopaper	Therapeutic	**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.
Journal of Clinical Virology 07MAY2020	**SARS-CoV-2 detection by direct rRT-PCR without RNA extraction**	Merindol, Natacha, and al. gotopaper	Diagnostic	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. ->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.

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JAMA 07MAY2020	**Necessity of a development and widespread distribution of COVID-19 medical treatments**	Bollyky, T. et al, US gotopaper	HSS/Politic	1- Equitable Distribution Plan for manufacturing capacity, financing, and distribution infrastructure necessary to produce sufficient quantities to meet global needs in a fair, public health–driven manner. 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.
The Lancet. Respiratory medicine 07MAY2020	**Tropism, replication competence, and innate immune responses of the coronavirus SARS-CoV-2 in human respiratory tract and conjunctiva: an analysis in ex-vivo and in-vitro cultures**	Hui, Kenrie P. Y.; et al. China gotopaper	Fundamental research	SARS-CoV-2 tissue and cellular tropism in ex-vivo cultures of human bronchus, lung, conjunctiva, and innate immune responses vs other coronavirus and influenza virus (H1N1). 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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Infect. Control Hosp. Epidemiol. MAY2020	**Effect of ambient air pollutants and meteorological variables on COVID-19 incidence**	Jiang et al, China gotopaper	Public Health/Epidemiology	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 raged from 0.915 (95% CL, 0.896 - 0.934) to 0.961 (95% CL, 0.95 - 0.972) while that of temperature was 0.738 (95% CL, 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.
Nature 07MAY2020	**The pathogenicity of SARS-CoV-2 in hACE2 transgenic mice**	Bao, Linlin; et al. China gotopaper	Animal model	**Human ACE2 transgenic mice infected with SARS-CoV-2** : - SARS-CoV-2 intranasal inoculation at 10^5 $TCID_{50}$/50 µL inoculum volume per mouse. (14 days observation) - 6-11 month-old, male and female WT (n=15) 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 titers at 3 dpi), but not WT mice. - **Viral antigens detected** in bronchial epithelial cells, macrophages and alveolar epithelia. **-> Confirmed pathogenicity of SARS-CoV-2 in hACE2 expressing mice and suggests that hACE2 was essential for infection and replication in mice.**
The Journal of Infectious Diseases 07MAY2020	**T cell subset counts in peripheral blood can be used as discriminatory biomarkers for diagnosis and severity prediction of COVID-19**	Jiang, Mei and al. China gotopaper	Diagnostic	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.
The Lancet Psychatry 07MAY2020	**COVID-19, unemployment, and suicide**	*Kawohl* And Nordt., Switzerland gotopaper	Psy	**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.
New England Journal of Medicine 07MAY2020	**Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19**	Geleris, Joshua et al. USA gotopaper	Therapeutic	**Observational study** involving consecutive patients with Covid-19 admitted to a hospital, and **comparaing 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.

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Nat Rev Immunology 06MAY2020	**Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages**	Merad et al., USA gotopaper	Immuno	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. **Conclusion:** 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
Antimicrobial agents and chemotherapy 06MAY2020	**Inhibition of SARS-CoV-2 infection by the cyclophilin inhibitor Alisporivir (Debio 025)**	Softic, Lauren et al. France, gotopaper	Therapeutic	Cyclophilins play a key role in the lifecycle of coronaviruses. **Alisporivir (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. => 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**. => Anti-SARS-CoV-2 effectiveness of alisporivir was confirmed by immunofluorescence. => 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**.
Journal of the American College of Cardiology 06MAY2020	**Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19**	Paranjpe, Ishan et al. USA gotopaper	Therapeutic	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. => **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. => **Association with AC and improved survival after adjusting for mechanical ventilation**. **Limitations**: observational study, unobserved confounding, unknown indication for AC, lack of metrics to further classify illness severity in the mechanically ventilated subgroup, and indication bias.

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BMC 06MAY2020	**A single-center, retrospective study of COVID-19 features in children: a descriptive investigation**	Ma H, and al China gotopaper	Clinic	50 children COVID19+ and 26 with PCR- and CT+ with history of exposure Symptoms: - More frequent: fever (64%) – cought (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-propiolactione 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-2strains 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 S 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 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 <u>Symptoms in both groups</u>: fever – cough – dyspnea – diarrhea/vomiting <u>Laboratory:</u> -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 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 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).
Cell 05MAY2020	**Structural Basis for Potent Neutralization of Betacoronaviruses by Single-domain Camelid Antibodies**	DanielWrapp and al, https://doi.org/10.1016/j.cell.2020.04.031	Therapeutic	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.

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Nature Communications 04MAY2020	**A human monoclonal antibody blocking SARS-CoV-2 infection**	Wang, Chunyan et al, https://www.nature.com/articles/s41467-020-16256-y	Therapeutic	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.
Intensive Care Med 04MAY2020	**High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study**	Helms J, and al France https://doi.org/10.1007/s00134-020-06062-x	Clinic	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: >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*<0,008) Thrombotic complications despite prophylactic or therapeutic anticoagulation → large number of patients still intubated → under-estimated → monitoring anticoagulant treatment/ higher targets than usual?
Nature 04MAY2020	**Effect of non-pharmaceutical interventions to contain COVID-19 in China**	Lai, Shengjie et al, https://www.nature.com/articles/s41586-020-2293-x	Public Health/Epidemio	**Modelling framework that uses daily travel networks to simulate different outbreak and intervention scenarios across China**, using epidemiological and anonymised human movement data. -> Total of 114,325 COVID-19 cases (interquartile range 76,776 - 164,576) estimated in mainland China as of February 29, 2020. -> 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. -> 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. -> 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.
Cell host & microbe 04MAY2020	**Heightened innate immune responses in the respiratory tract of COVID-19 patients**	Zhou, Zhuo; et al. China https://doi.org/10.1016/j.chom.2020.04.017	Immunology	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 immune cell populations, show increased activated dendritic cells and neutrophils.**
Science 04MAY2020	**Site-specific glycan analysis of the SARS-CoV-2 spike**	Watanabe, Yasunori, et al. UK - USA https://doi.org/10.1126/science.abb9983	Structural biology	**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. **-> 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 .**

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Nature 04MAY2020	**Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform**	Thao, Tran Thi Nhu, et al. Switzerland - Germany - Russia https://www.nature.com/articles/s41586-020-2294-9	Fundamental research	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.**
Autoimmunity reviews 03MAY2020	**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**	Toniati, Paola et al, Italy https://doi.org/10.1016/j.autrev.2020.102568	Therapeutic	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 administred 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.
Immunity 03MAY2020	**Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals**	Ling et al., China https://www.sciencedirect.com/science/article/pii/S1074761320301813	Diagnostic	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.
American journal of obstetrics and gynecology 03MAY2020	**Evidence for and against vertical transmission for SARS-CoV-2 (COVID-19)**	A, Amouroux; et al. France http://www.sciencedirect.com/science/article/pii/S000293782030524X	Clinic	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.

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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.ijid.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 ina Large Cohort of Infected Patients From New York: Clinical Implications**	Kaveh H and al USA https://doi.org/10.1053/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**
JAMA Cardiology 01MAY2020	**Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19)**	Mercuro, Nicholas J. Et al, USA https://jamanetwork.com/journals/jamacardiology/fullarticle/2765631	Therapeutic	**Cohort study of hospitalized patients** with coronavirus disease 2019. 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	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.**
New England Journal of Medicine 01MAY2020	**Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19**	Mehra M, and al USA https://doi.org/10.1056/NEJMoa2007621	Clinic	**RETRACTED**

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New England Journal of Medicine 01MAY2020	**Early Detection of Covid-19 through a Citywide Pandemic Surveillance Platform**	Chu, Helen Y. and al. USA https://www.nejm.org/doi/full/10.1056/NEJMc2008646	Public Health/Epidemio	The Seattle Flu Study is a multi-institutional, community-wide pandemic surveillance platform that was established in November 2018. -> 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. **Conclusion:** widespread implementation of simple methods that are scalable and require minimal interaction for collection of samples from persons who may not seek clinical care is critical for early detection of community cases. An ubiquitous, community-based sampling for respiratory illnesses appears as an essential infrastructure for early detection and mitigation of future pandemics
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	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. **Conclusion:** the assays developed here can screen medical staff, in-coming patients, passengers and people who are in close contact with the confirmed patients to identify the "innocent viral spreaders", protect the medical staff and stop the further spreading of the virus.
J. Clin. Virol. 01MAY2020	**A RT-PCR Assay for the Detection of Coronaviruses from Four Genera**	Xiu, Leshan and al. China https://www.sciencedirect.com/science/article/pii/S1386653220301335	Diagnostic	A better understanding of the natural hosts and genetic diversity of CoVs are needed to help mitigate these threats. Objective: to design and evaluate a molecular diagnostic tool for detection and identification of all currently recognized and potentially future emergent CoVs from the Orthocoronavirinae subfamily. **Conclusion:** a semi-nested, reverse transcription RT-PCR assay capable of detecting and identifying all previously recognized CoVs, including SARS-CoV-2, and potentially any emergent CoVs in this subfamily.
Science 01MAY2020	**SARS-CoV-2 productively infects human gut enterocytes**	Lamers, Mart M.; et al. Netherlands 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 (confocal- 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.**

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Emerging Microbes & Infections 01MAY2020	**Kinetics of SARS-CoV-2 specific IgM and IgG responses in COVID-19 patients**	Sun et al., China https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1762515#	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.
Science 01MAY2020	**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 form (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 struture 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.**
Gastroenterology 01MAY2020	**Taste Changes (Dysgeusia) in COVID-19: A systematic review and metaanalysis**	Aziz, Muhammad; et al. USA https://doi.org/10.1053/j.gastro.2020.05.003	Clinic	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 = 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.**
New England Journal of Medicine 01MAY2020	**Renin–Angiotensin–Aldosterone System Inhibitors and Risk of Covid-19**	Reynolds H, and al USA https://doi.org/10.1056/NEJMoa2008975	Clinic	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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NEJM 01MAY2020	**Inhibitors of the Renin–Angiotensin–Aldosterone System and Covid-19**	Jarcho, John A.; et al. USA https://doi.org/10.1056/NEJMe2012924 Mehra MR, et al. USA https://doi.org/10.1056/NEJMoa2007621 Mancia, Giuseppe; et al. Italy https://doi.org/10.1056/NEJMoa2006923 Reynolds HR, et al. USA https://doi.org/10.1056/NEJMoa2008975	Clinic	Analysis of 3 *N Engl J Med*articles, as clincians weigh alleged harm of continuing RAAS inhibitor medications (like ACE inhibitors and angiotensin-receptor blockers (ARBs)) often prescribed to patient with hypertension, diabetes, and coronary artery disease (high risk groups for severe COVID-19): - 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.** - 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.** - Reynolds et al. electronic health records, 12,594 people in New York University -> 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.** **-> none of the 3 studies showed evidence of harm with continued use of ACE inhibitors and ARBs.**
JAMA Cardiology 30APR2020	**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**	Bessiere, Francis et al, France https://jamanetwork.com/journals/jamacardiology/fullarticle/2765633	Therapeutic	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. -> 30 patients (75%) required invasive mechanical ventilation and 25 (63%) received vasoactive drugs. -> 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. ⇒ 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. ⇒ 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). ⇒ The antiviral treatment ceased before completion for 7 patients (17.5%) following ECG abnormalities and in 10 (25%) for acute renal failure.
Nature 30APR2020	**A SARS-CoV-2 protein interaction map reveals targets for drug repurposing**	Gordon, David E et al, https://www.nature.com/articles/s41586-020-2286-9#Abs1	Therapeutic	**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) -> Identification of 332 high-confidence SARS-CoV-2-human protein-protein interactions (PPIs). -> 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). -> 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.

