COVID-19

Literature review of accepted relevant papers

UPDATE OF

04 JUNE 2020

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.

Coordinated by:

REACTing:
Renaud Vatrinet
& Eric D'Ortenzio

Documented by:

Inserm- Collective Expertise Unit:
Bénédicte Varignon
& Laurent Fleury

Redaction committee

Inserm- Thematic Institute of Immunology, Inflammation, Infectiology, and Microbiology (I3M):
Guia Carrara; Eric D'Ortenzio; Evelyne Jouvin-Marche; Boris Lacarra; Claire Madelaine; Inmaculada Ortega-Perez; Oriane Puéchal; Erica Telford; Renaud Vatrinet

With a precious help fom:

- Inserm- Department of Partnerships and External Relations (DPRE)
- Inserm- USA office

Additionnal links:

Rapid Evidence Reviews Group: https://isaric.tghn.org/covid-19-rapid-evidence-reviews-group/
Bibliovid: https://bibliovid.org
CORD19 Publication Dashboard: https://france-science.com/en/homepage-english-2/

List of articles pre-selected by Inserm- Collective Expertise Unit available at:
https://insermbiblio.inist.fr/wp-content/uploads/2020/04/Littérature_Covid19_03062020.xlsx ← Please enter the date of access to the last available file

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 03JUN2020	**A Randomized Trial of Hydroxychloroquine as Postexposure Prophylaxis for Covid-19**	David R. Boulware et al. USA/Canada gotopaper	Therapeutic	**Randomized, double-blind, placebo-controlled trial** to evaluate **postexposure prophylaxis with hydroxychloroquine** after exposure to Covid-19. Participants had known exposure (by participant report) to a person with laboratory-confirmed Covid-19, whether as a **household contact**, a **health care worker**, or a person with other **occupational exposures**. The primary outcome was the incidence of either laboratory-confirmed Covid-19 or illness compatible with Covid-19 within 14 days. **821 asymptomatic adult** participants were randomly assigned to the hydroxychloroquine group (414 participants) or the placebo group (407 participants). Overall, 87.6% of the participants (719 of 821) had high-risk exposures without eye shields and surgical masks or respirators. - The **incidence of new illness** compatible with Covid-19 **did not differ significantly** between participants receiving hydroxychloroquine (49 of 414 [11.8%]) and those receiving placebo (58 of 407 [14.3%]); the absolute difference was −2.4 percentage points (95% confidence interval, −7.0 to 2.2; P=0.35). - Side effects were more common with hydroxychloroquine than with placebo (40.1% vs. 16.8%), but no serious adverse reactions were reported. Conclusion: **high doses of hydroxychloroquine did not prevent illness compatible with Covid-19 when initiated within 4 days after a high-risk or moderate-risk exposure.** **Limitation**: a priori symptomatic case definition used because majority of the participants, including health care workers, were unable to access testing ; Internet-based approach used to rapidly recruit participants in the context of a pandemic, data were obtained by means of participant report ; predictive power of the case definition is unknown, particularly in the younger populations studied.
Cell Systems 02JUN2020	**Ultra-high-throughput clinical proteomics reveals classifiers of COVID-19 infection**	Messner et al., UK,Germany,Sweden gotopaper	Diagnostic	-A standardized, ultra-highthroughput clinical platform for serum and plasma proteomics -Platform enables high precision quantification of 180 patient samples/day at low cost -27 biomarkers are differentially expressed between WHO severity grades for COVID-19 -Biomarkers include proteins not previously associated with COVID-19 infection
Lancet 01JUN2020	**Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis**	Chu et al, Canada gotopaper	Public Health/Epidemio	Aim: to investigate the effects of physical distance, face masks, and eye protection on virus transmission in health-care and community settings, through a systematic review and meta-analysis of 172 observational studies (25 697 patients in total). - Transmission of viruses was lower with physical distancing of 1 m or more, compared with a distance of less than 1. protection was increased as distance was lengthened. - Face mask use resulted in a large reduction in risk of infection, with stronger associations with N95 or similar respirators compared with disposable surgical masks or similar. - Eye protection was associated with less infection These findings support physical distancing of 1 m or more and provide quantitative estimates for models and contact tracing to inform policy.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Communications 01JUNE2020	**Two linear epitopes on the SARS-CoV-2 spike protein that elicit neutralising antibodies in COVID-19 patients**	Poh, Chek Meng et al; Singapore gotopaper	Therapeutic	**Identification of immunogenic targets against the coronavirus spike glycoprotein** • In this study, using pools of overlapping linear B-cell peptides, two immunodominant linear B-cell epitopes on the S glycoprotein of SARS-CoV-2 were identified. SP14P5 is located in close proximity to the receptor binding domain whereas S21P2 is in the region that encompasses the fusion peptide, which is highly conserved among coronaviruses suggesting a potential pan-SARS epitope at this location. • Detection for both S14P5 and S21P2 was consistently and significantly higher in COVID-19 patients • Interestingly, antibody depletion assays demonstrate that antibodies recognized these two linear epitopes and can neutralise SARS-CoV-2. Conclusion: SP14P5 et S21P2 epitopes can potentially be used in the design of more sensitive serological assays for epidemiological or vaccine efficiency assessments since that antibodies targeting these two linear epitopes account for a significant fraction of the anti-S-neutralising response.
Int. J. Infect. Dis. 31MAY2020	**Fast SARS-CoV-2 detection by RT-qPCR in preheated nasopharyngeal swab samples**	Alcoba-Florez, Julia et al. Spain gotopaper	Diagnostic	Performance of **three alternative, simple and affordable protocols to rapidly detect SARS-CoV-2**, bypassing the long and tedious RNA extraction step and reducing the time to viral detection: three methods based on direct nasopharyngeal swab viral transmission medium (VTM) heating before the RT-qPCR: a) direct without additives; b) in a formamide-EDTA (FAE) buffer, c) in a RNAsnap™ buffer. Although with a delay in cycle threshold compared to the gold-standard, we found consistent results in nasopharyngeal swab samples that were subject to a direct 70°C incubation for 10 min. **CI°**: This study provides valuable options **to overcome any supply chain issue** and help **to increase the throughput of diagnostic tests**, thereby complementing standard diagnosis.
Int. J. Infect. Dis. 31MAY2020	**Aberrant hyperactivation of cytotoxic T-cell as a potential determinant of COVID-19 severity**	Kang, Chang Kyung et al. Rep. of Korea gotopaper	Immuno	We hypothesized that **immune response may contribute to progression of coronavirus disease-19 (COVID-19)** at the second week of illness. Therefore, **we compared cell-mediated immune (CMI) responses between severe and mild COVID-19 cases**. We examined peripheral blood mononuclear cells of laboratory-confirmed COVID-19 patients from their first and third weeks of illness. **CI°**: **Severe COVID-19 had higher degree of proliferation, activation, and cytotoxicity of T-cells** at the late phase of illness without cytotoxic T-cell contraction, which might contribute to the development of severe COVID-19. **Limitations:** First, numbers of patients analyzed in this study was small. Second, it would be desirable if there were more time points to be examined to elucidate the exact temporal changes of such responses or when the persistent cytotoxic T-cell activity returns to normal in severe cases. Finally, the potential immunomodulatory effects of lopinavir/ritonavir could not be adjusted because the drug was prescribed to all severe patients in this study.

