

# COVID-19

## Literature review of accepted relevant papers

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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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- Inserm- Department of Partnerships and External Relations (DPRE)
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### Additional 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
Science 20MAY2020	<b>DNA vaccine protection against SARS-CoV-2 in rhesus macaques</b>	Yu et al., USA <a href="#">gotopaper</a>	Vaccine	<p><b>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.</b></p> <p>-&gt; humoral and cellular immune response with neutralizing antibody (titers = those found in convalescent humans and macaques).</p> <p>-&gt; challenged with SARS-CoV-2: the vaccine encoding the full-length S protein resulted in &gt;3.1 and &gt;3.7 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa.</p> <p>-&gt; Vaccine-elicited neutralizing antibody titers correlated with protective efficacy: <b>suggests an immune correlate of protection</b></p>
Nature Medicine 19MAY2020	<b>Artificial intelligence-enabled rapid diagnosis of patients with COVID-19</b>	Mei et al., USA <a href="#">gotopaper</a>	Diagnostic	<p>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.</p> <p>-&gt; 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.</p> <p>-&gt; 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</p> <p><b>When CT scans and associated clinical history are available, the proposed AI system can help to rapidly diagnose COVID-19 patients.</b></p>
Clinical Infectious Diseases 19MAY2020	<b>Early Short Course Corticosteroids in Hospitalized Patients with COVID-19</b>	Fadel, Raef et al. USA <a href="#">gotopaper</a>	Therapeutic	<p><b>Multi-center quasi-experimental study</b> of 213 adult patients with confirmed moderate to severe COVID, 81 (38%) and 132 (62%) in SOC and <b>early short course corticosteroid</b> (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.</p> <p>- 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.</p> <p>- Significant reduction in median hospital length of stay was also observed in the early corticosteroid group (8 vs. 5 days, p &lt; 0.001).</p> <p>- 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]).</p> <p><b>Conclusion: An early short course of methylprednisolone in patients with moderate to severe COVID-19 reduced escalation of care and improved clinical outcomes.</b></p> <p><b>Limitations:</b> 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.</p>

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Circulation 19MAY2020	<b>Deep Vein Thrombosis in Hospitalized Patients with Coronavirus Disease 2019 (COVID-19) in Wuhan, China: Prevalence, Risk Factors, and Outcome</b>	Zang L et al, China <a href="#">gotopaper</a>	Clinic	<p>Investigation of deep vein thrombosis (DVT) in hospitalized patient with COVID-19 143 patients from Jan 29 and Feb 29 <u>Demographic</u>: 51,7% man – median age= 63 46,1% (66) lower extremity DVT= 23 proximal DVT and 43 distal DVT <u>DVT vs no DVT</u>:</p> <ul style="list-style-type: none"> <li>- Older</li> <li>- Lower oxygenation index</li> <li>- Higher rate of cardiac injury</li> <li>- Increase death (23 vs 9, p=0,001)</li> </ul> <p><u>Multivariate analysis, DVT associated with</u></p> <ul style="list-style-type: none"> <li>- CURB-65 score3-5, OR:6,12</li> <li>- Padua prediction <math>\geq 4</math>, OR: 4,01</li> <li>- D-dimer&gt;1<math>\mu</math>g/ml OR :5,81</li> </ul> <p><u>Predicting DVT</u> <b>CURB-65 score3-5, Padua prediction score <math>\geq 4</math> + D-dimer&gt;1 had Se 88% and Spe 61,4%</b></p> <p>→ prevalence of DVT is high → importance of prophylaxis for venous thromboembolism (Padua prediction score <math>\geq 4</math>)</p>
Science 18MAY2020	<b>Susceptible supply limits the role of climate in the early SARS-CoV-2 pandemic</b>	Baker, Rachel E. et al. USA <a href="#">gotopaper</a>	Climate	<p>Climate-dependent model to simulate SARS-CoV-2 pandemic, probing different scenarios based on known coronavirus biology.</p> <p>Results suggest:</p> <ul style="list-style-type: none"> <li>• <b>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.</b></li> <li>• <b>Both tropical and temperate locations should prepare for severe outbreaks and summertime temperatures will not effectively limit spread of infection.</b></li> <li>• <b>Endemic cycles will likely be tied to climate factors and seasonal peaks may vary with latitude.</b></li> </ul>
Cell 18MAY2020	<b>Potent neutralizing antibodies against SARS-CoV-2 identified by high-throughput single-cell sequencing of convalescent patients' B cells</b>	Yunlong Cao et al., Chine, <a href="#">gotopaper</a>	Immunology	<p>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.</p> <p>=&gt; among of which,14 potent neutralizing mAbs were identified</p> <p>=&gt; one of them, BD-368-2, exhibited an IC50 of 1.2 ng/mL and 15 ng/mL against pseudotyped and authentic SARS-CoV-2.</p> <p>=&gt; in vivo experiments confirmed that BD-368-2 provide strong therapeutic efficacy and prophylactic protection against SARS-CoV-2, using the hACE2 transgenic mice model</p> <p>Conclusion: The potent neutralizing antibodies we identified may provide an effective therapeutic and prophylactic solution</p> <p>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.</p>

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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 <a href="#">gotopaper</a>	Population studies	<p><b>Lyon University Hospital admissions</b> 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.</p> <p>Results :</p> <ul style="list-style-type: none"> <li>- 25% of severe COVID-19 patients had obesity, vs 15-3% in French adult population in 2014.</li> <li>-&gt; <b>Obesity prevalence 1.35 times higher in severe COVID-19 patients vs general French population.</b></li> <li>-&gt; <b>In ICU, obesity prevalence 1.89 times higher vs general population.</b></li> <li>-&gt; <b>Obesity prevalence higher in critical vs non-critical COVID-19 patients.</b></li> </ul> <p>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 <i>et al.</i> 2020) :</p> <ul style="list-style-type: none"> <li>-&gt; <b>obesity prevalence 2.88 times higher in critical COVID-19 vs French general population</b></li> <li>-&gt; <b>Obesity prevalence higher in critical COVID-19 vs Lille ICU patients without COVID-19 (n=306).</b></li> </ul> <p><b>=&gt; Report significant association in obesity prevalence and severe COVID-19, including critical COVID-19, and suggests obesity =&gt; risk factor of pejorative evolution of COVID-19, increasing risk of ICU admission.</b></p>
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 <a href="#">gotopaper</a>	Clinic	<p>A series of children admitted to PICU for cardiogenic shock + left ventricular dysfunction + severe inflammatory state (14 centers)</p> <p>35 children – median age: 10 y [2 – 16]</p> <p>Comorbidities: 28% of the children which 17% were overweight</p> <p><u>Symptoms:</u> Fever and asthenia (100%) / Gastrointestinal symptoms (83%) / Respiratory distress (65%) – rhinorrhea (43%)</p> <p><u>Left ventricular ejection at baseline</u> &lt; 30 for 28% / 30 to 50 for 72%</p> <p><u>Laboratory:</u> 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)</p> <p><u>Treatment:</u> 94% Respiratory support: invasive (62%) – noninvasive (32%) / 28% ECMO / 80% inotropic support / 100% IV globuline / 1/3 received steroid therapy</p> <p><u>At discharge:</u> 25/35 had left ventricular function restored - no death</p> <p><b>→ SARS-COV-2 + severe inflammatory state in children → acute cardiac decompensation</b></p>
The Journal of Antimicrobial Chemotherapy 17MAY2020	COVID-19 infection also occurs in patients taking hydroxychloroquine	Lahouati, M et al. France <a href="#">gotopaper</a>	Therapeutic	<p>Report on <b>two severe cases of COVID-19 in patients already using hydroxychloroquine for a long time</b> to treat inflammatory disease.</p> <p><b>High plasma levels of hydroxychloroquine</b> collected on admission in those cases confirm chronic exposure and adherence to hydroxychloroquine. These values are <b>close to or higher than the EC50</b> 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.</p> <p>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.</p> <p>These <b>observational data are not in favour of a universal protective effect of hydroxychloroquine</b>, and clinicians should use it carefully, awaiting the results of clinical trials, particularly in the context of prevention.</p>

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Water research 16MAY2020	<b>SARS-CoV-2 RNA in wastewater anticipated COVID-19 occurrence in a low prevalence area</b>	Randazzo et al, Spain <a href="#">gotopaper</a>	Public Health/Epidemio	<p><b>Faecal shedding of SARS-CoV-2 RNA from COVID-19 patients has extensively been reported.</b></p> <p>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).</p> <p>-&gt; The estimated quantification of SARS-CoV-2 RNA titers in untreated wastewater waters of <math>5.4 \pm 0.2 \log_{10}</math> genomic copies/L on average.</p> <p>-&gt; Two secondary water samples resulted positive (2/18) and all tertiary water samples tested as negative (0/12).</p> <p>SARS-CoV-2 RNA shedding in stools was present even before the first cases were reported by the authorities.</p> <p><b>This strategy could be implemented in environmental surveillance as an early indicator of the infection within a specific population.</b></p>
Developmental Cell 16MAY2020	<b>Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract</b>	Smith, Joan C. <i>et al.</i> USA <a href="#">gotopaper</a>	Fundamental research	<p>Cigarette smoke causes dose-dependent upregulation of ACE2 receptor in rodent and human lungs.</p> <p>Single-cell sequencing data:</p> <ul style="list-style-type: none"> <li>- <b>ACE2 expressed in a subset of secretory cells in respiratory tract.</b></li> <li>- <b>Chronic smoke exposure triggers expansion of this cell population and increased ACE2 expression.</b></li> <li>- <b>Quitting smoking has convers effect</b> (decreases this cell population and ACE2 levels).</li> <li>- ACE2 expression responsive to inflammatory signalling and upregulated by viral infections / interferon treatment.</li> </ul> <p>-&gt; May partially explain why smokers are particularly susceptible to severe SARS-CoV-2 infections</p> <p>-&gt; <b>identifies ACE2 as interferon-stimulated gene in lung cells -&gt; possible positive-feedback loops increasing ACE2 levels and facilitating viral dissemination.</b></p>
J. Clin. Virol. 16MAY 2020	<b>A combined oropharyngeal/nares swab is a suitable alternative to nasopharyngeal swabs for the detection of SARS-CoV-2</b>	LeBlanc, Jason J. and al., Canada <a href="#">gotopaper</a>	Diagnostic	<p>Given the global shortage of nasopharyngeal (NP) swabs typically used for respiratory virus detection, alternative collection methods were evaluated during the COVID-19 pandemic.</p> <p>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.</p>
The Lancet Infectious Diseases 15MAY2020	<b>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</b>	Lusignan, Simon de et al. UK-South Africa <a href="#">gotopaper</a>	Clinic	<p>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):</p> <ul style="list-style-type: none"> <li>- 587 SARS-CoV-2 +ve out of 3802 test results.</li> <li>- male sex independently associated with testing +ve (18 vs 13 % for women)</li> </ul> <p><b>Clinical factors and demographics more likely to testing +ve :</b></p> <ul style="list-style-type: none"> <li>- Adults, in particular <b>ages 40-64</b>, vs children (19 % in aged 40-64 vs 5 % in children)</li> <li>- People with <b>chronic kidney disease</b> (33 vs 14 % without chronic kidney disease), but no significant association with other chronic conditions.</li> <li>- <b>Obese people</b> (21 vs 13 % for people of normal weight)</li> <li>- <b>Active smoking at decreased odds of testing +ve</b> (11 vs 18 % in non-smokers)</li> <li>- <b>black people</b> vs white (62 vs 16 %)</li> <li>- <b>People living in urban areas</b> vs rural areas (26 vs 5-6% in rural areas)</li> <li>- <b>People living in deprived areas</b> (30 vs 8% in least deprived areas)</li> </ul> <p>-&gt; +ve SARS-CoV-2 test results in primary care cohort was associated with similar risk factors as for severe outcomes of COVID-19 in hospital settings, except for smoking.</p> <p>-&gt; Provides evidence of potential sociodemographic factors associated with a +ve test : deprivation, population density, ethnicity and chronic kidney disease.</p>

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Gastroenterology 15MAY2020	<b>Associations between Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blocker Use, Gastrointestinal Symptoms, and Mortality among Patients with COVID-19</b>	Tan, Nian-Di et al. China <a href="#">gotopaper</a>	Therapeutic/ Clinic	<p><b>Retrospective cohort study</b> of consecutive patients with COVID-19. Among the <b>100 participants with hypertension</b>, 31 were classified as ACEI/ARB group and the remaining 69 were classified as non-ACEI/ARB group.</p> <p><b>Inpatient treatment with ACEI/ARB</b> was associated with <b>lower risk of digestive system involvement</b> and <b>lower risk of all-cause mortality</b> compared with ACEI/ARB non-users in COVID-19 patients with hypertension.</p> <p><b>Limitations:</b> small sample-size, possible unappreciated confounding effect.</p>
Science 15MAY2020	<b>Serology assays to manage COVID-19</b>	Krammer F., Simon V., USA <a href="#">gotopaper</a>	Public Health/Epidemiol	<p>Measurement of antibodies to SARS-CoV-2 will improve disease management if used correctly.</p> <p>This perspective article describes the serological assays available and discusses the potential applications, including:</p> <ul style="list-style-type: none"> <li>- understand the antibody responses mounted upon SARS-CoV-2 infection and vaccination;</li> <li>- inform on the prevalence of SARS-CoV-2 infection if different populations;</li> <li>- identification of donors for convalescent plasma therapy;</li> <li>- identify individuals who are immune (and the caveats concerning this point).</li> </ul> <p><b>With high-quality serological assays now available, the key challenge will be to apply and deploy these tests in a strategic manner.</b></p>
Clinical microbiology and infection 15MAY2020	<b>A multiple center clinical evaluation of an ultra-fast single-tube assay for SARS-CoV-2 RNA</b>	Wang, Ji and al. China <a href="#">gotopaper</a>	Diagnostic	<p>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.</p> <p>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.</p> <p>CI<sup>o</sup>: 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.</p>
Science 15MAY2020	<b>Inferring change points in the spread of COVID-19 reveals the effectiveness of interventions</b>	Dehning et al., Germany <a href="#">gotopaper</a>	PublicHealth/Epidemiology	<p><b>By combining an established epidemiological model with Bayesian inference -&gt; analysis of the time dependence of the effective growth rate of new infections</b></p> <p>Focusing on COVID-19 spread in Germany, detection of change points in the effective growth rate that correlate well with the times of publicly announced interventions -&gt; Possibility to quantify the effect of interventions, and we can incorporate the corresponding change points into forecasts of future scenarios and case numbers. This code is freely available and can be readily adapted to any country or region.</p>
Nature 14MAY2020	<b>Proteomics of SARS-CoV-2-infected host cells reveals therapy targets</b>	Bojkova, Denisa et al. Germany <a href="#">gotopaper</a>	Therapeutic	<p><b>Identification of the host cell pathways</b> modulated by SARS-CoV-2 infection and inhibition of these pathways showed to prevent viral replication in human cells. A <b>human cell culture model for infection</b> with SARS-CoV-2 clinical isolate was established. Employing this system, the <b>SARS-CoV-2 infection profile</b> was determined by translato3 and proteome proteomics at different times after infection. These analyses revealed that <b>SARS-CoV-2 reshapes central cellular pathways</b>, such as translation, splicing, carbon metabolism and nucleic acid metabolism. <b>Small molecule inhibitors targeting these pathways prevented viral replication in cells.</b></p>

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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 <a href="#">gotopaper</a>	Therapeutic/ Clinic	<p><b>Case-population study</b> 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. <b>1139 cases</b> and <b>11 390 population controls</b>.</p> <p>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.</p> <p>The <b>current use of RAAS inhibitors is not associated with an increased risk of COVID-19 requiring admission to hospital</b> (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.</p> <p><b>Limitations:</b> 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.</p>
BMJ 14MAY2020	Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial	Tang, Wei et al. China <a href="#">gotopaper</a>	Therapeutic	<p><b>Multicentre, randomised, parallel, open label trial of hydroxychloroquine</b> (1200 mg daily for three days, then 800 mg daily) versus standard of care in 150 patients admitted to hospital with covid-19.</p> <p><b>No evidence to support an increase in the probability of negative conversion</b> of SARS-CoV-2 conferred by the addition of hydroxychloroquine administration to the current standard of care in patients admitted to hospital with mainly <b>persistent mild to moderate covid-19</b>. <b>Adverse events</b>, particularly gastrointestinal events, were <b>more frequently reported</b> in patients receiving <b>hydroxychloroquine</b>.</p> <p><b>Limitations:</b> 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.</p>
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 <a href="#">gotopaper</a>	Clinic	<p>Description of maternal disease and obstetrical outcomes – 6 hospital in Washington state</p> <p><b>46 pregnant women</b></p> <p><b>Demographic:</b> median age: 29y – 6,5% in first &amp; 43,4% second &amp; 50% in third trimester</p> <p>26,1% had at least one comorbidity: asthma – hypertension – diabetes - ....</p> <p><b>28,6% were overweight and 35,7% obese</b></p> <p><b>Symptoms:</b> 93,5% had one – cough (70%) – fever (51%) – dyspnea – headache ....</p> <p><b>Outcomes:</b></p> <ul style="list-style-type: none"> <li>- 15% categorized has severe disease: overweight/obese/comorbidity</li> <li>- 16% hospitalized &amp; 1 to ICU (all severe disease)</li> <li>- 8 delivered during the study period (median: 38,4 week)</li> <li>- 1 stillbirth: unknown etiology</li> </ul> <p>→ <b>higher risk group: chronic comorbidity / obese / overweight</b></p>



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Clinica Chimica Acta 14MAY2020	<b>The underlying changes and predicting role of peripheral blood inflammatory cells in severe COVID-19 patients: a sentinel?</b>	Sun, Da-wei and al. China <a href="#">gotopaper</a>	Virology	<p>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.</p> <p>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.</p> <p>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.</p> <p>CI<sup>o</sup>: 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</p>
Journal of Allergy and Clinical Immunology 14MAY2020	<b>Complement activation in patients with COVID-19: a novel therapeutic target</b>	Cugno, Massimo et al. Italy <a href="#">gotopaper</a>	Therapeutic	<p>Preliminary data providing evidence of <b>complement activation</b> in patients with COVID-19 with <b>different degrees of respiratory failure</b>. Investigation of the <b>plasma levels of sC5b-9 and C5a</b> as markers of complement activation in 31 COVID-19 patients, compared with 27 healthy subjects.</p> <ul style="list-style-type: none"> <li>- <b>Plasma levels of sC5b-9</b> were <b>significantly higher</b> in the patients with moderate disease and those with severe disease <b>than in the healthy controls</b>, and <b>significantly higher</b> in the patients with <b>severe disease</b> than in those with moderate disease.</li> <li>- The <b>plasma levels of C5a</b> were <b>higher</b> in the patients with moderate disease and those with severe disease <b>than in the healthy</b> (P=0.0001 for both), with no statistically significant difference between the two patient groups.</li> <li>- The cohort of patients had <b>increased levels of acute-phase proteins and coagulation system abnormalities</b>.</li> </ul> <p>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.</p>
BMJ 14MAY2020	<b>Clinical efficacy of hydroxychloroquine in patients with covid-19 pneumonia who require oxygen: observational comparative study using routine care data</b>	Mahévas, Matthieu et al. France <a href="#">gotopaper</a>	Therapeutic	<p><b>Comparative study</b> that uses <b>real world data</b> collected from routine care to assess the <b>efficacy and safety of hydroxychloroquine</b> in a population of <b>181 patients</b> admitted to hospital with covid-19 hypoxaemic pneumonia.</p> <ul style="list-style-type: none"> <li>- Hydroxychloroquine treatment at 600 mg/day added to standard care was <b>not associated with a reduction of admissions to the intensive care unit or death</b> 21 days after hospital admission compared with standard care alone.</li> <li>- The <b>rate of survival without acute respiratory distress syndrome did not increase</b>.</li> <li>- Eight patients in the treatment group (10%) experienced <b>electrocardiographic modifications that required discontinuation of treatment</b>.</li> </ul> <p>The results of this study do not support its use in patients admitted to hospital with covid-19 who require oxygen. <b>Limitations:</b> observational data, centre effect not taken into account ; limited sample ; only patients admitted to hospital.</p>



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Clinical Infectious Disease 14MAY2020	<b>Risk Factors of Severe Disease and Efficacy of Treatment in Patients Infected with COVID-19: A Systematic Review, Meta-Analysis and Meta-Regression Analysis</b>	Zhang, John J. Y et al. Singapore <a href="#">gotopaper</a>	Therapeutic/ Clinic	<p><b>Systematic review and meta-analysis</b> on COVID-19 clinical features and/or treatment outcomes.</p> <p><b>45 studies</b> reporting <b>4203 patients</b> 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.</p> <ul style="list-style-type: none"> <li>- On meta-regression, <b>ICU admission</b> was <b>predicted by raised leukocyte count</b> (<math>p&lt;0.0001</math>), <b>raised alanine aminotransferase</b> (<math>p=0.024</math>), <b>raised aspartate transaminase</b> (<math>p=0.0040</math>), <b>elevated lactate dehydrogenase (LDH)</b> (<math>p&lt;0.0001</math>) and <b>increased procalcitonin</b> (<math>p&lt;0.0001</math>).</li> <li>- <b>ARDS</b> was <b>predicted by elevated LDH</b> (<math>p&lt;0.0001</math>), while <b>mortality</b> was <b>predicted by raised leukocyte count</b> (<math>p=0.0005</math>) and <b>elevated LDH</b> (<math>p&lt;0.0001</math>).</li> <li>- Treatment with <b>lopinavir-ritonavir</b> showed <b>no significant benefit in mortality and ARDS rates</b>. <b>Corticosteroids</b> were associated with a <b>higher rate of ARDS</b> (<math>p=0.0003</math>).</li> </ul> <p><b>Limitations:</b> 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.</p>
Nature 14MAY2020	<b>Infection of dogs with SARS-CoV-2</b>	Sit, Thomas H. C Hong Kong <a href="#">gotopaper</a>	Fundamental research	<p><b>2/15 dogs from households with confirmed human COVID-19 cases</b> in Hong Kong were found to be infected (qRT-PCR, serology, viral genome sequencing, and virus isolation in 1 dog):</p> <ul style="list-style-type: none"> <li>- a 17yr-old male Pomeranian (SARS-CoV-2 RNA detected from 5 nasal swabs over 13-days).</li> <li>- a 2.5yr-old male German Shepherd dog (SARS-CoV-2 RNA on two occasions and virus isolated from nasal and oral swabs)</li> <li>- Both had antibody responses (plaque reduction neutralization assays).</li> <li>- <b>Viral genetic sequences from both dogs were identical to virus detected in respective human cases. Animals asymptomatic during quarantine.</b></li> </ul> <p>-&gt; <b>These are instances of human-to-animal transmission of SARS-CoV-2.</b> Unclear whether infected dogs can transmit the virus to other animals or back to humans.</p>
Nature 14MAY2020	<b>Pathogenesis and transmission of SARS-CoV-2 in golden hamsters</b>	Sia, Sin Fun et al. Hong Kong <a href="#">gotopaper</a>	Animal model	<p>Pathogenesis and transmissibility of the SARS-CoV-2 in <b>golden Syrian hamsters</b> (intranasal infection):</p> <ul style="list-style-type: none"> <li>- 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.</li> <li>- Viral antigen found in duodenum epithelial cells and viral RNA in feces.</li> </ul> <p>-&gt; <b>Efficient SARS-CoV-2 transmission from inoculated hamsters to naïve by direct contact and via aerosols.</b> Transmission via fomites less efficient.</p> <p>-&gt; <b>Communicable period was short and correlated with detection of infectious virus but not viral RNA.</b></p> <p>-&gt; <b>Inoculated and naturally-infected hamsters showed apparent weight loss, and all animals recovered with detection of neutralizing antibodies.</b></p>
Proc. Natl. Acad. Sci. U. S. A. 13MAY2020	<b>The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission</b>	Stadnytskyi et al. USA <a href="#">gotopaper</a>	Public Health/Epidemiol	<p>Speech droplets generated by asymptomatic carriers of SARS-CoV-2 likely to be a mode of disease transmission.</p> <p>-&gt; Highly sensitive laser light scattering observations have revealed that loud speech can emit thousands of oral fluid droplets per second.</p> <p>-&gt; In a closed, stagnant air environment, they disappear from the window of view with time constants in the range of 8 to 14 min (droplet nuclei of ca. 4 µm diameter, or 12- to 21-µm droplets prior to dehydration).</p> <p><b>There is therefore a substantial probability that normal speaking causes airborne virus transmission in confined environments.</b></p>

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Science 13MAY2020	<b>Estimating the burden of SARS-CoV-2 in France</b>	Salje et al., France <a href="#">gotopaper</a>	Public Health/Epidemiol	<p>Using models applied to hospital and death data, we estimate the impact of the lockdown and current population immunity in France.</p> <p>-&gt; We find 3.6% of infected individuals are hospitalized and 0.7% die (0.001% in &lt;20 years of age (ya), 10.1% in &gt;80ya). The lockdown reduced the reproductive number from 2.90 to 0.67 (77% reduction). By 11 May 2020, when interventions are scheduled to be eased, we project that 4.4% (range: 2.8–7.2) of the population will have been infected.</p> <p>Population immunity appears insufficient to avoid a second wave if all control measures are released at the end of the lockdown</p>
Ann. Intern. Med. 13MAY2020	<b>Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure</b>	Kucirka, Lauren M. and al. USA <a href="#">gotopaper</a>	Virology	<p>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.</p> <p>Objective: To estimate the false-negative rate by day since infection.</p> <p>CI<sup>o</sup>: 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.</p>
N. Engl. J. Med. 13MAY2020	<b>Multiorgan and Renal Tropism of SARS-CoV-2</b>	Puelles, Victor G. et al Germany <a href="#">gotopaper</a>	Cellular tropism	<p><b>Autopsy series from 22 patients who died from Covid-19:</b></p> <ul style="list-style-type: none"> <li>- 77% had more than 2 coexisting conditions, and <b>greater coexisting conditions associated with SARS-CoV-2 tropism for kidneys.</b></li> <li>- <b>highest SARS-CoV-2 copies per cell = respiratory tract,</b></li> <li>- <b>lower viral copies per cell = kidneys, liver, heart, brain, and blood.</b></li> </ul> <p><b>Kidney</b> tissue microdissection from 6 patients :          - 3 = detectable SARS-CoV-2 <b>viral load in all kidney compartments</b> examined, with <b>preferential targeting of glomerular cells.</b>          -&gt; <b>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</b></p>
The Journal of Molecular Diagnostics 13MAY2020	<b>Detection of SARS-CoV-2 is comparable in clinical samples preserved in saline or viral transport media</b>	Radbel, Jared and al. USA <a href="#">gotopaper</a>	Virology	<p>The availability of viral transport media (VTM) has become severely limited, contributing to delays in diagnosis and rationing of diagnostic testing.</p> <p>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.</p> <p>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.</p> <p>CI<sup>o</sup>: 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</p>

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Lancet 13MAY2020	<b>An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study</b>	Verdoni L et al Italy <a href="#">gotopaper</a>	Clinic	<p>29 children with Kawasaki disease Group1(n=19): before SARS-CoV-2 outbreak Group2(n=10): after SARS-CoV-2 outbreak <u>Group1 versus group2:</u></p> <ul style="list-style-type: none"> <li>- Higher incidence in group2: 0,3 vs 10/month (p&lt;0,05)</li> <li>- Older group2: 3,0 vs 7,5 y (p&lt;0,05)</li> <li>- Abnormal echocardiogram: 60%(grp2) vs 10%(grp1), p&lt;0,05</li> <li>- More MAS group2: 50% vs 0%</li> </ul> <p>→ 30-fold increased incidence of KD in the past month</p> <p><b>→ SARS-CoV-2 outbreak is associated with high incidence of severe form of KD</b></p>
Nature Medicine 13MAY2020	<b>Infection of bat and human intestinal organoids by SARS-CoV-2</b>	Zhou, Jie et al. Hong Kong <a href="#">gotopaper</a>	Fundamental research	<p>Establishment and characterization of intestinal organoids derived from horseshoe bats (<i>Rhinolophus sinicus</i>) can recapitulate bat intestinal epithelium:</p> <ul style="list-style-type: none"> <li>- bat enteroids are fully susceptible to SARS-CoV-2 infection and robust viral replication.</li> <li>- human intestinal organoids also sustain active replication of SARS-CoV-2</li> </ul> <p><b>-&gt; First expandable organoid culture system of bat intestinal epithelium and evidence that SARS-CoV-2 can infect bat intestinal cells.</b></p> <p>-&gt; Robust SARS-CoV-2 replication in human intestinal organoids suggests that the human intestinal tract might be a transmission route of SARS-CoV-2.</p>
JAMA 13MAY2020	<b>SARS-CoV-2 Rates in BCG-Vaccinated and Unvaccinated Young Adult</b>	Hamiel et al., Israel <a href="#">gotopaper</a>	Vaccine	<p>The BCG vaccine was routinely administered to all newborns in Israel as part of the national immunization program between 1955 and 1982</p> <p>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 proportions 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.</p> <p><b>-&gt; This study does not support the idea that BCG vaccination in childhood has a protective effect against COVID-19 in adulthood.</b></p>
Annals of Internal Medicine 12MAY2020	<b>Pharmacokinetics of Lopinavir and Ritonavir in Patients Hospitalized With Coronavirus Disease 2019 (COVID-19)</b>	Schoergenhofer, Christian et al. Austria <a href="#">gotopaper</a>	Therapeutic	<p><b>First pharmacokinetic data of lopinavir and ritonavir in patients hospitalized with COVID-19.</b> Series of 8 patients.</p> <ul style="list-style-type: none"> <li>- Lopinavir trough levels were approximately <b>2-fold higher</b> in this population <b>than in patients with HIV</b> receiving the same dose (7.1 µg/mL).</li> <li>- A correlation of drug concentrations with C-reactive protein, a downstream marker of IL-6, was observed.</li> </ul> <p>However, approximately <b>60- to 120-fold higher concentrations are required to reach the assumed EC50 at trough levels</b>, making effective treatment of COVID-19 with lopinavir and ritonavir at the currently used doses unlikely.</p> <p><b>Limitations:</b> 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.</p>

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Nature 12MAY2020	<b>Respiratory disease in rhesus macaques inoculated with SARS-CoV-2</b>	Munster, Vincent J. et al. USA <a href="#">gotopaper</a>	Animal model	<p>SARS-CoV-2 causes respiratory disease in infected rhesus macaques, with disease lasting 8-16 days:</p> <ul style="list-style-type: none"> <li>- 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 <math>4 \times 10^5</math> TCID<sub>50</sub>/ml (<math>3 \times 10^8</math> genome copies/ml).</li> <li>- Pulmonary infiltrates visible in lung radiographs</li> <li>- High viral load in nose and throat swabs and bronchoalveolar lavages of all animals.</li> <li>- prolonged rectal shedding detected in 1 animal</li> </ul> <p><b>-&gt; Rhesus macaque recapitulates moderate disease with regard to virus replication, shedding, presence of pulmonary infiltrates, histological lesions and seroconversion.</b></p>
Nat Med 12MAY2020	<b>A serological assay to detect SARS-CoV-2 seroconversion in humans</b>	Amanat et al., USA <a href="#">gotopaper</a>	Diagnostic	<p><b>Describing a</b> a serological enzyme-linked immunosorbent assay for the screening and identification of human SARS-CoV-2 seroconverters.</p> <ul style="list-style-type: none"> <li>-&gt; 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</li> <li>-&gt; there is no or only negligible cross-reactivity from human coronaviruses to SARS-CoV-2 in the tested individuals</li> <li>-&gt; strong seroconversion with ELISA AUC values in the 1:1,000 range after natural infection with SARS-CoV-2</li> </ul>
Cancer discovery 12MAY2020	<b>Impact of PD-1 blockade on severity of COVID-19 in patients with lung cancers</b>	Luo, Jia et al. USA <a href="#">gotopaper</a>	Therapeutic/ Clinic	<p>Analyses on <b>69 consecutive patients with lung cancers</b> who were diagnosed with COVID-19. Severity based on no or prior receipt of PD-1 blockade was examined.</p> <ul style="list-style-type: none"> <li>- Overall, the <b>severity of COVID-19 in patients with lung cancer was high</b>, including need for hospitalization in more than half of patients and death in nearly a quarter.</li> <li>- Prior PD-1 blockade was, as expected, associated with smoking status.</li> <li>- After adjustment for smoking status, <b>PD-1 blockade exposure was not associated with increased risk of severity of COVID-19</b>. PD-1 blockade does not appear to impact the severity of COVID-19 in patients with lung cancers.</li> </ul> <p>These initial results in patients with lung cancers support the <b>safety of PD-1 blockade treatment to achieve optimal cancer outcomes</b>.</p>
JAMA Intern Med 12MAY2020	<b>Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19</b>	Liang W et al, China <a href="#">gotopaper</a>	Clinic	<p>Develop and validate a clinical score at admission for predicting critical illness</p> <p>Retrospective cohort (575 hospital in China)</p> <p><u>1590 patients with data were include for variable selection:</u></p> <ul style="list-style-type: none"> <li>- Mean age: 48,9y – 57,3% were men – 25,1% had at least 1 comorbidity</li> <li>- 72 variables entered in selection process (LASSO and logistic regression)</li> </ul> <p><u>10 variables were independently statistically significant predictors of critical illness:</u></p> <ul style="list-style-type: none"> <li>- CXR abnormality: OR: 3,39</li> <li>- Age OR: 1,03</li> <li>- Hemoptysis OR 4,53</li> <li>- Dyspnea OR 1,88</li> <li>- Unconsciousness OR 4,71</li> <li>- Number of comorbidities OR 1,60</li> <li>- Cancer history OR 4,07</li> <li>- Neutrophil to lymphocyte ratio OR 1,06</li> <li>- Lactate dehydrogenase OR: 1,002</li> <li>- Direct bilirubin OR: 1,15</li> </ul> <p><u>Validation:</u> cohort of 710 patients AUC of COVID-GRAM 0,88 IC<sub>95%</sub> [0,84 – 0,93]</p> <p><u>Limitations:</u> data are entirely from China <b>→ risk score at the admission for predicting critical illness</b></p>

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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 <a href="#">gotopaper</a>	Therapeutic	<p><b>Retrospective multicenter cohort study of 1438 hospitalized patients</b> who received both hydroxychloroquine and azithromycin, hydroxychloroquine alone, azithromycin alone, or neither.</p> <p>=&gt; Compared with patients receiving neither drug, there <b>were no significant differences in mortality</b> 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]).</p> <p>=&gt; Compared with patients receiving neither drug, <b>cardiac arrest was significantly more likely in patients receiving hydroxychloroquine + azithromycin</b> (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]).</p> <p>=&gt; No significant differences in the relative likelihood of abnormal electrocardiogram findings.</p> <p><b>Limitations:</b> 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</p>
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 <a href="#">gotopaper</a>	Diagnostic	<p>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.</p> <p>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.</p> <p>After extensive experimental study, a rapid test kit has been fabricated to satisfy all design criteria</p>
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 <a href="#">gotopaper</a>	Diagnostic	<p>To address the shortage of the nasopharyngeal swabs, we designed and executed a translational-research program to allow immediate mass production by 3D printing.</p> <p>We validated four prototypes through an institutional review board (IRB)-approved clinical trial that involved 276 outpatient volunteers.</p> <p>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.</p> <p>All prototypes displayed excellent concordance with the control. Contact information for ordering can be found at <a href="http://printedswabs.org">http://printedswabs.org</a></p>
Nature Medicine 11MAY2020	Real-time tracking of self-reported symptoms to predict potential COVID-19	Menni et al, UK <a href="#">gotopaper</a>	Public Health/Epidemiology	<p>A total of 2,618,862 participants reported their potential symptoms of COVID-19 on a smartphone-based app.</p> <p>-&gt; 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).</p> <p>-&gt;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</p>