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Jama Psychiatry 30APR2020	**Mental Health in the Coronavirus Disease 2019 Emergency—The Italian Response**	De Girolamo et al., Italy https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2765557	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 https://doi.org/10.1016/S0140-6736(20)31024-2	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 https://doi.org/10.3390/v12050497	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 http://www.sciencedirect.com/science/article/pii/S0092867420304864	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 http://www.ncbi.nlm.nih.gov/pubmed/32349121	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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International journal of antimicrobial agents 29APR2020	**Global coronavirus disease 2019: what has daily cumulative index taught us?**	Lai C, and al China http://www.sciencedirect.com/science/article/pii/S092485792030159X	Public Health/Epidemio	Rapid increase of COVID19 cases in short time = insufficiency of healthcare system and negatively affect patient's outcome? **Daily cumulative index (DCI)** = cumulative cases/number of days between the first reported case and March 6. DCI significantly positively correlated with incidence (aRR:1,01 [1,00 – 1,02]) After adjustment of HCI or HAQI, DCI associated with mortality per 1,000,000 (aRR:1,02 [1,01 – 1,03]) 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
Science 29APR2020	**Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China**	Zhang J, and al China https://doi.org/10.1126/science.abb8001	Public Health/Epidemio	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 The model consider potential age differences in susceptibility to infection <u>Susceptibility to SARS-CoV-2 infection increase with age:</u> - 0-14 years: OR=0,34 [0,24 – 0,49] (compared to 15-64y) - > 65 years: OR=1,47 [1,12 – 1,92] (compared to 15-64y) <u>Model to study the impact of social distancing and school closures</u>: - 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.
PNAS 29APR2020	**Effective treatment of severe COVID-19 patients with tocilizumab**	Xu, Xiaoling et al, China https://doi.org/10.1073/pnas.2005615117	Therapeutic	**Retrospective study with tocilizumab**, an IL6R inhibitor, in treatment of 21 patients with severe and critical COVID-19. **Clinical data showed that the symptoms, hypoxygenmia, 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.
The Lancet 29APR2020	**Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial**	Wang et al., China https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31022-9/fulltext?utm_campaign=tlcoronavirus20&utm_source=twitter&utm_medium=social	Therapeutic	-> 237 patients were enrolled and randomly assigned to a treatment group (158 to remdesivir and 79 to placebo) -> Remdesivir use was not associated with a difference in time to clinical improvement (hazard ratio 1·23 [95% CI 0·87–1·75]) -> Although not statistically significant, patients receiving remdesivir had a numerically faster time to clinical improvement than those receiving placebo among patients with symptom duration of 10 days or less (hazard ratio 1·52 [0·95–2·43]) -> Adverse events were reported in 102 (66%) of 155 remdesivir recipients versus 50 (64%) of 78 placebo recipients. Remdesivir was stopped early because of adverse events in 18 (12%) patients versus four (5%) patients who stopped placebo early.

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J Infect Dis 29APR2020	**Effect of Convalescent Plasma Therapy on Viral Shedding and Survival in COVID-19 Patients**	Zeng, Qing-Lei et al, China https://doi.org/10.1093/infdis/jiaa228	Therapeutic	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.
Cancer discovery 28APR2020	**Patients with cancer appear more vulnerable to SARS-COV-2: a multi-center study during the COVID-19 outbreak**	Dai M, and al USA https://doi.org/10.1158/2159-8290.CD-20-0422	Clinic	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 Patient with cancer had higher: - **ICU admission** [OR:2,84 (1,59 – 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**
Critical Care 28APR2020	**Clinical determinants for fatality of 44,672 patients with COVID-19**	Deng G, and al China https://doi.org/10.1186/s13054-020-02902-w	Clinic *Letter*	Meta-analysis, confirmed cases series in China of 44672 patients Mortality rate all age → 2,3% CFR increase with age to 14,8 % in patients > 80 years Risk factors for fatality: - Male [RR:1,67 (1,47 – 1,89)] - Cardiovascular disease [RR:6,75 (5,4 – 8,43)] - HTA [HR:4,48 (3,69 – 5,85)] - Diabetes [RR:4,43 (3,49 – 5,61)] - Cancer [RR:2,92 (1,34 – 6,41)] - Respiratory disease [RR:3,43 (2,42 – 4,87)] **More intensive surveillance for male and those with comorbidities**
Natl Sci Rev 28APR2020	**Plasma Metabolomic and Lipidomic Alterations Associated with COVID-19**	Di Wu; Shu, et al. China https://doi.org/10.1093/nsr/nwaa086	Metabolite and lipid alterations	**Targeted metabolomic and lipidomic** analyses of plasma from cohort of COVID-19 patients **to identify plasma biomarkers associated with COVID-19:** - malic acid of the TCA cycle and carbamoyl phosphate of urea cycle **reveal altered energy metabolism and hepatic dysfunction**, respectively. **- carbamoyl phosphate profoundly down-regulated in fatal patients compared with mild patients**. **- guanosine monophosphate (GMP)** (mediated by GMP synthase, CD39 and CD73) **significantly altered between healthy subjects vs COVID-19 patients, and between the mild vs fatal groups**.
Public Health 28APR2020	**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**	Cobb J and al, USA http://www.sciencedirect.com/science/article/pii/S0033350620301219	Public Health/Epidemio	Trends among US counties and COVID 19 growth rate in relation to existence of shelter in place (SIP) orders **Machin learning** **Limiting gatherings to < 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

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Cell 28APR2020	**Trained immunity: a tool for reducing susceptibility and severity of SARS-CoV-2 infection**	Neteal et al., The Netherlands https://www.cell.com/pb-assets/products/coronavirus/CELL_11391_S5.pdf	Fundamental research	-> Long-term boosting of innate immune responses, also termed 'trained immunity', by certain live vaccines (BCG, oral polio vaccine, measles) induces heterologous protection against infections, through epigenetic, transcriptional and functional reprogramming of innate immune cells. **-> We propose that induction of trained immunity by whole microorganism vaccines may represent an important tool for reducing susceptibility and severity to SARS-CoV-2.**
Cell PreProof	**Clinically Applicable AI System for Accurate Diagnosis, Quantitative Measurements and Prognosis of COVID-19 Pneumonia Using Computed Tomography**	Zhang et al., China https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00656.pdf	Diagnostic	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. -> Identification of important clinical and biochemical markers of multiple organs that correlated with the NCP lesion properties -> Together with the clinical data, this AI system was able to provide accurate clinical prognosis
Science Advances 27APR2020	**Squalene-based multidrug nanoparticles for improved mitigation of uncontrolled inflammation**	Dormont, Flavio et al, France https://doi.org/10.1126/sciadv.aaz5466	Therapeutic	Development of **multidrug nanoparticles for the mitigation of uncontrolled inflammation**. The nanoparticles are made by conjugating squalene, an endogenous lipid, to adenosine, an endogenous immunomodulator, and then encapsulating α-tocopherol, a natural antioxidant. This resulted in **high drug loading, biocompatible, multidrug nanoparticles**. By exploiting the vascular endothelial barrier dysfunction at sites of acute inflammation, these **multidrug nanoparticles could deliver the therapeutic agents in a targeted manner** and conferred a significant survival advantage to treated animals in lethal models of endotoxemia. **-> Selectively delivering adenosine and antioxidants together could serve as a novel approach for the treatment of acute inflammation with reduced-side effects and high therapeutic potential.**
European Journal of Clinical Microbiology & Infectious Diseases 27APR2020	**Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards**	La Scola, Bernard and al. France https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7185831/	Virology	It is of paramount importance to define when a treated patient can be considered as no longer contagious. Correlation between successful isolation of virus in cell culture and Ct value of quantitative RT-PCR targeting E gene suggests that patients with Ct above 33–34 using our RT-PCR system are not contagious and thus can be discharged from hospital care or strict confinement for non-hospitalized patients.
Microbial Pathogenesis 27APR2020	**Design of a peptide-based subunit vaccine against novel coronavirus SARSCoV-2**	Parismita Kalita et al ., India-Japan http://www.sciencedirect.com/science/article/pii/S0882401020305234	Vaccines	Multi-peptide subunit-based epitope vaccine against COVID-19 containing and adjuvant, CTL, HTL and B Cell epitopes -> 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 566 aa subunit vaccine - Human b-defensine 1 (68aa): as adjuvant Extensive bioinformatics analysis suggest that the vaccine is immunogenic, non-toxic, non-allergenic, 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

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Eurosurveillance 27APR2020	**Coronavirus disease (COVID-19) – impact on vaccine preventable diseases**	Hungerdord et al., UK https://doi.org/10.2807/1560-7917.ES.2020.25.18.2000756	HSS/Politic	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.
The Lancet. Infectious diseases 27APR2020	**Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study**	Qifang B and al, China/USA http://www.sciencedirect.com/science/article/pii/S1473309920302875	Public Health/Epidemio	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 trancing reduced isolation period by 1,9 days Higher risk of infection: - Household contact (OR6,27) - 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
Inter J Infectious Disease 27APR2020	**Coronavirus disease 2019 in pregnancy**	Xu Q and al, China http://www.sciencedirect.com/science/article/pii/S1201971220302800	Clinic	Pregnant woman (28) compared to non-pregnant woman (54) **Time from illness to admission: shorter pregnant womenk** <u>Laboratory</u>: significantly - Higher leukocyte in pregnant women (10 vs 2 x10^9/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** → no vertical transmission – good outcomes for both group
Pathogens 26APR2020	**Emergence of Drift Variants That May Affect COVID-19 Vaccine Development and Antibody Treatment**	Takahiko Koyama et al., USA https://doi.org/10.3390/pathogens9050324	Vaccines	> Twenty-one virus variants affecting T-cell epitopes identified. >Twelve virus variants affecting B-cell epitopes of spike protein (S), nucleocapsid protein (N), and membrane protein (M) identified 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 > Vaccine design and convalescent plasma antibody treatment might require specific considerations to accommodate the drift