Journal and date	Title	Authors and link	Field of expertise	Key facts
J. Clin. Virol. 30MAY2020	**Persistent detection of SARS-CoV-2 RNA in patients and healthcare workers with COVID-19**	Gombar, Saurabh et al. USA gotopaper	Diagnostic	Current **guidelines for returning health care workers (HCW) to service after a positive SARS-CoV-2 RT-PCR test** and ceasing of transmission precautions for patients is based on two general strategies: **A test-based strategy** that requires negative respiratory RT-PCR tests obtained after the resolution of symptoms; **a symptom-based strategy** that recommends excluding HCW from the workforce until a fixed period of time has elapsed from symptom recovery. **Objective**: to better understand the appropriate length of symptom-based return to work and contact precaution strategies. Observational analysis of 150 patients and HCW shows that the **average time to transition from RT-PCR positive to negative was 24 days** after symptom onset and 10 % remained positive even 33 days after symptom onset. **CL°**: the fixed length of time before returning to work or ceasing contract precautions be revised **to over one-month**. Note: our analysis could be overestimating the length of infectious spreading by detecting non-infectious viral shedding. Large trials that rely on methods that detect the infective virus (ie viral culture) have not yet been reported in the literature.
Brain, Behavior and Immunity 30MAY2020	**COVID-19 pandemic and mental health consequences: systematic review of the current evidence**	Vindegaard and Eriksen Benros, Denmark gotopaper	Psy	COVID-19 patients displayed high levels of PTSS and increased levels of depression. •Patients with preexisting psychiatric disorders reported worsening of psychiatric symptoms. •Higher levels of psychiatric symptoms were found among health care workers. •A decrease in psychological well-being was observed in the general public. •However, well conducted large-scale studies are highly needed.
Clin. Infect. Dis. 30MAY2020	**Maximum Daily Temperature, Precipitation, Ultra-Violet Light and Rates of Transmission of SARS-Cov-2 in the United States**	Shera T et al., USA gotopaper	Public Health/Epidemio	Aim: to investigate effects of temperature, precipitation, and UV Light on community transmission of SARS-CoV-2 in the USA. - A maximum temperature >52° F on a given day was associated with a lower rate of new cases at 5 days. - Below 52° F, there was a significant inverse association between the maximum daily temperature and the rate of cases at 5 days. - In a theoretical state with a stable maximum daily temperature >52° F, the rate of new cases is predicted to be of 23-fewer cases per-million per-day by 25 days of the epidemics. - A 1-unit higher UV index was associated with a lower rate at 5 days. - Precipitation was not associated with a greater rate of cases at 5 days. The incidence of disease is lower at warmer versus cooler temperatures, but this association is small, and transmission is likely to remain high at warmer temperatures.
Cell Reports 30MAY2020	**Structural and biochemical characterization of nsp12-nsp7-nsp8 core polymerase complex from SARS-CoV-2**	Peng, Qi et al. China gotopaper	Structural biology	Cryo-EM structure of SARS-CoV-2 core polymerase complex (nsp12 catalytic subunit + nsp7-nsp8 cofactors): - Structure highly resembles SARS-CoV counterpart with conserved motifs for all viral RNA-dependent RNA polymerases, and suggests a mechanism for activation by cofactors. **- SARS-CoV-2 core complex has lower enzymatic activity than SARS-CoV.** **- SARS-CoV-2 nsp7/8/12 subunits are less thermostable than the SARS-CoV counterpart.** -> Provides insights into RNA synthesis by coronavirus polymerase and **indicate adaptation of SARS-CoV-2 towards humans with relatively lower body temperatures than the natural bat hosts.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Clin. Infect. Dis. 30MAY2020	**Surgical mask partition reduces the risk of non-contact transmission in a golden Syrian hamster model for Coronavirus Disease 2019 (COVID-19)**	Chan, Jasper Fuk-Woo *et al.* China gotopaper	Transmission - Animal model	Golden Syrian hamster SARS-CoV-2 model to experimentally address effect of surgical mask on transmission : Surgical mask partition placed between cages of SARS-CoV-2-challenged index hamsters and naïve hamsters (closed system units separated by a polyvinyl chloride air porous partition + unidirectional airflow). **- Surgical mask partition for challenged hamsters significantly reduced transmission to 16.7% (2/12, P=0.019) of exposed naïve hamsters compared to exposed naïve hamsters without surgical mask partition (66.7%).** **- Unlike severe COVID-19 manifestations of challenged hamsters, infected naïve hamsters had lower clinical scores,** milder histopathological changes, and lower viral nucleocapsid antigen expression respiratory tract tissues. **-> SARS-CoV-2 could be transmitted by respiratory droplets or airborne droplet nuclei in the hamster model. Such transmission could be reduced by surgical mask usage, especially when masks were worn by infected individuals.**
J Med Virol 29MAY2020	**Serum KL-6 concentrations as a novel biomarker of severe COVID19**	d'Alessandro, Miriana et al. Italy gotopaper	Virology	SARS-CoV-2 induced direct cytopathic effects against type I and II pneumocytes mediate lung damage. **Krebs von den Lungen-6 (KL-6) is mainly produced by damaged or regenerating alveolar type II pneumocytes**. This preliminary study analysed **serum concentrations of KL-6 in COVID19 patients to verify its potential as a prognostic biomarker of severity**. **CI°: NK cell analysis and assay of KL-6 in serum can help identify severe COVID19 patients**. Increased KL-6 serum concentrations were observed in patients with severe pulmonary involvement, revealing a prognostic value and supporting the potential usefulness of KL-6 measurement to evaluate COVID19 patients prognosis. **Limitations**: these results are worthy of further validation in a larger cohort to define the cut-off value for identifying patients at high risk of severe respiratory failure.
BMJ 29MAY2020	**Covid-19: the ethics of clinical research in quarantine**	Nicholas G Evans, USA gotopaper	SHS/Sciences Po	Quarantine = an opportunity to gain scientific knowledge of covid-19. Quarantine provides a model community in which to study both the social and epidemiological characteristics of a disease outbreak. As a closed system, quarantine offers the possibility for highly controlled research into the development and transmission of covid-19 But this opportunity is also an ethical risk. This knowledge would be obtained with human rights violation (such as liberty). Moreover, individuals under quarantine seem to me more vulnerable to researchers. Confinement could affect their ability to choose or not to participate into research. Finally, research in this context could be a major opportunity to clarify when quarantine is, or is not, effective and proportionate (with high quality data on COVID-19).
Journal of Allergy and Clinical Immunology 29MAY2020	**Successful use of methylprednisolone for treating severe COVID-19**	Liu, Jing et al. China gotopaper	Therapeutic	**Case series** of **101 consecutive hospitalized patients** with confirmed COVID-19 infection, among which 26 were classified as severe or critical (25.74%), with at least 10 patients had a PaO2/FiO2 ratio of less than 150 mmHg, treated with methylprednisolone. -> **Timely and appropriate application** of glucocorticoid in severe and critical COVID-19 patients may **improve outcomes** and lung function and could avoid the need for invasive mechanical ventilation, compared with outcomes in reported studies. -> Single-dose pulse methylprednisolone (40-500mg methylprednisolone) had **no apparent negative impact on SARS-CoV-2 removal and production of specific IgG**.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Communications 29MAY2020	**Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients**	Chia, PY et al., Singapore gotopaper	Public Health/Epidemio	Screening for SARS-CoV-2 RNA on surface and air samples from 3 airborne infection isolation rooms (AIIRs) in ICU and 27 AIIRs in the hospital general ward hosting Covid-19 patients. From 245 surface samples collected: - 56.7% of rooms have at least one surface contaminated - High touch surface contamination is shown in 10 (66.7%) out of 15 patient environments in the first week of illness, and 3 (20%) beyond the first week of illness - Air sampling performed in 3 of 27 general ward AIIRs ward detected SARS-CoV-2 PCR-positive particles of sizes >4 microm and 1-4 microm in two rooms, despite these rooms having 12 air changes per hour. This warrants further study of the particle size distribution and airborne transmission potential of SARS-CoV-2.
Science 29MAY2020	**Introductions and early spread of SARS-CoV-2 in the New York City area**	Gonzalez-Reiche et al, USA gotopaper	Public Health/Epidemio	Aim: to identify the early transmission events underlying the rapid spread of the virus in the NYC metropolitan area, by sequencing SARS-CoV-2 from patients. Phylogenetic analysis of 84 distinct SARS-CoV-2 genomes indicated: - multiple, independent but isolated introductions mainly from Europe and other parts of the United States, - evidence for community transmission of SARS-CoV-2 as suggested by clusters of related viruses found in patients living in different neighborhoods of the city.
Science Advances 29MAY2020	**Emergence of SARS-CoV-2 through recombination and strong purifying selection**	Li, Xiaojun *et al.* USA - China gotopaper	Phylogenetic	Localised genomic analysis of patterns of evolutionary recombination between CoVs from distinct host species that likely originated SARS-CoV-2, reveal: **- Strong purifying selection around the receptor binding motif (RBM) of the spike among bat, pangolin, and human coronaviruses.** **- SARS-CoV-2's entire RBM was introduced through recombination with coronaviruses from pangolins**, possibly a critical step in the evolution of SARS-CoV-2's ability to infect humans. **Note:** all 3 human CoVs (SARS, MERS and SARS-2) are the result of recombination among CoVs involving the S gene, likely a precondition to zoonosis that enabled efficient binding to human receptors. **-> Similar evolutionary selection in different host species, together with frequent recombination among coronaviruses, suggest a common evolutionary mechanism that could lead to new emerging human coronaviruses.**
Lancet 29MAY2020	**Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study**	COVIDSurg Collaborative UK gotopaper	Clinic	International – multicentre – 235 hospitals – 24 countries Surgery + SARS-CoV-2 positive within 7 before or 30 days after → **1128 patients** Pulmonary complication: ARDS or pneumonia or unexpected postoperative ventilation 74% had emergency surgery and 24,8% elective surgery **30-day mortality= 23,8%** **Pulmonary complications= 51,2% with 38% of mortality** Association with mortality (adjusted analysis): - Male sex OR: 1,75 [1,28 – 2,40] - > or = 70 years OR: 2,30 [1,65 – 3,22] - ASAS grade 3-5 OR: 2,35 [1,57 – 3,53] - Malignant diagnosis OR: 1,55 [1,01 – 2,39] - Emergency surgery OR: 1,67 [1,06 – 2,63] - Major surgery OR: 1,52 [1,01 – 2,31] → pulmonary complication in more than half of patients with perioperative SARS-CoV-2 infection → **postponing non urgent procedure and promoting non operative treatment**

Journal and date	Title	Authors and link	Field of expertise	Key facts
The Journal of clinical investigation 28MAY2020	**Impaired immune cell cytotoxicity in severe COVID-19 is IL-6 dependent**	Mazzoni, Alessio et a, Italy gotopaper	Immuno	**Characterization of the immune response in SARS-CoV-2 infected patients hospitalized at the Careggi University Hospital, Florence, Italy** • A flow cytometric characterization of immune cells subsets from 30 COVID-19 patients correlated with clinical outcomes confirms a decreased number of circulating T, B and NK cells and that T CD4+, T CD8+ but also NK cells displayed reduced anti-viral cytokine production capability. • The study shows a skewing of CD8+ T cells towards a terminally differentiated/senescent phenotype via a TNF-mediated T cell apoptosis. This may contribute to an uncontrolled inflammatory response. • In a group of patients that required intensive care, serum IL-6 levels are inversely correlated with the frequency of granzyme-expressing NK cells. This underlines that the exposure to high levels of IL-6 inhibits NK cell cytotoxicity and down-regulates the expression of perforin and granzyme. • In all patients treated with tocilizumab an increased expression of both perforin and granzyme in NK cells was observed as well as a decrease of CRP, which is considered as a marker of IL-6 mediated inflammation. This study points out that tocilizumab might restore the cytotoxic potential of NK cells. Conclusion: This current work endorses that targeting IL-6 cytokine might restore anti-viral mechanisms and the use an anti-IL-6 receptor monoclonal antibody in COVID-19 patients remains a potential therapeutic option.
Natl Sci Rev 28MAY2020	**Preliminary evidence from a multicenter prospective observational study of the safety and efficacy of chloroquine for the treatment of COVID-19**	Huang, Mingxing et al. China gotopaper	Therapeutic	**Multicenter prospective observational study** to assess the **efficacy and safety of chloroquine** with different doses in COVID-19. A total of 197 patients completed chloroquine treatment, and 176 patients treated with non-chloroquine therapy were included as historical controls. Across the two treatment groups, the majority patients were classified as **moderate cases** (93.4% in chloroquine; 89.2% in nonchloroquine). The primary endpoint is the **time to undetectable viral RNA**. Secondary outcomes include the proportion of patients with undetectable viral RNA by day 10 and 14, hospitalization time, duration of fever, and adverse events. - Patients in the chloroquine group experienced **significantly faster and higher rate of viral suppression** comparing to the nonchloroquine group in both the full analysis and the post hoc stratified analysis. Even when the dose reduced to half, the benefit of chloroquine still remained. - **Duration of fever is shorter** in chloroquine (geometric mean ratio 0.6; 95% CI 0.5 to 0.8). - **No serious adverse events** were observed in the chloroquine group. Patients treated with half dose experienced lower rate of adverse events than with full dose. - **No beneficial effect** of chloroquine in the **length of hospital stay** and the **duration of oxygen support**. - Unprecedently, 3 cases of so called **"re-positive" patients** observed in the chloroquine group. **Limitations**: observational study ; dramatic improvement in the primary outcome in chloroquine could be due to the later treatment initiation since symptom onset ; relatively young study population with few patients with severe symptoms that requires ventilation.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet HIV 28MAY2020	**Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort**	Vizcarra P et al Spain gotopaper	Clinic	Observational & prospective study: 51 HIV-infected COVID-19+ & 1288 HIV-infected without 1 center in Madrid Mean age of COVID-19= 53,3y (SD:9,5) – 84% of men **No difference for age and CD4 cell counts** 63% with COVID-19 had at least one comorbity Clinical presentations similar than in general population 12% critically ill and 4% died Covid-19 vs without COVID-19: - 73% vs 32% received tenofovir before COVID-19 diagnosis (*p*=0,0036) - 22% vs 14% had previous protease inhibitor (*p*=0,578) RT-PCR remained positive after a median of 40 days in 6 patients → HIV-infected patients should receive the same treatment to the general population
Lancet 28MAY2020	**Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study**	Kuderer NM et al USA gotopaper	Clinic	Cohort study from the USA, Canada & Spain from the COVID-19 & cancer consortium (CCC19) Patients with active or previous malignancy & SARS-CoV-2 infection: **928 patients included** Malignancy: breast cancer (21%) – prostate (16%) – gastrointestinal (12%) – thoracic (10%) … Status: active cancer (43%) – remission (45%) – anticancer treatment (39%) **13% had died** Median age: 66 y IQR [57 – 76] – 50% were male Independent factor associated with increased 30-day mortality - Increased age per 10 years OR: 1,84 [1,53 – 2,21] - Male OR: 1,63 [1,07 – 2,28] - Former smoker vs never OR: 1,60 [1,03 – 2,47] - Two comorbidities vs none OR: 4,50 [1,33 – 15,28] - Active cancer OR: 5,2 [2,77 – 9,77] - Receipt azithro+hydroxy vs neither OR: 2,93 [1,79 – 4,79] →*confounding by indication not excluded* Obesity, cancer type, ethnicity, type of anticancer therapy, recent surgery → not associated Limits: regional variations in the primary and secondary outcomes → Hight mortality among patients with cancer + COVID-19 → **longer follow-up is needed**
The Lancet ID 28MAY2020	**Implication of SARS-CoV-2 evolution in the sensitivity of RT-qPCR diagnostic assays**	Sampaio Osorio and Correia-Neves, Portugal gotopaper	Diagnostic	Reports suggest the virus might be evolving –> redesign of the oligonucleotide sequences in use in RT-qPCR assays to circumvent potential primer–sample mismatches ? Analysis of all high-coverage SARS-CoV-2 genome sequences (1825 in total) deposited in the Global Initiative on Sharing All Influenza Data (GISAID) database nucleotide diversity (π) WAS CALCULATED in the binding region of each oligonucleotide. -> 79% (26 of 33) of the primer binding sites used in the RT-qPCR assays were mutated in at least one genome -> at least one of the previously designed primers is now likely to be ineffective at detecting up to 14% of the virus variants in circulation -> Oligonucleotide optimisation will be facilitated by global sharing of SARS-CoV-2 genomes and the frequently updated reports on sequence analysis that are available on the GISAID website.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Gene Reports 2020	**COVID-19 target: A specific target for novel coronavirus detection**	Kakhki, Reza Kamali et al. Iran gotopaper	Diagnostic	**The diagnosis and differentiation of this virus from other types of coronavirus is essential to control of the disease** The **analysis of genomics data** plays a vital role in introducing a stronger target and consequently provides better results in laboratory examinations. The modified comparative genomics approach helps us to find novel specific targets by comparing two or more sequences on the nucleotide collection database. Unlike previous reported genes (RdRP, E and N genes), **ORF8 is entirely specific to the novel coronavirus (COVID-19)** and has no cross-reactivity with other kinds of coronavirus **CI°**: ORF8 gene can be used as an additional confirmatory assay. **Limitations**: this study was conducted bioinformatically, and laboratory examinations are needed to confirm ORF8 gene as a potential target using RT-PCR, Real time PCR, or Line probe assay
Critical care medicine 27MAY2020	**Routine Venous Thromboembolism Prophylaxis May Be Inadequate in the Hypercoagulable State of Severe Coronavirus Disease 2019**	Maatman, Thomas K. et al.USA gotopaper	Therapeutic/ Clinic	**Observational multicenter study**, enrolled 240 consecutive patients among whom **109 critically ill COVID-19** patients admitted to the ICU were included in the analysis. All patients received **routine subcutaneous chemical venous thromboembolism prophylaxis**. Primary outcome: **frequency of venous thromboembolism** (VTE) and the degree of inflammatory and coagulation marker elevation associated with venous thromboembolism development. - **VTE was diagnosed in 31 patients (28%)** 8 ± 7 days after hospital admission, including two patients diagnosed with venous thromboembolism at presentation to the hospital. - Elevated admission D-dimer and peak D-dimer were associated with VTE development ($p < 0.05$). - D-dimer greater than 2,600 ng/mL predicted VTE with an area under the receiver operating characteristic curve of 0.760 (95% CI, 0.661-0.858; $p < 0.0001$), sensitivity of 89.7%, and specificity of 59.5%. - Twelve patients (11%) had thromboelastography performed and 58% of these patients had a hypercoagulable study. The calculated coagulation index was hypercoagulable in 50% of patients with thromboelastography -> SARS-CoV-2 infection results in **systemic hypercoagulability resulting in VTE**. Although current data on outcomes in patients receiving therapeutic anticoagulation in COVID-19 are lacking, it is apparent that **routine chemical VTE prophylaxis may be inadequate in preventing thrombotic complications in severe COVID-19**. **Limitations**: Although a relatively large series, it is an observational study ; retrospective study ; lack of comparator group of ICU patients without COVID-19 in which to compare VTE frequency ; degree of viremia not evaluated as a risk factor for VTE.
NEJM 27MAY2020	**Remdesivir for 5 or 10 Days in Patients with Severe Covid-19**	Jason D. Goldman et al. gotopaper	Therapeutic	**Open-label, randomized, multicenter trial** evaluating the **efficacy and safety** of treatment with **remdesivir for 5 or 10 days** in **397 patients** with **severe** Covid-19 disease. The primary end point was **clinical status on day 14**, assessed on a 7-point ordinal scale. => **No significant difference in efficacy between 5-day and 10-day courses of remdesivir**. After adjustment for baseline imbalances in disease severity, outcomes were similar as measured by a number of end points: clinical status at day 14, time to clinical improvement, recovery, and death from any cause. Similar percentages of patients experiencing adverse events. -> Results cannot be extrapolated to critically ill patients receiving mechanical ventilation; further evaluation of this subgroup and of other high-risk groups is needed to determine the shortest effective duration of therapy. **Limits**: lack of a randomized placebo control group (magnitude of benefit not determined); open-label design.