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Journal of Allergy and Clinical Immunology 11MAY2020	<b>Safety and efficacy of early high-dose IV anakinra in severe COVID-19 lung disease</b>	Pontali, Emanuele et al. Italy <a href="#">gotopaper</a>	Therapeutic	<p><b>Pilot study of early use of high IV doses of anti-IL-1 anakinra in 5 patients</b> with severe/moderate COVID-19 with pulmonary involvement.</p> <p>-&gt;All five patients experienced <b>rapid resolution of systemic inflammation</b>, and <b>remarkable improvement of respiratory parameters</b>, with reduction of oxygen support requirement and early amelioration of chest CT scan abnormalities before discharge in 3 patients.</p> <p>-&gt; All patients were discharged 6 to 13 days after the start of anakinra.</p> <p>-&gt; No secondary infections or other adverse events were observed.</p> <p><b>Limitations:</b> non-controlled study ; small size ; short-term duration of the treatment ; variability of laboratory biomarkers.</p>
Clin. Infect. Dis. 11MAY2020	<b>Hydroxychloroquine in COVID-19 patients: what still needs to be known about the kinetics</b>	Martin-Blondel, G. et al. France <a href="#">gotopaper</a>	Therapeutic	<p>Aim: to determine whether or not the pharmacokinetics in systemic lupus erythematosus (SLE) patients can be applied to COVID-19 patients.</p> <p>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).</p> <p>Blood samples (n=101) were collected from 57 COVID-19 patients for 7 days and concentrations were compared with simulated kinetic profiles.</p> <p>⇒ <b>Hydroxychloroquine exposure tends to be low</b> and in most instances lower than the values reported in SLE patients, in particular for the standard regimen of “200 mg x 3/day”.</p> <p>⇒ The <b>pharmacokinetic behavior in COVID-19 patients cannot be predicted by the SLE population or by rheumatoid arthritis patients</b>.</p>
European heart journal 11MAY2020	<b>Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019</b>	Shi S and al, China <a href="#">gotopaper</a>	Clinic	<p>671 hospitalized patients COVID-19 Median age: 63 years Main comorbidities: hypertension (29,7%) –diabetes (14,5%) – CHD(9%) Case fatality rate 9,2%</p> <p><u>Death versus survivor group</u></p> <ul style="list-style-type: none"> <li>- Older and more often male (p&lt;0,001)</li> <li>- More comorbidities (p&lt;0,001)</li> <li>- More myocardial injury: 75,8% vs 9,7% (p&lt;0,001)</li> </ul> <p><u>Cardiac troponin I predicting in-hospital mortality:</u></p> <ul style="list-style-type: none"> <li>- AUC 0,92</li> <li>- Se 86% and Spe 86%</li> <li>- Single cut-off concentrations 73 µg/L</li> </ul> <p><u>Predictor of myocardial injury:</u></p> <ul style="list-style-type: none"> <li>- Older age – comorbidities</li> <li>- High level of CRP</li> </ul> <p>Limitation: small sample size, cause of death or myocardial injury underestimated → <b>CtnI and CK-MB predict risk for in hospital mortality</b></p>



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JAMA ped 11MAY2020	<b>Characteristics and Outcomes of Children with Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units</b>	Shekerdeman LS and al, USA <a href="#">gotopaper</a>	Clinic	<p>46 PICU (March 14 and April 3) → 48 children (40 in US &amp; 6 in Canada)</p> <p>Median age: 13 years [4,2 – 16,6]</p> <p>Comorbidities (83%)</p> <p>Median PICU lenght of stay: 5 days</p> <p>Respiratory symptoms: 73 %</p> <p>→ 39/48 required ventilatory support: 21 non-invasively and 19 IMV</p> <p>Specific therapies (28/46): Hydroxychloroquine or hydroxy+azythro or remdesivir or tocilizumab</p> <p>Case fatality rate: 4,2% (2/48)</p> <p>→ <b>pre-hospital comorbidities = important factor</b></p>
Emerging Infectious Disease journal 08MAY2020	<b>Prolonged Persistence of SARS-CoV-2 RNA in Body Fluids</b>	Jiufeng Sun and al. <a href="#">gotopaper</a>	Virology	<p>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.</p> <p>43 patients with mild cases of COVID-19 - 490 specimens collected.</p> <p><b>Results:</b> through an AFT-based modeling study: persistent shedding of virus RNA in nasopharyngeal swab and feces samples. The estimated time until loss of virus RNA detection ranged from 45.6 days for nasopharyngeal swab samples to 46.3 days for feces samples in mild cases and from 48.9 days for nasopharyngeal swab samples to 49.4 days for feces samples in severe cases (longer than those for SARS-Cov and MERS-Cov).</p> <p><b>CI*:</b> 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.</p>
Pediatric Blood Cancer 08MAY2020	<b>COVID-19 infection in children and adolescents with cancer in Madrid</b>	De Roja T and al, Spain <a href="#">gotopaper</a>	Clinic	<p>15 pediatric oncology patients</p> <p>Median age: 10,6 years [0,6 – 18,6]</p> <p>Hematological malignancy (73%) and solid tumor (27%)</p> <p>60% received chemotherapy in the 15 days before infection</p> <p><b>Symptoms:</b> fever (67%) – cough (40%) – asymptomatic (13%)</p> <p><b>Radiological finding:</b> 8/14 pathological findings</p> <p>2 patients received oxygen therapy</p> <p>Median hospital stays: 8 days</p> <p><b>All favorable outcome</b></p> <p>→ <b>prevalence among children with cancer in Madrid: 1,3%</b></p> <p>→ mild symptomatic and better prognosis than adults</p>
American Journal of Obstetrics & Gynecology MFM 08MAY2020	<b>Clinical course of severe and critical COVID-19 in hospitalized pregnancies: a US cohort study</b>	Rebecca Am, and al USA <a href="#">gotopaper</a>	Clinic	<p><b>64 pregnant women</b> hospitalized: 44 severe and 20 critical – no death</p> <p>Gestational age at admission: 30 ± 6 weeks</p> <p>Admission: 7 days after onset symptoms</p> <p>Majoration of dyspnea at day 8 and MV at day 9</p> <p>Median duration of hospital stays: 6 day for severe and 12 for critical</p> <p><b>Delivery preterm:</b> 75% of critical women</p> <ul style="list-style-type: none"> <li>- Severe: 37 ± 2</li> <li>- Critical: 32 ± 4</li> </ul> <p><b>Critical cases:</b> 95% required MV - 70% ARDS - 20% prone position</p> <p><b>Neonate:</b></p> <ul style="list-style-type: none"> <li>- 64% need ICU</li> <li>- One tested positive at 48-h without any symptoms</li> </ul> <p>→ clinical course not different from not pregnant women</p> <p>→ <b>pregnancy should not be considered an independent risk of factor</b></p>



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Cell 08MAY2020	Host-viral infection maps reveal signatures of severe COVID-19 patients	Bost, Pierre; et al. Israel-France-China <a href="#">gotopaper</a>	Fundamental research	<p>Viral-Track, a new computational method to analyze host-viral infection maps :</p> <ul style="list-style-type: none"> <li>- <b>enables transcriptional sorting of infected vs bystander cells and reveals virus-induced expression</b> (scans unmapped scRNA-seq data for presence of viral RNA).</li> <li>- Applicable to multiple models of infection (HBV, HIV, VSV, etc)</li> </ul> <p>Applied to Bronchoalveolar-Lavage samples from severe vs mild COVID-19 patients, reveals:</p> <ul style="list-style-type: none"> <li>- SARS-CoV-2 infects epithelial cells and alters immune landscape in severe patients.</li> <li>- <b>detected unexpected coinfection with hMPV</b> (human MetaPneumoVirus) mainly in monocytes, dampening interferon response.</li> </ul> <p>-&gt; <b>robust technology for dissecting mechanisms of viral-infection and pathology.</b></p>
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 <a href="#">gotopaper</a>	Therapeutic	<p><b>Multicentre, prospective, open-label, randomised, phase 2 trial in 127 adults</b> with COVID-19 hospitalized in Hong Kong. Random assignement (2:1) to the <b>combination group (lopinavir-ritonavir + ribavirin+ interferon beta-1)</b> or to the <b>control group (lopinavir-ritonavir)</b>.</p> <p>=&gt; The <b>triple combination</b>, when <b>given within 7 days of symptom onset</b>, is <b>effective in suppressing the shedding of SARS-CoV-2</b>, not just in a nasopharyngeal swab, but in all clinical specimens, compared with lopinavir-ritonavir alone.</p> <p>=&gt; The <b>significant reductions in duration of RT-PCR positivity and viral load were associated with clinical improvement</b> as shown by the significant reduction in NEWS 2 and duration of hospital stay.</p> <p>=&gt; Subgroup comparison suggested interferon beta-1b to be a key component of the combination treatment.</p> <p><b>Limitations:</b> open label, no placebo group, confounded by a subgroup omitting interferon beta-1b within the combination group, no critically ill patients.</p>
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 <a href="#">gotopaper</a>	Fundamental research	<p><b>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 :</b></p> <ul style="list-style-type: none"> <li>- 3.1a resolution</li> </ul> <p>-&gt; <b>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.</b></p> <ul style="list-style-type: none"> <li>- CR3022 likely binds more tightly to SARS-CoV because its epitope contains a glycan absent in SARS-CoV-2.</li> </ul> <p>-&gt; Modeling showed this epitope only accessible when at least 2 of the 3 spike proteins are in a conformation competent to bind the receptor.</p>
Science 08MAY2020	Harnessing multiple models for outbreak management	Shea et al, USA <a href="#">gotopaper</a>	Public Health/Epidemiology	<p>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.</p> <p>We advocate a more systematic approach, by merging two well-established research fields.</p> <ol style="list-style-type: none"> <li>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.</li> <li>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.</li> </ol>

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JAMA 08MAY2020	<b>Changes in SARS-CoV-2 Positivity Rate in Outpatients in Seattle and Washington State, March 1-April 16, 2020</b>	Randhawa et al, USA <a href="#">gotopaper</a>	Public Health/Epidemiology	<p>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.</p> <p>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.</p> <p>SARS-CoV-2 infections in patients of Washington outpatient clinics and Seattle ED settings peaked in late March and have been declining.</p> <p>-&gt; This trajectory is aligned with local physical distancing and the “Stay Home, Stay Healthy” order announced March 23, 2020.</p>
Nature structural & molecular biology 07MAY2020	<b>Structural basis for the inhibition of SARS-CoV-2 main protease by antineoplastic drug carmofur</b>	Jin, Zhenming et al. China <a href="#">gotopaper</a>	Therapeutic	<p>The antineoplastic drug <b>carmofur is shown to inhibit the SARS-CoV-2 main protease (M<sup>pro</sup>)</b>. The X-ray crystal structure of M<sup>pro</sup> 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. <b>Carmofur inhibits viral replication in VeroE6 cells (EC50 = 24.30 µM)</b>. Carmofur has a favorable selectivity index (SI) of 5.36, but further optimization will be required to develop an effective drug.</p> <p>This study provides a basis for rational <b>design of carmofur analogs with enhanced inhibitory efficacy to treat COVID-19</b>.</p>
The Lancet Rheumatology 07MAY2020	<b>Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study</b>	Cavalli, Giulio et al. Italy <a href="#">gotopaper</a>	Therapeutic	<p><b>Retrospective cohort study</b> in adult patients with COVID-19, moderate-to-severe ARDS, and hyperinflammation, managed with non-invasive ventilation outside of the ICU and who received <b>standard treatment of hydroxychloroquine and lopinavir-ritonavir, with or without anakinra</b>.</p> <p><b>29 patients</b> received high-dose intravenous anakinra, <b>16 patients</b> comprised the comparison group for this study, and 7 patients received low-dose subcutaneous anakinra but treatment was interrupted after 7 days.</p> <p>At 21 days, <b>treatment with high-dose anakinra was associated with clinical improvement in 21 (72%)</b> of 29 patients versus 8 (50%) in the standard treatment group. At 21 days, <b>survival was 90% in the high-dose anakinra group</b> and 56% in the standard treatment group (<b>p=0.009</b>). Discontinuation of anakinra was not followed by inflammatory relapses.</p> <p><b>Limitations:</b> 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.</p>
Journal of Clinical Virology 07MAY2020	<b>SARS-CoV-2 detection by direct rRT-PCR without RNA extraction</b>	Merindol, Natacha, and al. <a href="#">gotopaper</a>	Diagnostic	<p>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.</p> <p>-&gt; Comparison of sensitivity of 2 approved rRT-QPCR Assays with and without RNA extraction.</p> <p><b>Conclusion :</b> 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.</p>

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JAMA 07MAY2020	<b>Necessity of a development and widespread distribution of COVID-19 medical treatments</b>	Bollyky, T. et al, US <a href="#">gotopaper</a>	HSS/Politic	<p>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.</p> <p>2- Framework for Distribution =&gt;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...)</p> <p>=&gt; Adequate, Predictable Financing Provide a funding mechanism to generate income for R&amp;D + deployment of vaccines and therapeutic products (advance purchase commitments (APC) for COVID-19 products + profiles of target products) Funds =&gt; 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.</p>
The Lancet. Respiratory medicine 07MAY2020	<b>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</b>	Hui, Kenrie P. Y.; et al. China <a href="#">gotopaper</a>	Fundamental research	<p>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).</p> <p>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. - <b>SARS-CoV-2 was a less potent inducer of proinflammatory cytokines than H5N1, H1N1pdm, or MERS-CoV.</b></p> <p>-&gt; <b>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.</b></p>
Cell 07MAY2020	<b>Coast-to-Coast Spread of SARS-CoV-2 during the Early Epidemic in the United States</b>	Fauver et al, USA <a href="#">gotopaper</a>	Public Health/Epidemiology	<p>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:</p> <p>- 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</p> <p>→ Widespread transmission of SARS-CoV-2 within USA, need for critical surveillance</p>

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Infect. Control Hosp. Epidemiol. MAY2020	<b>Effect of ambient air pollutants and meteorological variables on COVID-19 incidence</b>	Jiang et al, China <a href="#">gotopaper</a>	Public Health/Epidemiology	<p>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.</p> <p>Daily COVID-19 incidence was positively associated with PM2.5 and humidity in all cities. The relative risk (RR) of PM2.5 was 1.036 (95% CI, 1.032 -1.039), 1.059 (95% CI, 1.046 - 1.072) and 1.144 (95% CI, 1.12 - 1.169) for COVID-19 incidence per day in the three provinces. The RR of humidity was lower than that of PM2.5, difference ranging from 0.027 to 0.111. PM10 and temperature exhibited a negative correlation with daily COVID-19 incidence: the RR of PM10 ranged from 0.915 (95% 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).</p> <p>Data suggest that PM2.5/humidity and PM10/temperature could substantially increase and decrease the risk of COVID-19 incidence, respectively.</p>
Nature 07MAY2020	<b>The pathogenicity of SARS-CoV-2 in hACE2 transgenic mice</b>	Bao, Linlin; et al. China <a href="#">gotopaper</a>	Animal model	<p><b>Human ACE2 transgenic mice infected with SARS-CoV-2 :</b></p> <ul style="list-style-type: none"> <li>- SARS-CoV-2 intranasal inoculation at <math>10^5</math> TCID<sub>50</sub>/50 µL inoculum volume per mouse. (14 days observation)</li> <li>- 6-11 month-old, male and female WT (n=15) and hACE2 mice (n=19).</li> <li>- Typical histopathology: interstitial pneumonia with infiltration of significant macrophages and lymphocytes into the alveolar interstitium, and accumulation of macrophages in alveolar cavities.</li> <li>- <b>Weight loss observed in hACE2 mice (up to 8% at 5 dpi), not in WT mice.</b></li> <li>- <b>viral load detectable</b> (qRT-PCR) at 1, 3, 5 and 7 dpi (peak at 3 dpi) <b>in lungs of hACE2 mice but not in WT mice.</b></li> <li>- infectious virus isolated from lungs of hACE2 mice at 1, 3 dpi and 5 dpi (peak titers at 3 dpi), but not WT mice.</li> <li>- <b>Viral antigens detected</b> in bronchial epithelial cells, macrophages and alveolar epithelia.</li> </ul> <p>-&gt; <b>Confirmed pathogenicity of SARS-CoV-2 in hACE2 expressing mice and suggests that hACE2 was essential for infection and replication in mice.</b></p>
The Journal of Infectious Diseases 07MAY2020	<b>T cell subset counts in peripheral blood can be used as discriminatory biomarkers for diagnosis and severity prediction of COVID-19</b>	Jiang, Mei and al. China <a href="#">gotopaper</a>	Diagnostic	<p>Assessment of the significance of lymphocyte subsets detection in peripheral blood in the diagnosis and prognosis of Covid-19 disease.</p> <p>The counts of CD8+T and CD4+T cells can be used as diagnostic markers of COVID-19 and predictors of disease severity.</p>
The Lancet Psychiatry 07MAY2020	<b>COVID-19, unemployment, and suicide</b>	Kawohl And Nordt., Switzerland <a href="#">gotopaper</a>	Psy	<p><b>High scenario:</b> 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.</p> <p><b>Low scenario:</b> the unemployment would increase to 5-088%, associated with an increase of about 2135 suicides.</p>
New England Journal of Medicine 07MAY2020	<b>Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19</b>	Geleris, Joshua et al. USA <a href="#">gotopaper</a>	Therapeutic	<p><b>Observational study</b> involving consecutive patients with Covid-19 admitted to a hospital, and <b>comparing outcomes in patients who received hydroxychloroquine with those in patients who did not.</b> The primary end point was a composite of intubation or death in a time-to-event analysis.</p> <p>Of the <b>1376 patients</b>, 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.</p> <p>Overall, 346 patients (25.1%) had a primary end-point of respiratory failure. In the main analysis, there was <b>no significant association between hydroxychloroquine use and intubation or death</b> (hazard ratio, 1.04, 95% confidence interval, 0.82 to 1.32). Results were similar in multiple sensitivity analyses.</p>

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Nat Rev Immunology 06MAY2020	<b>Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages</b>	Merad et al., USA <a href="#">gotopaper</a>	Immuno	<p>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.</p> <ul style="list-style-type: none"> <li>· Monocytes differentiate into pro-inflammatory macrophages</li> <li>· 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-<math>\gamma</math> (IFN<math>\gamma</math>).</li> <li>· Oxidized phospholipids (OxPLs) are accumulated in infected lungs and activate monocyte-derived macrophages through the Toll-like receptor 4 (TLR4)–TRAF6–NF-<math>\kappa</math>B pathway.</li> <li>· 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-1<math>\beta</math> and/or IL-18.</li> <li>· IL-1<math>\beta</math> 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.</li> <li>· The engagement of Fc<math>\gamma</math> receptors (Fc<math>\gamma</math>R<math>s</math>) by anti-spike protein IgG immune complexes can contribute to increased inflammatory activation of monocyte-derived macrophages.</li> </ul> <p><b>Conclusion:</b> 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</p>
Antimicrobial agents and chemotherapy 06MAY2020	<b>Inhibition of SARS-CoV-2 infection by the cyclophilin inhibitor Alisporivir (Debio 025)</b>	Softic, Lauren et al. France, <a href="#">gotopaper</a>	Therapeutic	<p>Cyclophilins play a key role in the lifecycle of coronaviruses. <b>Alisporivir (Debio 025) is a non-immunosuppressive analogue of cyclosporin A with potent cyclophilin inhibition properties.</b> 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.</p> <p>=&gt; Alisporivir reduced SARS-CoV-2 RNA production in a dose-dependent manner in VeroE6 cell line, with an <b>EC50 of 0.46<math>\pm</math>0.04 <math>\mu</math>M</b>.</p> <p>=&gt; Anti-SARS-CoV-2 effectiveness of alisporivir was confirmed by immunofluorescence.</p> <p>=&gt; Alisporivir did not inhibit SARS-CoV-2 entry into VeroE6 cells. Effect of alisporivir was preserved when the compound was added 3 h post-infection. These results suggest that <b>alisporivir inhibits a post-entry step of the SARS-CoV-2 life cycle.</b></p>
Journal of the American College of Cardiology 06MAY2020	<b>Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19</b>	Paranjpe, Ishan et al. USA <a href="#">gotopaper</a>	Therapeutic	<p>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.</p> <p>=&gt; <b>Systemic AC may be associated with improved outcomes</b> 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.</p> <p>=&gt; <b>Association with AC and improved survival after adjusting for mechanical ventilation.</b></p> <p><b>Limitations:</b> observational study, unobserved confounding, unknown indication for AC, lack of metrics to further classify illness severity in the mechanically ventilated subgroup, and indication bias.</p>

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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 <a href="#">gotopaper</a>	Clinic	<p>50 children COVID19+ and 26 with PCR- and CT+ with history of exposure</p> <p><b>Symptoms:</b></p> <ul style="list-style-type: none"> <li>- More frequent: fever (64%) – cough (44%)</li> <li>- Less frequent: diarrhea (6%) – abdominal pain (4%) – rhinorrhea (16%)</li> <li>- Asymptomatic 12%</li> </ul> <p><b>Laboratory:</b></p> <ul style="list-style-type: none"> <li>- Lymphopenia (16%) – thrombocytopenia (14%)</li> <li>- Elevated CRP (20%) – anemia (12%)</li> </ul> <p>43/50 had abnormalities on CT:</p> <ul style="list-style-type: none"> <li>- Ground glass opacity (64%)</li> </ul> <p>29/50 &gt;1 CT which 65% had improved CT and 28% had more lesions</p> <p><b>At discharge: no association between changes in CT lesions</b> →CT allow to detect COVID19 but do not evaluated the resolution of illness for children</p>
Cell host & microbe PREPRINT	Identification of human single-domain antibodies against SARS-CoV-2	Yanling Wu et al, China <a href="#">gotopaper</a>	Therapeutic	<p>SARS-CoV-2 spike protein, containing the receptor-binding domain (RBD) and S1 subunit involved in receptor engagement, is a potential therapeutic target.</p> <ul style="list-style-type: none"> <li>- <b>Development of a phage-displayed single-domain antibody library</b> by grafting naïve complementarity-determining regions (CDRs) into framework regions of a human germline immunoglobulin heavy chain variable region (IGHV) allele.</li> <li>- Panning this library against SARS-CoV-2 RBD and S1 subunit <b>identified fully human single-domain antibodies targeting five distinct epitopes on SARS-CoV-2 RBD with subnanomolar to low nanomolar affinities</b>. Some of these antibodies neutralize SARS-CoV-2 by targeting a cryptic epitope located in the spike trimeric interface.</li> </ul>
SCIENCE 06MAY2020	Development of an inactivated vaccine candidate for SARS-CoV-2	Qiang Gao et al, China <a href="#">gotopaper</a>	Vaccine	<p><b>Development of PiCoVacc Vaccine based on the inactivated SARS-CoV-2 virus (Sinovac vaccine currently in ph1)</b> -&gt; 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-propionolactone was used for vaccine development (not causing severe disease).</p> <p><b>Immunogenicity in BAL/C mice:</b> -&gt; Inactivated Chinese patient virus+adjuvant (PiCoVacc) was injected at day 0 and 7 at different doses (0ug, 1,5ug, 3ug, 6ug) -&gt; SARS-CoV-2 S and RBD specific IgGs were developed very quickly in mice sera -&gt;The dominant immunogen was shown to be the RBD (no response to N protein) -&gt;Neutralizing antibodies against all the SARS-CoV-2strains were also produced</p> <p><b>Immunogenicity and protection in macaques</b> -&gt; 3 immunizations at d 0, 7 and 14 with at different doses of PiCoVacc (3 or 6ug) -&gt; Specific S IgG and neutralizing antibodies were induced from two weeks after vaccination -&gt; macaques at day 22 after fist immunization: viral loads were shown to decrease. -&gt; 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.</p>



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Pediatr Infect Dis J 6MAY2020	<b>The risk of children Hospitalized with severe COVID-19 in Wuhan</b>	Wang Y and al China <a href="https://doi.org/10.1097/INF.0000000000002739">https://doi.org/10.1097/INF.0000000000002739</a>	Clinic	<p>Retrospective case-control study – 8 severe children matched with 35 - Median age of severe cases: 5,06 years 2/8 had comorbidities</p> <p><u>Symptoms in both groups</u>: fever – cough – dyspnea – diarrhea/vomiting</p> <p><u>Laboratory</u>:</p> <ul style="list-style-type: none"> <li>-WBC higher in severe group</li> <li>-No difference for lymphocytes counts <math>p&gt;0,05</math></li> <li>-IL6 – IL10, D-dimer higher in severe group</li> </ul> <p>Hospital stay: 13,5 (severe) versus 11 days (non severe) Time for PCR turning negative: 10,5 (severe) versus 7,1 (<math>p&lt;0,05</math>)</p> <p><b>More lung segment involves in severe children</b> → unique risk factor for severe</p> <p>→ mild symptomatic (8 severe cases on 260 COVID-19) – rare mortality → <b>some factors associated with severity</b>: CT scan lesions – immune response (IL-6) – intravascular coagulation (D-dimer)</p>
Science 05MAY2020	<b>Rapid implementation of mobile technology for real-time epidemiology of COVID-19</b>	Drew et al, USA <a href="https://doi.org/10.1126/science.abc0473">https://doi.org/10.1126/science.abc0473</a>	Public Health/Epidemiology	<p>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.</p> <p>This mobile application offers data on risk factors, herald symptoms, clinical outcomes, and geographical hot spots.</p> <p>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.</p>
Autoimmunity reviews 05MAY2020	<b>Continuous hydroxychloroquine or colchicine therapy does not prevent infection with SARS-CoV-2: Insights from a large healthcare database analysis</b>	Gendelman, Omer et al, Israel <a href="https://doi.org/10.1016/j.autrev.2020.102566">https://doi.org/10.1016/j.autrev.2020.102566</a>	Therapeutic	<p><b>Retrospective study based on a large healthcare computerized database</b> including all patients that were screened for the SARS-CoV-2 in the study period from February 23rd 2020 to March 31st 2020.</p> <p>Comparison between subjects tested positive for SARS-CoV-2 and those found negative in terms of rate of <b>administration of hydroxychloroquine/ colchicine therapy</b>.</p> <ul style="list-style-type: none"> <li>- An overall sample of <b>14,520 subjects</b> were screened for SARS-CoV-2 infection and <b>1317 resulted positive</b>.</li> <li>- <b>No significant difference was found in terms of rates of usage of hydroxychloroquine or colchicine</b> 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).</li> </ul>
Cell 05MAY2020	<b>Structural Basis for Potent Neutralization of Betacoronaviruses by Single-domain Camelid Antibodies</b>	Daniel Wrapp and al, <a href="https://doi.org/10.1016/j.cell.2020.04.031">https://doi.org/10.1016/j.cell.2020.04.031</a>	Therapeutic	<p>Isolation of single-domain antibodies (VHHs) from a llama immunized with prefusion-stabilized coronavirus spikes.</p> <p>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.</p> <p>Cross-reactive VHH neutralizes SARS-CoV-2 S pseudotyped viruses as a bivalent human IgG Fc-fusion.</p> <p>=&gt; These data provide a <b>molecular basis for the neutralization of pathogenic betacoronaviruses by VHHs</b> and suggest that these molecules may serve as useful therapeutics during coronavirus outbreaks.</p>



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Nature Communications 04MAY2020	<b>A human monoclonal antibody blocking SARS-CoV-2 infection</b>	Wang, Chunyan et al, <a href="https://www.nature.com/articles/s41467-020-16256-y">https://www.nature.com/articles/s41467-020-16256-y</a>	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	<b>High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study</b>	Helms J, and al France <a href="https://doi.org/10.1007/s00134-020-06062-x">https://doi.org/10.1007/s00134-020-06062-x</a>	Clinic	Multicentric study – 4 ICU in France – 150 patients with ARDS Historical prospective cohort → comparison of COVID to non-COVID by propensity score matching <u>At baseline:</u> >95% patients elevated had D-dimer and fibrinogen Median age = 63 years 64/150 thrombotic complications and <b>16,7% pulmonary embolisms</b> <u>COVID19 (=77) vs non-COVID19 (=145):</u> - 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	<b>Effect of non-pharmaceutical interventions to contain COVID-19 in China</b>	Lai, Shengjie et al, <a href="https://www.nature.com/articles/s41586-020-2293-x">https://www.nature.com/articles/s41586-020-2293-x</a>	Public Health/Epidemiology	<b>Modelling framework that uses daily travel networks to simulate different outbreak and intervention scenarios across China</b> , 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	<b>Heightened innate immune responses in the respiratory tract of COVID-19 patients</b>	Zhou, Zhuo; et al. China <a href="https://doi.org/10.1016/j.chom.2020.04.017">https://doi.org/10.1016/j.chom.2020.04.017</a>	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, <b>suggesting SARS-CoV-2 causes hypercytokinemia.</b> - SARS-CoV-2 triggered <b>robust expression of IFN-inducible genes (ISGs) with immunopathogenic potential</b> (overrepresentation of genes involved in inflammation), unlike SARS-CoV which is thought to induce inadequate IFN. - <b>Estimations of immune cell populations, show increased activated dendritic cells and neutrophils.</b>
Science 04MAY2020	<b>Site-specific glycan analysis of the SARS-CoV-2 spike</b>	Watanabe, Yasunori, et al. UK - USA <a href="https://doi.org/10.1126/science.abb9983">https://doi.org/10.1126/science.abb9983</a>	Structural biology	<b>Revealing the glycan structures on a recombinant SARS-CoV-2 spike (S) glycoprotein immunogen by site-specific mass spectrometry.</b>  -SARS-CoV-2 S gene encodes 22 N-linked glycan sequons per protomer, which likely play a role in protein folding and immune evasion.  → <b>Glycosylation analysis enables detailed mapping of the glycan-processing states and signatures across the trimeric viral spike.</b> <b>Glycan profiling have implications in viral pathobiology as well as vaccine design for comparing immunogen integrity and monitoring manufacturing processes .</b>

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Nature 04MAY2020	<b>Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform</b>	Thao, Tran Thi Nhu, et al. Switzerland - Germany - Russia <a href="https://www.nature.com/articles/s41586-020-2294-9">https://www.nature.com/articles/s41586-020-2294-9</a>	Fundamental research	<p>Accelerated yeast-based reverse genetics pipeline can genetically reconstruct diverse long RNA viruses, including Coronaviridae, Flaviviridae and Paramyxoviridae families :</p> <ul style="list-style-type: none"> <li>- Viral subgenomic fragments (from viral isolates, cloned viral DNA, clinical samples, or synthetic DNA) are reassembled in one step in <i>S. cerevisiae</i> 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.</li> </ul> <p>-&gt; <b>Approach to generate SARS-CoV-2 is rapid</b> (1 week after receipt of synthetic DNA fragments) <b>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.</b></p> <p>- <b>Also possible to rapidly introduce sequence variations to functionally characterize phenotypic consequences of SARS-CoV-2 evolution in real-time.</b></p>
Autoimmunity reviews 03MAY2020	<b>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</b>	Toniati, Paola et al, Italy <a href="https://doi.org/10.1016/j.autrev.2020.102568">https://doi.org/10.1016/j.autrev.2020.102568</a>	Therapeutic	<p>A <b>prospective series of 100 consecutive patients</b> admitted to a Hospital in Brescia (Italy) between March 9th and March 20th with confirmed COVID-19 pneumonia and ARDS requiring ventilatory support <b>were administered Tocilizumab</b> (TCZ, monoclonal antibody that targets the interleukin 6 receptor).</p> <p>The outcome measure was an improvement in ARDS assessed by means of the Brescia COVID Respiratory Severity Score.</p> <p>Out of 100 treated patients (88 M, 12 F; median age: 62 years), the <b>respiratory condition was improved or stabilized in 77 (77%) patients</b>, 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.</p> <p>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.</p>
Immunity 03MAY2020	<b>Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals</b>	Ling et al., China <a href="https://www.sciencedirect.com/science/article/pii/S1074761320301813">https://www.sciencedirect.com/science/article/pii/S1074761320301813</a>	Diagnostic	<ol style="list-style-type: none"> <li>1. SARS-CoV-2-specific antibodies are detected in COVID-19 convalescent subjects.</li> <li>2. Most COVID-19 convalescent individuals have detectable neutralizing antibodies.</li> <li>3. Cellular immune responses to SARS-CoV-2 are found in COVID-19 convalescent subjects</li> <li>4. Neutralization antibody titers correlate with the numbers of virus-specific T cells.</li> </ol>
American journal of obstetrics and gynecology 03MAY2020	<b>Evidence for and against vertical transmission for SARS-CoV-2 (COVID-19)</b>	A, Amouroux; et al. France <a href="http://www.sciencedirect.com/science/article/pii/S000293782030524X">http://www.sciencedirect.com/science/article/pii/S000293782030524X</a>	Clinic	<p>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:</p> <ul style="list-style-type: none"> <li>- <b>SARS-CoV-2 recovered (RT-PCR) from</b> nasal and throat swabs, sputum and feces of symptomatic patients including <b>neonates but not from vaginal swabs, amniotic fluid, placenta, cord blood, neonatal blood or breast milk.</b></li> <li>- <b>Neonatal infection was diagnosed within 48 hours of life in 4 cases.</b></li> </ul> <p>-&gt; <b>More complete evidence and reliable serological studies needed</b> before counselling pregnant women on the risk of congenital infection with SARS-CoV-2.</p>