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The Lancet. Infectious diseases 27APR2020	**Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study**	Qifang B and al, China/USA http://www.sciencedirect.com/science/article/pii/S1473309920302875	Public Health/Epidemio	**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 trancing reduced isolation period by 1,9 days Higher risk of infection: - Household contact (OR6,27) - 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
An International Journal of Obstetrics & Gynaecology 27APR2020	**Vaginal delivery in SARS-CoV-2 infected pregnant women in Northern Italy: a retrospective analysis**	Ferrazzi E and al, Italy https://doi.org/10.1111/1471-0528.16278	Clinic	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 appropriated → cesarean: women with sever symptoms
Clinical microbiology and infection 25APR2020	**Umifenovir treatment is not associated with improved outcomes in patients with coronavirus disease 2019: A retrospective study**	Lian, Ningfang et al, China http://www.sciencedirect.com/science/article/pii/S1198743X20302342	Therapeutic	**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
Cell 24APR2020	**SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues**	Ziegler et al., USA https://www.cell.com/cell/fulltext/S0092-8674(20)30500-6	Fundamental research	-> Meta-analysis of human, primate & mouse scRNA-seq for putative SARS-CoV-2 targets -> Type II pneumocytes, nasal secretory cells & absorptive enterocytes are *ACE2+TMPRSS2+* -> Interferon & influenza increase *ACE2* in human nasal epithelia and lung tissue -> Mouse *Ace2* is not upregulated by interferon, raising implications for disease models
Infection, Genetics and Evolution 24APR2020	**Emerging genetic diversity among clinical isolates of SARS-CoV-2: Lessons for today**	Sheikh, Javaid Ahmad; et al. India-Germany-UK https://doi.org/10.1016/j.meegid.2020.104330	Phylogenetics	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 apears 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. **- ORF1ab, 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.**

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Annals of the rheumatic diseases 24APR2020	**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://ard.bmj.com/content/early/2020/04/24/annrheumdis-2020-217566.long	Therapeutic	**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.
Cell 24APR2020	**Clinically Applicable AI System for Accurate Diagnosis, Quantitative Measurements and Prognosis of COVID-19 Pneumonia Using Computed Tomography**	Zhang, Ket al., China https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00656.pdf	Diagnostics	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 identifyimportant 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 be made available globally to assist the clinicians to combat COVID-19.
J Med ViroL 24APR2020	**SARS-CoV-2 can be detected in urine, blood, anal swabs and oropharyngeal swabs specimens**	Peng, Liang and al. China https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25936	Diagnostics	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. CI°: 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
JAMA network open, 24APR2020	**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/jamanetworkopen.2020.8857	Therapeutic	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 for10 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 trail 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**

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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 https://doi.org/10.1038/s41591-020-0888-2	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 https://jamanetwork.com/journals/jamapediatrics/fullarticle/2765196	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 https://doi.org/10.1038/s41467-020-16048-4	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.
Clinica Chimica Acta 23APR2020	**Highly sensitive detection of SARS-CoV-2 RNA by multiplex rRT-PCR for molecular diagnosis of COVID-19 by clinical laboratories**	Shige, Takayuki and al. Japan https://www.sciencedirect.com/science/article/pii/S0009898120301789	Diagnostics	Three genes are used for multiplex rRT-PCR: the Sarbecovirus specific E gene, the SARS-CoV-2 specific N gene, and the human ABL1 gene as an internal control. Cl°: 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.
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 https://doi.org/10.1111/jth.14871	Therapeutic	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

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BMJ 23APR2020	**Covid-19: Two thirds of healthcare workers who have died were from ethnic minorities**	Rimmer et al., UK https://doi.org/10.1136/bmj.m1621	HSS/Politic	'- 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 => need for a concerted effort to seek explanations and solutions. Notable absence of deaths occurred among certain staff groups: '- Deaths notably in surgery (five cases), general practice (four), emergency medicine (two. No anaesthetists or intensivists. =>Better use of PPE? Need for a central registry of deaths among health and social care workers
Canadian Journal of Political Science 23APR2020	**Sociodemographic and psychological correlates of compliance with the Covid-19 public health measures in France**	Bouraurd et al., France https://doi.org/10.1017/S0008423920000335	HSS/Politic	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 => 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
Nature Medicine 23APR2020	**SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes**	Sungnak, Waradon; et al. UK-France-Netherlands-Germany-USA https://doi.org/10.1038/s41591-020-0868-6	Fundamental research	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 intal 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 **-> upper airway in viruses with higher R0/infectivity (SARS-CoV-2, influenza) vs lower airway/lung parenchyma for MERS-CoV** -> All data provided as a user-friendly an open resource: www.covid19cellatlas.org
Radiology 23APR2020	**Acute Pulmonary Embolism in COVID-19 Patients on CT Angiography and Relationship to D-Dimer Levels**	Leonard-Lorant I and al, France https://doi.org/10.1148/radiol.2020201561	Clinic/Radiology	106 patients COVID19+ and CT angiograms **32 (30%) positive for pulmonary embolus:** - Higher D-dimer levels (6110 vs 1920, p<0,01) - More in ICU (75% vs 32ù, p<0,01) - Treated more often with LWMH (78% vs 23%) D-dimer levels >2660µg/L : - Sensitivity 100% - Specificity 67%

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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.
Analytical chemistry 23APR2020	**Rapid and sensitive detection of anti-SARS-CoV-2 IgG using lanthanide-doped nanoparticles-based lateral flow immunoassay**	Chen, Zhenhua and al. China https://pubs.acs.org/doi/abs/10.1021/acs.analchem.0c00784	Diagnostics	Simple and rapid immunodiagnostic method based on lateral flow immunoassay (LFIA) that uses lanthanide-doped polysterene nanoparticles (LNPs) to detect anti-SARV-CoV-2 IgG in human serum. 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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European Journal of Epidemiology 22APR2020	**Vaccine confidence in the time of COVID-19**	Harrison et al,. US https://doi.org/10.1007/s10654-020-00634-3	HSS/Politic	**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 **4 points to consider:** 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 "care": 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.
The Lancet Infectious diseases 22APR2020	**No SARS-CoV-2 detected in amniotic fluid in mid-pregnancy**	Yu, Nan; et al. China https://doi.org/10.1016/S1473-3099(20)30320-0	Clinic	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.
Eur J Neurol 22APR2020	**Acute-onset smell and taste disorders in the context of Covid-19: a pilot multicenter PCR-based case-control study**	Beltran-Corbellini A and al, Spain https://doi.org/10.1111/ene.14273	Clinic	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
Radiology 22APR2020	**Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected by Pulmonary CT Angiography**	Grillet F and al, France https://doi.org/10.1148/radiol.2020201544	Clinic/Radiology	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<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. **Contrast enhanced CT rather for these patients**

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Science of the Total Environment journal 22APR2020	**COVID-19 outbreak: Migration, effects on society, global environment and prevention**	Chakraborty, I. 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
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**
Ophtalmology 21APR2020	**Ocular Findings and Proportion with Conjunctival SARS-COV-2 in COVID-19 Patients**	Zhou, Yunyun and al. China https://www.sciencedirect.com/science/article/pii/S014164202030405X	Virology	Study of 121 patients 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.
Gastroenterology 22APR2020	**Prevalence and Characteristics of Gastrointestinal Symptoms in Patients with SARS-CoV-2 Infection in the United States: A Multicenter Cohort Study**	Walker D.R and al, USA https://doi.org/10.1053/j.gastro.2020.04.045	Clinic	Multicenter study (9 centers) - **318 patients COVID+** **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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The Lancet Psychiarty 21APR2020	**Suicide risk and prevention during the COVID-19 pandemic**	Gunnel et al., UK https://doi.org/10.1016/S2215-0366(20)30171-1	Psy	->Suggestions that suicide rates will rise ->Many people vulnerable to mental health problems and suicidal behaviour ->Need fot timely public health responses: list of actions presented in the publication **Mental health consequences are likely to be present for longer and peak later than the actual pandemic.**
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://doi.org/10.3201/eid2607.200092	Virology	Phylogenetic 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.m1443	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 Respiratory 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
Thrombosis and haemostasis, 21APR2020	**COVID-19-Related Severe Hypercoagulability in Patients Admitted to Intensive Care Unit for Acute Respiratory Failure**	Spiezia, Luca et al, Italy https://www.ncbi.nlm.nih.gov/pubmed/32316063	Clinic Hematology	Evaluation of coagulation abnormalities via traditional tests and **whole blood thromboelastometry profiles** in a group of **22** patients with COVID and acute respiratory failure due to COVID-19 (mean age 67 ± 8 years, M:F 20:2) compared to 44 controls. 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 Poison Data System, United States, January 1, 2020–March 31, 2020**	Chang et al., USA https://www.cdc.gov/mmwr/volumes/69/wr/mm6916e1.htm?s_cid=mm6916e1_w#contribAff	Public Health/Epidemio	->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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Antimicrobial agents and chemotherapy 20APR2020	**Nafamostat mesylate blocks activation of SARS-CoV-2: New treatment option for COVID-19**	Hoffmann, Markus et al, Germany https://doi.org/10.1128/AAC.00754-20	Therapeutic	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 (FOY), 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. Gabexate mesylate slightly inhibited SARS-CoV-2 S-driven host cell entry while **camostat mesylate robustly suppressed entry**. Notably, **nafamostat mesylate**, which is FDA-approved for indications unrelated to coronavirus infection, **inhibited SARS-CoV-2 S-mediated entry into host cells with roughly 15-fold higher efficiency than camostat mesylate**, with an EC50 in the low nanomolar range. Moreover, **nafamostat mesylate blocked SARS-CoV-2 infection of human lung cells** with markedly **higher efficiency than camostat mesylate** while both compounds were not active against vesicular stomatitis virus infection, as expected.
J of Emerg Microb and Inf 20APR2020	**Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients**	Yongchen et al., China https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1756699	Diagnostic	-> 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. -> Seroconversion was observed in 100% (17/17) of symptomatic patients during the observation period -> Did not identify a strong association of seroconversion and disease severity in our cohort
Metabolism: clinical and experimental 19APR2020	**Obesity as a risk factor for greater severity of COVID-19 in patients with metabolic associated fatty liver disease**	Zheng, Kenneth I and al China http://www.sciencedirect.com/science/article/pii/S0026049520301086	Clinic	**Sixty six COVID-19 patients with metabolic associated fatty liver disease (MAFLD)** n=45 with Body mass index (BMI) > 25 and n=21 with BMI < 25 Mean age :47 years and 74,2% female Results : **BMI > 25 was related to more severe COVID 19** (adjusted-OR 6.32 95%CI 1.16 -34.54, p =0.033) even after adjusting for age, sex, smoking, diabetes, hypertension, and dyslipidaemia
Clin Inf Dis 19APR2020	**Profile of RT-PCR for SARS-CoV-2: a preliminary study from 56 COVID-19 patients**	Xiao et al., China https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa460/5822175	Diagnostic	Dynamics profile of SARS-CoV-2 from 56 recovered COVID-19 patients -> Virus shedding was up to 6 weeks after onset of symptoms -> Longest duration between RT-PCR test for SARS-CoV-2: 42 days after onset of symptoms. -> Median duration between onset of symptom to nucleic acid conversion: 24 days -> In first 3 weeks after symptoms onset, majority results of RT-PCR for SARS-CoV-2 were positive. From week 3 after symptoms onset, number of negative RT-PCR results increased. -> The positive rate of RT-PCR test results was highest at week 1 (100%), followed by 89.3%, 66.1%, 32.1%, 5.4% and 0% at week 2, week 3, week 4, week 5 and week 6 respectively.
Clinical Therapeutic 19APR2020	**Association between clinical manifestations and prognosis in patients with COVID-19**	Yu T and al, China https://doi.org/10.1016/j.clinthera.2020.04.009	Clinic	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) <u>Independent risk factors associated with ARDS:</u> - High systolic blood pressure (OR:1.04, p=0.025) - High LDH level (OR:1.01, p=0.021) <u>Association with pneumonia exacerbation (n=19):</u> - High BMI (OR: 1.28, p=0.017) - Tobacco smoking (OR: 16.13, p=0.032) <u>Limitations</u>: exacerbation based on CT scan findings