Journal and date	Title	Authors and link	Field of expertise	Key facts
SCIENCE 27MAY2020	**Reducing transmission of SARS-CoV-2**	Prather et al., USA-China gotopaper	Public Health/Epidemio	**PERSPECTIVE** - Traditional respiratory disease control measures: designed to reduce transmission by droplets produced in the sneezes and coughs of infected individuals. However, a large proportion of the spread: through **airborne transmission of aerosols** produced by asymptomatic individuals during breathing and speaking. Aerosols can **accumulate**, **remain infectious in indoor air for hours**, and be easily inhaled deep into the lungs. Contact (direct or indirect) is also a major source of contamination. - Respiratory droplet size has been shown to affect the severity of disease - "Silent shedders" (asymptomatic / pre-symptomatic) could be critical drivers. In China, undiagnosed cases, presumably asymptomatic, may be responsible for up to 79% of infections. - Many countries have not yet acknowledged airborne transmission as a possible pathway Recommendations for social distancing of 6 ft are based on studies of respiratory droplets carried out in the 1930s, but on large droplets (no technology for submicron aerosols). ->Intense coughs and sneezes that propel larger droplets more than 20 ft can also create thousands of aerosols that can travel even further (like a cigarette smoke)-> **6 ft WHO recommendation is likely not enough.** -Viruses can attach to other particles such as dust and pollution, which can modify the aerodynamic characteristics and increase dispersion **Aerosol transmission of viruses must be acknowledged as a key factor leading to the spread of infectious respiratory diseases. Evidence suggests that SARS-CoV-2 is silently spreading in aerosols exhaled by highly contagious infected individuals with no symptoms.** **-> It is essential that control measures be introduced to reduce aerosol transmission (face masks +++)**
Nature reviews Immunology 26MAY2020	**Dysregulation of type I interferon responses in COVID-19**	Dhiraj Acharya et al, USA gotopaper	Immuno	How imbalanced interferon responses may contribute to the pathology of COVID-19: • The lung injury in patients with severe COVID-19 underlines a possible failure to activate immuno-suppressive mechanisms in a timely manner. One suggestion is that the deficient or dysregulated IFN responses elicited by SARS-CoV-2 infection may influence the generation of regulatory T cells during the recovery phase of COVID-19. • The use of IFNs as a treatment for COVID-19 remains controversial, particularly regarding the timing of administration in mice model and in human • Since ACE2 has been identified as an ISG in human airway epithelial cells10. This finding raises the question of whether prophylactic or therapeutic IFN administration enhance the entry and replication of SARS-CoV-2 in target cells during disease progression **Conclusion**: a deeper understanding of the spatiotemporal kinetics of IFN responses during clinical SARS-CoV-2 infections is warranted to inform IFN-related therapeutics and vaccine design.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Cell Death Discovery 26MAY2020	**SARS-CoV-2 infection serology: a useful tool to overcome lockdown?**	Nuccetelli, M. et al, Italy gotopaper	Diagnostic	**Aim:** to compare and to evaluate different serological assays analytical performances (two different immunochromatographic cards, an immunofluorescence chromatographic card, and a chemiluminescence-automated immunoassay) on 43 positive samples with RT-qPCR-confirmed SARS-CoV-2 infection and 40 negative control subjects. → excellent IgG/IgM specificities for all the immunocromatographic card tests (100% IgG and 100% IgM) and for the chemiluminescence-automated assay (100% IgG and 94% IgM); → IgG/IgM sensitivities are moderately lower for all methods (94% and 84% for IgG and IgM, respectively), probably due to the assay viral antigen's nature and/or to the detection time of nasopharyngeal swab RT-qPCR, with respect to symptoms onset.
Clinical Infectious Diseases 25MAY2020	**Characterization of an asymptomatic cohort of SARS-COV-2 infected individuals outside of Wuhan, China**	Wang Y et al China gotopaper	Clinic	Epidemiologic and clinical characteristics of asymptomatic SARS-COV-2 infections 279 hospitalized SARS-CoV-2+ contacts of COVID-19 patients → **63 asymptomatic** included Mean time to diagnosis after contact: 16 days Mean age: 39,3 - 87,3% had no comorbidities Laboratory findings: quasi normal for all **2 groups**: abnormal chest CT findings (29) & normal chest CT findings (34) - Patient with abnormal findings were older (p<0,05) - Time from exposure to illness shorter in patient with abnormal CT (p>0,05) Outcomes: - 9 transmitted the virus to others with and without abnormal chest CT - No one died → asymptomatic infections play a large role in transmission → impact on treatment of symptomatic cases on transmission?
The Lancet 25MAY2020	**Assistance Publique–Hôpitaux de Paris' response to the COVID-19 pandemic**	The COVID19-APHP Group, France gotopaper	Public Health/Epidemio	**Key points of an effective AP-HP response to the Covid-19 crisis:** - Establishment of a medical organisation led by a central crisis medical director and supported by medical directors in each hospital - Allocation of human resources to recruit and train specialised staff from a single platform - Centralised logistics to adjust to shortages the equipment and consumables daily supply - Recruitment of students of various medical branches to support as paramedics, research assistants, operators of a telemedicine platform. - Regional centralised ICU bed-allocation system - Regularly updated practical guidelines for all hospitals - Development of a common research strategy prioritising patient cohorts, biobanking, clinical trial - Large scale initiatives: equipment 3D printing, Covidom telemedicine platfor - Setup of a region-wide patient-tracing programme