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Int. J. Infect. Dis. 03MAY2020	<b>Viral kinetics of SARS-CoV-2 in asymptomatic carriers and presymptomatic patients</b>	Kim, Seong Eun; et al. South Korea <a href="https://doi.org/10.1016/j.ijid.2020.04.083">https://doi.org/10.1016/j.ijid.2020.04.083</a>	Virology	<p>71 laboratory-confirmed SARS-CoV-2 cases, identified 3 presymptomatic patients and 10 entirely asymptomatic infections:</p> <ul style="list-style-type: none"> <li>- <b>2 out of 3 incubation period patients (presymptomatic) had very high viral titer (Ct value &lt;20).</b></li> <li>- <b>In entirely asymptomatic carriers : median days to first negative RT-PCR was 4.5 (2.5–9) days and all reached a first Ct&gt;35 RT-PCR within 14 days after diagnosis.</b></li> </ul> <p>-&gt; <b>COVID-19 patients may already be infectious before symptoms manifestation, and 14 days isolation after diagnosis may be sufficient in entirely asymptomatic cases.</b></p>
Gastroenterology 01MAY2020	<b>Gastrointestinal and Hepatic Manifestations of 2019 Novel Coronavirus Disease in a Large Cohort of Infected Patients From New York: Clinical Implications</b>	Kaveh H and al USA <a href="https://doi.org/10.1053/j.gastro.2020.05.010">https://doi.org/10.1053/j.gastro.2020.05.010</a>	Clinic	<p>1059 patients COVID-19 - 33% at least one gastrointestinal symptom</p> <p><b>GI symptom:</b> diarrhea (22%) – abdominal pain (7%) – nausea (16%)</p> <p>62% had biochemical liver injury</p> <p>GI manifestation and liver injury were associated with higher admission rate</p> <p><b>Multivariate analysis</b> → independent predictor of death or ICU admission</p> <ul style="list-style-type: none"> <li>- Liver injury at presentation OR:2,53</li> <li>- Older age OR:1,03</li> <li>- Tachypnea OR:1,73</li> <li>- Severe hypoxemia OR:1,47</li> </ul> <p>GI manifestation → no effect on the outcome</p> <p>→ <b>COVID-19 patients had commonly GI manifestation</b></p>
JAMA Cardiology 01MAY2020	<b>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)</b>	Mercurio, Nicholas J. Et al, USA <a href="https://jamanetwork.com/journals/jamacardiology/fullarticle/2765631">https://jamanetwork.com/journals/jamacardiology/fullarticle/2765631</a>	Therapeutic	<p><b>Cohort study of hospitalized patients with coronavirus disease 2019.</b></p> <p>Among <b>90 patients given hydroxychloroquine, 53 received concomitant azithromycin.</b> Those receiving concomitant azithromycin had a greater median change in QT interval compared with those receiving hydroxychloroquine.</p> <p>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 <b>1 case of torsades de pointes.</b></p>
Molecular Cell 01MAY2020	<b>A Multibasic Cleavage Site in the Spike Protein of SARS-CoV-2 Is Essential for Infection of Human Lung Cells</b>	Hoffmann, Markus; et al. Germany <a href="https://doi.org/10.1016/j.molcel.2020.04.022">https://doi.org/10.1016/j.molcel.2020.04.022</a>	Fundamental research	<p>The spike protein of SARS-CoV-2 harbors a multiple arginine residues (multibasic) S1/S2 site.</p> <ul style="list-style-type: none"> <li>- The host cell protease furin cleaves the SARS-CoV-2 spike protein at the S1/S2 site.</li> <li>- <b>Cleavage at the S1/S2 site is essential for spike-driven cell-cell fusion and viral entry into lung cells.</b></li> </ul> <p>-&gt; <b>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.</b></p>
New England Journal of Medicine 01MAY2020	<b>Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19</b>	Mehra M, and al USA <a href="https://doi.org/10.1056/NEJMoa2007621">https://doi.org/10.1056/NEJMoa2007621</a>	Clinic	<p>169 hospitals in Asia, Europe, North America</p> <p>8910 patients → 5,8 % died</p> <p>Use of ACE inhibitors or ARBDs → no associated to death</p> <p><b>Independently associated with increase of in hospital death:</b></p> <ul style="list-style-type: none"> <li>- <b>Age &gt; 65 y</b> [OR:1,93 (1,6 – 2,4)]</li> <li>- <b>Coronary artery disease</b> [OR:2,7 (2,08 – 3,51)]</li> <li>- <b>Heart failure</b> [OR:2,48 (1,62 – 3,79)]</li> <li>- <b>Cardiac arrhythmia</b> [OR:1,95 (1,33 – 2,86)]</li> <li>- <b>Chronic obstructive pulmonary disease</b> [OR:2,96 (2,0 – 4,4)]</li> <li>- <b>Current smoking</b> [OR:1,79 (1,29 – 2,47)]</li> </ul> <p>→ underlying cardiovascular disease is associated with an increased risk of in hospital death</p>

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New England Journal of Medicine 01MAY2020	<b>Early Detection of Covid-19 through a Citywide Pandemic Surveillance Platform</b>	Chu, Helen Y. and al. USA <a href="https://www.nejm.org/doi/full/10.1056/NEJM2008646">https://www.nejm.org/doi/full/10.1056/NEJM2008646</a>	Public Health/Epidemiology	<p>The Seattle Flu Study is a multi-institutional, community-wide pandemic surveillance platform that was established in November 2018.</p> <p>-&gt; Persons enrolled online and were sent kits, by rapid-delivery services, for home collection of a midnasal swab; samples were returned by mail.</p> <p>-&gt;Persons reporting symptoms of respiratory illness provided informed consent for testing to identify influenza and other respiratory pathogens.</p> <p>-&gt;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.</p> <p><b>Conclusion:</b> 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</p>
Clin. Infect. Dis 01MAY2020	<b>Early detection of SARS-CoV-2 antibodies in COVID-19 patients as a serologic marker of infection</b>	Zhao, Rongqing and al. <a href="https://doi.org/10.1093/cid/ciaa523">https://doi.org/10.1093/cid/ciaa523</a>	Diagnostic	<p><b>A COVID-19/SARS-CoV-2 S1 serology ELISA kit was developed.</b> 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.</p> <p><b>Conclusion:</b> 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.</p>
J. Clin. Virol. 01MAY2020	<b>A RT-PCR Assay for the Detection of Coronaviruses from Four Genera</b>	Xiu, Leshan and al. China <a href="https://www.sciencedirect.com/science/article/pii/S1386653220301335">https://www.sciencedirect.com/science/article/pii/S1386653220301335</a>	Diagnostic	<p>A better understanding of the natural hosts and genetic diversity of CoVs are needed to help mitigate these threats.</p> <p>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.</p> <p><b>Conclusion:</b> 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.</p>
Science 01MAY2020	<b>SARS-CoV-2 productively infects human gut enterocytes</b>	Lamers, Mart M.; et al. Netherlands <a href="https://doi.org/10.1126/science.abc1669">https://doi.org/10.1126/science.abc1669</a>	Fundamental research	<p>Infection of human small intestinal organoids (hSIOs) grown from primary gut epithelial stem cells to investigate intestine as another viral target organ :</p> <ul style="list-style-type: none"> <li>- hSIOs enterocytes were readily infected by SARS-CoV and SARS-CoV-2 (confocal- and electron-microscopy) and significant titers of infectious viral particles detected.</li> <li>- SARS-CoV-2 infected airway and gut organoids.</li> <li>- mRNA expression analysis revealed <b>strong induction of a generic viral response program. SARS-CoV-2 induced a stronger interferon response than SARS-CoV in HIOs.</b></li> </ul> <p>-&gt; <b>intestinal epithelium supports SARS-CoV-2 replication, and data imply that human organoids represent faithful experimental models to study of coronavirus infection and biology.</b></p>

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Emerging Microbes & Infections 01MAY2020	<b>Kinetics of SARS-CoV-2 specific IgM and IgG responses in COVID-19 patients</b>	Sun et al., China <a href="https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1762515#">https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1762515#</a>	Immuno	<ul style="list-style-type: none"> <li><b>Kinetic steps:</b> <ul style="list-style-type: none"> <li>- A total of 130 blood samples from 38 COVID-19 patients were analyzed.</li> <li>- 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.</li> <li>- 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.</li> <li>- 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%.</li> </ul> </li> <li><b>Comparison between ICU and non-ICU patients</b> <ul style="list-style-type: none"> <li>- Most ICU patients had higher N-IgG than S-IgG after the symptom onset</li> <li>- 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.</li> <li>- S-IgG in ICU patients was significantly lower than non-ICU patients by 2 weeks after the onset</li> </ul> </li> </ul> <p><b>Conclusion:</b> Intensive care unit monitoring the kinetics of S-IgG should help to predict prognosis.</p>
Science 01MAY2020	<b>Structural basis for inhibition of the RNA-dependent RNA polymerase from SARS-CoV-2 by remdesivir</b>	Yin, Wanchao; et al. China <a href="https://doi.org/10.1126/science.abc1560">https://doi.org/10.1126/science.abc1560</a>	Structural biology	<p>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).</p> <ul style="list-style-type: none"> <li>- Structure comparison and sequence alignment suggest that mode of substrate RNA recognition and Remdesivir inhibition of RdRp is highly conserved in diverse RNA viruses</li> <li>-&gt; <b>providing a basis for designing broad spectrum antiviral drugs based on nucleotide analogs and a template structure for modeling/modifying existing nucleotide drugs (ex. EIDD-2801).</b></li> <li>-&gt; <b>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.</b></li> </ul>
Gastroenterology 01MAY2020	<b>Taste Changes (Dysgeusia) in COVID-19: A systematic review and metaanalysis</b>	Aziz, Muhammad; et al. USA <a href="https://doi.org/10.1053/j.gastro.2020.05.003">https://doi.org/10.1053/j.gastro.2020.05.003</a>	Clinic	<p>Systematic review (case series/case-control/ cohort studies) (January 1st - April 21st, 2020) reporting on ageusia/dysgeusia:</p> <ul style="list-style-type: none"> <li>- 4 single-nation studies, 1 multinational study from Europe = total of 817 patients included.</li> <li>-&gt; <b>Prevalence : almost half of patients (49.8%) with COVID-19 have altered taste sensation across the five studies.</b></li> </ul> <p><b>Limitations :</b> lack of data comparing ageusia/dysgeusia in COVID-19 +ve vs -ve patients, or severe COVID-19.</p> <p>In contexts of lack of diagnostic tests (ex. developing world), <b>distinctive clinical features like ageusia/dysgeusia can be useful in identifying suspected COVID-19 patients.</b></p>
New England Journal of Medicine 01MAY2020	<b>Renin–Angiotensin–Aldosterone System Inhibitors and Risk of Covid-19</b>	Reynolds H, and al USA <a href="https://doi.org/10.1056/NEJMoa2008975">https://doi.org/10.1056/NEJMoa2008975</a>	Clinic	<p>Relation between previous treatment that act on the RAAS and the likelihood of a positive test or the likelihood of severe illness?</p> <p>Five class of antihypertensive medication examined. Estimated a propensity score for the likelihood of treatment with each medication class</p> <ul style="list-style-type: none"> <li>-&gt; 12594 patients were tested</li> <li>-&gt; 5894 patients positive COVID19 which 17% had severe illness</li> <li>-&gt; 2573/(5894) had HTA which 24,6% had severe illness</li> </ul> <p><b>No association between medication examined and increased likelihood of a positive test or in the risk of severe Covid19.</b></p>

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NEJM 01MAY2020	<b>Inhibitors of the Renin–Angiotensin–Aldosterone System and Covid-19</b>	<p>Jarcho, John A.; et al. USA <a href="https://doi.org/10.1056/NEJMe2012924">https://doi.org/10.1056/NEJMe2012924</a></p> <p>Mehra MR, et al. USA <a href="https://doi.org/10.1056/NEJMoa2007621">https://doi.org/10.1056/NEJMoa2007621</a></p> <p>Mancia, Giuseppe; et al. Italy <a href="https://doi.org/10.1056/NEJMoa2006923">https://doi.org/10.1056/NEJMoa2006923</a></p> <p>Reynolds HR, et al. USA <a href="https://doi.org/10.1056/NEJMoa2008975">https://doi.org/10.1056/NEJMoa2008975</a></p>	Clinic	<p>Analysis of 3 <i>N Engl J Med</i> articles, as clinicians 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):</p> <ul style="list-style-type: none"> <li>- Mehra et al. database study, 8910 hospitalised Covid-19 patients, 11 countries : <b>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.</b></li> <li>- Mancia et al. case–control study, 6272 confirmed SARS-CoV-2 patients in Lombardy (Italy) vs 30,759 matched controls : <b>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.</b></li> <li>- Reynolds et al. electronic health records, 12,594 people in New York University -&gt; 5894 tested +ve, of which 1002 had severe illness (admission to ICU/mechanical ventilation/death): <b>no +ve association for drug classes, ACE inhibitors and ARBs, for a +ve test result or severe illness.</b></li> </ul> <p><b>-&gt; none of the 3 studies showed evidence of harm with continued use of ACE inhibitors and ARBs.</b></p>
JAMA Cardiology 30APR2020	<b>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</b>	<p>Bessiere, Francis et al, France <a href="https://jamanetwork.com/journals/jamacardiology/fullarticle/2765633">https://jamanetwork.com/journals/jamacardiology/fullarticle/2765633</a></p>	Therapeutic	<p>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.</p> <ul style="list-style-type: none"> <li>-&gt; 30 patients (75%) required invasive mechanical ventilation and 25 (63%) received vasoactive drugs.</li> <li>-&gt; 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.</li> <li>⇒ 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.</li> <li>⇒ 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).</li> <li>⇒ The antiviral treatment ceased before completion for 7 patients (17.5%) following ECG abnormalities and in 10 (25%) for acute renal failure.</li> </ul>
Nature 30APR2020	<b>A SARS-CoV-2 protein interaction map reveals targets for drug repurposing</b>	<p>Gordon, David E et al, <a href="https://www.nature.com/articles/s41586-020-2286-9#Abs1">https://www.nature.com/articles/s41586-020-2286-9#Abs1</a></p>	Therapeutic	<p><b>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</b> using affinity-purification mass spectrometry (AP-MS)</p> <ul style="list-style-type: none"> <li>-&gt; Identification of 332 high-confidence SARS-CoV-2-human protein-protein interactions (PPIs).</li> <li>-&gt; 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).</li> <li>-&gt; Screening a subset of these in multiple viral assays identified <b>two sets of pharmacological agents that displayed antiviral activity</b>: inhibitors of mRNA translation and predicted regulators of the Sigma1 and Sigma2 receptors.</li> </ul> <p>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.</p>



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Jama Psychiatry 30APR2020	<b>Mental Health in the Coronavirus Disease 2019 Emergency—The Italian Response</b>	De Girolamo et al., Italy <a href="https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2765557">https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2765557</a>	Psy	<b>Experience of mental health services and the lessons learned in Italy</b> -> 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 <b>Need for a leadership position in the psychosocial management of disasterlike situations.</b>
Lancet 30APR2020	<b>Obesity could shift severe COVID-19 disease to younger ages</b>	Kass, David A.; et al. USA <a href="https://doi.org/10.1016/S0140-6736(20)31024-2">https://doi.org/10.1016/S0140-6736(20)31024-2</a>	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) : - <b>significant inverse correlation between age and BMI -&gt; younger individuals admitted to hospital more likely obese.</b> - no difference by sex -> <b>In populations with high prevalence of obesity, COVID-19 will affect younger populations more than previously reported.</b>
Viruses 30APR2020	The SARS-CoV-2 Exerts a Distinctive Strategy for Interacting with the ACE2 Human Receptor	Brielle, Esther S.; et al. Israel <a href="https://doi.org/10.3390/v12050497">https://doi.org/10.3390/v12050497</a>	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.  -> <b>SARS-CoV-2–ACE2 complex -&gt; higher number of interacting residues larger, larger interface area, decreased interface residue fluctuations relative to the SARS-CoV–ACE2 complex.</b>  -> <b>Data implies therapeutic challenge attributed to the enhanced rigidity of the COVID-19 RBD relative to that of SARS-2002.</b>
Cell 30APR2020	<b>Genomic Epidemiology of SARS-CoV-2 in Guangdong Province, China</b>	Lu, Jing; et al. China <a href="http://www.sciencedirect.com/science/article/pii/S0092867420304864">http://www.sciencedirect.com/science/article/pii/S0092867420304864</a>	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:  - <b>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).</b>  -> <b>national travel restrictions and province's large-scale intensive surveillance and intervention measures helped reduce/ eliminate transmission chains.</b> - vigilance still required following recent increase in COVID-19 cases imported to China from other countries.
Nature 29APR2020	<b>Massively multiplexed nucleic acid detection using Cas13</b>	Ackerman, Cheri M. and al. USA <a href="http://www.ncbi.nlm.nih.gov/pubmed/32349121">http://www.ncbi.nlm.nih.gov/pubmed/32349121</a>	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.  <b>Conclusion:</b> 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	<b>Global coronavirus disease 2019: what has daily cumulative index taught us?</b>	Lai C, and al China <a href="https://www.sciencedirect.com/science/article/pii/S092464602030159X">https://www.sciencedirect.com/science/article/pii/S092464602030159X</a>	Public Health/Epidemiology	<p>Rapid increase of COVID19 cases in short time = insufficiency of healthcare system and negatively affect patient's outcome?</p> <p><b>Daily cumulative index (DCI)</b> = 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 HCl or HAQI, DCI associated with mortality per 1,000,000 (aRR:1,02 [1,01 – 1,03])</p> <p>Higher level of healthcare performance is associated with higher incidence → ability to detect?</p> <p>→ Reduction of DCI:</p> <ul style="list-style-type: none"> <li>- slow the increasing number of COVID19</li> <li>- improve outcome in COVID-19 patients</li> </ul>
Science 29APR2020	<b>Changes in contact patterns shape the dynamics of the COVID-19 outbreak in China</b>	Zhang J, and al China <a href="https://doi.org/10.1126/science.abb8001">https://doi.org/10.1126/science.abb8001</a>	Public Health/Epidemiology	<p>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</p> <p>The model consider potential age differences in susceptibility to infection <u>Susceptibility to SARS-CoV-2 infection increase with age:</u></p> <ul style="list-style-type: none"> <li>- 0-14 years: OR=0,34 [0,24 – 0,49] (compared to 15-64y)</li> <li>- &gt; 65 years: OR=1,47 [1,12 – 1,92] (compared to 15-64y)</li> </ul> <p><u>Model to study the impact of social distancing and school closures:</u></p> <ul style="list-style-type: none"> <li>- social distancing alone is sufficient to control the outbreak</li> <li>- School closures → reduce peak incidence (40-60%) and delay the epidemic / impact on the disease dynamic and hospital surge capacity</li> </ul> <p>→ Refining age-specific estimates of susceptibility to infection → to evaluating the impact of interventions put in place.</p>
PNAS 29APR2020	<b>Effective treatment of severe COVID-19 patients with tocilizumab</b>	Xu, Xiaoling et al, China <a href="https://doi.org/10.1073/pnas.2005615117">https://doi.org/10.1073/pnas.2005615117</a>	Therapeutic	<p><b>Retrospective study with tocilizumab</b>, an IL6R inhibitor, in treatment of 21 patients with severe and critical COVID-19.</p> <p><b>Clinical data showed that the symptoms, hypoxymia, and CT opacity changes were improved immediately after the treatment</b> 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.</p> <p>Limitations: limited number of patients, single observation study.</p>
The Lancet 29APR2020	<b>Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial</b>	Wang et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31022-9/fulltext?utm_campaign=tlc-oronavirus20&amp;utm_source=twitter&amp;utm_medium=social">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31022-9/fulltext?utm_campaign=tlc-oronavirus20&amp;utm_source=twitter&amp;utm_medium=social</a>	Therapeutic	<p>-&gt; 237 patients were enrolled and randomly assigned to a treatment group (158 to remdesivir and 79 to placebo)</p> <p>-&gt; Remdesivir use was not associated with a difference in time to clinical improvement (hazard ratio 1.23 [95% CI 0.87–1.75])</p> <p>-&gt; 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])</p> <p>-&gt; 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.</p>

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J Infect Dis 29APR2020	<b>Effect of Convalescent Plasma Therapy on Viral Shedding and Survival in COVID-19 Patients</b>	Zeng, Qing-Lei et al, China <a href="https://doi.org/10.1093/infdis/jiaa228">https://doi.org/10.1093/infdis/jiaa228</a>	Therapeutic	<p>6 COVID-19 subjects with respiratory failure received <b>convalescent plasma</b> at a median of <b>21.5 days</b> after first detection of viral shedding. All tested <b>negative for SARS-CoV-2 RNA by 3 days after infusion</b>, and <b>5 died eventually</b>.</p> <p>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.</p>
Cancer discovery 28APR2020	<b>Patients with cancer appear more vulnerable to SARS-CoV-2: a multi-center study during the COVID-19 outbreak</b>	Dai M, and al USA <a href="https://doi.org/10.1158/2159-8290.CD-20-0422">https://doi.org/10.1158/2159-8290.CD-20-0422</a>	Clinic	<p>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</p> <p><u>Patient with cancer had higher:</u></p> <ul style="list-style-type: none"> <li>- <b>ICU admission</b> [OR:2,84 (1,59 – 5,08)]</li> <li>- <b>Death rate</b> [OR:2,34 (1 15 – 4, 77)]</li> <li>- <b>Having one or more severe/critical symptom</b> [OR:2,79 (1,74 – 4,41)]</li> <li>- <b>Changes of needing MV</b></li> </ul> <p>Hematological, lung, metastatic cancer → higher rates of severe events</p> <p>→ <b>patients with cancer tend to have more severe outcomes</b></p>
Critical Care 28APR2020	<b>Clinical determinants for fatality of 44,672 patients with COVID-19</b>	Deng G, and al China <a href="https://doi.org/10.1186/s13054-020-02902-w">https://doi.org/10.1186/s13054-020-02902-w</a>	Clinic Letter	<p>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 &gt; 80 years</p> <p><u>Risk factors for fatality:</u></p> <ul style="list-style-type: none"> <li>- Male [RR:1,67 (1,47 – 1,89)]</li> <li>- Cardiovascular disease [RR:6,75 (5,4 – 8,43)]</li> <li>- HTA [HR:4,48 (3,69 – 5,85)]</li> <li>- Diabetes [RR:4,43 (3,49 – 5,61)]</li> <li>- Cancer [RR:2,92 (1,34 – 6,41)]</li> <li>- Respiratory disease [RR:3,43 (2,42 – 4,87)]</li> </ul> <p><b>More intensive surveillance for male and those with comorbidities</b></p>
Natl Sci Rev 28APR2020	<b>Plasma Metabolomic and Lipidomic Alterations Associated with COVID-19</b>	Di Wu; Shu, et al. China <a href="https://doi.org/10.1093/nsr/nwaa086">https://doi.org/10.1093/nsr/nwaa086</a>	Metabolite and lipid alterations	<p><b>Targeted metabolomic and lipidomic analyses of plasma from cohort of COVID-19 patients to identify plasma biomarkers associated with COVID-19:</b></p> <ul style="list-style-type: none"> <li>- malic acid of the TCA cycle and carbamoyl phosphate of urea cycle <b>reveal altered energy metabolism and hepatic dysfunction</b>, respectively.</li> <li>- <b>carbamoyl phosphate profoundly down-regulated in fatal patients compared with mild patients.</b></li> <li>- <b>guanosine monophosphate (GMP)</b> (mediated by GMP synthase, CD39 and CD73) <b>significantly altered between healthy subjects vs COVID-19 patients, and between the mild vs fatal groups.</b></li> </ul>
Public Health 28APR2020	<b>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</b>	Cobb J and al, USA <a href="http://www.sciencedirect.com/science/article/pii/S0033350620301219">http://www.sciencedirect.com/science/article/pii/S0033350620301219</a>	Public Health/Epidemio	<p>Trends among US counties and COVID 19 growth rate in relation to existence of shelter in place (SIP) orders <b>Machin learning</b></p> <p><b>Limiting gatherings to &lt; 10 people reduced growth rate by 6,6%</b></p> <p><b>SIP → reduction of 7,8% versus counties with no SIP</b> <b>SIP orders and limitation gathering were additive</b></p> <p>Features predicting the effect of SIP:</p> <ul style="list-style-type: none"> <li>- Population / Longitude / Population per square</li> </ul> <p>→ SIP was effective → Counties with large population or high population density: benefit the most from a SIP</p>

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Cell 28APR2020	<b>Trained immunity: a tool for reducing susceptibility and severity of SARS-CoV-2 infection</b>	Neteal et al., The Netherlands <a href="https://www.cell.com/pb-assets/products/coronavirus/CELL_11391_S5.pdf">https://www.cell.com/pb-assets/products/coronavirus/CELL_11391_S5.pdf</a>	Fundamental research	<p>-&gt; 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.</p> <p><b>-&gt; 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.</b></p>
Cell PreProof	<b>Clinically Applicable AI System for Accurate Diagnosis, Quantitative Measurements and Prognosis of COVID-19 Pneumonia Using Computed Tomography</b>	Zhang et al., China <a href="https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00656.pdf">https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00656.pdf</a>	Diagnostic	<p>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.</p> <p>-&gt; Identification of important clinical and biochemical markers of multiple organs that correlated with the NCP lesion properties</p> <p>-&gt; Together with the clinical data, this AI system was able to provide accurate clinical prognosis</p>
Science Advances 27APR2020	<b>Squalene-based multidrug nanoparticles for improved mitigation of uncontrolled inflammation</b>	Dormont, Flavio et al, France <a href="https://doi.org/10.1126/sciadv.aaz5466">https://doi.org/10.1126/sciadv.aaz5466</a>	Therapeutic	<p>Development of <b>multidrug nanoparticles for the mitigation of uncontrolled inflammation</b>.</p> <p>The nanoparticles are made by conjugating squalene, an endogenous lipid, to adenosine, an endogenous immunomodulator, and then encapsulating <math>\alpha</math>-tocopherol, a natural antioxidant. This resulted in <b>high drug loading, biocompatible, multidrug nanoparticles</b>.</p> <p>By exploiting the vascular endothelial barrier dysfunction at sites of acute inflammation, these <b>multidrug nanoparticles could deliver the therapeutic agents in a targeted manner</b> and conferred a significant survival advantage to treated animals in lethal models of endotoxemia.</p> <p><b>-&gt; 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.</b></p>
European Journal of Clinical Microbiology & Infectious Diseases 27APR2020	<b>Viral RNA load as determined by cell culture as a management tool for discharge of SARS-CoV-2 patients from infectious disease wards</b>	La Scola, Bernard and al. France <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7185831/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7185831/</a>	Virology	<p>It is of paramount importance to define when a treated patient can be considered as no longer contagious.</p> <p>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.</p>
Microbial Pathogenesis 27APR2020	<b>Design of a peptide-based subunit vaccine against novel coronavirus SARSCoV-2</b>	Parismita Kalita et al., India-Japan <a href="http://www.sciencedirect.com/science/article/pii/S0882401020305234">http://www.sciencedirect.com/science/article/pii/S0882401020305234</a>	Vaccines	<p>Multi-peptide subunit-based epitope vaccine against COVID-19 containing and adjuvant, CTL, HTL and B Cell epitopes</p> <p>-&gt; Epitopes were selected from known SARS-CoV-2 antigenic proteins (Nucleocapside, membrane, Spike) by using <i>in silico</i> prediction tools.</p> <p>-&gt; Identification of 6 high immunogenic epitopes targeting HTL, 18 targeting CTL, 9 targeting B-cells.</p> <p>- Epitopes were linked together to build a 566 aa subunit vaccine</p> <p>- Human b-defensine 1 (68aa): as adjuvant</p> <p>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.</p> <p>The binding modes, dynamics, and stability of the vaccine-TLR3 complex were validated by using molecular dynamics simulation studies.</p> <p>Estimation of the half-life of the vaccine :</p> <ul style="list-style-type: none"> <li>- 30 h in mammalian reticulocytes (in vitro)</li> <li>- &gt; 20 h in yeast (in vivo)</li> <li>- &gt; 10 h in E. coli (in vivo), suggesting that the construct is stable in vivo</li> </ul> <p>-&gt; Probability of showing good protective efficacy and safety against SARS-CoV-2 infection in humans</p>

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Eurosurveillance 27APR2020	<b>Coronavirus disease (COVID-19) – impact on vaccine preventable diseases</b>	Hungerdord et al., UK <a href="https://doi.org/10.2807/1560-7917.ES.2020.25.18.2000756">https://doi.org/10.2807/1560-7917.ES.2020.25.18.2000756</a>	HSS/Politic	<p>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:</p> <ol style="list-style-type: none"> <li>1. Isolation + COVID-19 illness in families with newborn children</li> <li>2. Disruption of vaccine supplies</li> <li>3. Healthcare staffing issues</li> <li>4. Difficulty to launch a prevention campaign for adults at risk</li> </ol> <p><b>Impact:</b></p> <ul style="list-style-type: none"> <li>• Increase in number of sensitive children facing winter illnesses</li> <li>• The poorest populations are disproportionately affected</li> <li>• Risk of outbreaks of diseases such as measles...</li> </ul> <p><b>To deal with this impact,</b></p> <ul style="list-style-type: none"> <li>- ensure consideration + resources for delivery of routine vaccination</li> <li>- Vaccination rates should be monitored by analysts and immunization teams to identify hotspots = vaccine coverage surveillance + modeling.</li> </ul> <p>This will help face and not allow the Covid to increase the disability and mortality from vaccine preventable diseases.</p>
The Lancet. Infectious diseases 27APR2020	<b>Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study</b>	Qifang B and al, China/USA <a href="http://www.sciencedirect.com/science/article/pii/S1473309920302875">http://www.sciencedirect.com/science/article/pii/S1473309920302875</a>	Public Health/Epidemiology	<p>391 cases and 1286 close contact</p> <p>Cases were older - Most case mild or moderate and 9% severe</p> <p>Median incubation period: 4,8 days</p> <p>All those develop symptoms will do within 14 days</p> <p>Median time recovery: 20,8 days</p> <p>Contact tracing reduced isolation period by 1,9 days</p> <p>Higher risk of infection:</p> <ul style="list-style-type: none"> <li>- Household contact (OR6,27)</li> <li>- Contact travelling with a case (OR:7,06)</li> </ul> <p>Secondary attack = 11,2%</p> <p>Children likely to be infected (7,4%) than adults (6,6%)</p> <p>→ Isolation and contact tracing reduce the R and time during which cases are infectious</p> <p>→ children similar risk → analyses for transmission and control</p>
Inter J Infectious Disease 27APR2020	<b>Coronavirus disease 2019 in pregnancy</b>	Xu Q and al, China <a href="http://www.sciencedirect.com/science/article/pii/S1201971220302800">http://www.sciencedirect.com/science/article/pii/S1201971220302800</a>	Clinic	<p>Pregnant woman (28) compared to non-pregnant woman (54)</p> <p><b>Time from illness to admission: shorter pregnant women</b></p> <p><b>Laboratory:</b> significantly</p> <ul style="list-style-type: none"> <li>- Higher leukocyte in pregnant women (10 vs 2 x10<sup>9</sup>/L)</li> <li>- Higher CRP (17 vs 14 mg/dl)</li> </ul> <p>75% pregnant received antiviral vs 100% non-pregnant</p> <p><b>No association between</b></p> <ul style="list-style-type: none"> <li>- pregnancy and virus clearance time</li> <li>- pregnancy and LOS</li> <li>- pregnancy and severity of disease</li> </ul> <p>Median gestational age: 38 [IQR:36,5 – 39]</p> <p><b>None of neonates had a positive result for SARS-CoV-2</b></p> <p>→ no vertical transmission – good outcomes for both group</p>
Pathogens 26APR2020	<b>Emergence of Drift Variants That May Affect COVID-19 Vaccine Development and Antibody Treatment</b>	Takahiko Koyama et al., USA <a href="https://doi.org/10.3390/pathogens9050324">https://doi.org/10.3390/pathogens9050324</a>	Vaccines	<p>&gt; Twenty-one virus variants affecting T-cell epitopes identified.</p> <p>&gt; Twelve virus variants affecting B-cell epitopes of spike protein (S), nucleocapsid protein (N), and membrane protein (M) identified</p> <p>A variant replacing 23403A&gt;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.</p> <p>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&gt; Genetic drift</p> <p>&gt; Vaccine design and convalescent plasma antibody treatment might require specific considerations to accommodate the drift</p>

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The Lancet. Infectious diseases 27APR2020	<b>Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study</b>	Qifang B and al, China/USA <a href="http://www.sciencedirect.com/science/article/pii/S1473309920302875">http://www.sciencedirect.com/science/article/pii/S1473309920302875</a>	Public Health/Epidemiology	<p><b>391 cases and 1286 close contact</b></p> <p>Cases were older - Most case mild or moderate and 9% severe Median incubation period: 4,8 days All those develop symptoms will do within 14 days Median time recovery: 20,8 days Contact tracing reduced isolation period by 1,9 days Higher risk of infection:</p> <ul style="list-style-type: none"> <li>- Household contact (OR6,27)</li> <li>- Contact travelling with a case (OR:7,06)</li> </ul> <p>Secondary attack = 11,2% Children likely to be infected (7,4%) than adults (6,6%)</p> <p>→ Isolation and contact tracing reduce the R and time during which cases are infectious → children similar risk → analyses for transmission and control</p>
An International Journal of Obstetrics & Gynaecology 27APR2020	<b>Vaginal delivery in SARS-CoV-2 infected pregnant women in Northern Italy: a retrospective analysis</b>	Ferrazzi E and al, Italy <a href="https://doi.org/10.1111/1471-0528.16278">https://doi.org/10.1111/1471-0528.16278</a>	Clinic	<p>42-woman COVID-19 who delivered during study period <u>Diagnosis COVID:</u> 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 <b>Cesareans related to pneumonia (p=0,024)</b> <b>3 neonates positive for SARS-CoV:</b></p> <ul style="list-style-type: none"> <li>- 2 newborns of women diagnosed after delivery</li> <li>- 1 newborn after vaginal delivery: gastrointestinal and respiratory symptoms → ICU with 24h of MV</li> </ul> <p>→ vaginal delivery is appropriated → cesarean: women with sever symptoms</p>
Clinical microbiology and infection 25APR2020	<b>Umifenovir treatment is not associated with improved outcomes in patients with coronavirus disease 2019: A retrospective study</b>	Lian, Ningfang et al, China <a href="http://www.sciencedirect.com/science/article/pii/S1198743X20302342">http://www.sciencedirect.com/science/article/pii/S1198743X20302342</a>	Therapeutic	<p><b>Retrospective study</b>, 81 COVID-19 patients included, with 45 in umifenovir group and 36 in control group. Baseline clinical, laboratory characteristics were comparable between two groups.</p> <p><b>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.</b> No severe side effect was found in umifenovir treatment.</p> <p><b>Limitations :</b> 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</p>
Cell 24APR2020	<b>SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues</b>	Ziegler et al., USA <a href="https://www.cell.com/cell/fulltext/S0092-8674(20)30500-6">https://www.cell.com/cell/fulltext/S0092-8674(20)30500-6</a>	Fundamental research	<p>-&gt; Meta-analysis of human, primate &amp; mouse scRNA-seq for putative SARS-CoV-2 targets -&gt; Type II pneumocytes, nasal secretory cells &amp; absorptive enterocytes are ACE2+TMPRSS2+ -&gt; Interferon &amp; influenza increase ACE2 in human nasal epithelia and lung tissue -&gt; Mouse Ace2 is not upregulated by interferon, raising implications for disease models</p>
Infection, Genetics and Evolution 24APR2020	<b>Emerging genetic diversity among clinical isolates of SARS-CoV-2: Lessons for today</b>	Sheikh, Javaid Ahmad; et al. India-Germany-UK <a href="https://doi.org/10.1016/j.meegid.2020.104330">https://doi.org/10.1016/j.meegid.2020.104330</a>	Phylogenetics	<p>Machine learning approaches to analyse genome sequences of 257 available SARS-CoV-2 clinical isolates :</p> <ul style="list-style-type: none"> <li>- <b>At least 5 different clades of SARS-CoV-2, great deal of genetic diversity emerging among clinical isolates.</b></li> <li>- <b>Every continent appears to have multiple introductions of different viral strains</b> (no geographical clustering unlike previous pandemics).</li> <li>- 5' terminal of viral genome more prone to mutations compared to 3' end.</li> <li>- <b>ORF1ab, spike, ORF3a and E proteins most prone to mutations.</b></li> <li>- <b>RBD of spike protein is a mutational hotspot (major driver of diversity).</b></li> <li>- <b>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.</b></li> </ul>