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Clin Inf Dis 19APR2020	**Antibody Detection and Dynamic Characteristics in Patients with COVID-19**	Xiang et al., China https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa461/5822173	Diagnostic	**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, 83.3.3% 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.**
Med 18APR2020	**Efficacy and safety of lopinavir/ritonavir or arbidol in adult patients with mild/moderate COVID-19: an exploratory randomized controlled trial**	Li, Y et al, China https://marlin-prod.literatumonline.com/pb-assets/products/coronavirus/MEDJ1.pdf	Therapeutics	**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.
European urology 18APR2020	**Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China**	Zhu L and al, China http://www.sciencedirect.com/science/article/pii/S0302283820302141	Clinic	Controls: 10 family members **10 kidney transplant patients + COVID-19 pneumonia:** - Classical symptoms: fever, cough, shortness of breath, …. - 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
Science 17APR2020	**Comparative pathogenesis of COVID-19, MERS, and SARS in a nonhuman primate model**	Rockx, Barry; et al. Netherlands https://doi.org/10.1126/science.abb7314	Fundamental research	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 mucosae. - 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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J Thromb Haemost 17APR2020	**The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome**	Ranucci M and al, Italy https://doi.org/10.1111/jth.14854	Clinic	**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 ?
Circulation research 17APR2020	**Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19**	Zhang, Peng et al, China https://doi.org/10.1161/CIRCRESAHA.120.317134	Therapeutics	**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.
Gut 17APR2020	**Covid-19 and immunomodulation in IBD**	Neurath, Germany https://gut.bmj.com/content/early/2020/04/16/gutjnl-2020-321269	Immunology	***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.
Nature Biotechnology 16APR2020	**CRISPR–Cas12-based detection of SARS-CoV-2**	Broughton, James P. and al. USA https://doi.org/10.1038/s41587-020-0513-4	Diagnostic	Development of a rapid (<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.

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NEJM 16APR2020	**Not a Perfect Storm — Covid-19 and the Importance of Language**	Brandt M. et al., USA https://doi.org/10.1056/NEJMp2005032	HSS/Politic	Metaphors we use to describe disease shape our experience of illness : has an impact on the approach taken against the Covid => misguiding our approach. Covid characterized as a "perfect storm"="fierce storm arising from a rare combination of adverse meteorological factors" (randomness/volatility => 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 **Conclusion:** Covid is not a simple natural event. It is also the result of human actions. => 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.
Cell 16APR2020	**Development of CRISPR as an antiviral strategy to combat SARSCoV-2 and influenza**	Abbott, T et al, USA https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00736.pdf	Therapeutics	A CRISPR-Cas13-based strategy, PAC-MAN (Prophylactic Antiviral CRISPR in huMAN cells), for viral inhibition can **effectively degrade RNA from SARS-CoV-2 sequences** and live influenza A virus (IAV) in human lung epithelial cells. CRISPR RNAs (crRNAs) targeting conserved viral regions were designed and screened, and **functional crRNAs targeting SARS-CoV-2 were identified**. 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.
Plos One 16APR2020	**Mental health problems and social media exposure during COVID-19 outbreak**	Gao et al., China https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0231924	Psy	**Social media exposure (SME) +++ during Covid-19.** Study on 4872 participants from 31 provinces and autonomous region -> High prevalence of mental health problems ->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. -> Need to combat with "infodemic" while combating during public health emergency
International journal of antimicrobial agents 16APR2020	**Can post-exposure prophylaxis for COVID-19 be considered as one of outbreak response strategies in long-term care hospitals?**	Lee, Sun Hee et al, Republic of Korea https://doi.org/10.1016/j.ijantimicag.2020.105988	Therapeutics	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). => PEP was completed in 184 (97.4%) patients and 21 (95.5%) careworkers **without serious adverse events**. => At the end of 14 days of quarantine, **follow-up PCR tests were all negative**. Limitations: - 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.

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Respiratory Research 15APR2020	**Prognostic value of NT-proBNP in patients with severe COVID-19**	Gao L and al, China https://doi.org/10.1186/s12931-020-01352-w	Clinic	**54 patients – 2 groups**: high and low NT-proBNP NT-proBNP at admission High group significantly: - Older - More comorbidities - Pro inflammatory - Lymphopenia - **Higher risk of death** Cut-off of NT-proBNP for predicting **in hospital death**: 88,64 pg/ml (sensibility: 100% - specificity: 66,67%) AUC for in hospital death = 0,909 **NT-proBNP = independent risk factors for in hospital death** (after adjusting)
ACS nano 15APR2020	**Rapid Detection of COVID-19 Causative Virus (SARS-CoV-2) in Human Nasopharyngeal Swab Specimens Using Field-Effect Transistor-Based Biosensor**	Seo, Giwan and al Rep of Korea https://doi.org/10.1021/acsnano.0c02823	Diagnostic	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.
Nature Medicine 15APR2020	**Temporal dynamics in viral shedding and transmissibility of COVID-19**	He, Xi; et al. China https://doi.org/10.1038/s41591-020-0869-5	Virology	Pemporal 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.
Journal of Biomolecular Structure and Dynamics 15APR2020	**Reverse vaccinology approach to design a novel multi-epitope vaccine candidate against COVID-19: an in silico study**	Maryam Enayatkhani et al. Iran https://doi.org/10.1080/07391102.2020.1756411	Vaccine	3 known antigenic proteins of SARS-CoV-2 (Nucleocapsid, ORF3a, and Membrane protein) -> used to predict *in silico* the potential immunogenic B and T-cell epitopes. -> 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 -> predicted by bioinfomatic 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**
Nat Med 15APR2020	**Temporal dynamics in viral shedding and transmissibility of COVID-19**	He et al., China https://www.nature.com/articles/s41591-020-0869-5	Public Health/Epidemio	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** -> 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

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ACS nano 14APR2020	**Computational Design of ACE2-Based Peptide Inhibitors of SARS-CoV-2**	Han, Yanxiao et al, USA https://doi.org/10.1021/acsnano.0c02857	Therapeutics	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.
Kidney International 14APR2020	**Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China**	Su et al., China https://www.kidney-international.org/article/S0085-2538(20)30369-0/fulltext	Clinic	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.
Journal of Autoimmunity 14APR2020	**Assessing ACE2 expression patterns in lung tissues in the pathogenesis of COVID-19**	Li, Guoping; et al. China https://doi.org/10.1016/j.jaut.2020.102463	Fundamental research	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.

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Disaster medicine and public health preparedness 14APR2020	**Public Education and Electronic Awareness of the New Coronavirus (COVID-19): Experiences from Iran**	Peyravi, M. et al, Iran https://doi.org/10.1017/dmp.2020.94	HSS/Politic	When WHO declared a global health emergency, the Iranian Red Crescent Society and Ministry of Health took measures for public awareness (13 measures). - Training on preventive measures and how to deal with infection and exposure to patients are the most important steps to cope with COVID-19. - Take into account : new educational technologies and applications and the capacity of national and private media. - Necessity to develop content related to the individuals' ages. Adapt also to illiterate and disabled. - Messages adapted to certain special public groups (drivers, bakeries, ...) or social activities (shopping, ...) more impactful than some general advice. **In the cyberspace** - Effective and timely use of cyberspace=> acceptance and dissemination - Better effectiveness of E-training than ordinary training. - Infographics (humor, animation and kids-friendly themes) viewed more and possibly higher effectiveness than monolog lectures. - Exponential growth in sharing the materials **Conclusion :** to manage the virus, policymakers /organizations should provide innovative, unified and applied educational content to all people.
BMJ 14APR2020	**COVID-19: why we need a national health and social care service**	Pollock, A. et al, UK https://doi.org/10.1136/bmj.m1465	HSS/Politic	Social services in the UK: most privatized and fragmented in Western world. 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. Lack of access to, i.e., support after hospital discharge or mental health services: => more health crises & hospital admissions + essential care workers taking time off to care for family members. **Conclusion:** Universal integrated health and social care service => bring all services and staff under government control. => social care delivered by a trained and properly equipped workforce with decent terms of service. + mandate collection of data quantifying effect of COVID on social care sector.
Ear, nose, & throat journal 13APR2020	**Clinical Presentation of COVID-19: A Systematic Review Focusing on Upper Airway Symptoms**	Lovato A and al, Italy https://doi.org/10.1177/0145561320920762	Clinic	5 retrospective studies and cohort studies Quality of evidence = level 4 (low) **1556 patients: 57,5% males** **Mortality: 2,4% - ICU admission: 7,3%** Upper airways symptoms: - Pharyngodynia: 12,4% - Nasal congestion: 3,7% - Rhinorrhea: 4% (1 study) **None of the studies reported olfactory or gustative dysfunction** Rest symptoms: same other study (fever, cough, fatigue) Alteration chest CT: 83% → bilateral++++ Severe cases: older, lymphopenia, radiologic abnormalities Limits: only hospitalized patients → not full clinical spectrum of COVID-19 / olfactory disorders could have been underestimated

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Mayo Clinic Proceedings 13APR2020	**ST-segment Elevation, Myocardial Injury, and Suspected or Confirmed COVID-19 Patients: Diagnostic and Treatment Uncertainties**	Bennett et al., USA https://doi.org/10.1016/j.mayocp.2020.04.005	Diagnostic	-> 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 -> Institutions to define acute cardiac care pathways which balance the risks of complicating COVID-19 patients from invasive therapies and unnecessary contrast exposure versus the potential benefit if the patient is experiencing a MI from acute coronary occlusion
International Forum of Allergy & Rhinology 12APR2020	**Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms**	Carol Y and al, USA https://doi.org/10.1002/alr.22579	Clinic	**Cross sectional study – question survey – 2 groups** **All with influenza like symptoms** 59 COVID-19 positive and 203 COVID-19 negative Hospital admission low and comparable between groups Smell and taste loss: more frequent in COVID-19 group - 68% and 71% verus 16% and 17% respectively - Largest magnitude of association with COVID-19 **Independently associated with COVID-19:** - Anosmia: OR 10,9 [5,08 – 23,5] - Taste: OR 10,2 [4,74 – 22,1] Improvement of olfaction and taste that correlated with clinical resolution of illness.
Travel Med. Infect. Dis. 11APR2020	**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**	Gautret, Philippe et al, France https://doi.org/10.1016/j.tmaid.2020.101663	Therapeutic	**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.
The Lancet 11APR2020	**Centring sexual and reproductive health and justice in the global COVID-19 response**	Matthew J Harris et al., UK https://doi.org/10.1016/S0140-6736(20)30801-1	HSS/Politic	COVID-19 + existing sexual & reproductive health inequities => women, girls and vulnerable populations' health, wellbeing and economic stability disproportionately impacted. 1) COVID-19 = 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.