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Climate Change 23MAY2020	**Temporary reduction in daily global CO2 emissions during the COVID-19 forced confinement**	Le Quéré et al. UK, gotopaper	SHS/SciPo	> Emissions of carbon dioxide rise by about 1% per year over the previous decade > COVID 19 imposed confinement leads to drastic changes in energy use, with expected impacts on CO2 emissions. However CO2 emissions are reported as annual values and there is no available real time data > An alternative approach using a combination of energy, activity and policy data was used to estimate changes in CO2 daily emissions during the confinement is porposed (69 countries, 50 US states and 30 Chinese provinces; 85% of global population; 87% of global emissions) **Results** > Estimated decrease in daily fossil CO2 emissions from the severe and forced confinement of world populations: –17% (–11 to –25%) > Annual associated decrease: –4.2 to –7.5% (rates needed over the next decades to limit climate change to 1.5 °C warming) > However observed changes are likely to be temporary as they do not reflect structural changes in the economic, transport or energy systems.
Biosensors and Bioelectronics 23MAY2020	**Ultra-sensitive and high-throughput CRISPR-Powered COVID-19 diagnosis**	Huang, Zhen and al. USA gotopaper	Diagnostic	A rapid, sensitive SARS-CoV-2 diagnostic assay capable of high-throughput operation that can preferably utilize existing equipment to facilitate broad, large-scale screening efforts. The developed assay utilizes a custom CRISPR Cas12a/gRNA complex and a fluorescent probe to amplify target amplicons produced by standard RT-PCR or isothermal recombinase polymerase amplification (RPA), to allow sensitive detection at sites not equipped with real-time PCR systems required for qPCR diagnostics. The results obtained on nasal swab samples of individuals with suspected COVID-19 cases were comparable to paired results from a CDC-approved qPCR assay performed in a state testing lab, and superior to those produced by same assay in a clinical lab, where the qPCR assay exhibited multiple invalid or inconclusive results. It also demonstrated greater analytical sensitivity and more robust diagnostic performance than other recently reported CRISPR-based assays. CI°: a CRISPR-based fluorescent application has potential to improve current COVID-19 screening efforts.
BMJ 22MAY2020	**Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study**	Docherty, AB. Et al. UK gotopaper	Clinic	Aim: To characterise the clinical features of 20 133 hospital patients with Covid-19 enrolled in the ISARIC WHO CCP-UK prospective cohort study, and to explore risk factors associated with admission to critical care and mortality in hospital. Patient follow-up time was of two weeks minimum. → Median age: 73 years (interquartile range (IR) 58-82, range 0-104). 60% of patients were men, 40% women. Median duration of symptoms before admission was 4 days (IR 1-8). → Comorbidities: chronic cardiac disease (31%), uncomplicated diabetes (21%), non-asthmatic chronic pulmonary disease (18%), chronic kidney disease (16%); 23% had no reported major comorbidity. → 41% of patients were discharged alive, 26% died, 34% continued receiving care as of reporting date. 17% (3001/18 183) required admission to high dependency or ICU; of these, 28% were discharged alive, 32% died, and 41% continued to receive care. Of those receiving mechanical ventilation (1658), 17% were discharged alive, 37% died, and 46% remained in hospital. Increasing age, male sex, and chronic comorbidities were associated with higher mortality in hospital.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Circulation 22MAY2020	**Cardiovascular Toxicities Associated with Hydroxychloroquine and Azithromycin: An Analysis of the World Health Organization Pharmacovigilance Database**	Nguyen, Lee S. et al. France/USA gotopaper	Therapeutic	**Observational, retrospective study**, that used VigiBase®, the **WHO pharmacovigilance database** encompassing over 21 million reports from over 130 countries, to compare CV-ADR reporting in patients who received **hydroxychloroquine, azithromycin, or their combination** with **cardiovascular adverse-drug-reactions** (CV-ADRs) reported with all other drugs in the full database. Extraction of 76,822 ADR cases associated with hydroxychloroquine alone, 89,692 with azithromycin alone, and 607 with the combination of both drugs. The cases were retrieved from 21,275,867 total ADR reports in VigiBase®. The lower end of the IC's 95% credibility interval is IC025. It is considered significant when above 0. - Significant greater reporting of **prolonged-QT** (LQT) and/**or ventricular tachycardia** including **Torsades-de-Pointes** (TdP/VT) for each drug individually in suspected cases (IC025=1.67 for azithromycin and IC025=1.04 for hydroxychloroquine). - Hydroxychloroquine was also associated with **conduction disorders** (atrioventricular and bundle branch blocks) (IC025=1.04) and heart failure (HF, IC025=0.06). - Azithromycin monotherapy was associated with a greater reporting of LQT and/or TdP/VT than hydroxychloroquine monotherapy. The **combination of azithromycin and hydroxychloroquine** was associated with a **greater reporting of LQT and/or TdP/VT** than either drug in monotherapy. - The proportion that resulted in **death for TdP/VT** cases was 8.4% with hydroxychloroquine and 20.2% with azithromycin versus 0% and 5.4% for LQT without TdP/VT with hydroxychloroquine and azithromycin, respectively ($p<0.001$ for both). - Corresponding death rate was 20.7% for HF associated with hydroxychloroquine. Dose of hydroxychloroquine was higher in HF compared to LQT and/or TdP/VT cases. **Main limitation**: without data on numbers exposed in Vigibase, this work cannot assess the incidence or risk for QT prolongation with these drugs.
Annals of Translational Medicine MAY2020	**Preliminary study to identify severe from moderate cases of COVID-19 using combined hematology parameters**	Wang, Changzheng et al. China gotopaper	Diagnostic	The aim of this study was to investigate the **characteristics and rules of hematology changes in patients with COVID-19**, and to explore the possibility differentiating moderate and severe patients using conventional hematology parameters or combined parameters As the disease progressed, white blood cell count (WBC), neutrophil count, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), red blood cell distribution width-coefficient of variation (RDW-CV), and red cell volume distribution width-standard deviation (RDW-SD) parameters in the severe group were significantly higher than those in the moderate group. CI°: **the combined NLR and RDW-SD parameter is the best hematology index**. It may help clinicians to predict the severity of COVID-19 patients and can be used as a useful indicator to help prevent and control the epidemic

Journal and date	Title	Authors and link	Field of expertise	Key facts
Gastroenterology 22MAY2020	**Famotidine Use is Associated with Improved Clinical Outcomes in Hospitalized COVID-19 Patients: A Propensity Score Matched Retrospective Cohort Study**	Freedberg, Daniel E. et al. USA gotopaper	Therapeutic	**Retrospective cohort study** of 1,620 hospitalized patients tested positive for SARS-CoV-2 within 72 hours following admission including **84 patients** who received **famotidine** within 24 hours of hospital admission. **Primary outcome** was a composite of death or endotracheal intubatio n. Although Famotidine has not previously been studied in patients for antiviral effects, an untargeted computer modelling analysis identified famotidine as one of the highest-ranked matches for drugs **predicted to bind 3CLpro**, a SARS-CoV-2 protease which generates non-structure proteins critical to viral replication. 340 (21%) patients met the composite study outcome. Famotidine use was **significantly associated** with a **reduced risk of clinical deterioration leading to intubation or death**. A randomized controlled trial is currently underway to determine whether famotidine can improve clinical outcomes in hospitalized COVID-19 patients. **Limitations**: observational; no samples were gathered, and mechanism cannot be directly assessed; single center study.
Clinical infectious diseases 22MAY2020	**Association of renin-angiotensin-aldosterone system inhibitors with COVID-19-related outcomes in Korea: a nationwide population-based cohort study**	Jung, Sun-Young et al. Korea gotopaper	Therapeutic/ Clinic	**Nationwide population-based cohort study** in Korea comparing the **clinical outcomes** of confirmed COVID-19 cases between **RAAS inhibitor users and nonusers**. The study revealed a **significantly higher mortality rate** among patients with COVID-19 who were **using RAAS inhibitors**, relative to patients who were not receiving RAAS inhibitors. However, **RAAS inhibitor users were older**, had **more comorbidities**, and were **more likely to receive in-hospital treatments**. The **elevated risk of mortality** among RAAS inhibitor users **disappeared after adjusting for these confounding factors**. This study in an **Asian population** is clinically relevant, given that the East Asian populations **have higher ACE2 expression in tissues** than other populations under the similar conditions. **Limitations**: accuracy of diagnostic codes may be limited; retrospective observational design.
Clinical infectious diseases 22MAY2020	**Thymosin alpha 1 (Talpha1) reduces the mortality of severe COVID-19 by restoration of lymphocytopenia and reversion of exhausted T cells**	Liu, Yueping et al. China gotopaper	Therapeutic	**Retrospective cohort study** to evaluate the clinical outcomes of **severe or critical** COVID 19 hospitalized patients receiving **Thymosin alpha 1** (Tα1) supplement. A total of **76 patients** were enrolled (36 in the treatment group and 40 in the non treatment group) Compared with untreated group, **Tα1 treatment significantly reduces mortality** of severe COVID-19 patients (11% vs. 30%, p=0.044). **Tα1 timely enhances blood T cell numbers** in COVID-19 patients with **severe lymphocytopenia**. Under such conditions, Tα1 also successfully **restores CD8+ and CD4+ T cell numbers in aged patients**. Meanwhile, Tα1 **reduces PD-1 and Tim-3 expression on CD8+ T cells** from severe COVID-19 patients in comparison with untreated cases. **Limitations**: issue with the normalization of TREC levels among individuals; retrospective study and small sample size; mortality as primary clinical outcome and not clinical improvement.

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 22MAY2020	**Remdesivir for the Treatment of Covid-19 — Preliminary Report**	Beigel, John H. et al. , USA gotopaper	Therapeutic	**Double-blind, randomized, placebo-controlled trial** of **intravenous remdesivir** in **1063 adults hospitalized** with Covid-19 with evidence of lower respiratory tract involvement in 60 trial sites in 10 countries. The **primary outcome** was the **time to recovery**, defined by either discharge from the hospital or hospitalization for infection-control purposes only. **Early unblinding** of the results recommended by the DSMB based on findings from an analysis that showed shortened time to recovery in the remdesivir group. Preliminary results from the 1059 patients (538 assigned to remdesivir and 521 to placebo) suggest that a **10-day course of remdesivir was superior to placebo in the treatment of hospitalized patients with Covid-19**. - This benefit was seen in the **number of days to recovery** (median, 11 days, as compared with 15; rate ratio for recovery, 1.32 [95% CI, 1.12 to 1.55]) and in **recovery according to the ordinal scale score at day 15** (odds ratio, 1.50; 95% CI, 1.18 to 1.91). - Mortality was numerically lower in the remdesivir group than in the placebo group, but the difference was not significant (hazard ratio for death, 0.70; 95% CI, 0.47 to 1.04; 1059 patients). - Incidence of adverse events was not found to be significantly different between the remdesivir group and the placebo group. Awaiting final visits, data entry, monitoring, and data lock for the last of the 1063 patients enrolled, to provide an update of the results.
The Lancet 22MAY2020	**Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis**	Mandeep R Mehra et al., USA gotopaper	Therapeutic	**Multinational registry analysis** of the use of **hydroxychloroquine or chloroquine with or without a macrolide** for treatment of COVID-19. The registry comprised data from 671 hospitals in six continents. **96 032 patients** (mean age 53·8 years, 46·3% women) were enrolled, with **14 888 patients were in the treatment groups** and 81 144 patients were in the control group. The **main outcomes** of interest were **in-hospital mortality** and the occurrence of **de-novo ventricular arrhythmias** (non-sustained or sustained ventricular tachycardia or ventricular fibrillation). The study was **unable to confirm a benefit** of hydroxychloroquine or chloroquine, when used alone or with a macrolide, on in-hospital outcomes for COVID-19. **Each of these drug regimens** was **associated with decreased in-hospital survival** and an increased **frequency of ventricular arrhythmias** when used for treatment of COVID-19. Main **limitation**: observational study design.
mBio 22MAY2020	**Antiviral Efficacies of FDA-Approved Drugs against SARS-CoV-2 Infection in Ferrets**	Park, Su-Jin et al. Korea gotopaper	Therapeutic	FDA-approved drugs **lopinavir-ritonavir**, **hydroxychloroquine sulfate**, and **emtricitabine-tenofovir** were **tested against SARS-CoV-2** infection in a highly susceptible **ferret infection model**. While **most of the drug treatments marginally reduced clinical symptoms**, they **did not reduce virus titers**, with the **exception of emtricitabine-tenofovir** treatment, which led to diminished virus titers in nasal washes at 8 dpi. Further, the **azathioprine-treated immunosuppressed ferrets** showed delayed virus clearance and low SN titers, resulting in a prolonged infection.