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Annals of the rheumatic diseases 24APR2020	<b>Clinical course of coronavirus disease 2019 (COVID-19) in a series of 17 patients with systemic lupus erythematosus under long-term treatment with hydroxychloroquine</b>	Mathian, Alexis et al, France <a href="https://ard.bmj.com/content/early/2020/04/24/ard.2020-0424">https://ard.bmj.com/content/early/2020/04/24/ard.2020-0424</a>	Therapeutic	<p><b>Observational study</b> with the aim to follow the clinical course of COVID-19 in <b>patients with systemic lupus erythematosus (SLE) who received long-term treatment with HCQ</b> (17 patients).</p> <p>-&gt; 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.</p> <p>-&gt; 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.</p> <p>Based on the observation that <b>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</b>, in patients with SLE.</p>
Cell 24APR2020	<b>Clinically Applicable AI System for Accurate Diagnosis, Quantitative Measurements and Prognosis of COVID-19 Pneumonia Using Computed Tomography</b>	Zhang, Ket al., China <a href="https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00656.pdf">https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00656.pdf</a>	Diagnostics	<p>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.</p> <p>Development of an AI system that can diagnose NCP and differentiate it from other common pneumonia and normal controls.</p> <p>The AI system can assist radiologists and physicians in performing a quick diagnosis and is able to identify important clinical markers that correlated with the NCP lesion properties.</p> <p>It provides accurate clinical prognosis that can aid clinicians to consider appropriate early clinical management and allocate resources appropriately.</p> <p>This AI system has been made available globally to assist the clinicians to combat COVID-19.</p>
J Med Virol 24APR2020	<b>SARS-CoV-2 can be detected in urine, blood, anal swabs and oropharyngeal swabs specimens</b>	Peng, Liang and al. China <a href="https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25936">https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25936</a>	Diagnostics	<p>To assess the presence of the SARS-CoV-2 ribonucleic acid (RNA) in urine and blood specimens, and anal and oropharyngeal swabs.</p> <p>SARS-CoV-2 RNA was present in all 4 specimen types, though not all specimen types were positive simultaneously.</p> <p>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</p>
JAMA network open, 24APR2020	<b>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</b>	Borba, Mayla Gabriela Silva et al, Brazil, <a href="https://doi.org/10.1001/jamanetworkopen.2020.8857">https://doi.org/10.1001/jamanetworkopen.2020.8857</a>	Therapeutic	<p>Parallel, double-masked, randomized, phase IIb clinical trial <b>81 adult patients with severe acute respiratory syndrome SARS-CoV-2 infection</b></p> <p>High-dosage CQ (ie, <b>600 mg CQ twice daily for 10 days</b>) versus low-dosage CQ (ie, <b>450 mg twice daily on day 1 and once daily for 4 days</b>)</p> <p>At Day 13, 6 of 40 patients (15.0%) in the low-dose group had died, compared with 16 of 41 patients (39.0%) in the high-dose group. Prolongation of QTc interval was observed in 4 of 36 patients (11.1%) in the low-dose group and 7 of 37 patients (18.9%) in the high-dose group. In addition, 2 patients in the high-dose group (2.7%) experienced ventricular tachycardia. The trial was stopped.</p> <p><b>The preliminary findings of this study suggest that the higher CQ dosage should not be recommended for critically ill patients with COVID-19</b></p>



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Nature Medicine 24APR2020	<b>The QT interval in patients with COVID-19 treated with hydroxychloroquine and azithromycin</b>	Chorin, Ehud et al, USA <a href="https://doi.org/10.1038/s41591-020-0888-2">https://doi.org/10.1038/s41591-020-0888-2</a>	Therapeutic	<p>Charts review and corrected QT (QTc) interval follow-up in a consecutive <b>cohort of 84 patients receiving HY</b> (400mg daily on D1, then 200mg daily from D2 to D5)/<b>AZ</b> (500mg per day for 5 days).</p> <ul style="list-style-type: none"> <li><b>QTc significantly prolonged.</b></li> <li>In a subset of nine (11%) of those patients, the QTc was severely prolonged to &gt;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.</li> <li>No <i>torsades de pointes</i> events recorded for any patients, including those with a severely prolonged QTc.</li> </ul> <p>=&gt; Suggest that the <b>QTc should be followed repeatedly in patients with COVID-19 who are treated with HY/AZ</b>, particularly in those with co-morbidities and in those who are treated with other QT-prolonging medications.</p>
JAMA Pediatrics 24APR2020	<b>Mental Health Status Among Children in Home Confinement During the Coronavirus Disease 2019 Outbreak in Hubei Province, China</b>	Xinyan Xie et al., China <a href="https://jamanetwork.com/journals/jamapediatrics/fullarticle/2765196">https://jamanetwork.com/journals/jamapediatrics/fullarticle/2765196</a>	Psy	<p>Investigation of depressive and anxiety symptoms among students in Hubei province, China.</p> <p>Restricted to home for a mean (SD) of 33.7 days -&gt; A total of 403 students (22.6%) and 337 students (18.9%) reported depressive and anxiety symptoms, respectively. -&gt; Students in Wuhan: significantly higher CDI-S scores than those in Huangshi + greater risk of depressive symptoms -&gt; 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.</p> <p><b>There was no significant association between demographic characteristics and anxiety symptoms.</b></p>
Nat Com 24APR2020	<b>Neutralization of SARS-CoV-2 spike pseudotyped virus by recombinant ACE2-Ig</b>	Lei, Changhai et al, China <a href="https://doi.org/10.1038/s41467-020-16048-4">https://doi.org/10.1038/s41467-020-16048-4</a>	Therapeutic	<p>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.</p> <ul style="list-style-type: none"> <li>Both fusion proteins have a <b>high binding affinity for the receptor-binding domains of SARS-CoV and SARS-CoV-2</b> and exhibit <b>desirable pharmacological properties in mice.</b></li> <li>Moreover, the <b>fusion proteins neutralize virus pseudotyped with SARS-CoV or SARS-CoV-2 spike proteins in vitro.</b></li> </ul> <p>=&gt; As these fusion proteins exhibit cross-reactivity against coronaviruses, they have potential applications in the diagnosis, prophylaxis, and treatment of SARS-CoV-2.</p>
Clinica Chimica Acta 23APR2020	<b>Highly sensitive detection of SARS-CoV-2 RNA by multiplex rRT-PCR for molecular diagnosis of COVID-19 by clinical laboratories</b>	Shige, Takayuki and al. Japan <a href="https://www.sciencedirect.com/science/article/pii/S0009898120301789">https://www.sciencedirect.com/science/article/pii/S0009898120301789</a>	Diagnostics	<p>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.</p> <p>CI*: The proposed multiplex rRT-PCR methodology enable highly sensitive detection of SARS-CoV-2 RNA, reducing reagent use and cost, and time required by clinical laboratory technicians.</p>
Journal of Thrombosis and Haemostasis 23APR2020	<b>Direct oral anticoagulant plasma levels striking increase in severe COVID-19 respiratory syndrome patients treated with antiviral agents. The Cremona experience</b>	Testa, Sophie et al, Italy <a href="https://doi.org/10.1111/jth.14871">https://doi.org/10.1111/jth.14871</a>	Therapeutic	<p>32 patients with <b>COVID 19 and direct oral anticoagulants (DOACs) eligible for antiviral therapy</b> (lopinavir, ritonavir or darunavir)</p> <p>DOAC stopped in 20, and continued in 12. On average, <b>C-trough DOAC levels were 6.14 times higher</b> during hospitalization than in pre-hospitalization period</p> <p><b>Physicians should consider withholding DOACs from patients with SARS-CoV-2 and replacing them with alternative parenteral antithrombotic strategies</b> for as long as antiviral agents are deemed necessary and until discharge</p>



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BMJ 23APR2020	<b>Covid-19: Two thirds of healthcare workers who have died were from ethnic minorities</b>	Rimmer et al., UK <a href="https://doi.org/10.1136/bmj.m1621">https://doi.org/10.1136/bmj.m1621</a>	HSS/Politic	<p>'- Two thirds of healthcare workers who have died from covid-19 were from an ethnic minority background, and at least half were not born in the UK : causes could be biological, medical, or sociological =&gt; need for a concerted effort to seek explanations and solutions.</p> <p>Notable absence of deaths occurred among certain staff groups:</p> <p>'- Deaths notably in surgery (five cases), general practice (four), emergency medicine (two. No anaesthetists or intensivists. =&gt;Better use of PPE?</p> <p>Need for a central registry of deaths among health and social care workers</p>
Canadian Journal of Political Science 23APR2020	<b>Sociodemographic and psychological correlates of compliance with the Covid-19 public health measures in France</b>	Bouraurd et al., France <a href="https://doi.org/10.1017/S0008423920000335">https://doi.org/10.1017/S0008423920000335</a>	HSS/Politic	<p>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.</p> <p>However, compliance by citizens cannot be taken for granted.</p> <p>Individual panel data =&gt; personality and demographic characteristics are relevant predictors of compliance, more than ideology, trust (towards the government and scientists), and emotional reactions.</p> <p>Main characteristics that lead to complying with the measures are :</p> <ul style="list-style-type: none"> <li>- Age (older people)</li> <li>- Sex (women)</li> <li>- Conscientiousness</li> </ul> <p>Characteristics with no impact on behavior :</p> <ul style="list-style-type: none"> <li>- Education</li> <li>- Extraversion</li> <li>- Neuroticism</li> <li>- Ideological extremity</li> </ul>
Nature Medicine 23APR2020	<b>SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes</b>	Sungnak, Waradon; et al. UK-France-Netherlands-Germany-USA <a href="https://doi.org/10.1038/s41591-020-0868-6">https://doi.org/10.1038/s41591-020-0868-6</a>	Fundamental research	<p>Tropism analysis from single cell RNA-seq datasets from multiple tissues from healthy human donors (Human Cell Atlas tissue consortium):</p> <ul style="list-style-type: none"> <li>- <b>ACE2 expressed in cells from multiple tissues at generally low levels.</b></li> <li>- <b>TMPRSS2 highly expressed with a broader distribution, suggesting that ACE2, rather than TMPRSS2, may be a limiting factor for intal viral entry stage.</b></li> <li>- <b>ACE2 and TMPRSS2 highest co-expression in nasal secretory epithelial cells (nasal goblet and ciliated cells), co-expressed with genes involved in innate immunity.</b></li> </ul> <p>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 :</p> <ul style="list-style-type: none"> <li>- <b>expression distribution coincided with viral transmissibility based on a comparison to R0 -&gt; upper airway in viruses with higher R0/infectivity (SARS-CoV-2, influenza) vs lower airway/lung parenchyma for MERS-CoV</b></li> </ul> <p>-&gt; All data provided as a user-friendly an open resource: <a href="http://www.covid19cellatlas.org">www.covid19cellatlas.org</a></p>
Radiology 23APR2020	<b>Acute Pulmonary Embolism in COVID-19 Patients on CT Angiography and Relationship to D-Dimer Levels</b>	Leonard-Lorant I and al, France <a href="https://doi.org/10.1148/radiol.2020201561">https://doi.org/10.1148/radiol.2020201561</a>	Clinic/Radiology	<p>106 patients COVID19+ and CT angiograms</p> <p><b>32 (30%) positive for pulmonary embolus:</b></p> <ul style="list-style-type: none"> <li>- Higher D-dimer levels (6110 vs 1920, p&lt;0,01)</li> <li>- More in ICU (75% vs 32ù, p&lt;0,01)</li> <li>- Treated more often with LWMH (78% vs 23%)</li> </ul> <p>D-dimer levels &gt;2660µg/L :</p> <ul style="list-style-type: none"> <li>- Sensitivity 100%</li> <li>- Specificity 67%</li> </ul>

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Emerging Infectious Disease 23APR2020	<b>Population-Based Estimates of Chronic Conditions Affecting Risk for Complications from Coronavirus Disease, United States</b>	Mary L. Adams; USA <a href="https://doi.org/10.3201/eid2608.200679">https://doi.org/10.3201/eid2608.200679</a>	Demographic / Risk assessment	<p>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 (&gt;18 years of age) in the 50 states and District of Columbia).</p> <p><b>-&gt; 45.4% of US adults are potentially at increased risk of complications because of cardiovascular disease, diabetes, respiratory disease, hypertension, or cancer.</b></p> <p>- Rates increased by age: 19.8% for 18–29 years of age, 80.7% for persons &gt;80 years of age, and varied by state, race/ethnicity, health insurance status, and employment.</p>
Analytical chemistry 23APR2020	<b>Rapid and sensitive detection of anti-SARS-CoV-2 IgG using lanthanide-doped nanoparticles-based lateral flow immunoassay</b>	Chen, Zhenhua and al. China <a href="https://pubs.acs.org/doi/abs/10.1021/acs.analchem.0c00784">https://pubs.acs.org/doi/abs/10.1021/acs.analchem.0c00784</a>	Diagnostics	<p>Simple and rapid immunodiagnostic method based on lateral flow immunoassay (LFIA) that uses lanthanide-doped polystyrene nanoparticles (LNPs) to detect anti-SARV-CoV-2 IgG in human serum.</p> <p>The results of the validation experiment met the requirements for clinical diagnostic reagents</p> <p>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.</p>
Science of the Total Environment journal 22APR2020	<b>COVID-19 outbreak: Migration, effects on society, global environment and prevention</b>	Chakraborty et al., India <a href="https://doi.org/10.1016/j.scitotenv.2020.138882">https://doi.org/10.1016/j.scitotenv.2020.138882</a>	HSS/Politic	<p>Economic impact:</p> <ul style="list-style-type: none"> <li>- Threat of high inflation and high unemployment as a result of lack of productivity and increased expenditures</li> <li>- For each month there will be an approximate loss of 2% points in annual GDP growth</li> <li>- The tourism sector alone faces an output decrease as high as 50% to 70%</li> </ul> <p>Global environment :</p> <ul style="list-style-type: none"> <li>-&gt; Non-functioning of industries: decrease of industrial waste emission, recovery of ecosystems and revival of ozone layer.</li> <li>-&gt;Deforestation linked to disease outbreaks.</li> <li>-&gt;Population growth: increasing sources of pollution + deforestation = exposing populations to new pathogens</li> </ul> <p>The global strategy for COVID-19 prevention and control:</p> <ul style="list-style-type: none"> <li>• Global threat that requires a global response involving all countries – in the short term: Restricting mass gatherings + research for new drugs/vaccines/prevention</li> </ul> <ul style="list-style-type: none"> <li>• In the long run: <ul style="list-style-type: none"> <li>o Forestation/Respecting wildlife habitats.</li> <li>o Control of population growth</li> <li>o Global ban on wildlife trade</li> </ul> </li> </ul>
Science 22APR2020	<b>Structure-based design of antiviral drug candidates targeting the SARS-CoV-2 main protease</b>	Dai, Wenhao et al, China <a href="https://doi.org/10.1126/science.abb4489">https://doi.org/10.1126/science.abb4489</a>	Therapeutic	<p>The main protease (Mpro) of SARS-CoV-2 is a key enzyme that plays a pivotal role in mediating viral replication and transcription.</p> <p><b>Two lead compounds (11a and 11b) targeting Mpro were designed and synthesized.</b></p> <p>Both exhibited excellent inhibitory activity and <b>potent anti-SARS-CoV-2 infection activity.</b></p> <p>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 <b>aldehyde groups of 11a and 11b are covalently bound to Cys145 of Mpro.</b></p> <p>Both compounds showed <b>good PK properties in vivo</b>, and 11a also exhibited low toxicity, suggesting that these compounds are promising drug candidates.</p>

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European Journal of Epidemiology 22APR2020	<b>Vaccine confidence in the time of COVID-19</b>	Harrison et al., US <a href="https://doi.org/10.1007/s10654-020-00634-3">https://doi.org/10.1007/s10654-020-00634-3</a>	HSS/Politic	<p><b>Rushing for a vaccine in the Covid19 epidemic will not solve the problem of vaccine hesitation among the population.</b></p> <p>Need to re-imagine the culture of public health more broadly than the delivery of vaccine /technology</p> <p><b>4 points to consider:</b></p> <ol style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>3- Reluctance to vaccinate: symptom of a greater desire to ignore threats because they are not bothersome or do not constitute an emergency (yet).</li> <li>4- Essential ethical dilemma of public health: tension between autonomy and state power</li> </ol> <p>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.</p> <p>=&gt; 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.</p>
The Lancet Infectious diseases 22APR2020	<b>No SARS-CoV-2 detected in amniotic fluid in mid-pregnancy</b>	Yu, Nan; et al. China <a href="https://doi.org/10.1016/S1473-3099(20)30320-0">https://doi.org/10.1016/S1473-3099(20)30320-0</a>	Clinic	<p>2 pregnant women diagnosed with COVID-19 at first trimester :</p> <ul style="list-style-type: none"> <li>- In the second trimester, both positive for SARS-CoV-2 total antibodies in serum and negative for SARS-CoV-2 RNA in throat swabs.</li> <li>- Amniotic fluid : negative (RT-PCR) and SARS-CoV-2 IgM and IgG negative in both patients.</li> <li>- In serum : both IgG positive, and only case 1 tested positive for IgM.</li> </ul> <p><b>-&gt; No SARS-CoV-2 detected in the amniotic fluid of both women diagnosed with COVID-19 in early stage of pregnancy.</b></p> <p>- <b>Limit</b> : Only 2 patients, sensitivity (RNA is much less stable in amniotic fluid than is DNA), lack of cord blood.</p>
Eur J Neurol 22APR2020	<b>Acute-onset smell and taste disorders in the context of Covid-19: a pilot multicenter PCR-based case-control study</b>	Beltran-Corbellini A and al, Spain <a href="https://doi.org/10.1111/ene.14973">https://doi.org/10.1111/ene.14973</a>	Clinic	<p>Multicenter study – cases (79) controls (40) study</p> <p><i>Controls: historical group of season influenza patients</i></p> <p>Basal characteristics: no difference between group</p> <p><i>Cases: 31(39%) with new onset smell or taste disorders (STD):</i></p> <p>for 35.5% initial symptoms</p> <p>Now-set of STD more frequent in cases than controls:</p> <ul style="list-style-type: none"> <li>- Adjusted OR: 21,4 [2.77 – 165.4]</li> </ul> <p>No difference for gender/smoking habits/severity between STD or not in case group.</p> <p>Increased frequency of STD in young patients</p> <p><b>STD more frequent among COVID-19 patients</b></p> <p><u>Limitations:</u> historical controls – lack of comparison with others virus – self reported questionnaire</p>
Radiology 22APR2020	<b>Acute Pulmonary Embolism Associated with COVID-19 Pneumonia Detected by Pulmonary CT Angiography</b>	Grillet F and al, France <a href="https://doi.org/10.1148/radiol.2020201544">https://doi.org/10.1148/radiol.2020201544</a>	Clinic/Radiology	<p>100 patients COVID19+ and severely ill</p> <p>Mean age: 66 years and 70% males</p> <p>23% had acute pulmonary embolus:</p> <ul style="list-style-type: none"> <li>- More frequent in critical care unit (p&lt;0,01)</li> <li>- Longer delay from symptoms onset to CT (12 d)</li> </ul> <p>Requirement of mechanical ventilation was associated with pulmonary embolus (OR=3,8, p=0,049)</p> <p>Extent of lesions was not associated with pulmonary embolus.</p> <p><b>Contrast enhanced CT rather for these patients</b></p>

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Science of the Total Environment journal 22APR2020	<b>COVID-19 outbreak: Migration, effects on society, global environment and prevention</b>	Chakraborty, I. al., India <a href="https://doi.org/10.1016/j.scitotenv.2020.138882">https://doi.org/10.1016/j.scitotenv.2020.138882</a>	HSS/Politic	<p><b>Economic impact:</b></p> <ul style="list-style-type: none"> <li>- Threat of high inflation and high unemployment as a result of lack of productivity and increased expenditures</li> <li>- For each month there will be an approximate loss of 2% points in annual GDP growth</li> <li>- The tourism sector alone faces an output decrease as high as 50% to 70%</li> </ul> <p><b>Global environment :</b></p> <ul style="list-style-type: none"> <li>-Non-functioning of industries: decrease of industrial waste emission, recovery of ecosystems and revival of ozone layer.</li> <li>-Deforestation linked to disease outbreaks.</li> <li>-Population growth: increasing sources of pollution + deforestation = exposing populations to new pathogens</li> </ul> <p><b>The global strategy for COVID-19 prevention and control:</b></p> <ul style="list-style-type: none"> <li>• Global threat that requires a global response involving all countries – in the short term: Restricting mass gatherings + research for new drugs/vaccines/prevention</li> <li>• In the long run: <ul style="list-style-type: none"> <li>o Forestation/Respecting wildlife habitats.</li> <li>o Control of population growth</li> <li>o Global ban on wildlife trade</li> </ul> </li> </ul>
Gastroenterology, 21APR2020	<b>Characteristics and prognosis of patients with inflammatory bowel disease during the SARS-CoV-2 pandemic in the Basque Country (Spain)</b>	Rodríguez-Lago, Iago et al, Espagne, <a href="https://doi.org/10.1053/j.gastro.2020.04.043">https://doi.org/10.1053/j.gastro.2020.04.043</a>	Clinic Gastroenterology	<p><b>Patients (N=40) with inflammatory bowel disease (IBD) and a positive test for SARS-CoV-2</b> from 5 sites as for the 8th April 2020. Mean age: 59 (range 18 – 90)</p> <p><b>28% under immunomodulator (28%) and 18% under biologic monotherapy.</b></p> <p>Most frequent symptoms: fever (77%) and cough (67%), with 21% reporting diarrhea</p> <p>No patient was admitted to the ICU</p> <p><b>Two deaths</b> were reported (5%):</p> <ul style="list-style-type: none"> <li>a 86-year-old male with diabetes, prostate adenocarcinoma and ulcerative proctitis on mesalamine</li> <li>a 77-year-old male with dementia and left-sided ulcerative colitis under mesalamine and methotrexate.</li> </ul> <p><b>patients with IBD and COVID have a good overall prognosis</b></p>
Ophthalmology 21APR2020	<b>Ocular Findings and Proportion with Conjunctival SARS-COV-2 in COVID-19 Patients</b>	Zhou, Yunyun and al. China <a href="https://www.sciencedirect.com/science/article/pii/S016164202030405X">https://www.sciencedirect.com/science/article/pii/S016164202030405X</a>	Virology	<p>Study of 121 patients</p> <p>SARS-CoV-2 RNA could be detected in the conjunctival swabs of 2.5% (3/121) patients.</p> <p>-&gt;Eight patients (6.6%) had ocular symptoms: itching, redness, tearing, discharge, and foreign body sensation.</p> <p>-&gt;Two patients without ocular symptoms tested positive for conjunctival SARS-CoV-2.</p> <p>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.</p>
Gastroenterology 22APR2020	<b>Prevalence and Characteristics of Gastrointestinal Symptoms in Patients with SARS-CoV-2 Infection in the United States: A Multicenter Cohort Study</b>	Walker D.R and al, USA <a href="https://doi.org/10.1053/j.gastro.2020.04.045">https://doi.org/10.1053/j.gastro.2020.04.045</a>	Clinic	<p>Multicenter study (9 centers) - <b>318 patients COVID+</b></p> <p><b>61,3% reported at least 1 gastrointestinal symptom:</b> anorexia (34,8%), diarrhea (33,7%) and nausea (26,4%)</p> <p>Lost of smell/taste more frequent in gastrointestinal symptoms group (p&lt;0,05)</p> <p><b>No difference</b> in patients with gastrointestinal symptom and those without for:</p> <ul style="list-style-type: none"> <li>- Laboratory results</li> <li>- Rates of clinical deterioration</li> <li>- ICU admission, mechanical ventilation, mortality</li> </ul>

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The Lancet Psychiatry 21APR2020	<b>Suicide risk and prevention during the COVID-19 pandemic</b>	Gunnel et al., UK <a href="https://doi.org/10.1016/S2215-0366(20)30171-1">https://doi.org/10.1016/S2215-0366(20)30171-1</a>	Psy	<p>-&gt;Suggestions that suicide rates will rise</p> <p>-&gt;Many people vulnerable to mental health problems and suicidal behaviour</p> <p>-&gt;Need for timely public health responses: list of actions presented in the publication</p> <p><b>Mental health consequences are likely to be present for longer and peak later than the actual pandemic.</b></p>
Emerging Infectious Disease journal 21APR2020	<b>Possible Bat Origin of Severe Acute Respiratory Syndrome Coronavirus 2</b>	Susanna K.P. Lau; et al. Hong Kong, China <a href="https://doi.org/10.3201/eid2607.200092">https://doi.org/10.3201/eid2607.200092</a>	Virology	<p>Phylogenetic analysis :</p> <ul style="list-style-type: none"> <li>- SARS-CoV-2 <b>genome closest to that of SARS-related coronaviruses (SARSr-CoVs) from horseshoe bats, and receptor-binding domain (RBD) closest to that of pangolin viruses.</b></li> <li>- <b>Potential recombination sites identified around the RBD region</b></li> <li>- none of existing SARSr-CoVs represents its immediate ancestor.</li> </ul> <p>--&gt; <b>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).</b></p> <p>Its origin and direct ancestral viruses not identified.</p> <p><b>Retrospective study – hospitalized patients only</b></p> <p><b>3497 samples collected from 96 patients COVID-19</b></p> <p>Samples: serum/respiratory/stool/urine</p> <p>Duration of virus significantly longer in stool samples</p> <p><u>Respiratory samples:</u></p> <ul style="list-style-type: none"> <li>- median duration of virus in severe disease was significantly longer than in mild disease (14 days, 10-21 days; P=0.04)</li> <li>- patients with severe disease: significantly higher viral loads.</li> <li>- Later shedding peak in severe group</li> </ul> <p>Other samples: no difference</p> <p>No effect of the antiviral treatment on viral load/duration</p> <p><u>Factors associated significantly with duration of virus:</u></p> <ul style="list-style-type: none"> <li>- glucocorticoid &gt; 10 days in severe group</li> <li>- men</li> <li>- &gt; 60 years</li> </ul> <p><u>Limitations:</u> small sample size / viral load influenced by many factors</p>
BMJ 21APR2020	<b>Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study</b>	Zheng S and al, China <a href="https://doi.org/10.1136/bmj.m1443">https://doi.org/10.1136/bmj.m1443</a>	Clinic/Virology	<p><b>Retrospective study – hospitalized patients only</b></p> <p><b>3497 samples collected from 96 patients COVID-19</b></p> <p>Samples: serum/respiratory/stool/urine</p> <p>Duration of virus significantly longer in stool samples</p> <p><u>Respiratory samples:</u></p> <ul style="list-style-type: none"> <li>- median duration of virus in severe disease was significantly longer than in mild disease (14 days, 10-21 days; P=0.04)</li> <li>- patients with severe disease: significantly higher viral loads.</li> <li>- Later shedding peak in severe group</li> </ul> <p>Other samples: no difference</p> <p>No effect of the antiviral treatment on viral load/duration</p> <p><u>Factors associated significantly with duration of virus:</u></p> <ul style="list-style-type: none"> <li>- glucocorticoid &gt; 10 days in severe group</li> <li>- men</li> <li>- &gt; 60 years</li> </ul> <p><u>Limitations:</u> small sample size / viral load influenced by many factors</p>
Thrombosis and haemostasis, 21APR2020	<b>COVID-19-Related Severe Hypercoagulability in Patients Admitted to Intensive Care Unit for Acute Respiratory Failure</b>	Spiezia, Luca et al, Italy <a href="https://www.ncbi.nlm.nih.gov/pubmed/32316062">https://www.ncbi.nlm.nih.gov/pubmed/32316062</a>	Clinic Hematology	<p>Evaluation of coagulation abnormalities via traditional tests and <b>whole blood thromboelastometry profiles</b> in a group of <b>22 patients with COVID and acute respiratory failure due to COVID-19</b> (mean age 67 ± 8 years, M:F 20:2) compared to 44 controls.</p> <p>Cases showed significantly <b>higher fibrinogen and D-dimer plasma levels</b> versus healthy controls</p> <p><b>Markedly hypercoagulable thromboelastometry profiles</b> in COVID-19 patients,</p> <p>COVID-19 patients with acute respiratory failure present a <b>severe hypercoagulability rather than consumptive coagulopathy</b></p>
CDC Morbidity and Mortality Weekly Report 20APR2020	<b>Cleaning and Disinfectant Chemical Exposures and Temporal Associations with COVID-19 — National Poison Data System, United States, January 1, 2020–March 31, 2020</b>	Chang et al., USA <a href="https://www.cdc.gov/mmwr/volumes/69/wr/mm6916e1.htm?_cid=mm6916e1_wticontribAff">https://www.cdc.gov/mmwr/volumes/69/wr/mm6916e1.htm?_cid=mm6916e1_wticontribAff</a>	Public Health/Epidemiology	<p>-&gt;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)</p> <p>-&gt; 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.</p> <p><b>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.</b></p>

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Antimicrobial agents and chemotherapy 20APR2020	<b>Nafamostat mesylate blocks activation of SARS-CoV-2: New treatment option for COVID-19</b>	Hoffmann, Markus et al, Germany <a href="https://doi.org/10.1128/AAC.00754-20">https://doi.org/10.1128/AAC.00754-20</a>	Therapeutic	<p>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. <b>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.</b> All compounds are approved for human use in Japan.</p> <p>Gabexate mesylate slightly inhibited SARS-CoV-2 S-driven host cell entry while <b>camostat mesylate robustly suppressed entry.</b> Notably, <b>nafamostat mesylate</b>, which is FDA-approved for indications unrelated to coronavirus infection, <b>inhibited SARS-CoV-2 S-mediated entry into host cells with roughly 15-fold higher efficiency than camostat mesylate</b>, with an EC50 in the low nanomolar range. Moreover, <b>nafamostat mesylate blocked SARS-CoV-2 infection of human lung cells with markedly higher efficiency than camostat mesylate</b> while both compounds were not active against vesicular stomatitis virus infection, as expected.</p>
J of Emerg Microb and Inf 20APR2020	<b>Different longitudinal patterns of nucleic acid and serology testing results based on disease severity of COVID-19 patients</b>	Yongchen et al., China <a href="https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1756699">https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1756699</a>	Diagnostic	<p>-&gt; Detailed timeline of nucleic acid testing results for throat or anal samples along with the anti-SARS-CoV-2 IgM and IgG responses in 21 individuals infected with SARS-CoV-2, including 11 non-severe COVID-19 patients, 5 severe COVID-19 patients and 5 asymptomatic carriers.</p> <p>-&gt; Seroconversion was observed in 100% (17/17) of symptomatic patients during the observation period</p> <p>-&gt; Did not identify a strong association of seroconversion and disease severity in our cohort</p>
Metabolism: clinical and experimental 19APR2020	<b>Obesity as a risk factor for greater severity of COVID-19 in patients with metabolic associated fatty liver disease</b>	Zheng, Kenneth I and al China <a href="http://www.sciencedirect.com/science/article/pii/S0026049520301086">http://www.sciencedirect.com/science/article/pii/S0026049520301086</a>	Clinic	<p><b>Sixty six COVID-19 patients with metabolic associated fatty liver disease (MAFLD)</b></p> <p>n=45 with Body mass index (BMI) &gt; 25 and n=21 with BMI &lt; 25 Mean age :47 years and 74,2% female</p> <p>Results : <b>BMI &gt; 25 was related to more severe COVID 19</b> (adjusted-OR 6.32 95%CI 1.16 -34.54, p =0.033) even after adjusting for age, sex, smoking, diabetes, hypertension, and dyslipidaemia</p>
Clin Inf Dis 19APR2020	<b>Profile of RT-PCR for SARS-CoV-2: a preliminary study from 56 COVID-19 patients</b>	Xiao et al., China <a href="https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa460/5822175">https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa460/5822175</a>	Diagnostic	<p>Dynamics profile of SARS-CoV-2 from 56 recovered COVID-19 patients</p> <p>-&gt; Virus shedding was up to 6 weeks after onset of symptoms</p> <p>-&gt; Longest duration between RT-PCR test for SARS-CoV-2: 42 days after onset of symptoms.</p> <p>-&gt; Median duration between onset of symptom to nucleic acid conversion: 24 days</p> <p>-&gt; 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.</p> <p>-&gt; 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.</p>
Clinical Therapeutic 19APR2020	<b>Association between clinical manifestations and prognosis in patients with COVID-19</b>	Yu T and al, China <a href="https://doi.org/10.1016/j.clinthera.2020.04.009">https://doi.org/10.1016/j.clinthera.2020.04.009</a>	Clinic	<p>Multicenter study – 95 patients COVID-19+</p> <p><b>73 had pneumonia (CT findings)</b>, significantly:</p> <ul style="list-style-type: none"> <li>- <b>Older</b></li> <li>- <b>Higher BMI</b>, ASAT and LDH levels</li> <li>- Lower lymphocyte and platelet count</li> </ul> <p>ARDS (n=24) and non-ARDS (n=71)</p> <p><u><b>Independent risk factors associated with ARDS:</b></u></p> <ul style="list-style-type: none"> <li>- High systolic blood pressure (OR:1.04, p=0.025)</li> <li>- High LDH level (OR:1.01, p=0.021)</li> </ul> <p><u><b>Association with pneumonia exacerbation (n=19):</b></u></p> <ul style="list-style-type: none"> <li>- High BMI (OR: 1.28, p=0.017)</li> <li>- Tobacco smoking (OR: 16.13, p=0.032)</li> </ul> <p><u><b>Limitations:</b></u> exacerbation based on CT scan findings</p>



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Clin Inf Dis 19APR2020	<b>Antibody Detection and Dynamic Characteristics in Patients with COVID-19</b>	Xiang et al., China <a href="https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa461/5822173">https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa461/5822173</a>	Diagnostic	<p><b>ELISA based on the recombinant nucleocapsid protein of SARS-CoV-2</b> Seroconversion of specific IgM and IgG antibodies were observed as early as the 4<sup>th</sup> day after symptom onset.</p> <p>In confirmed patient: <b>IgM:</b> Sensitivity, 77.3% Specificity, 100% PPV, 100% NPV, 80.0% Consistency rate : 88.1% <b>IgG:</b> Sensitivity, 83.3.3% Specificity, 95.0% PPV, 94.8% NPV, 83.8% Consistency rate : 88.9 %</p> <p>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%.</p> <p><b>-&gt; Both antibodies performed well in serodiagnosis for COVID-19 rely on great specificity.</b></p>
Med 18APR2020	<b>Efficacy and safety of lopinavir/ritonavir or arbidol in adult patients with mild/moderate COVID-19: an exploratory randomized controlled trial</b>	Li, Y et al, China <a href="https://marlin-prod.literatumonline.com/pb-assets/products/coronavirus/MEDJ1.pdf">https://marlin-prod.literatumonline.com/pb-assets/products/coronavirus/MEDJ1.pdf</a>	Therapeutics	<p><b>Exploratory randomized (2:2:1) controlled trial</b> assessing the efficacy and safety of <b>lopinavir/ritonavir (LPV/r) or arbidol monotherapy</b> for treating patients with mild/moderate COVID-19. 86 patients with mild/moderate COVID-19 enrolled.</p> <p>LPV/r and arbidol <b>did not shorten the time of positive-to-negative conversion of COVID-19 nucleic acid in respiratory specimens</b> (9.0 vs. 9.1 vs. 9.3 days), <b>nor did they improve the symptoms of COVID-19 or pneumonia on lung CT imaging</b> 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.</p> <p>Limitations: small sample size, no severely or critically ill patients, or patients at increased risk of poor outcome with many comorbidities, not completely blinded.</p>
European urology 18APR2020	<b>Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China</b>	Zhu L and al, China <a href="http://www.sciencedirect.com/science/article/pii/S0302283820302141">http://www.sciencedirect.com/science/article/pii/S0302283820302141</a>	Clinic	<p>Controls: 10 family members <b>10 kidney transplant patients + COVID-19 pneumonia:</b></p> <ul style="list-style-type: none"> <li>- Classical symptoms: fever, cough, shortness of breath, ....</li> <li>- 100%: lymphopenia and elevated CRP</li> <li>- 50% had temporally increase of serum creatinine</li> <li>- Abnormalities on chest CT scan</li> <li>- <b>8/10 were severe or critical cases and 1 died</b></li> </ul> <p><b>Versus controls:</b></p> <ul style="list-style-type: none"> <li>- <b>Transplants patients more severe</b></li> <li>- <b>Much longer time to become negative for SARS-CoV-2</b> (median time: 28,4 d)</li> <li>- <b>Reduce fatal severe pneumonia:</b> suppressing the hyperimmune response</li> </ul>
Science 17APR2020	<b>Comparative pathogenesis of COVID-19, MERS, and SARS in a nonhuman primate model</b>	Rockx, Barry; et al. Netherlands <a href="https://doi.org/10.1126/science.abb7314">https://doi.org/10.1126/science.abb7314</a>	Fundamental research	<p>Cynomolgus macaques inoculated with SARS-CoV-2 or MERS-CoV.</p> <ul style="list-style-type: none"> <li>- 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.</li> <li>- lung lesions typically more severe with SARS-CoV-2 than in MERS-CoV infection, where virus was detected mainly in type II pneumocytes.</li> </ul> <p><b>-&gt; Cynomolgus macaques provide a new infection model to test preventive and therapeutic strategies.</b></p>