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Journal of Clinical Virology 11APR2020	**Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: a descriptive study**	Xiao et al., China https://www.sciencedirect.com/science/article/pii/S1386653220300883?via%3Dihub	Diagnostic	301 patients: -> median period between symptoms presence and positive SARS-CoV-2 RT-PCR results was 16 days -> 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.
Science 10APR2020	**Structure of the RNA-dependent RNA polymerase from COVID-19 virus**	Gao, Yan; et al. China - Australia https://doi.org/10.1126/science.abb7498	Structural biology	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: - Conserved architecture of nsp12 with polymerase core of SARS-CoV, and resolution of a newly identified β-hairpin domain at its N terminus. - Comparative modeling reveals how remdesivir binds to nsp12 polymerase, its primary antiviral drug target. -> provides basis for design of new antiviral therapeutics /cocktails targeting viral RdRp (nsp12).
Emerg. Infect. Dis. 10APR2020	**Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020**	Zhen-Dong Guo; et al. China https://doi.org/10.3201/eid2607.200885	Virology	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. -> Atricter protective measures should be taken by medical staff working in the ICUs then general wards. -> Aerosol distribution in the general ward indicate transmission distance of SARS-CoV-2 might be 4 m
NEJM 10APR2020	**Compassionate Use of Remdesivir for Patients with Severe Covid-19**	Grein, Jonathan et al, USA https://doi.org/10.1056/NEJMoa2007016	Therapeutic	**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
Journal of Clinical Virology 10APR2020	**Clinical characteristics and risk assessment of newborns born to mothers with COVID-19**	Yang, Pu et al Chine https://doi.org/10.1016/j.jcv.2020.104356	Clinic	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**
Euro Surv 9APR2020	**Excess cases of influenza-like illnesses synchronous with coronavirus disease (COVID-19) epidemic, France, March 2020**	Boëlle, Pierre-Yves et al, France *https://doi.org/10.2807/1560-7917.ES.2020.25.14.2000326*	HSS/Politic	**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.**

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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 https://doi.org/10.1093/cid/ciaa351	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 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 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 https://doi.org/10.1159/000507639	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, CXCL5, and CXCL10) of the 13 key inflammatory mediators tested (in contrast to 85 % for SARS-CoV).
The Lancet. Global health 9APR2020	**COVID-19 and risks to the supply and quality of tests, drugs, and vaccines**	Paul N Newton et al., US https://doi.org/10.1016/S2214-109X(20)30136-4	HSS/Politic	Production /supply chains for COVID-19 candidate drugs / essential medical products impaired. Supply chains for vital drugs for other diseases disrupted by repurposing without adequate evidence. • 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/NEJMp2007637	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 using 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.lfs.2020.117652	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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EuroSur 9APR2020	**An alternative workflow for molecular detection of SARS-CoV-2 – escape from the NA extraction kit-shortage, Copenhagen, Denmark, March 2020**	Fomsgaard et al., Denmark https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.14.2000398	Diagnostics	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
Clin Inf Dis 9APR2020	**Prediction for Progression Risk in Patients with COVID-19 Pneumonia: the CALL Score**	Ji, Dong and al., China https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa414/5818317	Diagnostics	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 incorporing 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.
Clin Inf Dis 8APR2020	**PCR Assays Turned Positive in 25 Discharged COVID-19 Patient**	Yuan, Jing and al., China https://doi.org/10.1093/cid/ciaa398	Clinic	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 ≥350. (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. -> 25 discharged patients sent to hospital again because of the positive RT-PCR results. They experienced an average of 7.32±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**.
Clinical Immunology 8APR2020	**Epigenetic dysregulation of ACE2 and interferon-regulated genes might suggest increased COVID-19 susceptibility and severity in lupus patients**	Sawalha, Amr H. et al. USA-China https://doi.org/10.1016/j.clim.2020.108410	Virology	Patients with **systemic lupus erythematous** 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 succeptibility to SARS-CoV-2 infection. - increased oxidative stress induced by viral infection **exacerbates ACE2demethylation defect** in lupus and **may enhance viremia**. > 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 likelyhood of cytokine storm.

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JAMA pediatric 8APR2020	**Screening and Severity of Coronavirus Disease 2019 (COVID-19) in Children in Madrid, Spain**	Tagarro A and al, Spain https://doi.org/10.1001/jamapediatrics.2020.1346	Clinic.	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.
The Lancet 8APR2020	**First-wave COVID-19 transmissibility and severity in China outside Hubei after control measures, and second-wave scenario planning: a modelling impact assessment**	Leung et al., China https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30746-7/fulltext?utm_campaign=tlcoronavirus20&utm_source=twitter&utm_medium=social	Public Health/Epidemio	-> The first wave of COVID-19 outside of Hubei has abated because of **aggressive non-pharmaceutical interventions.** -> the R_t decreased substantially since Jan 23, when control measures were implemented, and have since remained below 1. -> **Relaxing the interventions (resulting in R_t >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_t and cCFR is needed to inform strategies against a potential second wave to achieve an optimal balance between health and economic protection.
The European respiratory journal, 8APR2020	**Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China**	Wen-hua Liang et al, Chine https://doi.org/10.1183/13993003.00562-2020	Clinic	**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.**
Journal of biomolecular structure & dynamics, 8APR2020	**In-silico homology assisted identification of inhibitor of RNA binding against 2019-nCoV N-protein (N terminal domain)**	Sarma, Phulen et al, India https://doi.org/10.1080/07391102.2020.1753580	Therapeutic	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 pyrimidone derivaties as possible inhibitors of RNA binding to the N terminal domain of N protein of coronavirus, thus opening new avenues for in vitro validations**
Pediatric Critical Care 7APR2020	**Coronavirus Disease 2019 in Critically Ill Children: A Narrative Review of the Literature**	Ong J and al, Singapore/Italy /Canada https://journals.lww.com/pccmjournal/Abstract/onlinefirst/Coronavirus_Disease_2019_in_Critically_Ill.98057.aspx	Clinic	Children account for a few proportions of COVID19 diseases **Not severely ill**: asymptomatic++++ or mild Infant under 1 year appear to have an increased risk of severe disease. <u>Spared from severe disease</u>: - Less lymphopenia: 3,5% ≠ 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. <u>Management:</u> - 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

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The Lancet Public Health 07APR2020	**The French response to COVID-19: intrinsic difficulties at the interface of science, public health, and policy**	Moatti, Jean.P et al., France https://doi.org/10.1016/S2468-2667(20)30087-6	HSS/Politic	French authorities appointed an advisory board of 11 scientists to help manage the crisis =>evidence-based policy but: 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 hydroxycholoroquine without considering alternative evaluation methods for quicker evidence => 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.
J Mol Diag PRE-PROOF 7MAR2020	**Development of Reverse Transcription Loop-mediated Isothermal Amplification (RT-LAMP) Assays Targeting SARS-CoV-2**	Park et al., Republic of korea https://www.biorxiv.org/content/10.1101/2020.03.09.983064v1	Diagnostic	-> 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.
Clinical infectious diseases 7APR2020	**Towards Optimization of Hydroxychloroquine Dosing in Intensive Care Unit COVID-19 Patients**	Perinel, Sophie et al, France https://doi.org/10.1093/cid/ciaa394	Therapeutic	**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 >1 mg/L and <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**
Science Translational Medicine 6APR2020	**An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 in human airway epithelial cell cultures and multiple coronaviruses in mice**	Sheahan, Timothy P. et al. USA https://doi.org/10.1126/scitranslmed.abb5883	Therapeutic	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) -> potency of NHC/EIDD-2801 against multiple coronaviruses and oral bioavailability makes it a potential effective antiviral against SARS-CoV-2
Journal of Medical Virology 6APR2020	**Tocilizumab treatment in COVID-19: a single center experience**	Luo, Pan et al, China https://doi.org/10.1002/jmv.25801	Therapeutic	**15 COVID-19 patients** under **Tocilizumab** (TCZ) therapy were **retrospectively assessed**. - TCZ treatment ameliorated the increased CRP in all patients rapidly, - The 4 critically ill patients who received an only single dose of TCZ -> 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. => 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.

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JAMA 6APR2020	**Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy**	Grasselli G et al, Italy https://doi.org/10.1001/jama.2020.5394	Clinic	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_2O** - 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
Clin Chem 4APR2020	**Potential false-negative nucleic acid testing results for Severe Acute Respiratory Syndrome Coronavirus 2 from thermal inactivation of samples with low viral loads**	Pan et al., China https://academic.oup.com/clinchem/advance-article/doi/10.1093/clinchem/hvaa091/5815979	Diagnostic	-> Ct values are increased (**higher treshold 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.
Inter J Of Infect Dis 3APR2020	**A first Case of Meningitis/Encephalitis associated with SARS-Coronavirus-2**	Moriguchi, Takeshi et al, Japan https://doi.org/10.1016/j.ijid.2020.03.062	Clinic	**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 hyperintense 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**.
The Journal of infection 3APR2020	**Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19**	Liu et al., China https://www.journalofinfection.com/article/S0163-4453(20)30208-5/pdf	Clinic	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.**
The Journal of infection 3APR2020	**Arbidol Monotherapy is Superior to Lopinavir/ritonavir in Treating COVID-19**	Zhu, Zhen et al, China https://doi.org/10.1016/j.jinf.2020.03.060	Therapeutic	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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CELL preproof	**Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2**	Monteil, Kwon et al,	Therapeutic	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**.
Nature Medicine 3APR2020	**Respiratory virus shedding in exhaled breath and efficacy of face masks**	Leung, Nancy H. L. et al., https://doi.org/10.1038/s41591-020-0843-2 China - USA	Virology	Detection of **virus RNA shedding in exhaled breat**h 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. **<u>Without face mask:</u>** - 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**
Antiviral Research 3APR2020	**Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro**	Choy, Yin-Lam Wong et al, Hong Kong https://doi.org/10.1016/j.antiviral.2020.104786	Therapeutic	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.**
International Journal of Antimicrobial Agents 3APR2020	**Structural and molecular modeling studies reveal a new mechanism of action of chloroquine and hydroxychloroquine against SARS-CoV-2 infection**	Fantini, Di Scala et al, France https://doi.org/10.1016/j.ijantimicag.2020.105960	Therapeutic	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**.