Journal and date	Title	Authors and link	Field of expertise	Key facts
BMJ 22MAY2020	**Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study**	Petrilli CM, et al., USA gotopaper	Clinic	**Aim:** To describe outcomes, and clinical and laboratory characteristic associated with severity of illness of 5279 patients admitted with Covid-19 in NYC/Long Island (US). → 48.2% of people tested (5566/11544) were positive for SARS-CoV2; of the 5279 patients included, 51.9% were admitted to hospital. Of these, 69.5% were discharged without hospice care, 24.3% were discharged to hospice care or died. Of 647 (23.6% of hospitalised) patients requiring mechanical ventilation, 60.4% died and 26.2% were extubated or discharged. → Risk for hospital admission was associated with age (odd ratio >2 for age groups >44 years, 37.9 (95% CI[26.1 to 56.0]) for >75 years), heart failure (4.4, 2.6 to 8.0), male sex (2.8, 2.4 to 3.2), chronic kidney disease (2.6, 1.9 to 3.6), increase in body mass index (BMI) (eg, for BMI >40: 2.5, 1.8 to 3.4). → Risk for critical illness besides age was associated with heart failure (1.9, 1.4 to 2.5), BMI >40 (1.5, 1.0 to 2.2), and male sex (1.5, 1.3 to 1.8). Admission oxygen saturation of <88% (3.7, 2.8 to 4.8), troponin level >1 (4.8, 2.1 to 10.9), C reactive protein level >200 (5.1, 2.8 to 9.2), and D-dimer level >2500 (3.9, 2.6 to 6.0) were more strongly associated with critical illness than age or comorbidities. → Risk of critical illness decreased significantly over the study period, and similar associations were found for mortality alone, potentially **suggesting improvement in care.**
Science 22MAY2020	**Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial**	Zhu FC et al. China, gotopaper	Vaccine	Phase 1 vaccine trial using the recombinant non-replicating adenovirus 5 type vectored COVID 19 vaccine expressing the S protein (open label; non randomised; dose escalation- $5x10^{10}/1x10^{11}/5x10^{11}$ viral particles). NCT04313127 108 patients recruited (18-60 years; 51% male-49% female) **Endpoint for safety:** 7D post vaccination/recording of AE until 28D post-vaccination **Humoral immunogenicity endpoints:** The specific ELISA antibody titres to RBD and S protein, and the neutralising antibody amounts against live SARS-CoV-2 **Positive antibody response (seroconversion):** at least a four-fold increase in post-vaccination titre from baseline **SAE and Safety** > 83%/83%/75% (related to increasing dose, non-significant difference) of patients had at least an AE of moderate/mild severity within the first 7 days (pain, fever, fatigue, headache or muscle pain) > no serious AE were recorded at 28d post vaccination **Protection** Elisa antibodies and neutralizing antibodies increased at D14 and peaked at D28 post-vaccination. Specific T cells response peaked at D14 post-vaccination **Comments** > Older age participants could have a negative effect on the vaccine-elicited responses to SARS-CoV-2 > ADE not evaluted (because of low number of particiapnts) > Pre-existing Ad5 immunity might also have a negative effect on the persistence of the vaccine-elicited immune responses. Issues to evaluate in Phase 2

Journal and date	Title	Authors and link	Field of expertise	Key facts
Neurology 22MAY2020	**Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy**	Benussi A et al Italy gotopaper	Clinic	Outcomes of patients admitted with neurological disorders with and without COVID-19 173 patients included: **56 COVID-19 pos & 117 COVID-19 neg** No difference for comorbitities Patients with COVID-19: -Older: 77,0 versus 70,1 years (p=0,006) -More cerebrovascular disorders: 76,8% versus 58,1% (p=0,035) -Higher qSOFA: 0,9 versus 0,5 (p=0,006) -Higher incidence of delirium: 26,8% versus 7,7% (p=0,003) -Higher in-hospital mortality: 75,5% versus 4,3% (p<0,001) -Wider use of high flow oxygenation: 76,8% versus 9,4% (p<0,001) -Prolonged length of stay Potential risk factor of poor prognosis: high qSOFA score – thrombocytopenia – increase lactate deshydrogenase level
Clinical infectious diseases 22MAY2020	**Predicting infectious SARS-CoV-2 from diagnostic samples**	Bullard, Jared and al. Canada gotopaper	Diagnostic	RT-PCR detects RNA, not infectious virus, thus its ability to determine duration of infectivity of patients is limited. Objective: to determine the relationship between E gene SARS-CoV-2 RT-PCR cycle threshold (Ct) values from respiratory samples, symptom onset to test (STT) and infectivity in cell culture. => SARS-CoV-2 Vero cell infectivity was only observed for RT-PCR Ct < 24 and STT < 8 days. Infectivity of patients with Ct >24 and duration of symptoms >8 days may be low. Cl°: this information can inform public health policy and guide clinical, infection control and occupational health decisions.However, further studies of larger size are needed.
Analytical chemistry 22MAY2020	**A novel one-step single-tube nested quantitative Real-Time PCR assay for highly sensitive detection of SARS-CoV-2**	Wang, Ji and al. China gotopaper	Diagnostic	qRT-PCR results could be false-negative due to the inadequate sensitivity of qRT-PCR. In this study, we have developed and evaluated a novel one-step single-tube nested quantitative Real-Time PCR (OSN-qRT-PCR) assay for highly sensitive detection of SARS-CoV-2 targeting the ORF1aband N genes. The sensitivity of the OSN-qRT-PCR assay was 1 copy/reaction and 10-fold higher than that of commercial qRT-PCR kit (10 copies/reaction). Cl° : Compared to the qRT-PCR kit, OSN-qRT-PCR assay revealed higher sensitivity and specificity hence better suited to clinical applications for the detection of SARS-CoV-2 in patients with low viral load.
New England Journal of Medicine 21MAY2020	**Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19**	Ackermann, Maximilian, *et al.* Germany-Belgium-UK-USA gotopaper	Clinic	Lungs (autopsy) form patients: 7 who died from Covid-19 vs 7 who died from acute respiratory distress syndrome secondary to influenza A (H1N1) infection vs 10 age-matched, uninfected control lungs. Common to both Covid-19 and influenza-associated respiratory failure : - diffuse alveolar damage with perivascular T-cell infiltration **In Covid-19 patients :** **- severe endothelial injury** (associated to intracellular virus and disrupted cell membranes) **- widespread thrombosis with microangiopathy** **- capillary microthrombi 9x more prevalent** compared to influenza patients **- new vessel growth 2.7x** higher than in lungs from influenza patients **-> Vascular angiogenesis distinguished pulmonary pathobiology of Covid-19 from that of equally severe influenza virus infection**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 21MAY2020	**Postmortem Examination of Patients With COVID-19**	Schaller, Tina, *et al.* Germany gotopaper	Clinic	Serial postmortem examinations, 10 patients with proven SARS-CoV-2 infection who died at University Medical Center Augsburg. Median age: 79; range: 64-90 yrs, 7 male; all SARS-CoV-2 +ve by nasopharyngeal swab at hospital admission. Admission median till death: 7.5 days (range, 1-26 days), median of 4 known preexisting comorbidities. **- At autopsy, SARS-CoV-2 detectable in respiratory tracts of all patients, and PCR +ve in pleural effusion but not in all CSF samples.** - **Predominant histopathologic findings: acute and organizing diffuse alveolar damage and SARS-CoV-2 persistence in the respiratory tract, constituting the leading cause of death in patients with and without invasive ventilation.** - Periportal liver lymphocyte infiltration considered unspecific inflammation. - Whether myoepicardial alterations represented systemic inflammation or early myocarditis is unclear (criteria for true myocarditis not met). - **Central nervous system involvement by COVID-19 could not be detected** Limitations: small number of cases from a single center and missing proof of direct viral organ infection
Nature 21MAY2020	**Structure of replicating SARS-CoV-2 polymerase**	Hillen, Hauke S. *et al.* Germany gotopaper	Structural biology	Cryo-EM structure of SARS-CoV-2 RdRp in active form, mimicking the replicating enzyme: - Active site cleft of nsp12 binds first turn of RNA and mediates RdRp activity with conserved residues. - Two copies of nsp8 bind to opposite sides of the cleft and position the second turn of RNA. - Long helical extensions in nsp8 protrude along exiting RNA, forming +vely charged 'sliding poles'. -> sliding poles can account for known processivity of RdRp required for replicating the long coronavirus genome. - Previous study suggested remdesivir functions as 'immediate' RNA chain terminator, while t**his study showed that several more nucleotides can be added to RNA following remdesivir incorporation, leading to 'delayed' termination** -> mechanism that **could explain how remdesivir escapes removal from the RNA 3'-end by the viral exonuclease nsp14**.
Cell 21MAY2020	**Pathogenesis of SARS-CoV-2 in transgenic mice expressing human angiotensin-converting enzyme 2**	Jiang, Ren-Di. *et al.* China-USA gotopaper	Animal model	Developed a SARS-CoV-2 **hACE2 transgenic mouse** (HFH4-hACE2 in C3B6 mice) infection model, generating: - **Typical interstitial pneumonia and pathology, similar COVID-19 patients.** - Viral quantification: lungs are the major site of infection (**viral RNA also found in eye, heart, and brain in some mice**). - Full-genome sequences of virus identical to SARS-CoV-2 isolated from the infected lung and brain tissues. - **Pre-exposure to SARS-CoV-2 could protect mice from severe pneumonia**. **-> The hACE2 mouse would be a valuable tool** for testing potential vaccines and therapeutics.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 20MAY2020	**Viral and host factors related to the clinical outcome of COVID-19**	Zhang, Xiaonan, *et al.* China gotopaper	Clinic	326 confirmed COVID-19 cases in Shanghai. (SARS-CoV-2 genomic sequences assembled from 112 samples + sequences in the Global Initiative on Sharing All Influenza Data (GISAID)). Observations: - **stable evolution** and 2 major lineages suggested with differential exposure history during the early phase of outbreak in Wuhan (similar virulence and clinical outcomes for both lineages). - **Lymphocytopenia predictive of disease progression** (especially reduced CD4+ and CD8+ T cell counts upon admission). - **High IL-6 and IL-8 levels during treatment** in patients with severe/critical disease, which correlated with decreased lymphocyte count. **-> Determinants of disease severity seemed to stem mostly from host factors (age, lymphocytopenia and associated cytokine storm), whereas viral genetic variation did not significantly affect outcomes.**
Eur. Respir. J. MAY2020	**A Fully Automatic Deep Learning System for COVID-19 Diagnostic and Prognostic Analysis**	Wang et al., China gotopaper	Diagnostic	**Retrospective collection of 5372 patients** with **computed tomography images** from 7 cities or provinces. Steps: 1st-> 4106 patients with computed tomography images were used to pre-train the DL system, making it learn lung features 2nd-> 1266 patients from 6 cities or provinces were enrolled to train and externally validate the performance of the deep learning system **-> Deep learning system achieved good performance in identifying COVID-19 from other pneumonia (AUC=0.87 and 0.88) and viral pneumonia (AUC=0.86).** **-> Succeeded to stratify patients into high-risk and low-risk groups whose hospital-stay time have significant difference (p=0.013 and 0.014)** **-> Without human-assistance, the deep learning system automatically focused on abnormal areas that showed consistent characteristics with reported radiological findings**
Science 20MAY2020	**SARS-CoV-2 infection protects against rechallenge in rhesus macaques**	Chandrashekar A et al. USA gotopaper	Vaccine	Infection of macaques with SARS-CoV-2 results in protective immunity against re-exposure? **Methods:** Infection of 9 rhesus macaques (6-12 years) with SARS-CoV-2 showing high viral loads in the upper and lower respiratory tract, humoral and cellular immune responses and pathologic evidence of viral pneumonia, re-challenged after virus clearance (D35 post initial infection), + 3 naïve animals as positive controls in the rechallenge experiment **Results** > After primary infection all 9 macaques developed binding antibody responses to S protein and NAb responses and cellular immune responses. > 5 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa compared with primary infection and infected naïve animals > All animals developed anamnestic antibody responses following re-challenge→ protection mediated by immunologic control
Cell 20MAY2020	**Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals**	Grifoni et al., USA gotopaper	Immuno	Measuring immunity to SARS-CoV-2 is key for understanding COVID-19 and vaccine development •Epitope pools detect CD4+ and CD8+ T cells in 100% and 70% of convalescent COVID patients •T cell responses are focused not only on spike but also on M, N, and other ORFs •T cell reactivity to SARS-CoV-2 epitopes is also detected in non-exposed individuals