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J Thromb Haemost 17APR2020	<b>The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome</b>	Ranucci M and al, Italy <a href="https://doi.org/10.1111/jth.14854">https://doi.org/10.1111/jth.14854</a>	Clinic	<p><b>16 patients COVID-19 pneumonia and ARDS in ICU</b> 94% were male and 31% were obese D-Dimer, IL-6 and fibrinogen = <b>higher than upper limit</b> <b>Association between IL-6 and fibrinogen levels</b> Clot firmness higher than normal <u>Follow-up:</u> - 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. <u>Limitation:</u> lack of data on thrombin generation and fibrinolysis. Further studies: best prophylaxis and treatment ?</p>
Circulation research 17APR2020	<b>Association of Inpatient Use of Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blockers with Mortality Among Patients With Hypertension Hospitalized With COVID-19</b>	Zhang, Peng et al, China <a href="https://doi.org/10.1161/CIRCRESAHA.120.317134">https://doi.org/10.1161/CIRCRESAHA.120.317134</a>	Therapeutics	<p><b>Retrospective, multi-center study including 1128 adult patients with hypertension diagnosed with COVID-19</b>, including <b>188 taking ACEI/ARB</b> (ACEI/ARB group; median age 64 [IQR 55-68] years; 53.2% men) <b>and 940 without using ACEI/ARB</b> (non-ACEI/ARB group; median age 64 [IQR 57-69]; 53.5% men).</p> <p>Among hospitalized COVID-19 patients with hypertension, inpatient <b>use of ACEI/ARB was associated with lower risk of all-cause mortality compared with ACEI/ARB non-users.</b></p> <p>Limitations: hospital only, modest sample size, retrospective study.</p>
Gut 17APR2020	<b>Covid-19 and immunomodulation in IBD</b>	Neurath, Germany <a href="https://gut.bmj.com/content/early/2020/04/16/gutjnl-2020-321269">https://gut.bmj.com/content/early/2020/04/16/gutjnl-2020-321269</a>	Immunology	<p><b>Results/ recommendations:</b></p> <ul style="list-style-type: none"> <li>· No evidence for an increased risk or aggravated outcomes in patients with IBD in the context of covid-19</li> <li>· However, covid-19 risks situation comprise older patients with IBD with comorbidities as well as patients suffering from malnutrition</li> <li>· Experimental covid-19 treatment with hydroxychloroquine or remdesivir may increase the risks for drug-drug interactions with established IBD medications.</li> <li>· Currently available recommendations for patients with IBD are : <ul style="list-style-type: none"> <li>o Continue current treatment if disease is stable and discuss suitable medicine if disease has flared</li> <li>o Use of mesalamine should be continued and should not increase the risk of infection.</li> <li>o Corticosteroid use can be continued, but be cautious of possible side effects.</li> <li>o A new prescription of immunosuppressant or increase in dose of an ongoing immunosuppressant is not recommended in epidemic areas.</li> <li>o Use of biologics such as the antitumour necrosis factors infliximab or adalimumab should be continued.</li> <li>o If infliximab infusion is not accessible, switching to adalimumab injection at home should be considered.</li> <li>o Vedolizumab use can be continued due to the specificity of the drug for the intestine.</li> <li>o Ustekinumab use can be continued, but starting ustekinumab requires infusion centre visits and therefore should be discussed before initiation of therapy.</li> <li>o Enteral nutrition might be used if biologics are not accessible</li> <li>o Tofacitinib should not be newly prescribed in epidemic areas unless there are no other alternatives.</li> </ul> </li> </ul>
Nature Biotechnology 16APR2020	<b>CRISPR–Cas12-based detection of SARS-CoV-2</b>	Broughton, James P. and al. USA <a href="https://doi.org/10.1038/s41587-020-0513-4">https://doi.org/10.1038/s41587-020-0513-4</a>	Diagnostic	<p>Development of a rapid (&lt;40 min), easy-to-implement and accurate CRISPR–Cas12-based lateral flow assay for detection of SARS-CoV-2 from respiratory swab RNA extracts.</p> <p>Validation using contrived reference samples and clinical samples, including 36 patients with COVID-19 infection and 42 patients with other viral respiratory infections.</p> <p>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.</p>

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NEJM 16APR2020	<b>Not a Perfect Storm — Covid-19 and the Importance of Language</b>	Brandt M. et al., USA <a href="https://doi.org/10.1056/NEJMp2005032">https://doi.org/10.1056/NEJMp2005032</a>	HSS/Politic	<p>Metaphors we use to describe disease shape our experience of illness : has an impact on the approach taken against the Covid =&gt; misleading our approach. Covid characterized as a "perfect storm"="fierce storm arising from a rare combination of adverse meteorological factors"</p> <p>(randomness/volatility =&gt; reactive, disempowering). Vs developing and implementing preventive strategies to prepare for pandemics</p> <p>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</p> <p><b>Conclusion:</b> Covid is not a simple natural event. It is also the result of human actions. =&gt; Be conscientious about our language and its implications as a first step for reforms and preventive measures to strengthen our health infrastructure to face future disease outbreaks.</p>
Cell 16APR2020	<b>Development of CRISPR as an antiviral strategy to combat SARSCoV-2 and influenza</b>	Abbott, T et al, USA <a href="https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00736.pdf">https://www.cell.com/pb-assets/products/coronavirus/CELL_CELL-D-20-00736.pdf</a>	Therapeutics	<p>A CRISPR-Cas13-based strategy, PAC-MAN (Prophylactic Antiviral CRISPR in huMAN cells), for viral inhibition can <b>effectively degrade RNA from SARS-CoV-2 sequences</b> and live influenza A virus (IAV) in human lung epithelial cells. CRISPR RNAs (crRNAs) targeting conserved viral regions were designed and screened, and <b>functional crRNAs targeting SARS-CoV-2 were identified</b>. The bioinformatic analysis showed a group of only six crRNAs can target more than 90% of all coronaviruses.</p> <p>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.</p>
Plos One 16APR2020	<b>Mental health problems and social media exposure during COVID-19 outbreak</b>	Gao et al., China <a href="https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0231924">https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0231924</a>	Psy	<p><b>Social media exposure (SME) +++ during Covid-19.</b> Study on 4872 participants from 31 provinces and autonomous region -&gt; High prevalence of mental health problems -&gt; frequently SME was positively associated with high odds of anxiety (OR = 1.72, 95%CI: 1.31–2.26) and combination of depression and anxiety (CDA) (OR = 1.91, 95%CI: 1.52–2.41) compared with less SME.</p> <p>-&gt; Need to combat with "infodemic" while combating during public health emergency</p>
International journal of antimicrobial agents 16APR2020	<b>Can post-exposure prophylaxis for COVID-19 be considered as one of outbreak response strategies in long-term care hospitals?</b>	Lee, Sun Hee et al, Republic of Korea <a href="https://doi.org/10.1016/j.ijantimicag.2020.105988">https://doi.org/10.1016/j.ijantimicag.2020.105988</a>	Therapeutics	<p>After a large COVID-19 exposure event in a long-term care hospital (LTCH) in Korea, <b>PEP using hydroxychloroquine (HCQ)</b> was conducted to <b>211 persons</b> 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).</p> <p>=&gt; PEP was completed in 184 (97.4%) patients and 21 (95.5%) careworkers <b>without serious adverse events</b>. =&gt; At the end of 14 days of quarantine, <b>follow-up PCR tests were all negative</b>.</p> <p>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.</p>

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Respiratory Research 15APR2020	<b>Prognostic value of NT-proBNP in patients with severe COVID-19</b>	Gao L and al, China <a href="https://doi.org/10.1186/s12931-020-01352-w">https://doi.org/10.1186/s12931-020-01352-w</a>	Clinic	<p><b>54 patients – 2 groups:</b> high and low NT-proBNP</p> <p>NT-proBNP at admission</p> <p><u>High group significantly:</u></p> <ul style="list-style-type: none"> <li>- Older</li> <li>- More comorbidities</li> <li>- Pro inflammatory</li> <li>- Lymphopenia</li> <li>- <b>Higher risk of death</b></li> </ul> <p>Cut-off of NT-proBNP for predicting <b>in hospital death</b>: 88,64 pg/ml (sensitivity: 100% - specificity: 66,67%)</p> <p>AUC for in hospital death = 0,909</p> <p><b>NT-proBNP = independent risk factors for in hospital death</b> (after adjusting)</p>
ACS nano 15APR2020	<b>Rapid Detection of COVID-19 Causative Virus (SARS-CoV-2) in Human Nasopharyngeal Swab Specimens Using Field-Effect Transistor-Based Biosensor</b>	Seo, Giwan and al Rep of Korea <a href="https://doi.org/10.1021/acsnano.0c02823">https://doi.org/10.1021/acsnano.0c02823</a>	Diagnostic	<p>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.</p> <p>The performance of the sensor was determined using antigen protein, cultured virus, and nasopharyngeal swab specimens from COVID-19 patients.</p> <p>CI*: the device is a highly sensitive immunological diagnostic method for COVID-19 that requires no sample pretreatment or labeling.</p>
Nature Medicine 15APR2020	<b>Temporal dynamics in viral shedding and transmissibility of COVID-19</b>	He, Xi; et al. China <a href="https://doi.org/10.1038/s41591-020-0869-5">https://doi.org/10.1038/s41591-020-0869-5</a>	Virology	<p>Pemporal viral shedding (94 patients with lab-confirmed COVID-19) and modeling of COVID-19 infectiousness profiles (separate 77 infector–infectee transmission pairs):</p> <ul style="list-style-type: none"> <li>- highest viral load in throat swabs was at the time of symptom onset.</li> <li>- 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.</li> </ul> <p>-&gt; control measures should be adjusted to account for substantial presymptomatic transmission.</p>
Journal of Biomolecular Structure and Dynamics 15APR2020	<b>Reverse vaccinology approach to design a novel multi-epitope vaccine candidate against COVID-19: an in silico study</b>	Maryam Enayatkhani et al. Iran <a href="https://doi.org/10.1080/07391102.2020.1756411">https://doi.org/10.1080/07391102.2020.1756411</a>	Vaccine	<p>3 known antigenic proteins of SARS-CoV-2 (Nucleocapsid, ORF3a, and Membrane protein)</p> <p>-&gt; used to predict <i>in silico</i> the potential immunogenic B and T-cell epitopes.</p> <p>-&gt; Prediction of best tertiary structure of selected epitopes docking TLR4 and HLA-A + Evaluation of the end the stability of complex of these receptors with the selected epitopes , by molecular Dynamic simulation methods.</p> <p>Antigenicity of the designed antigenic sequence -&gt; predicted by bioinformatic methods.</p> <p><b>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</b></p>
Nat Med 15APR2020	<b>Temporal dynamics in viral shedding and transmissibility of COVID-19</b>	He et al., China <a href="https://www.nature.com/articles/s41591-020-0869-5">https://www.nature.com/articles/s41591-020-0869-5</a>	Public Health/Epidemiology	<p>94 COVID-19 patients:</p> <ul style="list-style-type: none"> <li>- Highest Viral loads in Throat swabs <b>at time of symptom onset</b></li> <li>- Estimation: 44% (95% confidence interval, 25–69%) of secondary cases were infected during the index cases' <b>presymptomatic stage</b></li> </ul> <p>-&gt; Infectiousness started from 2.3 days (95% CI, 0.8–3.0 days) before symptom onset and peaked at 0.7 days (95% CI, –0.2–2.0 days) before symptom onset</p>

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ACS nano 14APR2020	<b>Computational Design of ACE2-Based Peptide Inhibitors of SARS-CoV-2</b>	Han, Yanxiao et al, USA <a href="https://doi.org/10.1021/acsnano.0c02857">https://doi.org/10.1021/acsnano.0c02857</a>	Therapeutics	<p>Design of <b>peptide inhibitors against the SARS-CoV-2</b>, 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.</p> <p>Molecular dynamics simulations revealed that the alpha-helical peptides maintain their secondary structure and provide a <b>highly specific and stable binding (blocking) to SARS-CoV-2</b>. To provide a multivalent binding to the SARS-CoV-2 receptors, many such peptides could be attached to the surfaces of nanoparticle carriers.</p> <p>The proposed peptide inhibitors could provide simple and efficient therapeutics against the COVID-19 disease.</p>
Kidney International 14APR2020	<b>Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China</b>	Su et al., China <a href="https://www.kidney-international.org/article/S0085-2538(20)30369-0/fulltext">https://www.kidney-international.org/article/S0085-2538(20)30369-0/fulltext</a>	Clinic	<p>Analyzing <b>kidney abnormalities in 26 autopsies</b> -&gt; Patients: respiratory failure associated with multiple organ dysfunction syndrome as the cause of death.</p> <p>9/26: <u>clinical signs</u> of kidney injury that included increased serum creatinine and/or new-onset proteinuria.</p> <p><u>Light microscopy</u>: 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.</p> <p><u>Electron microscopic</u>: clusters of coronavirus particles with distinctive spikes in the tubular epithelium and podocytes.</p> <p>ACE2 was found to be upregulated in patients with COVID-19, and immunostaining with SARS-CoV nucleoprotein antibody was positive in tubules.</p>
Journal of Autoimmunity 14APR2020	<b>Assessing ACE2 expression patterns in lung tissues in the pathogenesis of COVID-19</b>	Li, Guoping; et al. China <a href="https://doi.org/10.1016/j.jaut.2020.102463">https://doi.org/10.1016/j.jaut.2020.102463</a>	Fundamental research	<p>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) :</p> <ul style="list-style-type: none"> <li>- no difference in ACE2 lung expression in healthy vs patients with chronic airway disease, suggesting no difference in susceptibility to SARS-CoV-2 infection.</li> <li>- long-term smokers have significantly greater ACE2 expression than healthy non-smokers (small airway epithelium), suggesting a risk factor for COVID-19.</li> <li>- ACE2 expression dramatically increased between 12-24h post SARS-CoV infection (airway epithelial cells), suggesting a role of ACE2 in post-infectious regulation.</li> <li>- 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).</li> </ul> <p>Protein-protein regulation networks before and after infection identify:</p> <ul style="list-style-type: none"> <li>- ribosomal protein RPS3 plays a key role in viral replication.</li> <li>- non-receptor protein kinase SRC has a role in macrophage mediated innate immunity and cytokine release.</li> </ul> <p><b>Working hypothesis</b> -&gt; SARS-CoV-2 infection increases ACE2 expression, which affects RPS3 and SRC activity, two key hub genes involved in viral replication and inflammatory responses.</p>

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



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Mayo Clinic Proceedings 13APR2020	<b>ST-segment Elevation, Myocardial Injury, and Suspected or Confirmed COVID-19 Patients: Diagnostic and Treatment Uncertainties</b>	Bennett et al., USA <a href="https://doi.org/10.1016/j.jmayocp.2020.04.005">https://doi.org/10.1016/j.jmayocp.2020.04.005</a>	Diagnostic	<p>-&gt; For patients with COVID-19, the evaluation can be challenging due to reports of STE without obstructive coronary disease, which creates diagnostic and management challenges</p> <p>-&gt; 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</p>
International Forum of Allergy & Rhinology 12APR2020	<b>Association of chemosensory dysfunction and Covid-19 in patients presenting with influenza-like symptoms</b>	Carol Y and al, USA <a href="https://doi.org/10.1002/all.22572">https://doi.org/10.1002/all.22572</a>	Clinic	<p><b>Cross sectional study – question survey – 2 groups</b> <b>All with influenza like symptoms</b> 59 COVID-19 positive and 203 COVID-19 negative Hospital admission low and comparable between groups</p> <p><b>Smell and taste loss:</b> more frequent in COVID-19 group</p> <ul style="list-style-type: none"> <li>- 68% and 71% versus 16% and 17% respectively</li> <li>- Largest magnitude of association with COVID-19</li> </ul> <p><b>Independently associated with COVID-19:</b></p> <ul style="list-style-type: none"> <li>- Anosmia: OR 10,9 [5,08 – 23,5]</li> <li>- Taste: OR 10,2 [4,74 – 22,1]</li> </ul> <p>Improvement of olfaction and taste that correlated with clinical resolution of illness.</p>
Travel Med. Infect. Dis. 11APR2020	<b>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</b>	Gautret, Philippe et al, France <a href="https://doi.org/10.1016/j.tmaid.2020.101663">https://doi.org/10.1016/j.tmaid.2020.101663</a>	Therapeutic	<p><b>Uncontrolled non-comparative observational study</b> in a cohort of <b>80 relatively mildly infected inpatients</b> treated with a combination of <b>hydroxychloroquine and azithromycin</b> over a period of at least three days.</p> <p>All patients <b>improved clinically</b> except one 86 year-old patient who died, and one 74 year-old patient still in intensive care. A <b>rapid fall of nasopharyngeal viral load</b> was noted, with 83% negative at Day7, and 93% at Day8. <b>Virus cultures from patient respiratory samples were negative in 97.5% of patients at Days5.</b></p> <p><b>Limitations:</b> 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.</p>
The Lancet 11APR2020	<b>Centring sexual and reproductive health and justice in the global COVID-19 response</b>	Matthew J Harris et al., UK <a href="https://doi.org/10.1016/S0140-6736(20)30801-1">https://doi.org/10.1016/S0140-6736(20)30801-1</a>	HSS/Politic	<p>COVID-19 + existing sexual &amp; reproductive health inequities =&gt; women, girls and vulnerable populations' health, wellbeing and economic stability disproportionately impacted.</p> <p>1) COVID-19 = Increased risks for women</p> <ul style="list-style-type: none"> <li>- Women's risk factors of contracting COVID-19 may be higher = 70% of the global health and social care workforce worldwide,</li> <li>- Potential pregnancy-related complications</li> </ul> <p>2) Impact on sexual/reproductive health care</p> <ul style="list-style-type: none"> <li>- Disruption/Diversion of resources away from essential sexual/reproductive health care for COVID</li> <li>- Restrictive global policies that target vulnerable populations (Protecting Life in Global Health Assistance + migration policies of deterrence)</li> </ul> <p><b>Solutions:</b></p> <ul style="list-style-type: none"> <li>- Additional resources for sexual/reproductive health care + increase of telemedicine</li> <li>- Sex-disaggregated mortality and morbidity surveillance for COVID-19 research</li> <li>- Community driven efforts: recognize inequitable power structures + collaborative response</li> <li>- Eliminate legal/policy restrictions to sexual/reproductive health care.</li> </ul>

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Journal of Clinical Virology 11APR2020	<b>Dynamic profile of RT-PCR findings from 301 COVID-19 patients in Wuhan, China: a descriptive study</b>	Xiao et al., China <a href="https://www.sciencedirect.com/science/article/pii/S1386653220300883?via%3Dihub">https://www.sciencedirect.com/science/article/pii/S1386653220300883?via%3Dihub</a>	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	<b>Structure of the RNA-dependent RNA polymerase from COVID-19 virus</b>	Gao, Yan; et al. China - Australia <a href="https://doi.org/10.1126/science.abb7498">https://doi.org/10.1126/science.abb7498</a>	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 $\beta$ -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	<b>Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020</b>	Zhen-Dong Guo; et al. China <a href="https://doi.org/10.3201/eid2607.200885">https://doi.org/10.3201/eid2607.200885</a>	Virology	Samples taken from <b>potentially contaminated objects and air from an ICU</b> (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 than general wards. -> Aerosol distribution in the general ward indicate transmission distance of SARS-CoV-2 might be 4 m
NEJM 10APR2020	<b>Compassionate Use of Remdesivir for Patients with Severe Covid-19</b>	Grein, Jonathan et al, USA <a href="https://doi.org/10.1056/NEJMoa2007016">https://doi.org/10.1056/NEJMoa2007016</a>	Therapeutic	<b>63 compassionate use of remdesivir for COVID patients</b> 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, <b>36 patients (68%) had an improvement in oxygen-support class</b> , including 17 of 30 patients (57%) receiving mechanical ventilation who were extubated. <b>A total of 25 patients (47%) were discharged, and 7 patients (13%) died</b>  <b>Point of attention</b> : Measurement of efficacy will require ongoing randomized, placebo-controlled trials
Journal of Clinical Virology 10APR2020	<b>Clinical characteristics and risk assessment of newborns born to mothers with COVID-19</b>	Yang, Pu et al Chine <a href="https://doi.org/10.1016/j.jcv.2020.104356">https://doi.org/10.1016/j.jcv.2020.104356</a>	Clinic	Case report of <b>7 newborns</b> delivered by <b>SARS-CoV-2 infected pregnant women</b>  The current data show that the infection of <b>SARS-CoV-2 in late pregnant women does not cause adverse outcomes in their newborns</b>
Euro Surv 9APR2020	<b>Excess cases of influenza-like illnesses synchronous with coronavirus disease (COVID-19) epidemic, France, March 2020</b>	Boëlle, Pierre-Yves et al, France <a href="https://doi.org/10.2807/1560-7917.ES.2020.25.14.2000326">https://doi.org/10.2807/1560-7917.ES.2020.25.14.2000326</a>	HSS/Politic	<b>Comparison of data from the Sentinelles network</b> monitors influenza-like illnesses (ILI) and acute respiratory infections (ARI) in general practice in France and <b>official COVID 19 reported cases in early March 2020 from the Santé Publique France</b>  It is estimated that <b>760 (95% CrI: 219–1,706) of acute respiratory infections</b> consultations in those older than 65 years in two regions of France (BFC and GRE) <b>could have been caused by COVID-19 during week 10.</b>

Journal and date	Title	Authors and link	Field of expertise	Key facts
Clinical infectious disease 9APR2020	<b>Factors associated with prolonged viral RNA shedding in patients with COVID-19</b>	Xu K and al, China <a href="https://doi.org/10.1093/cid/ciaa351">https://doi.org/10.1093/cid/ciaa351</a>	Clinic	<p>Retrospective study – Two hospital – <b>113 patients</b></p> <p>Median age: 52 years – 58,4% were male</p> <p>28,3% were diagnosed as severe illness</p> <p>Median hospital stays: 15 days</p> <p><b>74,3% had viral RNA clearance within 21 days after illness onset</b> (median: 15 days)</p> <p><u>Prolonged RNA shedding:</u></p> <ul style="list-style-type: none"> <li>- Male (p=0,009)</li> <li>- Old age (p=0,033)</li> <li>- Concomitant hypertension (p=0,009)</li> <li>- Invasive mechanical ventilation (p=0,006)</li> <li>- Use of corticosteroid (p=0,025)</li> <li>- Delay recovery on radiological image (p&lt;0,001)</li> </ul> <p>→ <u>Multivariate analysis:</u></p> <ul style="list-style-type: none"> <li>- Male (OR: 3,24)</li> <li>- Delay hospital admission (OR: 1,30)</li> <li>- Invasive mechanical support</li> </ul> <p><u>Limitations:</u></p> <ul style="list-style-type: none"> <li>- Viral RNA shedding ≠ viral shedding</li> <li>- Didn't not evaluated the effect of the treatment</li> </ul>
Obesity 9APR2020	<b>High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation</b>	Simonnet A and al, France <a href="https://doi.org/10.1002/obv.22831">https://doi.org/10.1002/obv.22831</a>	Clinic	<p><b>Retrospective study</b> – 124 patients in ICU</p> <p>Control group: non-SARS-CoV2 in ICU</p> <p>Median age: 60 years – 73% male -15% died</p> <p>68,6% required invasive mechanical ventilation (IMV)</p> <p><b>Obesity and severe obesity were significantly more frequent in SARS-CoV2 patients (p&lt;0,001)</b></p> <p>Median BMI in SARS-CoV2 patients higher than in non-SARS-CoV2: 29,6 vs 24,0 (p&lt;0,001)</p> <p><u>IMV vs non IMV:</u></p> <ul style="list-style-type: none"> <li>- BMI higher in IMV group: 31,1 vs 27,0 (p&lt;0,001)</li> </ul> <p><b>Need for IMV gradually increase with BMI category.</b></p> <p>Patients with obesity should take extra measure to avoid COVID19 contamination.</p>
F1000 Research 9APR2020	<b>In silico identification of vaccine targets for 2019-nCoV</b>	Chloe H. Lee and Hashem Koohy UK <a href="https://doi.org/10.12688/f1000research.22507.1">https://doi.org/10.12688/f1000research.22507.1</a>	Vaccine	<p>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).</p> <p>They found:</p> <ul style="list-style-type: none"> <li>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)</li> <li>ii) 22 nCoV peptides having a high sequence similarity with immunogenic peptides but with a greater predicted immunogenicity score</li> <li>iii) 44 nCoV peptides predicted to be immunogenic by the iPred algorithm and 1G4 TCR positional weight matrices respectively (<i>de novo in silico</i> search of immunogenic peptides against the 2019-nCoV proteome sequence)</li> </ul>
Psychotherapy and psychosomatics 9APR2020	<b>Mental Health and Psychosocial Problems of Medical Health Workers during the COVID-19 Epidemic in China</b>	Hong-xing Wang et al., China <a href="https://doi.org/10.1159/000507639">https://doi.org/10.1159/000507639</a>	Psy	<p>Method : <b>online survey (2182 participants from China)</b></p> <p><b>Result :</b></p> <ul style="list-style-type: none"> <li>• higher prevalence rates of psychological symptoms among medical health workers = insomnia, anxiety, depression, somatization, and obsessive-compulsive symptoms</li> <li>• risk factors : having organic disease, living in rural areas, being female, and being at risk of contact with COVID-19 patients</li> </ul> <p>Main reasons :</p> <ul style="list-style-type: none"> <li>• insufficient understanding of the virus initially</li> <li>• lack of prevention and control knowledge</li> <li>• long-term workload</li> <li>• high risk of exposure to patients with COVID-19</li> <li>• shortage of medical protective equipment,</li> <li>• lack of rest</li> <li>• exposure to critical life events, such as death.</li> </ul> <p>Need for :</p> <ul style="list-style-type: none"> <li>• health protection and adequate working conditions: lowering job demands and workload / increasing job control and reward, medical protective equipment, adequate rest...</li> <li>• recovery programs focused on resilience and psychological well-being</li> </ul>

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Clinical infectious diseases 9APR2020	<b>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</b>	Chu, Hin; et al. China <a href="https://doi.org/10.1093/cid/ciaa410">https://doi.org/10.1093/cid/ciaa410</a>	Virology	<p>Ex vivo human lung tissues infected with SARS-CoV-2 compared to SARS-CoV :</p> <ul style="list-style-type: none"> <li>- SARS-CoV-2 infected and replicated in human lung tissues more efficiently, generating 3.20 folds more infectious virus particles within 48hrs.</li> <li>- Both viruses were similar in cell tropism: both targeting types I and II pneumocytes, and alveolar macrophages.</li> </ul> <p>-&gt; 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).</p>
The Lancet. Global health 9APR2020	<b>COVID-19 and risks to the supply and quality of tests, drugs, and vaccines</b>	Paul N Newton et al., US <a href="https://doi.org/10.1016/S2214-109X(20)30136-4">https://doi.org/10.1016/S2214-109X(20)30136-4</a>	HSS/Politic	<p>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.</p> <ul style="list-style-type: none"> <li>• Substandard drugs driven by cost reduction</li> <li>• Falsified agents thrive on shortages, especially when buyers depart from regulated supply chains (masks, diagnostic tests, false claim of treatments...).</li> </ul> <p>When proven efficacious treatment, robust policies need to ensure prompt affordable, access for all people in need + quality assured, not diverted from other treatments:</p> <ul style="list-style-type: none"> <li>• Coordinated information-sharing among medicine regulators on authorizations for clinical trials</li> <li>• Ensure global manufacture + investigational interventions for unregistered + off label use</li> <li>• Comprehensive/rapid reporting of shortages of active ingredients and finished products</li> <li>• Robust evaluation of diagnostic tests</li> <li>• Innovative regional mechanisms (e.g. African Vaccine Regulatory Forum) for nations without robust regulatory systems</li> </ul>
NEJM 9APR2020	<b>Disease Control, Civil Liberties, and Mass Testing — Calibrating Restrictions during the Covid-19 Pandemic</b>	David M. Studdert et al., US <a href="https://doi.org/10.1056/NEJMo2007637">https://doi.org/10.1056/NEJMo2007637</a>	HSS/Politic	<p>Civil liberties: courts insist coercive restrictions must be 1) necessary, 2) crafted as narrowly as possible, 3) not used to target ostracized groups.</p> <p>Clear criteria for quarantine for other diseases don't apply to social restrictions for COVID-19:</p> <ol style="list-style-type: none"> <li>1) Quarantine is community-wide and applies to government and private actors;</li> <li>2) Transmission dynamics make it difficult to identify / target risk groups.</li> <li>3) Stay-at-home restrictions unlikely to be a one-shot deal</li> </ol> <p>=&gt; Need for a graduated approach to restrictive measures.</p> <p>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.</p> <p>Tailor restrictions using credible person-level information =&gt; identify people most likely to transmit infection through population wide program of testing and surveillance.</p> <p>Aggregate test results at community+state level to dial up or down.</p> <p>=&gt;Federal, state and local governments to finance &amp; oversee + rely on hospitals, pharmacies, private labs, mobile health services for implementation + civil organizations to foster compliance.</p>
Life Sciences 9APR2020	<b>In silico studies on therapeutic agents for COVID-19: Drug repurposing approach</b>	Shah, Bhumi et al, India <a href="https://doi.org/10.1016/j.lfs.2020.117652">https://doi.org/10.1016/j.lfs.2020.117652</a>	Therapeutic	<p>61 molecules that are already being used in clinics or under clinical scrutiny as antiviral agents are surveyed via <b>docking study</b>.</p> <p>37 molecules were found to interact with &gt;2 protein structures of COVID-19. Among them, <b>HIV protease inhibitors</b> and <b>RNA-dependent RNA polymerase inhibitors</b> showed promising features of binding to COVID-19 enzyme. Along with these, Methisazone an inhibitor of protein synthesis, <b>CGP42112A</b> an angiotensin AT2 receptor agonist and <b>ABT450</b> an inhibitor of the non-structural protein 3-4A might become convenient treatment option as well against COVID-19.</p>

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EuroSur 9APR2020	<b>An alternative workflow for molecular detection of SARS-CoV-2 – escape from the NA extraction kit-shortage, Copenhagen, Denmark, March 2020</b>	Fomsgaard et al., Denmark <a href="https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.14.2000398">https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.14.2000398</a>	Diagnostics	<p>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.</p> <p>Approach consists of heating samples at 98°C for 5 min</p> <p>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</p>
Clin Inf Dis 9APR2020	<b>Prediction for Progression Risk in Patients with COVID-19 Pneumonia: the CALL Score</b>	Ji, Dong and al., China <a href="https://academic.oup.com/cid/advance-article/doi/10.1093/cid/cia414/5818317">https://academic.oup.com/cid/advance-article/doi/10.1093/cid/cia414/5818317</a>	Diagnostics	<p>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.</p> <p>Comorbidity, older age, lower lymphocyte and higher lactate dehydrogenase were shown to be independent high-risk factors for COVID-19 progression.</p> <p>By incorporating these 4 factors a novel scoring model, named as CALL, was established and tested.</p> <p>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.</p>
Clin Inf Dis 8APR2020	<b>PCR Assays Turned Positive in 25 Discharged COVID-19 Patient</b>	Yuan, Jing and al., China <a href="https://doi.org/10.1093/cid/cia398">https://doi.org/10.1093/cid/cia398</a>	Clinic	<p>172 COVID-19 infected patients discharged from Hospital:</p> <ol style="list-style-type: none"> <li>(1) Normal body temperature for more than 3 consecutive days.</li> <li>(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 <math>\geq 350</math>.</li> <li>(3) Substantial improvement over conventional chest radiography detection.</li> <li>(4) At least two consecutively negative results of RT-PCR testing separated by at least 24-hour interval.</li> </ol> <p>All discharged patients were required another 14 days of self-segregating at home for further observation.</p> <p>-&gt; 25 discharged patients sent to hospital again because of the positive RT-PCR results. They experienced an average of <math>7.32 \pm 3.86</math> days from their last negative RT-PCR result to turning positive again.</p> <p><b>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.</b></p>
Clinical Immunology 8APR2020	<b>Epigenetic dysregulation of ACE2 and interferon-regulated genes might suggest increased COVID-19 susceptibility and severity in lupus patients</b>	Sawalha, Amr H. et al. USA-China <a href="https://doi.org/10.1016/j.clim.2020.108410">https://doi.org/10.1016/j.clim.2020.108410</a>	Virology	<p>Patients with <b>systemic lupus erythematosus</b> might be especially prone to severe COVID-19, independent of their immunosuppressed state.</p> <ul style="list-style-type: none"> <li>- <b>ACE2 is hypomethylated and overexpressed in lupus T cells</b> suggesting an increased susceptibility to SARS-CoV-2 infection.</li> <li>- increased oxidative stress induced by viral infection <b>exacerbates ACE2 demethylation defect</b> in lupus and <b>may enhance viremia</b>.</li> </ul> <p>&gt; Maintaining disease remission in lupus patients is critical to prevent DNA demethylation and increased oxidative stress, which may exacerbate susceptibility to SARS-CoV-2 infection and likelihood of cytokine storm.</p>

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JAMA pediatric 8APR2020	<b>Screening and Severity of Coronavirus Disease 2019 (COVID-19) in Children in Madrid, Spain</b>	Tagarro A and al, Spain <a href="https://doi.org/10.1001/jamapediatrics.2020.1346">https://doi.org/10.1001/jamapediatrics.2020.1346</a>	Clinic.	365 screened children and 41 were positive = <b>11%</b> Median age = 1 year 34% had upper respiratory tract infection – 127 % fever without source - 5% viral like pneumonia 60% were hospitalized and <b>9,7% were admitted to PICU and needed respiratory support</b> <b>No one died</b> Limitations: probably more hospitalisation because of an increase awareness of COVID-19.
The Lancet 8APR2020	<b>First-wave COVID-19 transmissibility and severity in China outside Hubei after control measures, and second-wave scenario planning: a modelling impact assessment</b>	Leung et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30746-7/fulltext?utm_campaign=tlcoronavirus20&amp;utm_source=twitter&amp;utm_medium=social">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30746-7/fulltext?utm_campaign=tlcoronavirus20&amp;utm_source=twitter&amp;utm_medium=social</a>	Public Health/Epidemiology	-> The first wave of COVID-19 outside of Hubei has abated because of <b>aggressive non-pharmaceutical interventions</b> .  -> the $R_t$ decreased substantially since Jan 23, when control measures were implemented, and have since remained below 1. -> <b>Relaxing the interventions (resulting in <math>R_t &gt; 1</math>)</b> when the epidemic size was still small would increase the cumulative case count <b>exponentially as a function of relaxation duration</b> , 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	<b>Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A Nationwide Analysis of China</b>	Wen-hua Liang et al, China <a href="https://doi.org/10.1183/13993003.00562-2020">https://doi.org/10.1183/13993003.00562-2020</a>	Clinic	<b>1590 cases from 575 hospitals in 31 provincial administrative regions</b> were collected (core cohort). <b>The overall rate of severe cases and mortality was 16.0% and 3.2%, respectively, but</b>  Potential risk factors analysed using proportional hazard (PH) Cox regression models <b>Patients in Hubei</b> [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] <b>have a poorer prognosis compared with patients outside of Hubei after adjusting for age and comorbidity</b> <b>This might be attributed to the prolonged duration of symptom onset to hospitalization in the epicenter.</b>
Journal of biomolecular structure & dynamics, 8APR2020	<b>In-silico homology assisted identification of inhibitor of RNA binding against 2019-nCoV N-protein (N terminal domain)</b>	Sarma, Phulen et al, India <a href="https://doi.org/10.1080/07391102.2020.1753580">https://doi.org/10.1080/07391102.2020.1753580</a>	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” <b>This study suggests two important class of compounds, theophylline and pyrimidone derivatives as possible inhibitors of RNA binding to the N terminal domain of N protein of coronavirus, thus opening new avenues for in vitro validations</b>
Pediatric Critical Care 7APR2020	<b>Coronavirus Disease 2019 in Critically Ill Children: A Narrative Review of the Literature</b>	Ong J and al, Singapore/Italy/Canada <a href="https://journals.lww.com/pccmjournal/Abstract/onlinefirst/Coronavirus_Disease_2019_in_Critically_Ill_98057.aspx">https://journals.lww.com/pccmjournal/Abstract/onlinefirst/Coronavirus_Disease_2019_in_Critically_Ill_98057.aspx</a>	Clinic	Children account for a few proportions of COVID19 diseases <b>Not severely ill:</b> 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 high-flow nasal cannula 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	<b>The French response to COVID-19: intrinsic difficulties at the interface of science, public health, and policy</b>	Moatti, Jean.P et al., France <a href="https://doi.org/10.1016/S2468-2667(20)30087-6">https://doi.org/10.1016/S2468-2667(20)30087-6</a>	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 hydroxychloroquine 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	<b>Development of Reverse Transcription Loop-mediated Isothermal Amplification (RT-LAMP) Assays Targeting SARS-CoV-2</b>	Park et al., Republic of Korea <a href="https://www.biorxiv.org/content/10.1101/2020.03.09.983064v1">https://www.biorxiv.org/content/10.1101/2020.03.09.983064v1</a>	Diagnostic	-> Development of <b>highly specific RT-LAMP assays</b> 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	<b>Towards Optimization of Hydroxychloroquine Dosing in Intensive Care Unit COVID-19 Patients</b>	Perinel, Sophie et al, France <a href="https://doi.org/10.1093/cid/ciaa394">https://doi.org/10.1093/cid/ciaa394</a>	Therapeutic	<b>Prospective pharmacokinetic study : 13 patients in intensive care unit received 200 mg x 3 of oral HCQ daily</b> , 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.  <b>PK studies are needed to define the optimal dosing regimen.</b> Based on simulations, <b>a loading dose of 800 mg once daily on day 1, followed by 200 mg twice daily for 7 days is proposed</b>
Science Translational Medicine 6APR2020	<b>An orally bioavailable broad-spectrum antiviral inhibits SARS-CoV-2 in human airway epithelial cell cultures and multiple coronaviruses in mice</b>	Sheahan, Timothy P. et al. USA <a href="https://doi.org/10.1126/scitranslmed.abb5883">https://doi.org/10.1126/scitranslmed.abb5883</a>	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	<b>Tocilizumab treatment in COVID-19: a single center experience</b>	Luo, Pan et al, China <a href="https://doi.org/10.1002/jmv.25801">https://doi.org/10.1002/jmv.25801</a>	Therapeutic	<b>15 COVID-19 patients</b> under <b>Tocilizumab (TCZ)</b> therapy were <b>retrospectively assessed</b> . - 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.  <b>=&gt; A single dose of TCZ seems to fail to improve the disease activity in critically ill patients</b> although it was used in combination with glucocorticoid. However, <b>repeated doses of TCZ might improve the condition of critically ill patients.</b> <b>Limitations:</b> 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.