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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/10.1007/s11239-020-02105-8	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	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	HSS/Politic	Health workers with **pre-existing medical conditions**/in **older age groups** are at **greater risk** of severe illness and death if exposed to COVOD-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**
Physical and Engineering Sciences in Medicine, 3APR2020	**Covid-19: automatic detection from X-ray images utilizing transfer learning with convolutional neural networks**	Apostolopoulos et al., Greece https://link.springer.com/article/10.1007/s13246-020-00865-4	Diagnostic	Technology evaluated is called **Transfer Learning** 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 technlogy 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	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 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., Chine, 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.
American journal of nephrology 2APR2020	**Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China**	Wang Lu et al, China https://doi.org/10.1159/000507471	Clinic	**116 patients** – Retrospective study 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.**
Liver Int 2APR2020	**Liver impairment in COVID-19 patients: a retrospective analysis of 115 cases from a single center in Wuhan city, China**	Zhang Y et al, China https://doi.org/10.1111/liv.14455	Clinic	**2 groups: 115 COVID-19 and 114 controls (community acquired pneumonia)** 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**
CDC 1APR2020	**Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020**	Wei et al., China https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm?s_cid=mm6914e1_w#contribAff	Public Health/Epidemio	-> Identification of **7 clusters** of COVID-19 in Singapore in which **presymptomatic transmission** likely occurred and which may explain the occurrence of secondary cases

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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/laneur/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.**
Nature 1APR2020	**Virological assessment of hospitalized patients with COVID-2019**	Wolfel et al. Germany https://www.nature.com/articles/s41586-020-2196-x	Virology	A detailed virological analysis of 9 cases, providing proof of active virus replication in upper respiratory tract tissues. -> 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. Seroconversion 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/NEJMe2007263	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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The Lancet) 01APR2020	**Racism and discrimination in COVID-19 responses**	Devakumar, D. et al., UK https://doi.org/10.1016/S0140-6736(20)30792-	HSS/Politic	**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
Virol Sin 31MAR2020	**Inefficiency of Sera from Mice Treated with Pseudotyped SARS-CoV to Neutralize 2019-nCoV Infection**	Zezhong Liu et al., China https://doi.org/10.1007/s12250-020-00214-5	Therapeutic	**S proteins:** - 76% homology SARS CoV / SARS CoV-2 - 29% homology SARS CoV / MERSCoV. **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. -> Sera tested on ACE2 expressing 293T cells. -> 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 -> no neutralization effect was evidenced. **It may not be practical to treat SARS-CoV-2 patients.**
Emerging microbes & infections 31MAR2020	**Renin-angiotensin system inhibitors improve the clinical outcomes of COVID-19 patients with hypertension**	Meng, Juan et al, Chine, https://doi.org/10.1080/22221751.2020.1746200	Therapeutic	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.
Annals of internal medicine 30MAR2020	**A Rush to Judgment? Rapid Reporting and Dissemination of Results and Its Consequences Regarding the Use of Hydroxychloroquine for COVID-19**	Kim, Alfred H.J et al., USA https://doi.org/10.7326/M20-1223	HSS/Politic	**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:** **->** Sufficient justification to continue investigation of the efficacy and safety of HCQ in patients hospitalized with COVID-19. **->** No data currently to recommend the use of HCQ as a prophylaxis for COVID-19. **->**No recommendation of its use outside of marketing authorization until it is justified and offer is reinforced. **->** Risk of penury to patients with rheumatic diseases who depend on HCQ for their survival. **->** HCQ shortage will limit availability to patients with COVID-19 if efficacy truly established.

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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 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 *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**
The Lancet ID 30MAR2020	**Estimates of the severity of coronavirus disease 2019: a model-based analysis**	Verity et al., UK https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30243-7/fulltext#	Public Health/Epidemio	**Using data on 24 deaths that occurred in mainland China and 165 recoveries outside of China:** - Mean duration from onset of symptoms to death : 17,8 days - Mean durantion 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.
Journal of Gastroenterology and Hepatology 27MAR2020	**Covid-19 and the Digestive System**	Wong S et al, China https://doi.org/10.1111/jgh.15047	Clinic	**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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The Lancet ID 27MAR2020	**Clinical and virological data of the first cases of COVID-19 in Europe: a case series**	Lescure et al., France https://doi.org/10.1016/S1473-3099(20)30200-0	Clinic	**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 paucisymptomatic 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.
Clinical Infectious Disease 27MAR2020	**Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China**	Mo P et al, China https://doi.org/10.1093/cid/ciaa270	Clinic	**155 patients** with median age of 54 years – **85 refractory COVID-19:** - Older and more male (p< 0,05) - More comorbidities: diabetes, cardiovascular disease, cerebrovascular disease (p<0,05) - Higher incidence of breath shortness and anorexia (p<0,05) - Bilateral pneumonia - Higher CRP, LDH, ASAT and neutrophile 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])
JAMA 27MAR2020	**Treatment of 5 critically ill patients with COVID-19 with convalescent plasma**	Shen C et al, China https://jamanetwork-com.proxy.insermbiblio.inist.fr/journals/jama/fullarticle/2763983	Therapeutic	**5 patients**: severe pneumonia + P_{AO2}/F_{IO2}<300mmHg + 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_{AO2}/F_{IO2} , 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?
The Lancet 27MAR2020	**Historical linkages: epidemic threat, economic risk, and xenophobia**	White, A. et al,. USA https://doi.org/10.1016/S0140-6736(20)30737-6	HSS/Politic	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 (=> 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.

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J. Med. Virol. 26MAR2020	**Stability Issues of RT-PCR Testing of SARS-CoV-2 for Hospitalized Patients Clinically Diagnosed with COVID-19**	Li et al., China https://doi.org/10.1002/jmv.25786	Diagnostic	610 hospitalized patients from Wuhan -> High false negtive 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	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 newsborns : · 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 placentas 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.m1205	HSS/Politic	**Biggest camp in Cox's Bazar (Bengladesh):** - 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 : creaion 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	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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Lancet 25MAR2020	**Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study**	Yu N. et al, China *https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30176-6.pdf*	Clinic	**Pregnant patients with COVID 19 – no ICU :** 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/early/2020/03/25/science.abb4218	Public Health/Epidemio	**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 https://www.ijidonline.com/article/S1201-9712(20)30172-7/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 http://www.ncbi.nlm.nih.gov/pubmed/32207674	HSS/Politic	**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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The Lancet Global Health 24MAR2020	**Early in the epidemic: impact of preprints on global discourse about COVID-19 transmissibility COMMENT**	Maimuna et al., USA https://doi.org/10.1016/S2214-109X(20)30113-3	HSS/Politic	**Novelty of SARS-CoV-2, so scientists rushed to fill epidemiological, virological, and clinical knowledge gap** -> 50 new studies about the virus between January 10 and January 30 alone. Use of a simple method to plot the ten R0 estimations posted as preprints before publication of the first peer-reviewed study on Jan 29. Result of the peer review R0 estimations are very similar to those in the peer-reviewed studies published on and after Jan 29. **Conclusions :** - 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)
Emerging microbes and Infections 24MAR2020	**Establishment and validation of a pseudovirus neutralization assay for SARS-CoV-2**	Jianhui Nie et al, China http://www.ncbi.nlm.nih.gov/pubmed/32207377	Therapeutic	Necessity of **handling SARS-CoV-2 in BSL-3 facilities** and **accessibility to virus strains** -> **barriers to develop candidate vaccines and therapeutics**. -> Hence, development of a SARS-CoV-2 pseudovirus based in neutralization assays using S viral genes cloned into pcDAN3.1 plasmids. -> Expressed in a VSV pseudoviral platform. -> Huh7 cells platted at 5x104/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.**
The Lancet Child & Adolescent Health 24MAR2020	**Mental health considerations for children quarantined because of COVID-19**	Liu, Jia Jia; Bao, Yanping et al,. China https://doi.org/10.1016/S2352-4642(20)30096-1	HSS/Politic	**• at home = stress can be eased** **• in local hospitals/ collective medical observation centers = 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** **Chinese gov. strategies to prevent risks :** **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** **Guidelines issued: 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** **Need for :** **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**

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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 https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30196-1/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 onse**t 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 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, Chine 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
International journal of antimicrobial agents 20MAR2020	**Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial**	Gautret, and al, France https://www.sciencedirect.com/science/article/pii/S0924857920300996	Therapeutic	**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 virologicaly 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 http://www.ncbi.nlm.nih.gov/pubmed/32205272	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 http://www.ncbi.nlm.nih.gov/pubmed/32205269	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.
Cell Mol Immunol 19MAR2020	**Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine**	Wanbo Tai et al., China https://www-nature-com.proxy.insermbiblio.inist.fr/articles/s41423-020-0400-4	Vaccine	-> SARS-CoV-2 **receptor-binding domain (RBD)** protein could be used **as a therapeutic agent** against SARS-CoV-2 and SARS-CoV infection (from results *invitro*) -> 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 antisera could cross-neutralize SARS-CoV-2 -> **potential to develop SARS-CoV RBD-based vaccines for prevention of SARS-CoV-2 and SARS-CoV infection**.
NEJM 19MAR2020	**A trial of liponavir-ritonavir in adults hospitalized with severe Covid-19**	Cao B et al, China https://www.nejm.org/doi/pdf/10.1056/NEJMoa2001282?articleTools=true	Therapeutic	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 beneficit was observed with lopinavir-ritonavir treatment**

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NEJM 19MAR2020	**SARS-CoV2 Infection in children**	Lu X. et al, China https://www.nejm.org/doi/pdf/10.1056/NEJMc2005073?articleTools=true	Clinic	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 % Pneumonia: 64.9 % **3 patients** (with coexisting conditions) **require intensive care and 1 death** **Most children appear to be mild symptomatic.**
World Journal of Pediatrics 19MAR2020	**Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study**	Sun D et al, China *https://link-springer-com.proxy.insermbiblio.inist.fr/content/pdf/10.1007/s12519-020-00354-4.pdf*	Clinic	**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 lund damage and severe health complication**
Cell and Mol Biol 17MAR2020	**Elevated exhaustion levels and reduced functional diversity of T cells in peripheral blood may predict severe progression in COVID-19 patients**	Zheng et al., https://www.nature.com/articles/s41423-020-0401-3	Immunology	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 **-> Identifcation of potential immunological risk factors for COVID-19 pneumonia and provided clues for its clinical treatment.**
The NEJM 17MAR2020	**Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1**	Doremalen et al., USA https://www.nejm.org/doi/pdf/10.1056/NEJMc2004973?articleTools=true	Virology	-> Stability of **SARS-CoV-2** was similar to that of **SARS-CoV-1** under the experimental circumstances tested. -> 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**

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The Lancet 17MAR2020	**Prevention of SARS-CoV-2 infection in patients with decompensated cirrhosis**	Xiao et al., China https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30080-7/fulltext	Clinic	**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.
International journal of infectious diseases 17MAR2020	**Transmission potential and severity of COVID-19 in South Korea**	Shim et al., Rep of Korea https://www.ijidonline.com/article/S1201-9712(20)30150-8/fulltext	Public Health/Epidemio	- COVID-19 caused 6,284 cases and 42 deaths in South Korea as of March 8, 2020. - The mean reproduction number Rt 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 > = 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.
J Inf Dis 17MAR2020	**Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China.**	Wang et al., China https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa119/5807958	Clinic	**55 asymptomatic carriers** Conclusions: -> 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
Am J Transplant. 17MAR2020	**Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression.**	Zhu et al., China https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.15869	Clinic	**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.**
J Med Virol 17MAR2020	**Platelet-to-lymphocyte ratio is associated with prognosis in patients with Corona Virus Disease-19.**	Qu et al., China https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25767	Clinic	-Retrospective analysis of **30 hospitalized patients** -> Patients with platelet peaks during treatment: longer hospitalization. -> Patients with platelet peaks were **older** -> **Higher PLT** (platelet to lymphocyte ratio): **longer hospitalisation**. It may be related to **cytokine storm**.