Journal and date	Title	Authors and link	Field of expertise	Key facts
The Lancet Infectious Diseases 20MAY2020	**Individual quarantine versus active monitoring of contacts for the mitigation of COVID-19: a modelling study**	Peak, C. et al, USA gotopaper	Public Health/Epidemio	**Aim:** to estimate the comparative efficacy of individual quarantine and active monitoring of contacts to control SARS-CoV-2, fitting a model to the incubation period distribution (mean 5.2 days) and to two estimates of the serial interval distribution (4.8 and 7.5 days). Two feasibility settings: - high-feasibility (90% of contacts traced, half-day average delay in tracing and symptom recognition, 90% effective isolation) - low-feasibility (50% of contacts traced, 2-day average delay, 50% effective isolation). → Mean time of infectiousness onset before symptom onset : 0.77 days (shorter serial interval) and 0.51 days (longer serial interval). → Individual quarantine in high-feasibility settings (>75% of infected contacts individually quarantined), contains an outbreak of SARS-CoV-2 with a short serial interval 84% of the time. In low-feasibility setting: the outbreak continues to grow and so does the burden of the number of contacts traced for active monitoring or quarantine, particularly asymptomatic contacts. **Conclusion:** When resources are prioritised for scalable interventions such as physical distancing, active monitoring or individual quarantine of high-risk contacts, this can contribute synergistically to mitigation efforts.
Science 20MAY2020	**DNA vaccine protection against SARS-CoV-2 in rhesus macaques**	Yu et al., USA gotopaper	Vaccine	**Development of a series of DNA vaccine candidates expressing different forms of the SARS-CoV-2 Spike (S) protein and evaluated them in 35 rhesus macaques.** -> humoral and cellular immune response with neutralizing antibody (titers = those found in convalescent humans and macaques). -> challenged with SARS-CoV-2: the vaccine encoding the full-length S protein resulted in >3.1 and >3.7 log10 reductions in median viral loads in bronchoalveolar lavage and nasal mucosa. -> Vaccine-elicited neutralizing antibody titers correlated with protective efficacy: **suggests an immune correlate of protection**
JAMA 20MAY2020	**Nasal Gene Expression of Angiotensin-Converting Enzyme 2 in Children and Adults**	Bunyavanich, Supinda, *et al.* USA gotopaper	Clinic	Nasal epithelium from 305 individuals aged 4-60, with or without asthma (Mount Sinai Health System, New York, during 2015-2018) collected using a cytology brush. **ACE2 gene expression in nasal epithelium:** **- lowest in aged <10 yrs, and significantly higher in older children (10-17 yrs), young adults (18-24 yrs), and adults (≥25 yrs).** - ACE2 gene expression and age was independent of sex and asthma. **-> Lower ACE2 expression in children nasal epithelium relative to adults may help explain why COVID-19 is less prevalent in children.** Limitation: study did not include individuals older than 60 years.

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 19MAY2020	**Respecting disability rights – towards improved crisis standards of care**	Mello M. et al, US gotopaper	HSS/Politic	Policymakers and hospitals can take key steps to honor commitments to antidiscrimination principles while appropriately stewarding scarce resources during a public health emergency. **1- Do not use categorical exclusions**. Patients must not be categorically excluded from access to treatment because of a disability or diagnosis. Consider not whether someone has a disability but patient's prospects of benefiting from treatment. **2- Do not use perceived quality of life** = biases in how the public/physicians evaluate the quality of life of persons with disabilities. **3- Use hospital survival and near-term prognosis but not long-term life expectancy**. Predictions of long-term life expectancy are much more uncertain + prone to bias than predictions of short-term survival + affected by social circumstances (poverty). Ignoring near-term prognosis can produce outcomes inconsistent with responsible stewardship of scarce resources. **4- Designate triage officers as the decision-makers and train them to respect disability rights.** **Include disability rights advocates in policy development and dissemination =** it will also help in avoiding inflammatory language and ensure public understanding for operationalization.
Clinical Infectious Diseases 19MAY2020	**Early Short Course Corticosteroids in Hospitalized Patients with COVID-19**	Fadel, Raef et al. USA gotopaper	Therapeutic	**Multi-center quasi-experimental study** of 213 adult patients with confirmed moderate to severe COVID, 81 (38%) and 132 (62%) in SOC and **early short course corticosteroid** (methylprednisolone) groups, respectively. Outcomes were evaluated with a primary composite endpoint of escalation of care from ward to ICU, new requirement for mechanical ventilation, and mortality. - The composite endpoint occurred at a significantly lower rate in the early corticosteroid group (34.9% vs. 54.3%, p=0.005). Treatment effect observed within each individual component of the composite endpoint. - Significant reduction in median hospital length of stay was also observed in the early corticosteroid group (8 vs. 5 days, $p < 0.001$). - Multivariate regression analysis demonstrated an independent reduction in the composite endpoint at 14-days controlling for other factors (aOR: 0.41; 95% CI [0.22 – 0.77]). Conclusion: **An early short course of methylprednisolone in patients with moderate to severe COVID-19 reduced escalation of care and improved clinical outcomes**. **Limitations**: pragmatic quasi-experimental design was used and there are some differences in the baseline characteristics of the comparator groups ; limited follow up period of 14 days.

Journal and date	Title	Authors and link	Field of expertise	Key facts
J Infect Dis 19MAY2020	**Influence of storage conditions on SARS-CoV-2 nucleic acid detection in throat swabs**	Li, Lin and al. China gotopaper	Virology	For the detection of SARS-CoV-2 infection, samples often need to be shipped or inactivated before SARS-CoV-2 testing. In this study, we checked the influence of sample storage conditions on SARS-CoV-2 nucleic acid testing results, including sample inactivation time, storage temperature and the time. All of these conditions caused an increase in the Ct values of the nucleic acid tests and led to the misclassification of at least 10.2% of positive cases as negative or suspected. CL°: results highlight the importance of immediate testing of samples for SARS-CoV-2 nucleic acid and detection.
Lancet 19MAY2020	**Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study**	Cummings MJ et al USA gotopaper	Clinic	2 hospitals in NY – critically ill patient with COVID-19 – At least 28 days of observation 1150 adults admitted COVID-19 which **257 (22%) were critically ill (**included) Median age: 62 years – 67% male – 82% at least one comorbidity (HTA, diabetes) 46% had obesity Treatment - 72% received hydroxychloroquine and 9% remdesivir - 26% received corticosteroid - 66% received vasopressor - 31% received RRT Outcomes: - 79% received IMV median of 18 days - **39% died (median of 9 days in the hospital)** and 37% remained hospitalized Association with in hospital death (significantly) - Older age aHR: 1,31 [1,09 – 1,57] per 10 years increase - Chronic cardiac disease aHR: 1,76 [1,08 – 2,86] - Chronic pulmonary disease aHR: 2,94 [1,48 – 5,84] - Concentration of IL-6 aHR: 1,11 [1?02 – 1,20] per decile increase - Concentration of D-dimer aHR: 1,10 [1,01 – 1,19] per decile increase → **high frequency of IMV & in hospital mortality**
Nature Medicine 19MAY2020	**Artificial intelligence–enabled rapid diagnosis of patients with COVID-19**	Mei et al., USA gotopaper	Diagnostic	Use of artificial intelligence (AI) algorithms to integrate chest CT findings with clinical symptoms, exposure history and laboratory testing to rapidly diagnose patients who are positive for COVID-19. -> In a test set of 279 patients, the AI system achieved an area under the curve of 0.92 and had equal sensitivity as compared to a senior thoracic radiologist. -> The AI system also improved the detection of patients who were positive for COVID-19 via RT–PCR who presented with normal CT scans, correctly identifying 17 of 25 (68%) patients, whereas radiologists classified all of these patients as COVID-19 negative **When CT scans and associated clinical history are available, the proposed AI system can help to rapidly diagnose COVID-19 patients.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Circulation 19MAY2020	**Deep Vein Thrombosis in Hospitalized Patients with Coronavirus Disease 2019 (COVID-19) in Wuhan, China: Prevalence, Risk Factors, and Outcome**	Zang L et al, China gotopaper	Clinic	Investigation of deep vein thrombosis (DVT) in hospitalized patient with COVID-19 143 patients from Jan 29 and Feb 29 Demographic: 51,7% man – median age= 63 46,1% (66) lower extremity DVT= 23 proximal DVT and 43 distal DVT DVT vs no DVT: - Older - Lower oxygenation index - Higher rate of cardiac injury - Increase death (23 vs 9, p=0,001) Multivariate analysis, DVT associated with - CURB-65 score3-5, OR:6,12 - Padua prediction ≥ 4, OR: 4,01 - D-dimer>1µg/ml OR :5,81 Predicting DVT **CURB-65 score3-5, Padua prediction score ≥ 4 + D-dimer>1 had Se 88% and Spe 61,4%** → prevalence of DVT is high → importance of prophylaxis for venous thromboembolism (Padua prediction score ≥ 4)
Science 18MAY2020	**Susceptible supply limits the role of climate in the early SARS-CoV-2 pandemic**	Baker, Rachel E. et al. USA gotopaper	Climate	Climate-dependent model to simulate SARS-CoV-2 pandemic, probing different scenarios based on known coronavirus biology. Results suggest: • **While climate may play a role in details of the size and timescales of an endemic outbreak, population immunity is a much more fundamental driver of pandemic invasion dynamics**. • **Both tropical and temperate locations should prepare** for severe outbreaks and **summertime temperatures will not effectively limit spread** of infection. • **Endemic cycles will likely be tied to climate factors and seasonal peaks may vary with latitude.**
Cell 18MAY2020	**Potent neutralizing antibodies against SARS-CoV-2 identified by high-throughput single-cell sequencing of convalescent patients' B cells**	Yunlong Cao et al., Chine, gotopaper	Immunology	Rapid and efficient identification of SARS-CoV-2 neutralizing antibodies achieved by high-throughput single-cell RNA and VDJ sequencing of antigen-binding B cells from 60 convalescent COVID-19 patients reveal over 8,500 antigen-binding B cell clonotypes expressing IgG1 antibodies. => among of which,14 potent neutralizing mAbs were identified => one of them, BD-368-2, exhibited an IC50 of 1.2 ng/mL and 15 ng/mL against pseudotyped and authentic SARS-CoV-2. => in vivo experiments confirmed that BD-368-2 provide strong therapeutic efficacy and prophylactic protection against SARS-CoV-2, using the hACE2 transgenic mice model Conclusion: The potent neutralizing antibodies we identified may provide an effective therapeutic and prophylactic solution Limitation: deeper sequencing of the scRNA libraries is needed to further evaluate the effectiveness of removing exhausted memory B cells to improve the identification of neutralizing mAbs.
Ann. Intern. Med. 18MAY2020	**Tocilizumab for Hemophagocytic Syndrome in a Kidney Transplant Recipient With COVID-19**	Faguer, Stanislas et al. France, gotopaper	Therapeutic	**Case Report** describing an i**mmunocompromised patient with COVID-19 and a related hemophagocytic syndrome** who was treated with **tocilizumab**. The cytokine storm and multiorgan failure **rapidly reversed**, and the patient made a **speedy recovery**. On hospital day 30, the patient was breathing spontaneously with protective tracheotomy, and rehabilitation is ongoing.