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 6APR2020	<b>Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy</b>	Grasselli G et al, Italy <a href="https://doi.org/10.1001/jama.2020.5394">https://doi.org/10.1001/jama.2020.5394</a>	Clinic	<p>Retrospective - 1591 patients COVID-19 – multicentric</p> <p><u>Demographic:</u></p> <ul style="list-style-type: none"> <li>- <b>82% male</b> - median age: 63 years</li> <li>- 68% had at least 1 comorbidity (HTA+++)</li> </ul> <p><u>Clinical data</u></p> <ul style="list-style-type: none"> <li>- 1150 patients required mechanical ventilation (higher than reported for other ICU patients)</li> <li>- <b>Median PEEP: 14 cmH<sub>2</sub>O</b></li> <li>- Median P<sub>aO2</sub>/F<sub>IO2</sub> = 166 (IQR:114-220), higher in young patients (&lt; 63 years)</li> <li>- <b>Mortality: 26%</b>, higher in older patients (15% vs 36%, p&lt;0,001)</li> <li>- Median length of stay: 9 days in ICU</li> </ul> <p><u>Limitation:</u></p> <ul style="list-style-type: none"> <li>- Short follow up → mortality rate could change?</li> <li>- Missing data for some patients</li> </ul>
Clin Chem 4APR2020	<b>Potential false-negative nucleic acid testing results for Severe Acute Respiratory Syndrome Coronavirus 2 from thermal inactivation of samples with low viral loads</b>	Pan et al., China <a href="https://academic.oup.com/clinchem/advance-article/doi/10.1093/clinchem/hvaa091/5815979">https://academic.oup.com/clinchem/advance-article/doi/10.1093/clinchem/hvaa091/5815979</a>	Diagnostic	<p>-&gt; Ct values are increased (<b>higher threshold for detection</b>) in specimens from diagnosed COVID-19 patients in RT-PCR tests <b>after thermal incubation</b>.</p> <p>-&gt; 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</p> <p>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.</p>
Inter J Of Infect Dis 3APR2020	<b>A first Case of Meningitis/Encephalitis associated with SARS-Coronavirus-2</b>	Moriguchi, Takeshi et al, Japan <a href="https://doi.org/10.1016/j.ijid.2020.03.062">https://doi.org/10.1016/j.ijid.2020.03.062</a>	Clinic	<p><b>Case report : 23-year old male, with seizure accompanied by unconsciousness.</b></p> <p>The specific <b>SARS-CoV-2 RNA</b> was not detected in the nasopharyngeal swab but <b>was detected in a CSF brain MRI</b> : hyperintensity along the wall of right lateral ventricle and hyperintense signal changes in the right mesial temporal lobe and hippocampus, <b>suggesting the possibility of SARS-CoV-2 meningitis</b></p> <p>Chest CT <b>small ground glass opacities</b></p> <p>At D15 : still ventilated and with impaired consciousness</p> <p><b>This case warns the physicians of patients who have CNS symptoms.</b></p>
The Journal of infection 3APR2020	<b>Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19</b>	Liu et al., China <a href="https://www.journalofinfection.com/article/S0163-4453(20)30208-5/pdf">https://www.journalofinfection.com/article/S0163-4453(20)30208-5/pdf</a>	Clinic	<p>245 COVID-19 patients :</p> <p>-&gt; Multivariate analysis demonstrated that there was 8% higher risk of in-hospital mortality for each unit increase in NLR.</p> <p>-&gt; 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</p> <p>-&gt; Fully adjusted OR for mortality was 1.10 in males for each unit increase of NLR</p> <p><b>NLR is an independent risk factor of the in-hospital mortality for COVID-19 patients especially for male.</b></p>
The Journal of infection 3APR2020	<b>Arbidol Monotherapy is Superior to Lopinavir/ritonavir in Treating COVID-19</b>	Zhu, Zhen et al, China <a href="https://doi.org/10.1016/j.jinf.2020.03.060">https://doi.org/10.1016/j.jinf.2020.03.060</a>	Therapeutic	<p>50 patients into 2 groups</p> <ul style="list-style-type: none"> <li>- <b>lopinavir/ritonavir group (34 cases)</b></li> <li>- <b>arbidol group (16 cases).</b></li> </ul> <p>Data from these patients were <b>retrospectively analyzed</b>.</p> <p><b>At D14 post admission: no viral load was detected in arbidol group.</b></p> <p><b>44.1%</b> of patients in <b>lopinavir/ritonavir</b> group had <b>positive RNA test</b> on day 14.</p> <p>Patients in the arbidol group had a shorter duration of positive RNA test.</p> <p>No apparent side effects were found in both groups.</p> <p><b>=&gt; Arbidol monotherapy may be superior to lopinavir/ritonavir in treating COVID-19.</b></p> <p>The sample size is the major limitation of this study.</p>

Journal and date	Title	Authors and link	Field of expertise	Key facts
CELL preproof	<b>Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2</b>	Monteil, Kwon et al,	Therapeutic	<p>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 (<b>hrsACE2</b>) <b>reduced SARS-CoV-2 recovery from Vero cells by a factor of 1,000-5,000</b>. 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.</p> <p><b>These data demonstrate that hrsACE2 can significantly block early stages of SARS-CoV-2 infections.</b></p>
Nature Medicine 3APR2020	<b>Respiratory virus shedding in exhaled breath and efficacy of face masks</b>	Leung, Nancy H. L. et al., <a href="https://doi.org/10.1038/s41591-020-0843-2">https://doi.org/10.1038/s41591-020-0843-2</a> China - USA	Virology	<p>Detection of <b>virus RNA shedding in exhaled breath and coughs</b> 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.</p> <p><b><u>Without face mask:</u></b></p> <ul style="list-style-type: none"> <li>- 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)</li> </ul> <p>Surgical face masks significantly reduced detection of viral RNA for:</p> <ul style="list-style-type: none"> <li>- Influenza virus in respiratory droplets, but not in aerosol.</li> <li>- Coronavirus in aerosols (≤5 µm particles), and non-significant reduction in respiratory droplets.</li> </ul> <p>Limitation: infectivity of detected virus not tested.</p> <p><b>--&gt; Surgical face masks could prevent transmission of human coronaviruses and influenza viruses from symptomatic individuals</b></p>
Antiviral Research 3APR2020	<b>Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro</b>	Choy, Yin-Lam Wong et al, Hong Kong <a href="https://doi.org/10.1016/j.antiviral.2020.104786">https://doi.org/10.1016/j.antiviral.2020.104786</a>	Therapeutic	<p>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.</p> <p><b>=&gt; Antiviral effect of remdesivir, lopinavir, homoharringtonine, 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.</b></p> <p><b>=&gt; Ribavirin or favipiravir that are currently evaluated under clinical trials showed no inhibition at 100 µM.</b></p> <p><b>=&gt; Synergy between remdesivir and emetine</b> was observed, and remdesivir at 6.25 µM in combination with emetine at 0.195 µM may achieve 64.9% inhibition in viral yield.</p> <p><b>Combinational therapy may help to reduce the effective concentration of compounds below the therapeutic plasma concentrations and provide better clinical benefits.</b></p>
International Journal of Antimicrobial Agents 3APR2020	<b>Structural and molecular modeling studies reveal a new mechanism of action of chloroquine and hydroxychloroquine against SARS-CoV-2 infection</b>	Fantini, Di Scala et al, France <a href="https://doi.org/10.1016/j.jantimicag.2020.105960">https://doi.org/10.1016/j.jantimicag.2020.105960</a>	Therapeutic	<p>Identification of a <b>new mechanism of action of CLQ and CLQ-OH</b> supporting the use of these repositioned drugs to cure SARS-CoV-2 infected patients.</p> <p>Using a combination of structural and molecular modeling approaches :</p> <p><b>=&gt; chloroquine (CLQ) binds sialic acids and gangliosides with high affinity.</b></p> <p><b>=&gt; New type of ganglioside-binding domain at the tip of the N-terminal domain of the SARS-CoV-2 spike (S) protein identified.</b> This domain (aa 111-158), which is fully conserved among clinical isolates worldwide, may <b>improve the attachment of the virus to lipid rafts and facilitate the contact with the ACE-2 receptor.</b></p> <p><b>=&gt; In presence of CLQ (or of the more active derivative hydroxychloroquine, CLQ-OH), the viral spike is no longer able to bind gangliosides.</b></p>

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Journal of Thrombosis and Thrombolysis 3APR2020	<b>Difference of coagulation features between severe pneumonia induced by SARS-CoV2 and non-SARS-CoV2</b>	Shiyu Y et al, China <a href="https://doi.org/10.1007/s11239-020-02105-8">https://doi.org/10.1007/s11239-020-02105-8</a>	Clinic	<p>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&lt;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 <b>Anticoagulant therapy may benefit to selected COVID patients (elevated D-Dimer)?</b> <u>Limits:</u></p> <ul style="list-style-type: none"> <li>- Retrospective</li> <li>- Influence of others therapies?</li> </ul>
Circulation 3APR2020	<b>The Variety of Cardiovascular Presentations of COVID-19</b>	Fried J et al, USA <a href="https://doi.org/10.1161/CIRCULATIONAHA.120.047164">https://doi.org/10.1161/CIRCULATIONAHA.120.047164</a>	Clinic	<p><b>4 cases reports</b></p> <ul style="list-style-type: none"> <li>- SARS-CoV2 infection should be in the differential of typical cardiac syndrome during pandemic event without infection signs</li> <li>- Myocarditis like presentations with COVID-19 → <b>further study</b></li> <li>- Direct cardiac injury = result of viral invasion OR cytokine storm induced by SARS-CoV2 → toxic effect on myocardium</li> <li>- COVID-19 can cause decompensation of heart failure → mixed shock</li> </ul>
JAMA 3APR2020	<b>Personal Risk and Societal Obligation Amidst COVID-19</b>	Tsai et al., USA <a href="https://doi.org/10.1001/jama.2020.5450">https://doi.org/10.1001/jama.2020.5450</a>	HSS/Politic	<p>Health workers with <b>pre-existing medical conditions</b>/in <b>older age groups</b> are at <b>greater risk</b> of severe illness and death if exposed to COVID-19. =&gt; Telemedicine</p> <p>Issue : <b>guilt</b> – 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</p> <p><b>Comforted by :</b></p> <ol style="list-style-type: none"> <li>1) High need for virtual-based care</li> <li>2) Sense of purpose in the community</li> </ol> <p>How much risk in the career of medicine should be acceptable to physicians? → <b>Need for medical profession to balance the obligations and duties of this profession with physicians' fundamentally human limitations and fears</b></p>
Physical and Engineering Sciences in Medicine, 3APR2020	<b>Covid-19: automatic detection from X-ray images utilizing transfer learning with convolutional neural networks</b>	Apostolopoulou et al., Greece <a href="https://link.springer.com/article/10.1007/s13246-020-00865-4">https://link.springer.com/article/10.1007/s13246-020-00865-4</a>	Diagnostic	<p>Technology evaluated is called <b>Transfer Learning</b></p> <p><u>Two sets of X-Ray images from patients were used as follow:</u></p> <ul style="list-style-type: none"> <li>- 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.</li> <li>- 2nd set : 224 images with confirmed Covid-19 disease, 714 images with confirmed bacterial and viral pneumonia, and 504 images of normal conditions.</li> </ul> <p>Deep Learning with X-ray imaging would extract significant biomarkers related to the Covid-19 disease, while the best accuracy, sensitivity, and specificity obtained is 96.78%, 98.66%, and 96.46% respectively. Further research are needed to confirm the efficiency of this type of technology for automatic detection of Covid-19 cases; moreover, it is necessary to develop models capable of distinguishing Covid-19 cases from other similar viral cases, but also from a greater variety of common pneumonia or even physiological X-rays</p>
Antiviral Research, 3APR2020	<b>The FDA-approved Drug Ivermectin inhibits the replication of SARS-CoV-2 in vitro</b>	Caly, Leon et al, Australia <a href="https://doi.org/10.1016/j.antiviral.2020.104787">https://doi.org/10.1016/j.antiviral.2020.104787</a>	Therapeutic	<p><b>Ivermectin is an inhibitor of the COVID-19 causative virus (SARS-CoV-2) on Vero/hSLAM cells.</b> A single treatment able to effect ~5000-fold reduction in virus at 48h in cell culture compared to control sample.</p> <p><b>Ivermectin is FDA-approved for parasitic infections, Ivermectin is widely available, due to its inclusion on the WHO model list of essential medicines</b></p>

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The Lancet Microbe 2APR2020	<b>Stability of SARS-CoV-2 in different environmental conditions</b>	Chin, Alex W. H. et al., China <a href="https://doi.org/10.1016/S2666-5247(20)30003-3">https://doi.org/10.1016/S2666-5247(20)30003-3</a>	Virology	<p><u>Infectious SARS-CoV-2 Stability at different temperatures (in virus transport medium) :</u></p> <ul style="list-style-type: none"> <li>- highly stable at 4°C (only ~ 0.7 log-unit reduction of infectious titre on day 14)</li> <li>- at 70°C, virus inactivation reduced to 5 mins</li> <li>- On a surgical mask, infectious virus detectable on day 7 (~0.1% of the original inoculum).</li> <li>- 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%), ...).</li> </ul> <p>--&gt; <b>SARS-CoV-2 can be highly stable in a favourable environment, but also susceptible to standard disinfection methods.</b></p>
Liver Int 2APR2020	<b>Clinical characteristics of Non-ICU hospitalized patients with coronavirus disease 2019 and liver injury : A Retrospective study</b>	Xie et al., China, <a href="https://doi.org/10.1111/iv.14449">https://doi.org/10.1111/iv.14449</a>	Clinic	<p><b>Retrospective study of 79 patients</b>, median age 60 years and 55.7% male. <b>29 had liver injury</b> (elevated ALT, AST and/or bilirubin)</p> <p>Multivariate analysis suggested that <b>CT scores was an independent predictor for liver injury</b>. Patients with liver injury stayed longer in the hospital.</p>
American journal of nephrology 2APR2020	<b>Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China</b>	Wang Lu et al, China <a href="https://doi.org/10.1159/000507471">https://doi.org/10.1159/000507471</a>	Clinic	<p><b>116 patients</b> – Retrospective study</p> <p>Median age: 54y and 58% male 40% severe pneumonia and 9% were ARDS 4,3% had CKD with long-term hemodialysis</p> <p><b>None patient meet criteria for AKI</b> 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%</p> <p><b>Results are similar with study on SARS-CoV infection in 2003</b> <b>Be careful because ACE2 expression is high in kidney.</b></p>
Liver Int 2APR2020	<b>Liver impairment in COVID-19 patients: a retrospective analysis of 115 cases from a single center in Wuhan city, China</b>	Zhang Y et al, China <a href="https://doi.org/10.1111/iv.14455">https://doi.org/10.1111/iv.14455</a>	Clinic	<p><b>2 groups: 115 COVID-19 and 114 controls (community acquired pneumonia)</b></p> <p>Controls significantly older – no other difference <b>No difference between group in the level of ALT or AST</b> Majority of COVID19 had mild abnormalities COVID-19 had reduction of albumin Liver is not the main target organ</p> <p><u>Relationship with the disease progression:</u></p> <ul style="list-style-type: none"> <li>- Higher level of ALT or AST in severe cases than mild cases,</li> <li>- Higher total bilirubin in severe cases,</li> <li>- Lower level of albumin in severe cases,</li> </ul> <p><b>Liver function did not show an independent association with severe COVID19</b></p>
CDC 1APR2020	<b>Presymptomatic Transmission of SARS-CoV-2 — Singapore, January 23–March 16, 2020</b>	Wei et al., China <a href="https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm?s_cid=mm6914e1_w#contribAff">https://www.cdc.gov/mmwr/volumes/69/wr/mm6914e1.htm?s_cid=mm6914e1_w#contribAff</a>	Public Health/Epidemiology	<p>-&gt; Identification of <b>7 clusters</b> of COVID-19 in Singapore in which <b>presymptomatic transmission</b> likely occurred and which may explain the occurrence of secondary cases</p>

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The Lancet Neurology 1APR2020	<b>Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence?</b>	Zhao, Hua; et al. China <a href="https://www.thelancet.com/journals/lanneur/article/PIIS1474-4422(20)30109-5/fulltext">https://www.thelancet.com/journals/lanneur/article/PIIS1474-4422(20)30109-5/fulltext</a>	Clinic	<p>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.</p> <p>Patient then developed symptoms of SARS-CoV-2 on day 8 and tested +ve by RT-PCR.</p> <p>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.</p> <p>Limitations: patient was not tested for SARS-CoV-2 upon admission, so causality is not clear.</p> <p><b>-&gt;This is the first, and single case report. It only suggests a possible association and more cases are necessary to support a causal relationship.</b></p>
Nature 1APR2020	<b>Virological assessment of hospitalized patients with COVID-2019</b>	Wolfel et al. Germany <a href="https://www.nature.com/articles/s41586-020-2196-x">https://www.nature.com/articles/s41586-020-2196-x</a>	Virology	<p>A detailed virological analysis of 9 cases, providing proof of active virus replication in upper respiratory tract tissues.</p> <p>-&gt; Pharyngeal virus shedding: very high during 1st week of symptoms.</p> <p>-&gt; Infectious virus was readily isolated from throat- and lung-derived samples, but not from stool samples (in spite of high virus RNA concentration).</p> <p>-&gt; Blood and urine never yielded virus.</p> <p>Active replication in the throat is confirmed by viral replicative RNA intermediates in throat samples.</p> <p>Sequence-distinct virus populations were consistently detected in throat and lung samples from the same patient, proving independent replication.</p> <p>Shedding of viral RNA from sputum outlasted the end of symptoms.</p> <p>Seroconversion occurred after 7 days in 50% of patients (14 days in all), but was not followed by a rapid decline in viral load.</p> <p>COVID-19 can present as a mild upper respiratory tract illness.</p> <p><b>Active virus replication in the upper respiratory tract puts the prospects of COVID-19 containment in perspective.</b></p>
NEJM 01APR2020	<b>Ten Weeks to Crush the Curve</b>	Fineberg, Harvey v. et al. USA <a href="https://doi.org/10.1056/NEJMe2007263">https://doi.org/10.1056/NEJMe2007263</a>	HSS/Politic	<p><b>1.</b> 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.</p> <p><b>2.</b> Perform millions of diagnostic tests over the next 2 weeks Organize dedicated clinical trial sites, physically separate from other health centers.</p> <p><b>3.</b> Provide all health workers with personal protective equipment.</p> <p><b>4.</b> 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 &amp; 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.</p> <p><b>5.</b> 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.</p> <p><b>6.</b> Learn through real-time, fundamental research.</p> <p>Over the long-term: Reinvigorate the public health infrastructure for future threats.</p>



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The Lancet) 01APR2020	<b>Racism and discrimination in COVID-19 responses</b>	Devakumar, D. et al., UK <a href="https://doi.org/10.1016/S0140-6736(20)30792-">https://doi.org/10.1016/S0140-6736(20)30792-</a>	HSS/Politic	<p><b>COVID 19 engenders fear =&gt; social, political racism and xenophobia with racialised/ discriminatory responses to fear + disproportionately affecting marginalised groups</b></p> <p>Social dimension : COVID could have been an equalizer but disproportionately affects people of color + migrants</p> <ol style="list-style-type: none"> <li>1) Microaggression/Violence towards different ethnic groups (i.e.: Chinese)</li> <li>2) lower socio-economic groups (limited access to healthcare + precarious jobs)</li> <li>3) Ethnic minority groups at greater risk (comorbidities)</li> <li>4) Migrants avoid hospitals for fear of identification/reporting</li> </ol> <p>Political dimension : Misappropriation of Covid-19 crisis for political purpose (racial discrimination, conflating public health restrictions and border policies + trade policies).</p> <p>Health protection relies on a well functioning health system with universal coverage, + social inclusion, justice, and solidarity</p>
Virology 31MAR2020	<b>Inefficiency of Sera from Mice Treated with Pseudotyped SARS-CoV to Neutralize 2019-nCoV Infection</b>	Ze Zhong Liu et al., China <a href="https://doi.org/10.1007/s12250-020-00214-5">https://doi.org/10.1007/s12250-020-00214-5</a>	Therapeutic	<p><b>S proteins:</b></p> <ul style="list-style-type: none"> <li>- 76% homology SARS CoV / SARS CoV-2</li> <li>- 29% homology SARS CoV / MERSCoV.</li> </ul> <p><b>RBS:</b></p> <ul style="list-style-type: none"> <li>- Significantly different, even if the bind to the same receptor (ACE2).</li> </ul> <p><b>Cross-reaction of sera ?</b></p> <p>SARS-CoV and MERCoV pseudovirus expression S protein: produced and injected into BALBc mice.</p> <ul style="list-style-type: none"> <li>-&gt; Sera tested on ACE2 expressing 293T cells.</li> <li>-&gt; Effective neutralization for SARS-PsV-treated mice but not MERS-PsV treated mice.</li> </ul> <p>When SARS-PsV-treated mice was exposed to a SARS-CoV-2 pseudovirus -&gt; no neutralization effect was evidenced.</p> <p><b>It may not be practical to treat SARS-CoV-2 patients.</b></p>
Emerging microbes & infections 31MAR2020	<b>Renin-angiotensin system inhibitors improve the clinical outcomes of COVID-19 patients with hypertension</b>	Meng, Juan et al, Chine, <a href="https://doi.org/10.1080/22221751.2020.1746200">https://doi.org/10.1080/22221751.2020.1746200</a>	Therapeutic	<p>Retrospective study of <b>42 patients with treated hypertension</b> admitted in hospitalization for COVID 19.</p> <p>Before hospitalization, <b>17 were on angiotensin-converting enzyme inhibitors (ACEIs)</b> or angiotensin II type 1 receptor blockers (ARBs), 25 were on other drugs.</p> <p><b>Results :</b> in patients from the ACEI/ARB group :</p> <ul style="list-style-type: none"> <li>- <b>Less severe cases</b></li> <li>- <b>trend toward lower IL-6 levels</b></li> <li>- <b>increased CD3 and CD8 T cell counts</b></li> <li>- <b>peak viral load during hospitalization significantly lower</b></li> </ul> <p>ACEI/ARB therapy may attenuate the inflammatory response, potentially through the inhibition of IL-6 levels</p> <p><b>Point of attention :</b> retrospective study, small sample.</p>
Annals of internal medicine 30MAR2020	<b>A Rush to Judgment? Rapid Reporting and Dissemination of Results and Its Consequences Regarding the Use of Hydroxychloroquine for COVID-19</b>	Kim, Alfred H.J et al., USA <a href="https://doi.org/10.7326/M20-1223">https://doi.org/10.7326/M20-1223</a>	HSS/Politic	<p><b>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 :</b></p> <p><b>Conclusion:</b></p> <ul style="list-style-type: none"> <li>-&gt; Sufficient justification to continue investigation of the efficacy and safety of HCQ in patients hospitalized with COVID-19.</li> <li>-&gt; No data currently to recommend the use of HCQ as a prophylaxis for COVID-19.</li> <li>-&gt;No recommendation of its use outside of marketing authorization until it is justified and offer is reinforced.</li> <li>-&gt; Risk of penury to patients with rheumatic diseases who depend on HCQ for their survival.</li> <li>-&gt; HCQ shortage will limit availability to patients with COVID-19 if efficacy truly established.</li> </ul>

Journal and date	Title	Authors and link	Field of expertise	Key facts
Medicine in Drug Discovery – pre-Proof 22MAR2020	<b>Novel decoy cellular vaccine strategy utilizing transgenic antigen-expressing cells as immune presenter and adjuvant in vaccine prototype against SARS-CoV-2 virus</b>	Henry Ji et al., China <a href="https://doi.org/10.1016/j.medidd.2020.100026">https://doi.org/10.1016/j.medidd.2020.100026</a>	Vaccine	<p>S1 SARS-CoV-2 protein is expressed on the surface of K562 human myelogenous leukemia cells (HLA negative - highly sensitive to NK mediating kills):</p> <p>-&gt; Provides a means of targeting and activating an innate driver of the host adaptive immune response.</p> <p>-&gt; 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.</p> <p><b>This approach has already being used for cancer vaccine treatments inducing robust cellular and humoral anti-tumor immune responses.</b></p>
Journal of infectious Disease 31MAR2020	<b>Characteristics of peripheral lymphocyte subset alteration in COVID-19 pneumonia</b>	Fan W et al, China <a href="https://doi.org/10.1093/infdis/jiaa150">https://doi.org/10.1093/infdis/jiaa150</a>	Immunology	<p><b>60 patients – monocentric – total lymphocytes in COVID-19 were compared to healthy controls (HC)</b> Median age 60 y 32% were serious illness <u>Compared to HCs, COVID-19 had a decrease in:</u></p> <ul style="list-style-type: none"> <li>- Total lymphocytes</li> <li>- CD4 + - CD8+ - NK cells and B cells</li> </ul> <p><u>Serious compared to mild patient:</u></p> <ul style="list-style-type: none"> <li>- Decrease total lymphocytes, CD4+, CD8+ and B cells in serious patients</li> </ul> <p><u>Post-treatment:</u></p> <ul style="list-style-type: none"> <li>- Total lymphocytes, CD8+ and B cells increased significantly in responders</li> <li>- No significant change in non responder's</li> </ul> <p><b>CD8+ cells potential predictor for disease severity and poor clinical efficacy</b></p>
The Lancet ID 30MAR2020	<b>Estimates of the severity of coronavirus disease 2019: a model-based analysis</b>	Verity et al., UK <a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30243-7/fulltext#">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30243-7/fulltext#</a>	Public Health/Epidemiology	<p><b><u>Using data on 24 deaths that occurred in mainland China and 165 recoveries outside of China:</u></b></p> <ul style="list-style-type: none"> <li>- Mean duration from onset of symptoms to death : 17,8 days</li> <li>- Mean duration from onset to hospital discharge: 24,7 days</li> <li>- Crude case fatality ratio: 3,67%</li> </ul> <p>After further adjusting for demography and under-ascertainment:</p> <ul style="list-style-type: none"> <li>- Case fatality ratio: 1,38% / &lt;60 y : 0,32% / &gt;60y: 6,4% / &gt;80y: 13,4%</li> </ul> <p>Estimates of case fatality ratio from international cases stratified by age were consistent with those from China (see paper for data)</p> <p>Estimated overall infection fatality ratio for China: 0-66%, with an increasing profile with age.</p> <p>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.</p>
Journal of Gastroenterology and Hepatology 27MAR2020	<b>Covid-19 and the Digestive System</b>	Wong S et al, China <a href="https://doi.org/10.1111/jgh.15047">https://doi.org/10.1111/jgh.15047</a>	Clinic	<p><b>Diarrhoea</b> (2 to 10%) and <b>nausea/vomiting</b> (1 to 10%) are the most frequent gastrointestinal symptoms.</p> <p>Early in the disease course: earlier than pyrexia</p> <p><b>Liver injury:</b> abnormal level of ALAT and ASAT in 15 to 53 % of patients – <b>mild and transient</b></p> <ul style="list-style-type: none"> <li>→ microvesicular steatosis and mild lobular activity</li> <li>→ direct viral infection of hepatocytes (ACE2 receptor) or drug toxicity or immune-related injury</li> </ul> <p><b>Possible tropism of SARS-CoV-2 for gastrointestinal tract:</b> ACE2 receptor</p> <p><b>Faecal source: viral transmission ?</b></p>

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The Lancet ID 27MAR2020	<b>Clinical and virological data of the first cases of COVID-19 in Europe: a case series</b>	Lescure et al., France <a href="https://doi.org/10.1016/S1473-3099(20)30200-0">https://doi.org/10.1016/S1473-3099(20)30200-0</a>	Clinic	<p><b>5 Patients:</b> 3 men: aged 31 years, 48 years, and 80 years – 2 women: aged 30 years and 46 years</p> <p><b>3 different clinical evolutions:</b>  <ul style="list-style-type: none"> <li>- 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</li> <li>- 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</li> <li>- 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.</li> </ul> </p> <p>The 80-year-old patient died on day 14 of illness. All other patients had recovered and been discharged by Feb 19, 2020.</p>
Clinical Infectious Disease 27MAR2020	<b>Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China</b>	Mo P et al, China <a href="https://doi.org/10.1093/cid/ciaa270">https://doi.org/10.1093/cid/ciaa270</a>	Clinic	<p><b>155 patients</b> with median age of 54 years –  <b>85 refractory COVID-19:</b></p> <ul style="list-style-type: none"> <li>- Older and more male (<math>p &lt; 0,05</math>)</li> <li>- More comorbidities: diabetes, cardiovascular disease, cerebrovascular disease (<math>p &lt; 0,05</math>)</li> <li>- Higher incidence of breath shortness and anorexia (<math>p &lt; 0,05</math>)</li> <li>- Bilateral pneumonia</li> <li>- Higher CRP, LDH, ASAT and neutrophile</li> </ul> <p><b>Risk factors:</b>  <ul style="list-style-type: none"> <li>- <b>Male (OR: 2,3 [1,0-4,8]) and anorexia admission (OR:3,9 [1,1-13,4])</b></li> </ul> </p> <p>Received more oxygen (OR: 3,0), corticosteroid (OR:2,32)  <b>Protective factor:</b> fever on admission (OR: 0,33 [0,1 – 0,9])</p>
JAMA 27MAR2020	<b>Treatment of 5 critically ill patients with COVID-19 with convalescent plasma</b>	Shen C et al, China <a href="https://jamanetwork.com.proxy.insermbiblio.inist.fr/journals/jama/fullarticle/2763983">https://jamanetwork.com.proxy.insermbiblio.inist.fr/journals/jama/fullarticle/2763983</a>	Therapeutic	<p><b>5 patients:</b> severe pneumonia + <math>P_{AO_2}/F_{IO_2} &lt; 300 \text{ mmHg}</math> + currently or has been supported by mechanical ventilation  All received antiviral agents and steroids  <b>Administered between 10 and 22 days after admission</b></p> <p><b>After transfusion:</b>  <ul style="list-style-type: none"> <li>- Ct value and viral load declined</li> <li>- Value of inflammatory biomarkers decreased</li> <li>- Clinical improvement: improved <math>P_{AO_2}/F_{IO_2}</math>, reduced body temperature, improved chest imaging</li> <li>- No longer required respiratory support by 9 days after transfusion</li> </ul> </p> <p><b>Limitations:</b>  <ul style="list-style-type: none"> <li>- No control group and small cases</li> <li>- Improved without transfusion? / Improvement related to transfusion or other therapies?</li> <li>- Late administration of transfusion: different timing would be associated with different outcomes?</li> </ul> </p>
The Lancet 27MAR2020	<b>Historical linkages: epidemic threat, economic risk, and xenophobia</b>	White, A. et al., USA <a href="https://doi.org/10.1016/S0140-6736(20)30737-6">https://doi.org/10.1016/S0140-6736(20)30737-6</a>	HSS/Politic	<p>Global management of pandemic disease threats and global commerce historically linked:  <ul style="list-style-type: none"> <li>- History of international infectious disease control shaped by a distinctly European/US perspective prioritizing epidemic threats from colonial/post-colonial sites potentially affecting trade (</li> </ul> =&gt; aggressive control in sites of epidemic outbreak and aggressive scrutiny of those deemed responsible.</p> <p>- 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.</p> <p><b>Aggressive racist and xenophobic responses in the name of health controls.</b></p> <ul style="list-style-type: none"> <li>- Concern for trading relationships central to US economic growth pivotal for US Congress to endorse creation of WHO.</li> <li>- Nations have recently aligned infectious disease control policy alongside concerns for national security.</li> </ul>