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The Lancet 17MAR2020	**Prisons and custodial settings are part of a comprehensive response to COVID-19**	Kinnet et al., Australia https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30058-X/fulltext	Public Health/Epidemio	**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.
Arch Pathol Lab Med. 17MAR2020	**An Analysis of 38 Pregnant Women with COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2: Maternal Coronavirus Infections and Pregnancy Outcomes**	Schwartz et al., USA https://www.archivesofpathology.org/doi/pdf/10.5858/arpa.2020-0901-SA	Clinic	Analyzing literature describing 38 pregnant women with COVID-19 and their newborns in China -> 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 16 MAR2020	**Infection with SARS-CoV-2 in pregnancy. Information and proposed care. CNGOF**	Peyronnet et al, France 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
Nat Med 16MAR2020	**Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19**	Thevarajan et al., Australia https://www.nature.com/articles/s41591-020-0819-2	Immunology	-> Kinetics of immune responses in relation to clinical and virological features of a patient with mild-to-moderate coronavirus disease 2019 (COVID-19) that required hospitalization. **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.abb3221.long	Public Health/Epidemio	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**
The Lancet 16MAR2020	**Preparedness is essential for malaria-endemic regions during the COVID-19 pandemic**	Wang et al., China https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30561-4/fulltext	Public Health/Epidemio	-> Relevant lessons from the 2014–16 outbreak of Ebola virus disease in west Africa -> 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/langas/article/PIIS2468-1253(20)30082-0/fulltext	Public Health/Epidemio	-> 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-CoV-2
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.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000199	Public Health/Epidemio	**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/laninf/article/PIIS1473-3099(20)30174-2/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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The Lancet 12MAR2020	**Real estimates of mortality following COVID-19 infection**	Baud et al., Switzerland https://www.thelancet.com/action/showPdf?pii=S1473-3099%2820%2930195-X	Public Health/Epidemio	Mortality rate estimates are based on the number of deaths relative to number of confirmed cases of infection -> **not representative of actual death rate.** **Real rates:** - 5·6% for China - 15·2% outside China **Current figures might underestimate the potential threat of COVID-19 in symptomatic patients**
The Lancet 11MAR2020	**Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?**	Fang et al., Switzerland https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30116-8/fulltext	Clinic	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.
The Lancet 11MAR2020	**Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.**	Zhou et al., China https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30566-3/fulltext	Clinic	-> 191 patients: 137 discharged and 54 died 1- Comorbidity: 48%, with hypertension (30%), diabetes (19%), coronary heart disease (8%). 2- Death associated with older age, higher SOFA score, d-dimer greater than 1 µg/mL on admission. 3- Viral shedding: median 20 days in survivors, otherwise until death. Longest viral shedding: 37 days
The Lancet 11MAR2020	**Early dynamics of transmission and control of COVID-19: a mathematical modelling study**	Kucharski et al., UK https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30144-4/fulltext	Public Health/Epidemio	Calculation the **probability that newly introduced cases might generate outbreaks in other areas.** **->** Estimations: The median daily reproduction number (R_t) 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**.
JAMA 11MAR2020	**Detection of SARS-CoV-2 in Different Types of Clinical Specimens**	Wang et al., China https://jamanetwork.com/journals/jama/fullarticle/2762997	Diagnostic	**-> 1070 specimens collected from 205 patients** **POSITIVITY** by RT-PCR: Bronchoalveolar lavage fluid (**93%**) Sputum (**72%**) Nasal Swabs (**63%**) Fibrobronchoscope brush biopsy (**46%**) Pharyngeal swabs (**32%**) Feces (**29%**) Blood (**1%**) Urine (**0%**)
Sci Rep 11MAR2020	**A high ATP concentration enhances the cooperative translocation of the SARS coronavirus helicase nsP13 in the unwinding of duplex RNA**	Jang et al., Republic of Korea https://www.nature.com/articles/s41598-020-61432-1	Fundamental Research	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.**

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Emerge Inf Dis 09MAR2020	**Detection of Novel Coronavirus by RT-PCR in Stool Specimen from Asymptomatic Child, China**	Tang et al., China https://wwwnc.cdc.gov/eid/article/26/6/20-0301_article	Public Health/Epidemio	**-> Asymptomatic** child **positive** for COVID-19 by RT-PCR **in stool, 17 days after the last virus exposure** -> Still positive 9 days after that (in stool) -> **Never positive** in **respiratory tracts specimens** -> no data on urine and blood -> The child might have transmitted the virus to numerous persons. **Stool from COVID-19 patients might serve as another vehicle for virus transmission**
Clin Inf Dis 09MAR2020	**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)**	Yao et al., China https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa237/5801998	Therapeutic	-> Vero cells were treated by **Choloroquine and Hydroxychloroquine** before (prophylaxy) and after (anti-viral) infection by SARS-CoV-2. -> **EC50** are calculated ->**Hydroxychloroquine has superior antiviral and prophylactic activity than chloroquine** -> Physiologically-based pharmacokinetic (PBPK) -> 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**).
Science 06MAR2020	**The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak.**	Chinazzi et al., USA https://science.sciencemag.org/content/early/2020/03/05/science.aba9757.long	Public Health/Epidemio	-> **Global metapopulation disease transmission model** to project the impact of travel limitations on the national and international spread of the epidemic. ->**Travel quarantine of Wuhan** delayed the overall epidemic progression by **only 3 to 5 days** in Mainland China -> More marked effect at the international scale, where case importations were **reduced by nearly 80%** until mid February -> 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** **->** Potential uses for the **definition of optimized containment** schemes and **mitigation policies** that includes **the local and international dimension** of the COVID-19 epidemic
EuroSurveillance 05MAR2020	Evaluation of a quantitative RT-PCR assay for the detection of the emerging coronavirus SARS-CoV-2 using a high throughput system	Pfefferle et al. Germany https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7068162	Diagnostic	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
Cell 04MAR2020	**SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor**	Hoffman et al., Germany https://www.cell.com/cell/fulltext/S0092-8674(20)30229-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0092867420302294%3Fshowall%3Dtrue	Therapeutic	-> **Priming of S proteins** by host **cell proteases (TMPRSS2)** is **essential for viral entry** into cells. -> **ACE 2 can be blocked** by a clinically proven **inhibitor** of **TMPRSS2** -> **The study suggests that antibody responses raised against SARS-CoV could at least partially protect against SARS- CoV-2 infection**

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Science 04MAR2020	**Structural basis for the recognition of the SARS-CoV-2 by full-length human ACE2**	Yan et al., China https://science.sciencemag.org/content/early/2020/03/03/science.abb2762/tab-pdf	Fundamental Research	-> **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 -> **ACE2 may be a homodimer even in the absence of B0AT1** -> **A dimeric ACE2 can accommodate two S protein trimers**, each through a monomer of ACE2 -> Structure-based rational **design of binders with enhanced affinities to either ACE2 or the S protein of the coronaviruses** may facilitate development of **decoy ligands** or **neutralizing antibodies** for suppression of viral infection.
J Clin Microbiol 04MAR2020	**Multicenter Evaluation of the QIAstat-Dx Respiratory Panel for the Detection of Viruses and Bacteria in Nasopharyngeal Swab Specimens**	Leber et al., USA https://jcm.asm.org/content/early/2020/02/28/JCM.00155-20.long	Diagnostic	**-> Multiplex** *in vitro* **diagnostic test** for the **qualitative** detection of **20 pathogens** directly from **nasopharyngeal swab specimens.** -> Results available in approximately **69 minutes** **-> Pathogens identified:** adenovirus, coronavirus 229E, coronavirus HKU1, coronavirus NL63, coronavirus OC43, human metapneumovirus A+B, influenza A, influenza A H1, influenza A H3, influenza A H1N1/2009, influenza B, parainfluenza virus 1, parainfluenza virus 2, parainfluenza virus 3, parainfluenza virus 4, rhinovirus/enterovirus, respiratory syncytial virus A+B, Bordetella pertussis, Chlamydophila pneumoniae and Mycoplasma pneumoniae -> Compared to the BioFire FilmArray Respiratory Panel version 1.7: **percent agreement: 99,5%** . **negative percent agreement of ≥ 97.9%** **Robust and accurate assay for rapid, comprehensive testing for respiratory pathogens.**
Sci. China Life Sci. 04MAR2020	**Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China**	https://link.springer.com/article/10.1007%2Fs11427-020-1661-4	Clinic	**->** Laboratory-confirmed positive for the COVID-19 (pharyngeal swab) -> No obvious symptoms **at time of screening** (all of them) -> **20.8%** developed symptoms (fever, cough, fatigue, etc.) -> 50.0% cases showed typical CT images of ground-glass chest ->20.8% presented stripe shadowing in the lungs -> 29.2% cases showed normal CT image and had no symptoms during hospitalization (**these cases were younger**) -> **Epidemiological investigation revealed asymptomatic transmission**
JAMA 04MAR2020	**Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient**	Ong et al., Singapore https://jamanetwork.com/journals/jama/fullarticle/2762692?resultClick=1	Public Health/Epidemio	Extensive **environmental contamination** by 1 SARS-CoV-2 patient with mild upper respiratory tract involvement -> Toilet bowl and sink samples were positive -> Swabs taken from the air exhaust outlets tested positive -> Air samples were negative -> Risk of transmission from contaminated footwear is likely low: negative results in the anteroom and clean corridor **Limit of the study:** viral culture was not done to demonstrate viability
Nat Sci Rev 03MAR2020	**On the origin and continuing evolution of SARS-CoV-2**	Tang et al., China https://academic.oup.com/nsr/advance-article/doi/10.1093/nsr/nwaa036/5775463?searchresult=1	Genomic	-> Assessment of the **molecular phylogeny** and the divergence between **SARS-CoV-2** and **related coronaviruses**. ->Population genetic analyses of 103 genomes of SARS-CoV-2 incate that there are **two major types of viruses** (designated **L and S**) currently circulating between humans. -> 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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JAMA 03MAR2020	**Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore**	Young et al., Singapore https://jamanetwork.com/journals/jama/fullarticle/2762688	Clinic	**-> 18patients** diagnosed with SARS-CoV-2 infection in Singapore between January 23 and February 3, 2020 -> Respiratory tract infection with **prolonged viral shedding from the nasopharynx** of **7 days or longer** in 15 patients (83%) -> Supplemental oxygen was required in 6 patients (33%), **5 of whom** were treated with **lopinavir-ritonavir**, with **variable clinical outcomes** following treatment.
Int J Infect Dis 02MAR2020	**Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report**	Chen et al., China https://www.ijidonline.com/article/S1201-9712(20)30122-3/pdf	Virology	- 46-year-old woman with multiple patchy ground glass opacities in bilateral subpleural areas by CT - **Oropharyngeal swab test was positive by RT-PCR.** -> Received **symptomatic treatment** and **antimicrobial therapy** including oseltamivir, arbidol, Lopinavir/ritonavir and moxifloxacin -> 6 testing from 28 Jan to 17FEB, all negative **but one the 2FEB** Discharged on 9FEB and testing remained negative during follow-up. **SARS-CoV-2 RNA of respiratory tract specimen may be persistent or recurrent positive during the course.**
Jour of Infect 29FEB2020	**Identification of the hyper-variable genomic hotspot for the novel coronavirus SARS-CoV-2**	Wen et al., China https://www.journalofinfection.com/article/S0163-4453(20)30108-0/pdf	Genomic	-> Confirmation of the relationship of SARS-CoV-2 with other beta coronaviruses on the amino acid level. -> Hyper-variable genomic hotspot established in SARS-CoV-2 **population at the nucleotide but not the amino acid level** -> means **no beneficial mutations**. -> **Mutations in nsp1, nsp3, nsp15, and gene S would be associated with the SARS-CoV-2 epidemic (compared with RaTG13) / required for human adaptation?**
J Med Virol 28FEV2020	**Development of Epitope-Based Peptide Vaccine Against Novel Coronavirus 2019 (SARS-COV-2): Immunoinformatics Approach**	Bhattacharya et al., India https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25736	Vaccine	1-> Characterization of the **spike glycoprotein** to obtain immunogenic epitopes 2-> Immunoinformatic analysis of 13 MHC I and 3 MHC II epitopes which **have antigenic properties** 3-> These identified epitopes are candidate to formulate a **multi-epitopic peptide vaccine.** **Need for *in vitro* and *in vivo* validations**
The NEJM 28FEB2020	**Clinical Characteristics of Coronavirus Disease 2019 in China**	Ni et al., China https://www.nejm.org/doi/pdf/10.1056/NEJMoa2002032?articleTools=true&downloadfile=showPdf&articleTools=true&doi=10.1056/NEJMoa2002032	Clinic	Median age : **47 years** / Female: 41.9% **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**. 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. Most common symptoms: fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%). Diarrhea was uncommon (3.8%). Median **incubation period**: **4 days** (interquartile range, 2 to 7). **CT:** ground-glass opacity was the most common radiologic: 56.4%. **No radiographic or CT abnormality:** 17.9% with nonsevere disease and 2.9% with severe disease. **Lymphocytopenia: 83.2%**