Journal and date	Title	Authors and link	Field of expertise	Key facts
The Lancet Diabetes & Endocrinology 18MAY2020	**Prevalence of obesity among adult inpatients with COVID-19 in France**	Caussy, Cyrielle et al. France gotopaper	Population studies	**Lyon University Hospital admissions** with BMI values: 340 patients with confirmed severe COVID-19 (68% non-critical and 32% critical COVID-19 patients) vs 1210 retrospective non-COVID-19 ICU patients admitted each year between 2007 - 2019. Results : - 25% of severe COVID-19 patients had obesity, vs 15·3% in French adult population in 2014. **-> Obesity prevalence 1·35 times higher in severe COVID-19 patients vs general French population.** **-> In ICU, obesity prevalence 1.89 times higher vs general population.** **-> Obesity prevalence higher in critical vs non-critical COVID-19 patients.** In agreement with preliminary data from 124 patients with critical COVID-19 and 306 ICU patients without COVID-19 from **Lille University Hospital (Simonnet A *et al.* 2020)** : **-> obesity prevalence 2·88 times higher in critical COVID-19 vs French general population** **-> Obesity prevalence higher in critical COVID-19 vs Lille ICU patients without COVID-19 (n=306).** **=> Report significant association in obesity prevalence and severe COVID-19, including critical COVID-19, and suggests obesity => risk factor of pejorative evolution of COVID-19, increasing risk of ICU admission.**
Circulation 17MAY2020	**Acute heart failure in multisystem inflammatory syndrome in children (MIS-C) in the context of global SARS-CoV-2 pandemic**	Belhadjer S et al, France gotopaper	Clinic	A series of children admitted to PICU for cardiogenic shock + left ventricular dysfunction + severe inflammatory state (14 centers) 35 children – median age: 10 y [2 – 16] Comorbidities: 28% of the children which 17% were overweight Symptoms: Fever and asthenia (100%) / Gastrointestinal symptoms (83%) / Respiratory distress (65%) – rhinorrhea (43%) Left ventricular ejection at baseline < 30 for 28% / 30 to 50 for 72% Laboratory: cytokine storm → high IL-6 and D-dimer (= macrophage activation) + elevation of CRP and PCT 88% were positive for SARS-CoV-2 (nasopharyngeal swabs or serology) Treatment: 94% Respiratory support: invasive (62%) – noninvasive (32%) / 28% ECMO / 80% inotropic support / 100% IV globuline / 1/3 received steroid therapy At discharge: 25/35 had left ventricular function restored - no death **→ SARS-COV-2 + severe inflammatory state in children → acute cardiac decompensation**
The Journal of Antimicrobial Chemotherapy 17MAY2020	**COVID-19 infection also occurs in patients taking hydroxychloroquine**	Lahouati, M et al. France gotopaper	Therapeutic	Report on **two severe cases of COVID-19 in patients already using hydroxychloroquine for a long time** to treat inflammatory disease. **High plasma levels of hydroxychloroquine** collected on admission in those cases confirm chronic exposure and adherence to hydroxychloroquine. These values are **close to or higher than the EC50** described by Yao et al. not taking into account lung diffusion. Those potentially immunosuppressed patients do not represent the general population exposed to COVID-19. It cannot be excluded that chloroquine and hydroxychloroquine negatively impact the early inflammatory response to the virus and the risk of acquisition of infection owing to their anti-inflammatory activity. These **observational data** are **not in favour of a universal protective effect of hydroxychloroquine**, and clinicians should use it carefully, awaiting the results of clinical trials, particularly in the context of prevention.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Water research 16MAY2020	**SARS-CoV-2 RNA in wastewater anticipated COVID-19 occurrence in a low prevalence area**	Randazzo et al, Spain gotopaper	Public Health/Epidemio	**Faecal shedding of SARS-CoV-2 RNA from COVID-19 patients has extensively been reported.** We investigated the occurrence of SARS-CoV-2 RNA in six wastewater treatments plants serving the major municipalities within the Region of Murcia, Spain (low COVID-19 prevalence). -> The estimated quantification of SARS-CoV-2 RNA titers in untreated wastewater waters of 5.4 ± 0.2 log10 genomic copies/L on average. -> Two secondary water samples resulted positive (2/18) and all tertiary water samples tested as negative (0/12). SARS-CoV-2 RNA shedding in stools was present even before the first cases were reported by the authorities. **This strategy could be implemented in environmental surveillance as an early indicator of the infection within a specific population.**
Developmental Cell 16MAY2020	**Cigarette smoke exposure and inflammatory signaling increase the expression of the SARS-CoV-2 receptor ACE2 in the respiratory tract**	Smith, Joan C. *et al.* USA gotopaper	Fundamental research	Cigarette smoke causes dose-dependent upregulation of ACE2 receptor in rodent and human lungs. Single-cell sequencing data: - **ACE2 expressed in a subset of secretory cells in respiratory tract**. - **Chronic smoke exposure** triggers **expansion of this cell population** and **increased ACE2 expression**. - **Quitting smoking has convers effect** (decreases this cell population and ACE2 levels). - ACE2 expression responsive to inflammatory signalling and upregulated by viral infections / interferon treatment. -> May partially explain why smokers are particularly susceptible to severe SARS-CoV-2 infections **-> identifies ACE2 as interferon-stimulated gene in lung cells -> possible positive-feedback loops increasing ACE2 levels and facilitating viral dissemination.**
J. Clin. Virol. 16MAY 2020	**A combined oropharyngeal/nares swab is a suitable alternative to nasopharyngeal swabs for the detection of SARS-CoV-2**	LeBlanc, Jason J. and al., Canada gotopaper	Diagnostic	Given the global shortage of nasopharyngeal (NP) swabs typically used for respiratory virus detection, alternative collection methods were evaluated during the COVID-19 pandemic. This study showed that a combined oropharyngeal/nares swab is a suitable alternative to NP swabs for the detection of SARS-CoV-2, with sensitivities of 91.7% and 94.4%, respectively.
The Lancet Infectious Diseases 15MAY2020	**Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study**	Lusignan, Simon de et al. UK-South Africa gotopaper	Clinic	Routinely collected, pseudonymised data for patients in the RCGP Research and Surveillance Centre primary care network +ve for SARS-CoV-2 (Jan 28 - April 4 2020): - 587 SARS-CoV-2 +ve out of 3802 test results. - male sex independently associated with testing +ve (18 vs 13 % for women) **Clinical factors and demographics more likely to testing +ve :** - Adults, in particular **ages 40-64**, vs children (19 % in aged 40-64 vs 5 % in children) - People with **chronic kidney disease** (33 vs 14 % without chronic kidney disease), but no significant association with other chronic conditions. - **Obese people** (21 vs 13 % for people of normal weight) - **Active smoking at decreased odds of testing +ve** (11 vs 18 % in non-smokers) - **black people** vs white (62 vs 16 %) - **People living in urban areas** vs rural areas (26 vs 5·6% in rural areas) - **People living in deprived areas** (30 vs 8% in least deprived areas) -> +ve SARS-CoV-2 test results in primary care cohort was associated with similar risk factors as for severe outcomes of COVID-19 in hospital settings, except for smoking. -> Provides evidence of potential sociodemographic factors associated with a +ve test : deprivation, population density, ethnicity and chronic kidney disease.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Gastroenterology 15MAY2020	**Associations between Angiotensin Converting Enzyme Inhibitors and Angiotensin II Receptor Blocker Use, Gastrointestinal Symptoms, and Mortality among Patients with COVID-19**	Tan, Nian-Di et al. China gotopaper	Therapeutic/ Clinic	**Retrospective cohort study** of consecutive patients with COVID-19. Among the **100 participants with hypertension**, 31 were classified as ACEI/ARB group and the remaining 69 were classified as non-ACEI/ARB group. **Inpatient treatment with ACEI/ARB** was associated with **lower risk of digestive system involvement** and **lower risk of all-cause mortality** compared with ACEI/ARB non-users in COVID-19 patients with hypertension. **Limitations**: small sample-size, possible unappreciated confounding effect.
Science 15MAY2020	**Serology assays to manage COVID-19**	Krammer F., Simon V., USA gotopaper	Public Health/Epidemiol	Measurement of antibodies to SARS-CoV-2 will improve disease management if used correctly. This perspective article describes the serological assays available and discusses the potential applications, including: - understand the antibody responses mounted upon SARS-CoV-2 infection and vaccination; - inform on the prevalence of SARS-CoV-2 infection if different populations; - identification of donors for convalescent plasma therapy; - identify individuals who are immune (and the caveats concerning this point). **With high-quality serological assays now available, the key challenge will be to apply and deploy these tests in a strategic manner.**
Clinical microbiology and infection 15MAY2020	**A multiple center clinical evaluation of an ultra-fast single-tube assay for SARS-CoV-2 RNA**	Wang, Ji and al. China gotopaper	Diagnostic	To evaluate the performance of an ultra-fast single-tube nucleic acid isothermal amplification detection assay for SARS-CoV-2 RNA using clinical samples from multiple centers. A reverse transcription recombinase-aided amplification (RT-RAA) assay for SARS-CoV-2 was conducted within 15minutes at 39°C with portable instruments after addition of extracted RNA. The clinical performance of RT-RAA assay was evaluated using 947 clinical samples and the approved commercial real-time fluorescent RT-PCR (qRT-PCR) kits were used for parallel detection. The sensitivity and specificity of RT-RAA were compared and analyzed. CI°: with comparable sensitivity and specificity to the commercial qRT-PCR kits, RT-RAA assay for SARS-CoV-2 exhibited distinctive advantages of simplicity and rapidity in terms of operation and turn-around time.
Science 15MAY2020	**Inferring change points in the spread of COVID-19 reveals the effectiveness of interventions**	Dehning et al., Germany gotopaper	PublicHealth/Epidemio	**By combining an established epidemiological model with Bayesian inference -> analysis of the time dependence of the effective growth rate of new infections** Focusing on COVID-19 spread in Germany, detection of change points in the effective growth rate that correlate well with the times of publicly announced interventions -> Possibility to quantify the effect of interventions, and we can incorporate the corresponding change points into forecasts of future scenarios and case numbers. This code is freely available and can be readily adapted to any country or region.
Nature 14MAY2020	**Proteomics of SARS-CoV-2-infected host cells reveals therapy targets**	Bojkova, Denisa et al. Germany gotopaper	Therapeutic	**Identification of the host cell pathways** modulated by SARS-CoV-2 infection and inhibition of these pathways showed to prevent viral replication in human cells. A **human cell culture model for infection** with SARS-CoV-2 clinical isolate was established. Employing this system, the **SARS-CoV-2 infection profile** was determined by translatome3 and proteome proteomics at different times after infection. These analyses revealed that SARS-**CoV-2 reshapes central cellular pathways, such as translation, splicing, carbon metabolism and nucleic acid metabolism**. **Small molecule inhibitors targeting these pathways prevented viral replication in cells**.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 14MAY2020	**Use of renin–angiotensin–aldosterone system inhibitors and risk of COVID-19 requiring admission to hospital: a case-population study**	Abajo, Francisco J. De, et al. Spain gotopaper	Therapeutic/ Clinic	**Case-population study** of consecutively selected hospitalized patients with a PCR-confirmed diagnosis of COVID-19, and randomly sampled ten patients per case, individually matched for age, sex, region, and date of admission to hospital as a reference group. **1139 cases** and **11 390 population controls**. Despite being matched on sex and age, a significantly higher proportion of cases had pre-existing cardiovascular disease (OR 1·98, 95% CI 1·62–2·41) and risk factors (1·46, 1·23–1·73) than did controls. The **current use of RAAS inhibitors** is **not associated with an increased risk of COVID-19 requiring admission to hospital** (including fatal cases and those admitted to an ICU) compared with other antihypertensive drugs. No substantial difference was observed between ACE inhibitors and angiotensin-receptor blockers, nor among short-term and long-term users. Sex, age, and background cardiovascular risk did not significantly affect the results, although use of RAAS inhibitors was associated with a reduced risk of COVID-19 requiring admission to hospital in patients with diabetes. **Limitations**: different data sources to extract information from cases and controls ; cases and controls were recorded at different dates ; data on smoking and other lifestyle habits not collected; observational study, residual confounding due to unmeasured or unknown confounders cannot be ruled out.