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J. Med. Virol. 26MAR2020	<b>Stability Issues of RT-PCR Testing of SARS-CoV-2 for Hospitalized Patients Clinically Diagnosed with COVID-19</b>	Li et al., China <a href="https://doi.org/10.1002/jmv.25786">https://doi.org/10.1002/jmv.25786</a>	Diagnostic	<p><u>610 hospitalized patients from Wuhan</u></p> <p>-&gt; High false negative rate of RT-PCR testing</p> <p>-&gt; 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</p> <p><b>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.</b></p>
JAMA 26MAR2020	<b>Antibodies in Infants Born to Mothers With COVID-19 Pneumonia</b>	Zeng et al., China <a href="https://jamanetwork.com/journals/jama/fullarticle/2763854">https://jamanetwork.com/journals/jama/fullarticle/2763854</a>	Clinic	<p>A novel study on 6 pregnant women and their infants confirm no maternal-infant transmission of SARS-CoV-2 based on reverse transcriptase–polymerase chain reaction (RT-PCR) and reveals the presence of antibodies in all newborns :</p> <ul style="list-style-type: none"> <li>· 6 mothers had mild clinical manifestations and had cesarean deliveries in their third trimester</li> <li>· Neonatal throat swabs and blood samples are negative by RT-PCR test</li> <li>· All 6 infants had IgG and IgM virus-specific antibodies in their serum and their mothers also had elevated levels of IgG and IgM</li> <li>· Inflammatory cytokine IL-6 was significantly increased in all infants.</li> </ul> <p><b>Point of care/conclusion</b></p> <p>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.</p>
BMJ 26MARS2020	<b>The world's largest refugee camp prepares for covid-19</b>	Gaia Vince, UK <a href="https://doi.org/10.1136/bmj.m1205">https://doi.org/10.1136/bmj.m1205</a>	HSS/Politic	<p><u><b>Biggest camp in Cox's Bazar (Bengladesh):</b></u></p> <ul style="list-style-type: none"> <li>- Nearly 1 million people live in overcrowded conditions.</li> <li>- Particularly vulnerable (physical distancing impossible).</li> </ul> <p>United Nations Refugee Agency coordinate efforts to increase hand washing, using community leaders to inform (imams and women group leaders).</p> <p>Other initiative for preparedness : creasion 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.</p>
The Lancet Public Health 25MAR2020	<b>The Italian health system and the COVID-19 challenge</b>	Armocida et al., Italy <a href="https://doi.org/10.1016/S2468-2667(20)30074-8">https://doi.org/10.1016/S2468-2667(20)30074-8</a>	HSS/Politic	<p>In Italy, National Healthcare Service is regionally based, with <b>local authorities responsible for the organisation</b> and delivery of health services. Due to progressive privatisation and finance cuts, system close to collapse. 4 lessons to be learned :</p> <ul style="list-style-type: none"> <li>- <b>Decentralisation and fragmentation of health services seems to have restricted timely interventions and effectiveness</b></li> <li>- Health-care systems capacity and financing need to be more flexible in case of emergencies</li> <li>- Solid partnerships between the private and public sector should be institutionalised</li> <li>- Recruitment of HR must be planned and financed with a long-term vision</li> </ul>

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Lancet 25MAR2020	<b>Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study</b>	Yu N. et al, China <a href="https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30176-6.pdf">https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30176-6.pdf</a>	Clinic	<p><b><u>Pregnant patients with COVID 19 – no ICU :</u></b></p> <p>Mean age gestational: 39 + 1 - All caesarean section Fever (6) - Cough (1) - Shortness of breath (1) - Diarrhea (1) Laboratory tests:</p> <ul style="list-style-type: none"> <li>- Elevated CRP (7)</li> <li>- Lymphopenia (5) – thrombopenia (2)</li> <li>- Elevated IL-6 (4)</li> </ul> <p><b>Chest CT:</b> all pneumonia → bilateral (6), unilateral (1) Treatment: oxygen + antiviral + antibiotic (single or combination) + traditional medicine. Methylprednisolone for 5 after caesarean section. <b>Neonatal:</b> 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 <b>No arguments for vertical transmission</b></p>
SCIENCE 25MAR2020	<b>The effect of human mobility and control measures on the COVID-19 epidemic in China</b>	Kraemer et al., UK <a href="https://science.sciencemag.org/content/early/2020/03/25/science.abb4218">https://science.sciencemag.org/content/early/2020/03/25/science.abb4218</a>	Public Health/Epidemiology	<p><b><u>Use of real-time mobility data from Wuhan and detailed case data including travel history</u></b></p> <p>-&gt; Early: spatial distribution of COVID-19 cases in China was explained well by human mobility data -&gt; After implementation of control measures: this correlation dropped and growth rates became negative in most locations</p> <p><b>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.</b></p>
Inter J of Infectious Diseases 25MAR2020	<b>Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings</b>	Zhang X et al, China <a href="https://www.ijidonline.com/article/S1201-9712(20)30172-7/fulltext">https://www.ijidonline.com/article/S1201-9712(20)30172-7/fulltext</a>	Clinic	<p><b>645 patients with 72 no-pneumonia and 573 pneumonia</b> Bilateral lung disease: 432 (67%) <b>Group with pneumonia:</b></p> <ul style="list-style-type: none"> <li>- Older: 46,6 vs 34,9 years</li> <li>- One coexisting underlying: 28,8% vs 16%</li> <li>- Less exposure to Wuhan or confirmed patient</li> <li>- Time from onset to COVID-19 was longer: 5 days vs 2 days</li> <li>- Symptoms: fever and cough</li> <li>- Lower lymphocyte, albumin and NaCl</li> <li>- Higher LDH and CRP</li> </ul> <p><b><u>Predictive factor of severe pneumonia:</u></b></p> <ul style="list-style-type: none"> <li>- Lymphopenia and higher creatinine</li> <li>- Shortness of breath</li> </ul>
Disaster medicine and public health preparedness 24MAR2020	<b>Chronology of COVID-19 cases on the Diamond Princess cruise ship and ethical considerations: a report from Japan</b>	Nakazawa, et al. Japan <a href="http://www.ncbi.nlm.nih.gov/pubmed/32207674">http://www.ncbi.nlm.nih.gov/pubmed/32207674</a>	HSS/Political	<p><b><u>Ship = virus incubator + "international miniature company"</u></b></p> <p>-&gt; Difficulty in testing such a large number of people of various origins and faiths <b><u>Recommendations of the article:</u></b> <b>Politically:</b> -&gt; Alert political decision-makers to the impact of multiple, contradictory, false or unconfirmed information on the health of confined passengers -&gt; Mobilize collective intelligence / academic consensus by involving a large number of experts</p> <p><b>In terms of ethics and public health:</b> -&gt; 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) -&gt; 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 ». -&gt; 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</p> <p><b>Legally:</b> -&gt; 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) -&gt; Strengthen international cooperation.</p>

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The Lancet Global Health 24MAR2020	<b>Early in the epidemic: impact of preprints on global discourse about COVID-19 transmissibility</b> COMMENT	Maimuna et al., USA <a href="https://doi.org/10.1016/S2214-109X(20)30113-3">https://doi.org/10.1016/S2214-109X(20)30113-3</a>	HSS/Politic	<p><b><u>Novelty of SARS-CoV-2, so scientists rushed to fill epidemiological, virological, and clinical knowledge gap</u></b></p> <p>-&gt; 50 new studies about the virus between January 10 and January 30 alone.</p> <p>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.</p> <p><b><u>Conclusions :</u></b></p> <ul style="list-style-type: none"> <li>- Powerful role preprints can have during public health crises because of the timeliness with which they can disseminate new information.</li> <li>- Use of preprint does not jeopardise future peer-reviewed publication (first step : preprint and then peer reviewed)</li> <li>- 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)</li> </ul>
Emerging microbes and Infections 24MAR2020	<b>Establishment and validation of a pseudovirus neutralization assay for SARS-CoV-2</b>	Jianhui Nie et al., China <a href="http://www.ncbi.nlm.nih.gov/pubmed/32207377">http://www.ncbi.nlm.nih.gov/pubmed/32207377</a>	Therapeutic	<p>Necessity of <b>handling SARS-CoV-2 in BSL-3 facilities and accessibility to virus strains -&gt; barriers to develop candidate vaccines and therapeutics.</b></p> <p>-&gt; Hence, development of a SARS-CoV-2 pseudovirus based in neutralization assays using S viral genes cloned into pcDNA3.1 plasmids. -&gt; Expressed in a VSV pseudoviral platform. -&gt; Huh7 cells plated at 5x10<sup>4</sup>/well were identified as the best cell system for SARS-CoV2 pseudovirus infection (inocula of 650 TCID<sub>50</sub>/well).</p> <p><b>When tested against the SARS-CoV-2 pseudovirus, SARS-CoV-2 convalescent patient sera showed high neutralizing potency, which underscore its potential as therapeutics.</b></p> <ul style="list-style-type: none"> <li>• at home = stress can be eased</li> <li>• 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</li> </ul> <p><b>30% = post-traumatic stress disorder</b></p> <p><b>Chinese gov. strategies to prevent risks :</b></p> <ol style="list-style-type: none"> <li>1. nurses 24 h per day</li> <li>2. guidance by nutritionists for children's diets</li> <li>3. communication with parents any time</li> <li>4. citizens volunteering as temporary mothers</li> <li>5. 24 h free psychological counselling hotlines</li> </ol> <p><b>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</b></p> <p><b>Need for :</b></p> <ol style="list-style-type: none"> <li>1. formal training for paediatric health-care workers</li> <li>2. evidence-based guidelines</li> <li>3. national collaborative networks (psychiatrists, psychotherapists, researchers, community volunteers)</li> <li>4. post-pandemic surveillance of children</li> </ol>
The Lancet Child & Adolescent Health 24MAR2020	<b>Mental health considerations for children quarantined because of COVID-19</b>	Liu, Jia Jia; Bao, Yanping et al., China <a href="https://doi.org/10.1016/S2352-4642(20)30096-1">https://doi.org/10.1016/S2352-4642(20)30096-1</a>	HSS/Politic	<p><b>30% = post-traumatic stress disorder</b></p> <p><b>Chinese gov. strategies to prevent risks :</b></p> <ol style="list-style-type: none"> <li>1. nurses 24 h per day</li> <li>2. guidance by nutritionists for children's diets</li> <li>3. communication with parents any time</li> <li>4. citizens volunteering as temporary mothers</li> <li>5. 24 h free psychological counselling hotlines</li> </ol> <p><b>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</b></p> <p><b>Need for :</b></p> <ol style="list-style-type: none"> <li>1. formal training for paediatric health-care workers</li> <li>2. evidence-based guidelines</li> <li>3. national collaborative networks (psychiatrists, psychotherapists, researchers, community volunteers)</li> <li>4. post-pandemic surveillance of children</li> </ol>



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The Lancet 23MAR2020	<b>Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study</b>	Kai-Wang et al., China <a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30196-1/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30196-1/fulltext</a>	Virology	<p><b>23 persons were included</b></p> <ul style="list-style-type: none"> <li>- Median viral load in posterior oropharyngeal saliva or other respiratory specimens at presentation was 5.2 log<sub>10</sub> copies per mL</li> <li>- Salivary viral load: <b>highest during the first week after symptom onset</b> and subsequently declined with time</li> <li>- In one patient, viral RNA was detected <b>25 days after symptom onset</b>.</li> <li>- <b>Older age</b> was correlated with <b>higher viral load</b></li> <li>- For 16 patients with serum samples available 14 days or longer after symptom onset, <b>rates of seropositivity</b> were 94% for <b>anti-NP IgG</b>, 88% for <b>anti-NP IgM</b>, 100% for <b>anti-RBD IgG</b>, and 94% for <b>anti-RBD IgM</b>.</li> <li>- <b>Anti-SARS-CoV-2-NP</b> or <b>anti-SARS-CoV-2-RBD IgG</b> levels correlated with <b>virus neutralisation titre</b>.</li> </ul>
JAMA 23MAR2020	<b>Ethics Committee Reviews of Applications for Research Studies at 1 Hospital in China During the 2019 Novel Coronavirus Epidemic</b>	Zhang H et al.- China <a href="https://doi.org/10.1001/jama.2020.4362">https://doi.org/10.1001/jama.2020.4362</a>	HSS/Politic	<ul style="list-style-type: none"> <li>- <b>Henan hospital</b>: designated to provide care to COVID-19 patients.</li> <li>- Hospital ethics committee organized <b>4 emergency video conference in 35 days</b>.</li> <li>- Projects evaluated <b>within 2,13 days after submission: more quickly</b> than other previous boards organized in an outbreak context.</li> <li>- 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. <b>Although the rush, review standards were not lowered during the outbreak.</b></li> </ul>
Open Forum Infect Dis 21MAR2020	<b>High-dose intravenous immunoglobulin as a therapeutic option for deteriorating patients with Coronavirus Disease 2019</b>	Wei Cao and al, Chine <a href="https://doi.org/10.1093/ofid/ofaa102">https://doi.org/10.1093/ofid/ofaa102</a>	Therapeutic	<p><b>3 adults (56, 34 and 35 y)</b></p> <ul style="list-style-type: none"> <li>- treated by <b>25 grams per day for five days</b> of <b>immunoglobulins</b> at the time of respiratory distress initiation + <b>antibiotic</b></li> <li>- <b>temperature back to normal in one to two days, and breathing difficulties alleviating in 3-5 days</b></li> </ul> <p>Point of attention: other treatments were given, antiviral for 2/3 patients, corticoid for 1.</p> <p>The <b>first few days of deterioration</b> may present a <b>critical point</b> when <b>potent suppression of inflammatory cascade could save the patients</b> from fatal immune-mediated injuries</p> <p><b>Hospitalized patients</b> : i) age &gt;12 years and ii) <b>PCR documented SARS-CoV-2 carriage in nasopharyngeal sample at admission</b></p>
International journal of antimicrobial agents 20MAR2020	<b>Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial</b>	Gautret, and al, France <a href="https://www.sciencedirect.com/science/article/pii/S0924857920300996">https://www.sciencedirect.com/science/article/pii/S0924857920300996</a>	Therapeutic	<ul style="list-style-type: none"> <li>- Treatment: <b>oral hydroxychloroquine sulfate</b> 200 mg, 3/day during 10 days.</li> <li>- 26 treated among them, six patients received additional azithromycin.</li> <li>- Control group : 16 patients from another centre or refusal to participate</li> <li>- 6 patients treated were excluded from the analysis</li> </ul> <p><b>Primary endpoint</b> : <b>virological clearance at day-6 post-inclusion</b></p> <p><b>70% of hydroxychloroquine-treated patients (N=20) were virologically cured</b> comparing with 12.5% in the control group (N=16) (p= 0.001)</p>

Journal and date	Title	Authors and link	Field of expertise	Key facts
Journal Travel Medicine and Infectious Disease 20MAR2020	<b>COVID-19: Active measures to support community-dwelling older adults</b>	K, Kuwahara et al., Japan <a href="http://www.ncbi.nlm.nih.gov/pubmed/32205272">http://www.ncbi.nlm.nih.gov/pubmed/32205272</a>	HSS/Politic	<p>-&gt; With no proven drug and vaccine treatments, non-pharmaceutical measures, especially social distancing, are an essential to slow the spread of the epidemic.</p> <p>-&gt; Given the higher risk associated with older adults, practical information should be provided to community-dwelling adults to help maintain appropriate community activity levels.</p> <p>-&gt; 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.</p>
Travel Med Infect Dis 20MAR2020	<b>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</b>	Amrane et al, France <a href="http://www.ncbi.nlm.nih.gov/pubmed/32205269">http://www.ncbi.nlm.nih.gov/pubmed/32205269</a>	Public Health/Epidemiology	<p>Rapid viral detection performed on sputum and nasopharyngeal samples from the first 280 patients suspected to have COVID-19.</p> <p>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.</p>
Cell Mol Immunol 19MAR2020	<b>Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine</b>	Wanbo Tai et al., China <a href="https://www.nature.com.proxy.insermbiblio.inist.fr/articles/s41423-020-0400-4">https://www.nature.com.proxy.insermbiblio.inist.fr/articles/s41423-020-0400-4</a>	Vaccine	<p>-&gt; SARS-CoV-2 <b>receptor-binding domain (RBD)</b> protein could be used <b>as a therapeutic agent</b> against SARS-CoV-2 and SARS-CoV infection (from results <i>in vitro</i>)</p> <p>-&gt; RBD in SARS-CoV-2 S protein was identified</p> <p>-&gt; RBD protein bound strongly to human and bat angiotensin-converting enzyme 2 (ACE2) receptors.</p> <p>- SARS-CoV RBD-specific antibodies could crossreact with SARS-CoV-2 RBD protein</p> <p>- SARS-CoV RBD-induced antisera could cross-neutralize SARS-CoV-2 -&gt; <b>potential to develop SARS-CoV RBD-based vaccines for prevention of SARS-CoV-2 and SARS-CoV infection.</b></p>
NEJM 19MAR2020	<b>A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19</b>	Cao B et al, China <a href="https://www.nejm.org/doi/pdf/10.1056/NEJMoa2001282?articleTools=true">https://www.nejm.org/doi/pdf/10.1056/NEJMoa2001282?articleTools=true</a>	Therapeutic	<p>Randomized, controlled trial, open-label trial</p> <p>☑ <b>199 patients included:</b> 99 received lopinavir-ritonavir and 100 standard care alone:</p> <ul style="list-style-type: none"> <li><b>Lopinavir-ritonavir was not associated with clinical improvement or mortality:</b> median time to clinical improvement 16 days vs 16 days, HR = 1.31 [0.95 – 1.85]</li> </ul> <p>Others outcomes:</p> <ul style="list-style-type: none"> <li>28-days mortality lower in the lopinavir-ritonavir group: 19.2% vs 25%, difference -5.8 % [-17.3 – 5.7]</li> <li>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)</li> <li>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.</li> <li>No difference on duration of oxygen therapy and duration hospitalization.</li> <li>Post hoc finding that early initiation of lopinavir-ritonavir might accelerate clinical recovery and reduced mortality</li> </ul> <p>Overall mortality at 22.1%</p> <p><b>No benefit was observed with lopinavir-ritonavir treatment</b></p>

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NEJM 19MAR2020	<b>SARS-CoV2 Infection in children</b>	Lu X. et al, China <a href="https://www.nejm.org/doi/pdf/10.1056/NEJMc2005073?articleTools=true">https://www.nejm.org/doi/pdf/10.1056/NEJMc2005073?articleTools=true</a>	Clinic	On the 1391 children tested at Wuhan Children's Hospital, <b>171 (12.3%) were positive for SARS-CoV2 infection.</b>  Median age: <b>6.7 years</b> - Male: 60.8 % Fever: <b>41.5 %</b> - Cough: 48.5 % Pneumonia: 64.9 % <b>3 patients</b> (with coexisting conditions) <b>require intensive care and 1 death</b> <b>Most children appear to be mild symptomatic.</b>
World Journal of Pediatrics 19MAR2020	<b>Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study</b>	Sun D et al, China <a href="https://link.springer.com.proxy.insermbiblio.inist.fr/content/pdf/10.1007/s12519-020-00354-4.pdf">https://link.springer.com.proxy.insermbiblio.inist.fr/content/pdf/10.1007/s12519-020-00354-4.pdf</a>	Clinic	<b>8 children included:</b> 5 severely ill and 3 critically ill 2 months to 15 years <b>Symptoms:</b> - Polypnea 100% - Fever (6/8) - Cough (6/8) - Expectoration (4/8) <b>Abnormalities in chest scanning 100% patients:</b> - multiple patch-like shadows - ground glass opacity <b>Biological:</b> - increase CRP, PCT and LDH - elevated ALAT - increase IL6 (2/8), IL10 (5/8), IFN- $\gamma$ (2/8) Level of IL6 and IL10 were significantly increase in 2 critically ill patient who remained in ICU for 20 days. <b>Specific laboratory abnormalities and excessive immune responses may lead to long-term lung damage and severe health complication</b>
Cell and Mol Biol 17MAR2020	<b>Elevated exhaustion levels and reduced functional diversity of T cells in peripheral blood may predict severe progression in COVID-19 patients</b>	Zheng et al., <a href="https://www.nature.com/articles/s41423-020-0401-3">https://www.nature.com/articles/s41423-020-0401-3</a>	Immunology	Immunological characteristics of peripheral blood leukocytes from 16 patients:  <b>Compared to healthy group (n=6):</b> - 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- $\gamma$ -TNF- $\alpha$ -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- $\alpha$ (TNF- $\alpha$ ) plasma concentrations were found among the three groups  - Levels of interferon- $\gamma$ (IFN- $\gamma$ ) and TNF- $\alpha$ 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  <b>-&gt; Identification of potential immunological risk factors for COVID-19 pneumonia and provided clues for its clinical treatment.</b>
The NEJM 17MAR2020	<b>Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1</b>	Doremalen et al., USA <a href="https://www.nejm.org/doi/pdf/10.1056/NEJMc2004973?articleTools=true">https://www.nejm.org/doi/pdf/10.1056/NEJMc2004973?articleTools=true</a>	Virology	-> Stability of <b>SARS-CoV-2</b> was similar to that of <b>SARS-CoV-1</b> under the experimental circumstances tested.  -> Detectable in <b>aerosols</b> for up to <b>three hours</b> , up to <b>four hours on copper</b> , up to <b>24 hours on cardboard</b> and up to <b>two to three days on plastic and stainless steel.</b>  <b>Aerosol and fomite transmission of SARS-CoV-2 is plausible</b>

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The Lancet 17MAR2020	<b>Prevention of SARS-CoV-2 infection in patients with decompensated cirrhosis</b>	Xiao et al., China <a href="https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30080-7/fulltext">https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30080-7/fulltext</a>	Clinic	<p><b>Previously known:</b> Patients with decompensated cirrhosis have a higher risk of, and mortality from, infection.</p> <p>-&gt; 111 patients with decompensated cirrhosis (were included) -&gt; <b>New precautionary procedures</b> were implemented (<b>see paper</b>) -&gt; Incidence of COVID19 was lower than in other groups.</p> <p>The simple approach (<b>see paper</b>) could be an effective means of preventing COVID-19 in patients with decompensated cirrhosis.</p>
International journal of infectious diseases 17MAR2020	<b>Transmission potential and severity of COVID-19 in South Korea</b>	Shim et al., Rep of Korea <a href="https://www.ijidonline.com/article/S1201-9712(20)30150-8/fulltext">https://www.ijidonline.com/article/S1201-9712(20)30150-8/fulltext</a>	Public Health/Epidemiology	<p>- COVID-19 caused 6,284 cases and 42 deaths in South Korea as of March 8, 2020.</p> <p>- The mean reproduction number <math>R_t</math> of COVID-19 in Korea was estimated at 1.5 (95% CI: 1.4-1.6)</p> <p>- 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</p> <p>- The crude case fatality rate is higher among males (1.1%) compared to females (0.4%) and increases with older age, from 0.1% among those 30-39 yrs to 6% among those &gt;= 80 yrs as of March 6, 2020.</p> <p>- Results indicate early sustained transmission of COVID-19 in South Korea and support the implementation of social distancing measures to rapidly control the outbreak.</p>
J Inf Dis 17MAR2020	<b>Clinical outcome of 55 asymptomatic cases at the time of hospital admission infected with SARS-Coronavirus-2 in Shenzhen, China.</b>	Wang et al., China <a href="https://academic.oup.com/ijid/advance-article/doi/10.1093/infdis/jiaa119/5807958">https://academic.oup.com/ijid/advance-article/doi/10.1093/infdis/jiaa119/5807958</a>	Clinic	<p><b>55 asymptomatic carriers</b></p> <p><b>Conclusions:</b> -&gt; Asymptomatic carriers occurred <b>more often in middle aged</b> people who had <b>close contact</b> with infected family members -&gt; Majority of the cases <b>developed to be mild and ordinary COVID-19</b> during hospital</p>
Am J Transplant. 17MAR2020	<b>Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression.</b>	Zhu et al., China <a href="https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.15869">https://onlinelibrary.wiley.com/doi/abs/10.1111/ajt.15869</a>	Clinic	<p><b>52-year-old man</b> who received <b>kidney transplantation 12 years ago</b></p> <p>-&gt; Clinical characteristics (symptoms, laboratory examinations, and chest CT) were <b>similar to those of non-transplanted COVID-19 patients</b> -&gt; Following a treatment regimen: reduced immunosuppressant use and low dose methylprednisolone-based therapy</p> <p><b>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.</b></p>
J Med Virol 17MAR2020	<b>Platelet-to-lymphocyte ratio is associated with prognosis in patients with Corona Virus Disease-19.</b>	Qu et al., China <a href="https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25767">https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25767</a>	Clinic	<p>-Retrospective analysis of <b>30 hospitalized patients</b> -&gt; Patients with platelet peaks during treatment: longer hospitalization. -&gt; Patients with platelet peaks were <b>older</b> -&gt; <b>Higher PLT</b> (platelet to lymphocyte ratio): <b>longer hospitalisation</b>. It may be related to <b>cytokine storm</b>.</p>

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The Lancet 17MAR2020	<b>Prisons and custodial settings are part of a comprehensive response to COVID-19</b>	Kinnet et al., Australia <a href="https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30058-X/fulltext">https://www.thelancet.com/journals/lanpub/article/PIIS2468-2667(20)30058-X/fulltext</a>	Public Health/Epidemiology	<p><b>Prisons are epicentres for infectious diseases:</b></p> <ul style="list-style-type: none"> <li>- higher background prevalence of infection</li> <li>- higher levels of risk factors for infection</li> <li>- unavoidable close contact in often overcrowded, poorly ventilated, and unsanitary facilities,</li> <li>- poor access to health-care services relative to that in community settings</li> </ul> <p>-&gt; 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.</p>
Arch Pathol Lab Med. 17MAR2020	<b>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</b>	Schwartz et al., USA <a href="https://www.archivesofpathology.org/doi/pdf/10.5858/arpa.2020-0901-SA">https://www.archivesofpathology.org/doi/pdf/10.5858/arpa.2020-0901-SA</a>	Clinic	<p>Analyzing literature describing 38 pregnant women with COVID-19 and their newborns in China</p> <p>-&gt; Unlike coronavirus infections of pregnant women caused by SARS and MERS, COVID-19 did not lead to maternal deaths</p> <p>-&gt; Similar to pregnancies with SARS and MERS: no confirmed cases of intrauterine transmission of SARS-CoV-2</p> <p><b>There is no evidence that SARS-CoV-2 undergoes intrauterine or transplacental transmission from infected pregnant women to their fetuses.</b></p>
Gynécologie, obstétrique, fertilité & sénologie 16 MAR2020	<b>Infection with SARS-CoV-2 in pregnancy. Information and proposed care. CNGOF</b>	Peyronnet et al., France <a href="https://www.sciencedirect.com/science/article/pii/S2468718920301100?via%3Dihub">https://www.sciencedirect.com/science/article/pii/S2468718920301100?via%3Dihub</a>	Clinic	<p>Few pregnant women have been described</p> <p>Same symptoms as rest of adult's patients</p> <p>Some cases of ARDS or pneumonia</p> <p><b>2 pregnant women with invasive ventilation have been described</b></p> <p>Risk: cesarean and prematurity</p> <p>No miscarriage described</p> <p><b>Neonatal:</b></p> <ul style="list-style-type: none"> <li>- no case of vertical transmission</li> <li>- milder symptomatic</li> <li>- symptoms probably due to maternal hypoxemia</li> </ul>
Nat Med 16MAR2020	<b>Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19</b>	Thevarajan et al., Australia <a href="https://www.nature.com/articles/s41591-020-0819-2">https://www.nature.com/articles/s41591-020-0819-2</a>	Immunology	<p>-&gt; 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.</p> <p><b>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:</b></p> <p>-&gt; ASCs appeared in the blood at the time of viral clearance (day 7; 1.48%) and peaked on day 8 (6.91%).</p> <p>-&gt; Emergence of cTFH cells in blood at day 7 (1.98%), increasing on day 8 (3.25%) and day 9 (4.46%)</p> <p>-&gt; 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.</p> <p>-&gt; 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).</p> <p>-&gt; Interestingly, minimal pro-inflammatory cytokines and chemokines were found in this patient with COVID-19, even at days 7–9.</p>

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SCIENCE 16MAR2020	<b>Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus(SARS-CoV2).</b>	Li et al, UK <a href="https://science.sciencemag.org/content/early/2020/03/13/science.abb3221.long">https://science.sciencemag.org/content/early/2020/03/13/science.abb3221.long</a>	Public Health/Epidemiology	<p>From observations of reported infection within China + mobility data + a networked dynamic metapopulation model and Bayesian inference</p> <p>-&gt; <b>86%</b> of all infections were undocumented (95% CI: [82%–90%]) prior to 23 January 2020 travel restrictions.</p> <p>-&gt; <b>Undocumented infections</b> were the infection <b>source for 79%</b> of documented cases</p> <p><b>It explain the rapid geographic spread of SARS-CoV2 and indicate containment of this virus will be particularly challenging</b></p>
The Lancet 16MAR2020	<b>Preparedness is essential for malaria-endemic regions during the COVID-19 pandemic</b>	Wang et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30561-4/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30561-4/fulltext</a>	Public Health/Epidemiology	<p>-&gt; Relevant lessons from the 2014–16 outbreak of Ebola virus disease in west Africa</p> <p>-&gt; 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</p>
The Lancet 16MAR2020	<b>Screening of faecal microbiota transplant donors during the COVID-19 outbreak: suggestions for urgent updates from an international expert panel</b>	Ianiro et al., Italy <a href="https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30082-0/fulltext">https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30082-0/fulltext</a>	Public Health/Epidemiology	<p>-&gt; Before each donation, physicians should screen for two main items: the presence of typical COVID-19 symptoms</p> <p>-&gt; In endemic countries, the RT-PCR assay should be considered in all donors</p> <p>-&gt; 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</p>
JAMA 13MAR2020	<b>Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China</b>	Wu et al., China <a href="https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2763184?resultClick=1">https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2763184?resultClick=1</a>	Clinic	<p>-&gt; <b>201 patients</b> included in the study</p> <p><b>Risk factors to develop ARDS:</b></p> <ul style="list-style-type: none"> <li>Older age, neutrophilia, and organ and coagulation dysfunction (eg, higher LDH and D-dimer)</li> <li>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</li> <li>Although <b>high fever</b> was <b>positively associated</b> with development of <b>ARDS</b>, it was <b>negatively related to death</b></li> <li><b>Higher CD3 and CD4 T-cell counts</b> might <b>protect</b> patients from developing ARDS</li> <li><b>Persistent and gradual increases in lymphocyte responses</b> might be required for effective immunity against SARS-CoV-2 infection.</li> </ul>
Euro Surveill 12MAR2020	<b>Retrospective analysis of the possibility of predicting the COVID-19 outbreak from Internet searches and social media data, China, 2020</b>	Li et al., China <a href="https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000199">https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.10.2000199</a>	Public Health/Epidemiology	<p><b>To predict the development of this outbreak as early and as reliably as possible</b></p> <p>-&gt; 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 <math>r &gt; 0.89</math>.</p> <p>-&gt; Peak interest for these keywords in Internet search engines and social media data was <b>10–14 days earlier than the incidence peak of COVID-19 published by the NHC</b>.</p> <p>-&gt; The lag correlation showed a maximum correlation at 8–12 days for laboratory-confirmed cases and 6–8 days for suspected cases</p>
The Lancet 12MAR2020	<b>SARS-CoV-2 RNA more readily detected in induced sputum than in throat swabs of convalescent COVID-19 patients</b>	Han et al., China <a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30174-2/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30174-2/fulltext</a>	Diagnostic	<p>-&gt; 2 cases in <b>convalescence</b></p> <p>-&gt; Both <b>negative</b> with throat swab and anal swabs</p> <p>-&gt; <b>Positive in induced sputum</b></p> <p>To reduce the risk of disease spread, <b>viral RNA tests of induced sputum, not throat swabs</b>, should be assessed as a criterion for releasing COVID-19 patients.</p>



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The Lancet 12MAR2020	<b>Real estimates of mortality following COVID-19 infection</b>	Baud et al., Switzerland <a href="https://www.thelancet.com/action/showPdf?pii=S1473-3099%2820%2930195-X">https://www.thelancet.com/action/showPdf?pii=S1473-3099%2820%2930195-X</a>	Public Health/Epidemiology	Mortality rate estimates are based on the number of deaths relative to number of confirmed cases of infection -> <b>not representative of actual death rate.</b>  <b>Real rates:</b> - 5-6% for China - 15-2% outside China <b>Current figures might underestimate the potential threat of COVID-19 in symptomatic patients</b>
The Lancet 11MAR2020	<b>Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection?</b>	Fang et al., Switzerland <a href="https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30116-8/fulltext">https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30116-8/fulltext</a>	Clinic	Patients with <b>cardiac diseases, hypertension, or diabetes</b> , who are treated with <b>ACE2-increasing drugs</b> , may be at <b>higher risk</b> for severe COVID-19 infection -> They <b>should be monitored for ACE2-modulating medications</b> , such as ACE inhibitors or ARBs. -> No evidence to suggest that <b>antihypertensive calcium channel blockers increased ACE2 expression or activity</b> ; these could be a <b>suitable alternative treatment</b> in these patients.
The Lancet 11MAR2020	<b>Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.</b>	Zhou et al., China <a href="https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30566-3/fulltext">https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30566-3/fulltext</a>	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	<b>Early dynamics of transmission and control of COVID-19: a mathematical modelling study</b>	Kucharski et al., UK <a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30144-4/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30144-4/fulltext</a>	Public Health/Epidemiology	Calculation the <b>probability that newly introduced cases might generate outbreaks in other areas.</b>  -> Estimations: The median daily reproduction number ( $R_t$ ) in Wuhan <b>declined from 2.35</b> (95% CI 1.15–4.77) 1 week before travel restrictions were introduced on Jan 23, 2020, <b>to 1.05</b> (0.41–2.39) 1 week after.  -> In locations with similar transmission potential to Wuhan in early January, <b>once there are at least four independently introduced cases, there is a more than 50% chance the infection will establish within that population.</b>
JAMA 11MAR2020	<b>Detection of SARS-CoV-2 in Different Types of Clinical Specimens</b>	Wang et al., China <a href="https://jamanetwork.com/journals/jama/fullarticle/2762997">https://jamanetwork.com/journals/jama/fullarticle/2762997</a>	Diagnostic	-> <b>1070 specimens collected from 205 patients POSITIVITY</b> by RT-PCR: Bronchoalveolar lavage fluid ( <b>93%</b> ) Sputum ( <b>72%</b> ) Nasal Swabs ( <b>63%</b> ) Fibrobronchoscope brush biopsy ( <b>46%</b> ) Pharyngeal swabs ( <b>32%</b> ) Feces ( <b>29%</b> ) Blood ( <b>1%</b> ) Urine ( <b>0%</b> )
Sci Rep 11MAR2020	<b>A high ATP concentration enhances the cooperative translocation of the SARS coronavirus helicase nsP13 in the unwinding of duplex RNA</b>	Jang et al., Republic of Korea <a href="https://www.nature.com/articles/s41598-020-61432-1">https://www.nature.com/articles/s41598-020-61432-1</a>	Fundamental Research	<b>To know: RNA Helicase nsP13 is essential for the viral RNA replication of the SARS coronavirus</b> <b>Here:</b> ->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 <b>SARS coronavirus nsP13 may require more ATPs to promote stable helicase translocation necessary for delicate RNA replication.</b>