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EuroSurv 27FEB2020	**Early transmission patterns of coronavirus disease 2019 (COVID-19) in travellers from Wuhan to Thailand, January 2020**	Okada et al., Thailand https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.8.2000097	Public Health/Epidemio	-> 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.**
J Clin Med 27FEB2020	**Epidemiological Identification of A Novel Pathogen in Real Time: Analysis of the Atypical Pneumonia Outbreak in Wuhan, China, 2019—2020**	Jung et al., Japan https://www.mdpi.com/2077-0383/9/3/637	Public Health/Epidemio	->**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.**
The Lancet 27FEB2020	**Secondary attack rate and superspreading events for SARS-CoV-2**	Liu et al., UK https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30462-1/fulltext	Public Health/Epidemio	**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 R0 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 R0 would be larger. **More data are needed.**
The Lancet 27FEB2020	**COVID-19: combining antiviral and anti-inflammatory treatments** **COMMENT**	Stebbing et al., UK https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30132-8/fulltext	Therapeutic	-> 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**
The Lancet 27FEB2020	**Positive RT-PCR Test Results in Patients Recovered From COVID-19**	Lan et al, China https://jamanetwork.com/journals/jama/fullarticle/2762452	Public Health/Epidemio	**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.**

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The Lancet 27FEB2020	**Convalescent plasma as a potential therapy for COVID-19** **COMMENT**	Chen et al., China https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30141-9.pdf	Therapeutic	-> In 2014, the use of convalescent plasma collected from patients who had recovered from **Ebola virus disease** 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**
Emerg Microb Infects 26FEB2020	**Detectable 2019-nCoV viral RNA in blood is a strong indicator for the further clinical severity**	Chen et al., China https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1732837	Clinic	-> 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**
The Lancet, 26FEB2020	**The psychological impact of quarantine and how to reduce it: rapid review of the evidence**	Brooks et al., UK https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30460-8/fulltext	HSS/Politic	-> 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**
Viruses 25FEB2020	**Preliminary Identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies**	Ahmed et al., China https://www.mdpi.com/1999-4915/12/3/254	Vaccine	**-> High genetic similarity** between **SARS-CoV-2 and SARS-Co**. **->** 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
EuroSurv 25FEV2020	**Differential diagnosis of illness in patients under investigation for the novel coronavirus (SARS-CoV-2), Italy, February 2020.**	Bordi et al., Italy https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.8.2000170	Public Health/Epidemio	-> **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.**
The Lancet 25FEB2020	**Potential association between COVID-19 mortality and health-care resource availability**	Ji et al., China https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30068-1/fulltext	Public Health/Epidemio	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 health-care burden**
The Lancet 24FEB2020	**COVID-19 control in China during mass population movements at New Year**	Chen et al., China https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30421-9/fulltext	Public Health/Epidemio	Several lessons that can be drawn from China's extension of the Lunar New Year holiday: 1-> Countries should consider **periods of recommended or mandatory closure of non-essential workplaces and public institutions**— to slow the rate of transmission. 2-> To tailor the design of these actions according to specific epidemic characteristics (incubation period and transmission routes). 3-> 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.

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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/2077-0383/9/2/601	Public Health/Epidemio	**->** 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	Fondamental 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/lanres/article/PIIS2213-2600(20)30079-5/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	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.
The Lancet 24FEB2020	**COVID-19 pneumonia: what has CT taught us?**	Lee et al., China https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30134-1/fulltext	Diagnostic	- The predominant CT findings included **ground-glass opacification, consolidation, bilateral involvement, and peripheral and diffuse distribution**. - 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.
J Med Virol 21FEB2020	**COVID-2019: the role of the nsp2 and nsp3 in its pathogenesis.**	Angeletti et al., Rome, Italy https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25719	Fondamental Research	The Open Reading Frame 1ab (ORF1ab) of COVID-2019 has been analyzed to evidence the **presence of mutation caused by selective pressure** on the virus. 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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Radiology 20 FEB 2020	**Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection.**	Bernheim et al., https://pubs.rsna.org/doi/10.1148/radiol.2020200463	Diagnostic	Frequency of CT findings is related to infection time course.
The Lancet, 20 FEB 2020	**Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study.**	Gilbert et al., Vittoria's team https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30411-6/fulltext	Public Health/Epidemio	- Highest importation risk: Egypt, Algeria, and South Africa -> moderate to high capacity to respond to outbreaks - Moderate risk: Nigeria, Ethiopia, Sudan, Angola, Tanzania, Ghana, and Kenya -> variable capacity and high vulnerability
The Lancet 19FEB2020	**Asymptomatic cases in a family cluster with SARS-CoV-2 infection**	Pan et al., China https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30114-6/fulltext	Public Health/Epidemio	- 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.
The Lancet 19FEB2020	**Enteric involvement of coronaviruses: is faecal–oral transmission of SARS-CoV-2 possible?**	Yeo et al., Singapore https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30048-0/fulltext	Virology	- 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.
THE NEJM, 19FEB2020	**SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients**	Zou et al, Chinq https://www.nejm.org/doi/full/10.1056/NEJMc2001737	Virology	**- 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.**
Biosci Trends, 19FEB2020	**Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies.**	Gao et al., https://www.ncbi.nlm.nih.gov/pubmed/32074550	Therapeutic	**Chloroquine phosphate,** an old drug for treatment of malaria, is shown to have apparent efficacy and acceptable safety against COVID-19 associated pneumonia in multicenter clinical trials conducted in China. (**DATA NOT SHOWN !**). The drug is recommended to be included in the next version of the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 issued by the National Health Commission of the People's Republic of China for treatment of COVID-19 infection in larger populations in the future.

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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 https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa077/5739751	Public Health/Epidemio	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.
The Lancet 18FEB2020	**Tracking online heroisation and blame in epidemics** **COMMENT**	Atlani Duault et al., France https://www.thelancet.com/action/showPdf?pii=S2468-2667%2820%2930033-5	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 of 2019-nCoV**	Chen et al., China and USA https://www.sciencedirect.com/science/article/pii/S0006291X20303399	Fondamental 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 <u>throughout</u> the animal kingdom (**<u>possible hosts ?)</u>** Since ACE2 is predominantly expressed in intestines, testis, and kidney, **<u>fecal-oral</u>** and **<u>other routes</u>** of transmission are also **<u>possible</u>**. 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 https://www.mdpi.com/2077-0383/9/2/538	Public Health/Epidemio	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 https://www.pnas.org/content/early/2020/02/12/1922083117	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 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30365-2/fulltext	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 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30360-3/fulltext	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.**
Cell Res 4FEB2020	**Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro**	Wang et al., China https://www.nature.com/articles/s41422-020-0282-0	Therapeutic	Remdesivir and chloroquine **are highly effective** in the control of 2019-nCoV infection **in vitro**. 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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Euro Surveill 6FEB2020	**Effectiveness of airport screening at detecting travellers infected with novel coronavirus (2019-nCoV).**	Quilty et al., UK https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.5.2000080	Public Health/Epidemio	Estimation: **46%** of infected travellers would **not be detected**, depending on incubation period, sensitivity of exit and entry screening, and proportion of asymptomatic cases. -> Airport screening is unlikely to detect a sufficient proportion of 2019-nCoV infected travellers to avoid entry of infected travellers.
The Lancet 03FEB2020	**Baricitinib as potential treatment for 2019-nCoV acute respiratory disease**	Richardson et al., UK https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(20)30304-4.pdf	Therapeutic	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.
Emerge Microbes Infect 03FEB2020	**Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody.**	Tian et al., China https://www.biorxiv.org/content/10.1101/2020.01.28.923011v1	Fondamental Research	A SARS-CoV-specific human monoclonal antibody, CR3022, could bind potently with 2019-nCoV RBD. ->Potential to be developed as candidate therapeutics ? Some of the most potent SARS-CoV-specific neutralizing antibodies that target the ACE2 binding site of SARS-CoV failed to bind 2019-nCoV spike protein. -> It is still **necessary to develop novel monoclonal antibodies** that could bind specifically to 2019-nCoV RBD.