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Emerge Inf Dis 09MAR2020	<b>Detection of Novel Coronavirus by RT-PCR in Stool Specimen from Asymptomatic Child, China</b>	Tang et al., China <a href="https://wwwnc.cdc.gov/eid/article/26/6/20-0301_article">https://wwwnc.cdc.gov/eid/article/26/6/20-0301_article</a>	Public Health/Epidemio	<ul style="list-style-type: none"> <li>-&gt; <b>Asymptomatic child positive</b> for COVID-19 by RT-PCR in stool, <b>17 days after the last virus exposure</b></li> <li>-&gt; Still positive 9 days after that (in stool)</li> <li>-&gt; <b>Never positive in respiratory tracts specimens</b></li> <li>-&gt; no data on urine and blood</li> <li>-&gt; The child might have transmitted the virus to numerous persons.</li> <li><b>Stool from COVID-19 patients might serve as another vehicle for virus transmission</b></li> </ul>
Clin Inf Dis 09MAR2020	<b>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)</b>	Yao et al., China <a href="https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa237/5801998">https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa237/5801998</a>	Therapeutic	<ul style="list-style-type: none"> <li>-&gt; Vero cells were treated by <b>Choloroquine and Hydroxychloroquine</b> before (prophylaxy) and after (anti-viral) infection by SARS-CoV-2.</li> <li>-&gt; <b>EC50</b> are calculated</li> <li>-&gt; <b>Hydroxychloroquine has superior antiviral and prophylactic activity than chloroquine</b></li> <li>-&gt; Physiologically-based pharmacokinetic (PBPK) -&gt; to <b>predict</b> (in silico) <b>drug concentrations</b> in lung, plasma and blood.</li> <li>-PBPK model has acceptable prediction accuracy.</li> <li>-Kinetics were simulated with different scenari of dose regimens</li> <li>-Dose regiment was optimized (<b>recommendations</b>).</li> </ul>
Science 06MAR2020	<b>The effect of travel restrictions on the spread of the 2019 novel coronavirus (COVID-19) outbreak.</b>	Chinazzi et al., USA <a href="https://science.sciencemag.org/content/early/2020/03/05/science.aba9757.long">https://science.sciencemag.org/content/early/2020/03/05/science.aba9757.long</a>	Public Health/Epidemio	<ul style="list-style-type: none"> <li>-&gt; <b>Global metapopulation disease transmission model</b> to project the impact of travel limitations on the national and international spread of the epidemic.</li> <li>-&gt; <b>Travel quarantine of Wuhan</b> delayed the overall epidemic progression by <b>only 3 to 5 days in Mainland China</b></li> <li>-&gt; More marked effect <u>at the international scale</u>, where case importations were <b>reduced by nearly 80%</b> until mid February</li> <li>-&gt; Sustained 90% travel restrictions to and from Mainland China <b>only modestly affect</b> the epidemic trajectory <b>unless combined with a 50% or higher reduction of transmission in the community</b></li> <li>-&gt; Potential uses for the <b>definition of optimized containment schemes and mitigation policies</b> that includes <b>the local and international dimension</b> of the COVID-19 epidemic</li> </ul>
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 <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7068162">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7068162</a>	Diagnostic	<p>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.</p> <p>Evaluated samples are swab samples.</p> <p>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.</p> <p>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</p>
Cell 04MAR2020	<b>SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor</b>	Hoffman et al., Germany <a href="https://www.cell.com/cell/fulltext/S0092-8674(20)30229-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2F0092867420302294%3Fshoall%3Dtrue">https://www.cell.com/cell/fulltext/S0092-8674(20)30229-4?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2F0092867420302294%3Fshoall%3Dtrue</a>	Therapeutic	<ul style="list-style-type: none"> <li>-&gt; <b>Priming of S proteins</b> by host <b>cell proteases (TMPRSS2)</b> is <b>essential for viral entry</b> into cells.</li> <li>-&gt; <b>ACE 2 can be blocked</b> by a clinically proven <b>inhibitor of TMPRSS2</b></li> <li>-&gt; <b>The study suggests that antibody responses raised against SARS-CoV could at least partially protect against SARS- CoV-2 infection</b></li> </ul>

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Science 04MAR2020	<b>Structural basis for the recognition of the SARS-CoV-2 by full-length human ACE2</b>	Yan et al., China <a href="https://science.sciencemag.org/content/early/2020/03/03/science.abb2762/ta-b-pdf">https://science.sciencemag.org/content/early/2020/03/03/science.abb2762/ta-b-pdf</a>	Fundamental Research	<p>-&gt; <b>Cryo-EM structures of human ACE2</b>, 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</p> <p>-&gt; <b>ACE2 may be a homodimer even in the absence of B0AT1</b></p> <p>-&gt; <b>A dimeric ACE2 can accommodate two S protein trimers</b>, each through a monomer of ACE2</p> <p>-&gt; Structure-based rational <b>design of binders with enhanced affinities to either ACE2 or the S protein of the coronaviruses</b> may facilitate development of <b>decoy ligands or neutralizing antibodies</b> for suppression of viral infection.</p>
J Clin Microbiol 04MAR2020	<b>Multicenter Evaluation of the QIAstat-Dx Respiratory Panel for the Detection of Viruses and Bacteria in Nasopharyngeal Swab Specimens</b>	Leber et al., USA <a href="https://jcm.asm.org/content/early/2020/02/28/JCM.00155-20.long">https://jcm.asm.org/content/early/2020/02/28/JCM.00155-20.long</a>	Diagnostic	<p>-&gt; <b>Multiplex <i>in vitro</i> diagnostic test</b> for the <b>qualitative</b> detection of <b>20 pathogens</b> directly from <b>nasopharyngeal swab specimens</b>.</p> <p>-&gt; Results available in approximately <b>69 minutes</b></p> <p>-&gt; <b>Pathogens identified:</b> 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, Chlamydia pneumoniae and Mycoplasma pneumoniae</p> <p>-&gt; Compared to the BioFire FilmArray Respiratory Panel version 1.7: <b>percent agreement: 99,5% . negative percent agreement of ≥ 97.9%</b></p> <p><b>Robust and accurate assay for rapid, comprehensive testing for respiratory pathogens.</b></p>
Sci. China Life Sci. 04MAR2020	<b>Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China</b>	<a href="https://link.springer.com/article/10.1007%2Fs11427-020-1661-4">https://link.springer.com/article/10.1007%2Fs11427-020-1661-4</a>	Clinic	<p>-&gt; Laboratory-confirmed positive for the COVID-19 (pharyngeal swab)</p> <p>-&gt; No obvious symptoms <b>at time of screening</b> (all of them)</p> <p>-&gt; <b>20.8%</b> developed symptoms (fever, cough, fatigue, etc.)</p> <p>-&gt; 50.0% cases showed typical CT images of ground-glass chest</p> <p>-&gt; 20.8% presented stripe shadowing in the lungs</p> <p>-&gt; 29.2% cases showed normal CT image and had no symptoms during hospitalization (<b>these cases were younger</b>)</p> <p>-&gt; <b>Epidemiological investigation revealed asymptomatic transmission</b></p>
JAMA 04MAR2020	<b>Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient</b>	Ong et al., Singapore <a href="https://jamanetwork.com/journals/jama/fullarticle/2762692?resultClick=1">https://jamanetwork.com/journals/jama/fullarticle/2762692?resultClick=1</a>	Public Health/Epidemiology	<p>Extensive <b>environmental contamination</b> by 1 SARS-CoV-2 patient with mild upper respiratory tract involvement</p> <p>-&gt; Toilet bowl and sink samples were positive</p> <p>-&gt; Swabs taken from the air exhaust outlets tested positive</p> <p>-&gt; Air samples were negative</p> <p>-&gt; Risk of transmission from contaminated footwear is likely low: negative results in the anteroom and clean corridor</p> <p><b>Limit of the study:</b> viral culture was not done to demonstrate viability</p>
Nat Sci Rev 03MAR2020	<b>On the origin and continuing evolution of SARS-CoV-2</b>	Tang et al., China <a href="https://academic.oup.com/nsr/advance-article/doi/10.1093/nsr/nwaa036/5775463?searchres=ult=1">https://academic.oup.com/nsr/advance-article/doi/10.1093/nsr/nwaa036/5775463?searchres=ult=1</a>	Genomic	<p>-&gt; Assessment of the <b>molecular phylogeny</b> and the divergence between <b>SARS-CoV-2</b> and <b>related coronaviruses</b>.</p> <p>-&gt; Population genetic analyses of 103 genomes of SARS-CoV-2 indicate that there are <b>two major types of viruses</b> (designated <b>L</b> and <b>S</b>) currently circulating between humans.</p> <p>-&gt; The <b>L type is predominant (70%)</b> against 30% for S type).</p> <p>-&gt; <b>This article suggests that the L type is more aggressive.</b></p>

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JAMA 03MAR2020	<b>Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore</b>	Young et al., Singapore <a href="https://jamanetwork.com/journals/jama/fullarticle/2762688">https://jamanetwork.com/journals/jama/fullarticle/2762688</a>	Clinic	<p>-&gt; <b>18patients</b> diagnosed with SARS-CoV-2 infection in Singapore between January 23 and February 3, 2020</p> <p>-&gt; Respiratory tract infection with <b>prolonged viral shedding from the nasopharynx of 7 days or longer</b> in 15 patients (83%)</p> <p>-&gt; Supplemental oxygen was required in 6 patients (33%), <b>5 of whom</b> were treated with <b>lopinavir-ritonavir</b>, with <b>variable clinical outcomes</b> following treatment.</p>
Int J Infect Dis 02MAR2020	<b>Recurrence of positive SARS-CoV-2 RNA in COVID-19: A case report</b>	Chen et al., China <a href="https://www.ijidonline.com/article/S1201-9712(20)30122-3/pdf">https://www.ijidonline.com/article/S1201-9712(20)30122-3/pdf</a>	Virology	<p>- 46-year-old woman with multiple patchy ground glass opacities in bilateral subpleural areas by CT</p> <p>- <b>Oropharyngeal swab test was positive by RT-PCR.</b></p> <p>-&gt; Received <b>symptomatic treatment</b> and <b>antimicrobial therapy</b> including oseltamivir, arbidol, Lopinavir/ritonavir and moxifloxacin</p> <p>-&gt; 6 testing from 28 Jan to 17FEB, all negative <b>but one the 2FEB</b> Discharged on 9FEB and testing remained negative during follow-up.</p> <p><b>SARS-CoV-2 RNA of respiratory tract specimen may be persistent or recurrent positive during the course.</b></p>
Jour of Infect 29FEB2020	<b>Identification of the hyper-variable genomic hotspot for the novel coronavirus SARS-CoV-2</b>	Wen et al., China <a href="https://www.journalofinfection.com/article/S0163-4453(20)30108-0/pdf">https://www.journalofinfection.com/article/S0163-4453(20)30108-0/pdf</a>	Genomic	<p>-&gt; Confirmation of the relationship of SARS-CoV-2 with other beta coronaviruses on the amino acid level.</p> <p>-&gt; Hyper-variable genomic hotspot established in SARS-CoV-2 <b>population at the nucleotide but not the amino acid level</b> -&gt; means <b>no beneficial mutations</b>.</p> <p>-&gt; <b>Mutations in nsp1, nsp3, nsp15, and gene S would be associated with the SARS-CoV-2 epidemic (compared with RaTG13) / required for human adaptation?</b></p>
J Med Virol 28FEB2020	<b>Development of Epitope-Based Peptide Vaccine Against Novel Coronavirus 2019 (SARS-COV-2): Immunoinformatics Approach</b>	Bhattacharya et al., India <a href="https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25736">https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25736</a>	Vaccine	<p>1-&gt; Characterization of the <b>spike glycoprotein</b> to obtain immunogenic epitopes</p> <p>2-&gt; Immunoinformatic analysis of 13 MHC I and 3 MHC II epitopes which <b>have antigenic properties</b></p> <p>3-&gt; These identified epitopes are candidate to formulate a <b>multi-epitopic peptide vaccine</b>.</p> <p><b>Need for <i>in vitro</i> and <i>in vivo</i> validations</b></p>
The NEJM 28FEB2020	<b>Clinical Characteristics of Coronavirus Disease 2019 in China</b>	Ni et al., China <a href="https://www.nejm.org/doi/pdf/10.1056/NEJMoa2002032?articleTools=true&amp;downloadfile=showPdf&amp;articleTools=true&amp;doi=10.1056/NEJMoa2002032">https://www.nejm.org/doi/pdf/10.1056/NEJMoa2002032?articleTools=true&amp;downloadfile=showPdf&amp;articleTools=true&amp;doi=10.1056/NEJMoa2002032</a>	Clinic	<p>Median age : <b>47 years</b> / Female: 41.9%</p> <p><b>Primary composite end point</b> (admission in ICU, use of mechanical ventilation and death) in <b>6.1%</b>, with <b>5.0% in ICU</b>, <b>2.3% with invasive mechanical ventilation</b>, and <b>1.4% who died</b>.</p> <p>History of direct contact with <b>wildlife: 1.9%</b></p> <p>Among nonresidents of Wuhan, <b>72.3% had contact with residents of Wuhan</b>, including 31.3% who had visited the city.</p> <p>Most common symptoms: fever (43.8% on admission and 88.7% during hospitalization) and cough (67.8%). Diarrhea was uncommon (3.8%).</p> <p>Median <b>incubation period: 4 days</b> (interquartile range, 2 to 7).</p> <p><b>CT:</b> ground-glass opacity was the most common radiologic: 56.4%.</p> <p><b>No radiographic or CT abnormality:</b> 17.9% with nonsevere disease and 2.9% with severe disease.</p> <p><b>Lymphocytopenia: 83.2%</b></p>

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EuroSurv 27FEB2020	<b>Early transmission patterns of coronavirus disease 2019 (COVID-19) in travellers from Wuhan to Thailand, January 2020</b>	Okada et al., Thailand <a href="https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.8.2000097">https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.8.2000097</a>	Public Health/Epidemiology	<p>-&gt; 2 women arriving in Thailand at different times (8 and 13 January)</p> <p>-&gt; The <b>two viral genomes are identical</b> to four sequences from Wuhan, while no direct link to the Huanan Seafood Market.</p> <p>-&gt; <b>Identical genomes of up to 30 kb are rare and a strong sign of recent transmission linkage</b></p> <p>-&gt; Data suggest that <b>transmission within Wuhan beyond the Huanan Seafood Market is likely to have occurred in the first week of January or earlier.</b></p>
J Clin Med 27FEB2020	<b>Epidemiological Identification of A Novel Pathogen in Real Time: Analysis of the Atypical Pneumonia Outbreak in Wuhan, China, 2019—2020</b>	Jung et al., Japan <a href="https://www.mdpi.com/2077-0383/9/3/637">https://www.mdpi.com/2077-0383/9/3/637</a>	Public Health/Epidemiology	<p>-&gt; <b>Non-virological descriptive characteristics</b> could have determined that the outbreak is caused by a novel pathogen in <b>advance of virological testing.</b></p> <p>-&gt; Characteristics of the outbreak <b>were collected in real time and compared with characteristics of eleven pathogens</b> that have previously caused cases of atypical pneumonia.</p> <p>-&gt; The <b>probability that a new virus was driving</b> the outbreak was assessed as <b>over 29%</b> on 31 December 2019, <b>one week before virus identification.</b></p>
The Lancet 27FEB2020	<b>Secondary attack rate and superspreading events for SARS-CoV-2</b>	Liu et al., UK <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30462-1/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30462-1/fulltext</a>	Public Health/Epidemiology	<p><b>The R<sub>0</sub> value</b> only captures the average dynamics of transmission.</p> <p><b>The secondary attack rate (SAR)</b> is the probability that an infection occurs among susceptible people <b>within a specific group.</b></p> <p><b>SAR among close contacts would be of 35%</b> (95% CI 27–44).</p> <p>-&gt; An infection with a high household SAR but a modest R<sub>0</sub> suggests transmission is driven by a relatively small number of high-risk contacts.</p> <p>-&gt; A large household SAR further suggests that between-household transmission risk is lower; otherwise the observed R<sub>0</sub> would be larger.</p> <p><b>More data are needed.</b></p>
The Lancet 27FEB2020	<b>COVID-19: combining antiviral and anti-inflammatory treatments</b>  <b>COMMENT</b>	Stebbing et al., UK <a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30132-8/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30132-8/fulltext</a>	Therapeutic	<p>-&gt; COVID-19 characterised by an overexuberant inflammatory response</p> <p>SARS -&gt; viral load is not correlated with the worsening of symptoms</p> <p>-&gt; Inhibition of <b>numb-associated kinase (NAK)</b> family would reduce viral infection in vitro (inhibit clathrin-mediated endocytosis and thereby inhibit viral infection of cells)</p> <p>-&gt; <b>JAK–STAT</b> signalling inhibitors, could be effective against the consequences of the elevated levels of cytokines (including interferon) typically observed in people with COVID-19</p> <p>-&gt; Baricitinib is a NAK inhibitor (<b>anti-viral</b>)</p> <p>-&gt; Baricitinib, fedratinib, and ruxolitinib are JAK inhibitors (<b>anti-inflammatory</b>)</p> <p><b>-&gt; Baricitinib is the best of the group</b></p>
The Lancet 27FEB2020	<b>Positive RT-PCR Test Results in Patients Recovered From COVID-19</b>	Lan et al., China <a href="https://jamanetwork.com/journals/jama/fullarticle/2762452">https://jamanetwork.com/journals/jama/fullarticle/2762452</a>	Public Health/Epidemiology	<p><b>Little attention</b> has been paid to the <b>follow-up of recovered</b> patients so far.</p> <p><b>4 patients</b> 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 <b>positive RT-PCR test results 5 to 13 days later</b>, while they were still <b>asymptomatic.</b></p>

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The Lancet 27FEB2020	<b>Convalescent plasma as a potential therapy for COVID-19</b>  <b>COMMENT</b>	Chen et al., China <a href="https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30141-9.pdf">https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30141-9.pdf</a>	Therapeutic	-> In 2014, the use of convalescent plasma collected from patients who had recovered from <b>Ebola virus disease</b> was <b>recommended by WHO</b> as an empirical treatment during outbreaks. -> A protocol for the use of convalescent plasma in the treatment of MERS coronavirus was established in 2015. -> <b>H1N1</b> : significant reduction of relative risk of mortality / <b>no adverse event</b> . -> and other studies <b>Antibodies from convalescent plasma might suppress viraemia</b>
Emerg Microb Infects 26FEB2020	<b>Detectable 2019-nCoV viral RNA in blood is a strong indicator for the further clinical severity</b>	Chen et al., China <a href="https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1732837">https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1732837</a>	Clinic	-> All patients (n=6 / 57) with <b>detectable viral RNA in the blood</b> progressed to severe symptom stage, indicating a strong <b>correlation of serum viral RNA with the disease severity</b> (p-value = 0.0001). -> 8 of the 11 patients with <b>annal swab virus-positive</b> was in <b>severe clinical stage</b> . -> Concentration of viral RNA in the <b>anal swab was higher than in the blood: virus might replicate in the digestive tract</b>
The Lancet, 26FEB2020	<b>The psychological impact of quarantine and how to reduce it: rapid review of the evidence</b>	Brooks et al., UK <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30460-8/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30460-8/fulltext</a>	HSS/Politic	-> Information is key; people who are quarantined need to understand the situation -> The quarantine period should be short and the duration <b>should not be changed</b> 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 -> <b>Public health officials should emphasise the altruistic choice of self-isolating</b>
Viruses 25FEB2020	<b>Preliminary Identification of Potential Vaccine Targets for the COVID-19 Coronavirus (SARS-CoV-2) Based on SARS-CoV Immunological Studies</b>	Ahmed et al., China <a href="https://www.mdpi.com/1999-4915/12/3/254">https://www.mdpi.com/1999-4915/12/3/254</a>	Vaccine	-> <b>High genetic similarity</b> between <b>SARS-CoV-2 and SARS-Co</b> . -> Identification of a set of <b>B cell and T cell epitopes</b> derived from the spike (S) and nucleocapsid (N) proteins that <b>map identically</b> to SARS-CoV-2 proteins. -> <b>No mutation</b> has been observed in these epitopes (as of 21 February 2020). -> <b>Immune targeting of these epitopes</b> may offer protection against this novel virus
EuroSurv 25FEV2020	<b>Differential diagnosis of illness in patients under investigation for the novel coronavirus (SARS-CoV-2), Italy, February 2020.</b>	Bordi et al., Italy <a href="https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.8.2000170">https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.8.2000170</a>	Public Health/Epidemio	-> <b>Similarity of symptoms</b> shared with more common respiratory infections. -> <b>Broad screening</b> requested. -> <b>Influenza virus</b> infections: <b>28.5% of all suspected cases</b> of SARS-CoV-2 infection. -> <b>Alternative diagnoses may clarify an individual patient's risk and may allow adjusting public health containment measures.</b>
The Lancet 25FEB2020	<b>Potential association between COVID-19 mortality and health-care resource availability</b>	Ji et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30068-1/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30068-1/fulltext</a>	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 <b>mortality is correlated with health-care burden</b>
The Lancet 24FEB2020	<b>COVID-19 control in China during mass population movements at New Year</b>	Chen et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30421-9/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30421-9/fulltext</a>	Public Health/Epidemio	Several lessons that can be drawn from China's extension of the Lunar New Year holiday: 1-> Countries should consider <b>periods of recommended or mandatory closure of non-essential workplaces and public institutions</b> — 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, <b>governments should use the closure period for information and education campaigns, community screening, active contact tracing, and isolation and quarantine</b> to maximise impact.



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J Clin Med 24FEB2020	<b>Assessing the Impact of Reduced Travel on Exportation Dynamics of Novel Coronavirus Infection (COVID-19)</b>	Anzai et al., Japan <a href="https://www.mdpi.com/2077-0383/9/2/601">https://www.mdpi.com/2077-0383/9/2/601</a>	Public Health/Epidemiology	<p>-&gt; From <b>28 January to 7 February 2020</b>, around 226 exported cases were prevented (=70.4% reduction in incidence)</p> <p>-&gt; Reduced probability of a major epidemic in Japan: from 7% to 20% (=median time delay: of 2 days)</p> <p>-&gt; Depending on the scenario, the estimated delay may be less than one day. As the <b>delay is small</b>, the decision to control travel volume through restrictions on freedom of movement should be <b>balanced</b> between the <b>resulting estimated epidemiological impact</b> and <b>predicted economic fallout</b>.</p>
Cell Discov 24FEB2020	<b>Comparative genetic analysis of the novel coronavirus (2019-nCoV/SARS-CoV-2) receptor ACE2 in different populations</b>	Cao et al., China <a href="https://jcm.asm.org/content/early/2020/02/28/jcm.00155-20.long">https://jcm.asm.org/content/early/2020/02/28/jcm.00155-20.long</a>	Fundamental Research	<p>-&gt; Previous studies demonstrated the <b>positive correlation of ACE2 expression and the infection of SARS-CoV in vitro</b></p> <p>-&gt; <b>Here:</b> Systematic analysis of coding-region variants in <i>ACE2</i> and the eQTL variants (may affect the expression of <i>ACE2</i>) among different populations (GTEx database)/</p> <p>-&gt; The <b>East Asian</b> populations have <b>much higher AFs</b> in the <b>eQTL variants</b> associated with <b>higher ACE2 expression</b> in tissues which may suggest <b>different susceptibility or response</b> to 2019-nCoV/SARS-CoV-2 <b>from different populations</b> under the similar conditions.</p> <p>-&gt; No direct evidence supporting the existence of <b>coronavirus S-protein binding-resistant ACE2 mutants</b> in different populations.</p>
The Lancet 24FEB2020	<b>Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study</b>	Xiaobo Yang et al., China <a href="https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30079-5/fulltext">https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30079-5/fulltext</a>	Clinic	<p>- <b>Mortality is high.</b> The survival term of the non-survivors is likely to be within 1–2 weeks after ICU admission.</p> <p>- Older patients (&gt;65 years) with comorbidities and ARDS are at increased risk of death.</p>
The Lancet 24FEB2020	<b>Viral load of SARS-CoV-2 in clinical samples</b>	Pan et al., China <a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30113-4/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30113-4/fulltext</a>	Virology	<p>- The <b>viral loads</b> in throat swab and sputum samples peaked at around <b>5–6 days after symptom onset</b>, ranging from around 104 to 107 copies per mL during this time</p> <p>- <b>Sputum samples</b> generally showed higher viral loads than throat swab samples.</p>
The Lancet 24FEB2020	<b>COVID-19 pneumonia: what has CT taught us?</b>	Lee et al., China <a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30134-1/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30134-1/fulltext</a>	Diagnostic	<p>- The predominant CT findings included <b>ground-glass opacification, consolidation, bilateral involvement, and peripheral and diffuse distribution</b>.</p> <p>- 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.</p>
J Med Virol 21FEB2020	<b>COVID-2019: the role of the nsp2 and nsp3 in its pathogenesis.</b>	Angeletti et al., Rome, Italy <a href="https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25719">https://onlinelibrary.wiley.com/doi/abs/10.1002/jmv.25719</a>	Fundamental Research	<p>The Open Reading Frame 1ab (ORF1ab) of COVID-2019 has been analyzed to evidence the <b>presence of mutation caused by selective pressure</b> on the virus.</p> <p>Which are the probably most common sites undergoing to an aminoacidic change ?</p> <p>-&gt; Insight of some important proteins of the COVID-2019 that are involved in the mechanism of viral entry and viral replication</p> <p>Results: Both nsp2 and nsp3 are under selective pressure. <b>nsp2</b>-&gt; could explain why this virus is more contagious than SARS <b>nsp 3</b>-&gt; could suggest a potential mechanism differentiating COVID-2019 from SARS</p>

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Radiology 20 FEB 2020	<b>Chest CT Findings in Coronavirus Disease-19 (COVID-19): Relationship to Duration of Infection.</b>	Bernheim et al., <a href="https://pubs.rsna.org/doi/10.1148/radiol.2020200463">https://pubs.rsna.org/doi/10.1148/radiol.2020200463</a>	Diagnostic	Frequency of CT findings is related to infection time course.
The Lancet, 20 FEB 2020	<b>Preparedness and vulnerability of African countries against importations of COVID-19: a modelling study.</b>	Gilbert et al., Vittoria's team <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30411-6/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30411-6/fulltext</a>	Public Health/Epidemiology	<ul style="list-style-type: none"> <li>- Highest importation risk: Egypt, Algeria, and South Africa -&gt; moderate to high capacity to respond to outbreaks</li> <li>- Moderate risk: Nigeria, Ethiopia, Sudan, Angola, Tanzania, Ghana, and Kenya -&gt; variable capacity and high vulnerability</li> </ul>
The Lancet 19FEB2020	<b>Asymptomatic cases in a family cluster with SARS-CoV-2 infection</b>	Pan et al., China <a href="https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30114-6/fulltext">https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30114-6/fulltext</a>	Public Health/Epidemiology	<ul style="list-style-type: none"> <li>- In this family cluster, although <b>all individuals tested positive</b> for SARS-CoV-2 infection on qRT-PCR, only patient 1 showed clinical symptoms, decreased lymphocyte count, and abnormal chest CT images.</li> <li>- However, <b>any of the three individuals could have been the first one to become infected</b> and thus transmitted the virus to the other two family members.</li> </ul>
The Lancet 19FEB2020	<b>Enteric involvement of coronaviruses: is faecal–oral transmission of SARS-CoV-2 possible?</b>	Yeo et al., Singapore <a href="https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30048-0/fulltext">https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30048-0/fulltext</a>	Virology	<ul style="list-style-type: none"> <li>- 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.</li> <li>-&gt;When <b>SARS-CoV</b> 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.</li> <li>-&gt; <b>MERS-CoV</b> 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.</li> </ul>
THE NEJM, 19FEB2020	<b>SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients</b>	Zou et al., China <a href="https://www.nejm.org/doi/full/10.1056/NEJMc2001737">https://www.nejm.org/doi/full/10.1056/NEJMc2001737</a>	Virology	<ul style="list-style-type: none"> <li>- <b>The higher viral loads were detected soon after symptom onset.</b></li> <li>- <b>Higher viral loads detected in the nose</b> than in the throat.</li> <li>- Our analysis <b>suggests</b> 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.</li> <li>- The viral load that was detected in the <b>asymptomatic patient</b> was <b>similar</b> to that in the <b>symptomatic patients</b>, which <b>suggests the transmission potential of asymptomatic or minimally symptomatic patients.</b></li> </ul>
Biosci Trends, 19FEB2020	<b>Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies.</b>	Gao et al., <a href="https://www.ncbi.nlm.nih.gov/pubmed/32074550">https://www.ncbi.nlm.nih.gov/pubmed/32074550</a>	Therapeutic	<p><b>Chloroquine phosphate</b>, 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. <b>(DATA NOT SHOWN !)</b>.</p> <p>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.</p>

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J Infect Dis. 18FEB2020	<b>A familial cluster of infection associated with the 2019 novel coronavirus indicating potential person-to-person transmission during the incubation period.</b>	Yu et al., China <a href="https://academic.oup.com/jid/advance-article/doi/10.1093/jid/iaa077/5739751">https://academic.oup.com/jid/advance-article/doi/10.1093/jid/iaa077/5739751</a>	Public Health/Epidemiology	Familial cluster of four patients in Shanghai. One was 88 years old man with moving difficulties and was only exposed to his asymptomatic family members who <b>developed symptoms later</b> .  The epidemiological evidence has shown a potential transmission of the 2019-nCoV during the incubation period.
The Lancet 18FEB2020	<b>Tracking online heroisation and blame in epidemics</b>  <b>COMMENT</b>	Atlani Duault et al., France <a href="https://www.thelancet.com/action/showPdf?pii=S2468-2667%2820%2930033-5">https://www.thelancet.com/action/showPdf?pii=S2468-2667%2820%2930033-5</a>	HSS/Politics	-> Gathering online <b>data on local perceptions</b> 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 <b>real time</b> , both <b>to correct inaccurate</b> information and <b>to respond to online scapegoating</b> . -> <b>Trust is a crucial</b> support to public health systems. <b>Public health authorities need to be aware of « complex geographies of hope and blame » while planning responses to the epidemic.</b>
Biochem Biophys Res Comm 17 FEB 2020	<b>Structure analysis of the receptor binding of 2019-nCoV</b>	Chen et al., China and USA <a href="https://www.sciencedirect.com/science/article/pii/S006291X20303399">https://www.sciencedirect.com/science/article/pii/S006291X20303399</a>	Fundamental Research	Structural analysis of the receptor binding domain (RBD) -> 72% identity with SARS CoV / Higher affinity with ACE 2.  ACE2 is widely expressed with conserved primary structures <u>throughout</u> the animal kingdom ( <b>possible hosts ?</b> ) Since ACE2 is predominantly expressed in intestines, testis, and kidney, <b>fecal-oral</b> and <b>other routes</b> of transmission are also <b>possible</b> .  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	<b>Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data.</b>	Linton et al., Japan <a href="https://www.mdpi.com/2077-0383/9/2/538">https://www.mdpi.com/2077-0383/9/2/538</a>	Public Health/Epidemiology	Incubation period falls within the range of 2–14 days with 95% confidence and has a mean of around 5 days.  The mean time from illness onset to hospital admission (for treatment and/or isolation) was estimated at 3–4 days without truncation and at 5–9 days.
PNAS, 13FEB2020	<b>Prophylactic and therapeutic remdesivir (GS-5734) treatment in the rhesus macaque model of MERS-CoV infection</b>	De Wit et al., USA <a href="https://www.pnas.org/content/early/2020/02/12/1922083117">https://www.pnas.org/content/early/2020/02/12/1922083117</a>	Therapeutic	- 24 h prior to inoculation -> <b>completely prevented MERS-CoV-induced clinical disease</b> , strongly inhibited MERS-CoV replication in respiratory tissues, and prevented the formation of lung lesions. - 12 h postinoculation -> <b>clear clinical benefit</b> , with a reduction in clinical signs, reduced virus replication in the lungs, and decreased presence and severity of lung lesions.  <b>- Remdesivir may be considered for SARS-CoV -2</b>
The Lancet 12 FEB 2020	<b>What are the risks of COVID-19 infection in pregnant women?</b>	Qiao et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30365-2/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30365-2/fulltext</a>	Clinic	The clinical characteristics reported in pregnant women with confirmed COVID-19 infection are <b>similar to those reported for non-pregnant</b> 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	<b>Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records</b>	Chen et al., China <a href="https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30360-3/fulltext">https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30360-3/fulltext</a>	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. <b>All samples tested negative</b> <b>None of the 9 patients developed severe COVID-19 pneumonia or died.</b>
Cell Res 4FEB2020	<b>Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro</b>	Wang et al., China <a href="https://www.nature.com/articles/s41422-020-0282-0">https://www.nature.com/articles/s41422-020-0282-0</a>	Therapeutic	Remdesivir and chloroquine <b>are highly effective</b> in the control of 2019-nCoV infection <b>in vitro</b> . 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 <b>novel coronavirus disease</b> .

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Euro Surveill 6FEB2020	<b>Effectiveness of airport screening at detecting travellers infected with novel coronavirus (2019-nCoV).</b>	Quilty et al., UK <a href="https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.5.2000080">https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.5.2000080</a>	Public Health/Epidemiology	<p>Estimation: <b>46%</b> of infected travellers would <b>not be detected</b>, depending on incubation period, sensitivity of exit and entry screening, and proportion of asymptomatic cases.</p> <p>-&gt; Airport screening is unlikely to detect a sufficient proportion of 2019-nCoV infected travellers to avoid entry of infected travellers.</p>
The Lancet 03FEB2020	<b>Baricitinib as potential treatment for 2019-nCoV acute respiratory disease</b>	Richardson et al., UK <a href="https://www.thelancet.com/pdfs/journals/lancet/PII/S0140-6736(20)30304-4.pdf">https://www.thelancet.com/pdfs/journals/lancet/PII/S0140-6736(20)30304-4.pdf</a>	Therapeutic	<p>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.</p>
Emerge Microbes Infect 03FEB2020	<b>Potent binding of 2019 novel coronavirus spike protein by a SARS coronavirus-specific human monoclonal antibody.</b>	Tian et al., China <a href="https://www.biorxiv.org/content/10.1101/2020.01.28.923011v1">https://www.biorxiv.org/content/10.1101/2020.01.28.923011v1</a>	Fundamental Research	<p>A SARS-CoV-specific human monoclonal antibody, CR3022, could bind potently with 2019-nCoV RBD.</p> <p>-&gt; Potential to be developed as candidate therapeutics ?</p> <p>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. -&gt; It is still <b>necessary to develop novel monoclonal antibodies</b> that could bind specifically to 2019-nCoV RBD.</p>