BMJ 14MAY2020	**Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial**	Tang, Wei et al. China gotopaper	Therapeutic	**Multicentre, randomised, parallel, open label trial** of **hydroxychloroquine** (1200 mg daily for three days, then 800 mg daily) versus standard of care in 150 patients admitted to hospital with covid-19. **No evidence to support an increase in the probability of negative conversion** of SARS-CoV-2 conferred by the addition of hydroxychloroquine administration to the current standard of care in patients admitted to hospital with mainly **persistent mild to moderate covid-19**. **Adverse events**, particularly gastrointestinal events, were **more frequently reported** in patients receiving **hydroxychloroquine**. **Limitations**: open label ; use of sequential envelopes for randomisation ; no patients at the early stage of disease ; 148/150 (99%) patients had mild to moderate disease ; underpowered sample size due to the lack of enough eligible patients to enrol.
American journal of obstetrics and gynecology 14MAY2020	**Clinical Characteristics of 46 Pregnant Women with a SARS-CoV-2 Infection in Washington State**	Lokken EM et al, USA gotopaper	Clinic	Description of maternal disease and obstetrical outcomes – 6 hospital in Washington state **46 pregnant women** Demographic: median age: 29y – 6,5% in first & 43,4% second & 50% in third trimester 26,1% had at least one comorbidity: asthma – hypertension – diabetes - …. **28,6% were overweight and 35,7% obese** Symptoms: 93,5% had one – cought (70%) – fever (51%) – dyspnea – headache …. Outcomes: - 15% categorized has severe disease: overweight/obese/comorbidity - 16% hospitalized & 1 to ICU (all severe disease) - 8 delivered during the study period (median: 38,4 week) - 1 stillbirth: unknown etiology → **higher risk group: chronic comorbidity / obese / overweight**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Clinica Chimica Acta 14MAY2020	**The underlying changes and predicting role of peripheral blood inflammatory cells in severe COVID-19 patients: a sentinel?**	Sun, Da-wei and al. China gotopaper	Virology	The underlying changes of peripheral blood inflammatory cells (PBICs) in COVID-19 patients are little known. Moreover, the risk factors for the underlying changes of PBICs and their predicting role in severe COVID-19 patients remain uncertain. This retrospective study includes two cohorts: the main cohort enrolling 45 patients of severe type serving as study group, and the secondary cohort enrolling 12 patients of no-severe type serving as control group. The PBICs analysis was based on blood routine and lymphocyte subsets. The inflammatory cell levels were compared among patients according to clinical classifications, disease-associated phases, as well as one-month outcomes. Results: the patients of severe type suffered from significantly decreased counts of lymphocytes, eosinophils, basophils, but increased counts of neutrophils. These PBICs alterations got improved in recovery phase, but persisted or got worse in aggravated phase. CI°: lymphopenia and eosinopenia may serve as predictors of disease severity and disease progression in COVID-19 patients, and enhancing the cellular immunity may contribute to COVID-19 treatment. Thus, PBICs might become a sentinel of COVID-19, and it deserves attention during COVID-19 treatment
Journal of Allergy and Clinical Immunology 14MAY2020	**Complement activation in patients with COVID-19: a novel therapeutic target**	Cugno, Massimo et al. Italy gotopaper	Therapeutic	Preliminary data providing evidence of **complement activation** in patients with COVID-19 with **different degrees of respiratory failure**. Investigation of the **plasma levels of sC5b-9 and C5a** as markers of complement activation in 31 COVID-19 patients, compared with 27 healthy subjects. - **Plasma levels of sC5b-9** were **significantly higher** in the patients with moderate disease and those with severe disease **than in the healthy controls**, and **significantly higher** in the patients with **severe disease** than in those with moderate disease. - The **plasma levels of C5a** were **higher** in the patients with moderate disease and those with severe disease **than in the healthy** (P=0.0001 for both), with no statistically significant difference between the two patient groups. - The cohort of patients had **increased levels of acute-phase proteins and coagulation system abnormalities**. Complement activation may contribute to the development of lung and endothelial damage in patients. Possibility that the coronavirus may directly cause damage to endothelial cells.
BMJ 14MAY2020	**Clinical efficacy of hydroxychloroquine in patients with covid-19 pneumonia who require oxygen: observational comparative study using routine care data**	Mahévas, Matthieu et al. France gotopaper	Therapeutic	**Comparative study** that uses **real world data** collected from routine care to assess the **efficacy and safety of hydroxychloroquine** in a population of **181 patients** admitted to hospital with covid-19 hypoxaemic pneumonia. - Hydroxychloroquine treatment at 600 mg/day added to standard care was **not associated with a reduction of admissions to the intensive care unit or death** 21 days after hospital admission compared with standard care alone. - The **rate of survival without acute respiratory distress syndrome did not increase**. - Eight patients in the treatment group (10%) experienced **electrocardiographic modifications that required discontinuation of treatment**. The results of this study do not support its use in patients admitted to hospital with covid-19 who require oxygen. **Limitations**: observational data, centre effect not taken into account ; limited sample ; only patients admitted to hospital.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Clinical Infectious Disease 14MAY2020	**Risk Factors of Severe Disease and Efficacy of Treatment in Patients Infected with COVID-19: A Systematic Review, Meta-Analysis and Meta-Regression Analysis**	Zhang, John J. Y et al. Singapore gotopaper	Therapeutic/ Clinic	**Systematic review and meta-analysis** on COVID-19 clinical features and/or treatment outcomes. **45 studies** reporting **4203 patients** were included. Pooled rates of intensive care unit (ICU) admission, mortality and acute respiratory distress syndrome (ARDS) were 10.9%, 4.3% and 18.4%, respectively. - On meta-regression, **ICU admission** was **predicted by raised leukocyte count** (p<0.0001), **raised alanine aminotransferase** (p=0.024), **raised aspartate transaminase** (p=0.0040), **elevated lactate dehydrogenase** (LDH) (p<0.0001) and **increased procalcitonin** (p<0.0001). - **ARDS** was **predicted by elevated LDH** (p<0.0001), while **mortality** was **predicted by raised leukocyte count** (p=0.0005) and **elevated LDH** (p<0.0001). - Treatment with **lopinavir-ritonavir** showed **no significant benefit in mortality and ARDS rates**. **Corticosteroids** were associated with a **higher rate of ARDS** (p=0.0003). **Limitations**: possible selection bias (publications in English) ; only studies from Asia at the time of the literature search ; studies included were observational ; heterogeneity in the range of symptoms and comorbidities recorded in the different studies.
Nature 14MAY2020	**Infection of dogs with SARS-CoV-2**	Sit, Thomas H. C Hong Kong gotopaper	Fundamental research	**2/15 dogs from households with confirmed human COVID-19 cases** in Hong Kong were found to be infected (qRT–PCR, serology, viral genome sequencing, and virus isolation in 1 dog): - a 17yr-old male Pomeranian (SARS-CoV-2 RNA detected from 5 nasal swabs over 13-days). - a 2.5yr-old male German Shepherd dog (SARS-CoV-2 RNA on two occasions and virus isolated from nasal and oral swabs) - Both had antibody responses (plaque reduction neutralization assays). **- Viral genetic sequences from both dogs were identical to virus detected in respective human cases. Animals asymptomatic during quarantine.** **-> These are instances of human-to-animal transmission of SARS-CoV-2**. Unclear whether infected dogs can transmit the virus to other animals or back to humans.
Nature 14MAY2020	**Pathogenesis and transmission of SARS-CoV-2 in golden hamsters**	Sia, Sin Fun et al. Hong Kong gotopaper	Animal model	Pathogenesis and transmissibility of the SARS-CoV-2 in **golden Syrian hamsters** (intranasal infection): - viral antigens (immunohistochemistry) in nasal mucosa, bronchial epithelial cells and in areas of lung on 2 and 5 dpi, followed by rapid viral clearance and pneumocyte hyperplasia on 7 dpi. - Viral antigen found in duodenum epithelial cells and viral RNA in feces. -> **Efficient SARS-CoV-2 transmission from inoculated hamsters to naïve by direct contact and via aerosols**. Transmission via fomites less efficient. **-> Communicable period was short and correlated with detection of infectious virus but not viral RNA.** **-> Inoculated and naturally-infected hamsters showed apparent weight loss, and all animals recovered with detection of neutralizing antibodies.**
Proc. Natl. Acad. Sci. U. S. A. 13MAY2020	**The airborne lifetime of small speech droplets and their potential importance in SARS-CoV-2 transmission**	Stadnytskyi et al. USA gotopaper	Public Health/Epidemio	Speech droplets generated by asymptomatic carriers of SARS-CoV-2 likely to be a mode of disease transmission. -> Highly sensitive laser light scattering observations have revealed that loud speech can emit thousands of oral fluid droplets per second. -> In a closed, stagnant air environment, they disappear from the window of view with time constants in the range of 8 to 14 min (droplet nuclei of *ca.* 4 µm diameter, or 12- to 21-µm droplets prior to dehydration). **There is therefore a substantial probability that normal speaking causes airborne virus transmission in confined environments**.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Science 13MAY2020	**Estimating the burden of SARS-CoV-2 in France**	Salje et al., France gotopaper	Public Health/Epidemio	Using models applied to hospital and death data, we estimate the impact of the lockdown and current population immunity in France. -> We find 3.6% of infected individuals are hospitalized and 0.7% die (0.001% in <20 years of age (ya), 10.1% in >80ya). The lockdown reduced the reproductive number from 2.90 to 0.67 (77% reduction). By 11 May 2020, when interventions are scheduled to be eased, we project that 4.4% (range: 2.8–7.2) of the population will have been infected. Population immunity appears insufficient to avoid a second wave if all control measures are released at the end of the lockdown
Ann. Intern. Med. 13MAY2020	**Variation in False-Negative Rate of Reverse Transcriptase Polymerase Chain Reaction–Based SARS-CoV-2 Tests by Time Since Exposure**	Kucirka, Lauren M. and al. USA gotopaper	Virology	Tests for SARS-CoV-2 based on RT-PCR are being used to "rule out" infection among high-risk persons, such as exposed inpatients and health care workers. It is critical to understand how the predictive value of the test varies with time from exposure and symptom onset to avoid being falsely reassured by negative test results. Objective: To estimate the false-negative rate by day since infection. CI°: care must be taken in interpreting RT-PCR tests for SARS-CoV-2 infection—particularly early in the course of infection—when using these results as a basis for removing precautions intended to prevent onward transmission. If clinical suspicion is high, infection should not be ruled out on the basis of RT-PCR alone, and the clinical and epidemiologic situation should be carefully considered.
N. Engl. J. Med. 13MAY2020	**Multiorgan and Renal Tropism of SARS-CoV-2**	Puelles, Victor G. et al Germany gotopaper	Cellular tropism	**Autopsy series from** 22 patients who died from Covid-19: - 77% had more than 2 coexisting conditions, and **greater coexisting conditions associated with SARS-CoV-2 tropism for kidneys.** **- highest SARS-CoV-2 copies per cell = respiratory tract,** **- lower viral copies per cell = kidneys, liver, heart, brain, and blood.** **Kidney** tissue microdissection from 6 patients : - 3 = detectable SARS-CoV-2 **viral load in all kidney compartments** examined, with **preferential targeting of glomerular cells**. **-> SARS-CoV-2 organotropism beyond respiratory tract includes heart, liver, brain, and kidneys. Renal tropism is a potential explanation of commonly reported new clinical signs of kidney injury in Covid-19 patients**
The Journal of Molecular Diagnostics 13MAY2020	**Detection of SARS-CoV-2 is comparable in clinical samples preserved in saline or viral transport media**	Radbel, Jared and al. USA gotopaper	Virology	The availability of viral transport media (VTM) has become severely limited, contributing to delays in diagnosis and rationing of diagnostic testing. The phosphate buffered saline (PBS) may be a viable transport medium, as an alternative to VTM, for clinical qPCR testing. We assessed the intra- and inter-individual reliability of SARS-CoV-2 qPCR in clinical endotracheal secretion samples transported in VTM or PBS, evaluating the stability of the RT-qPCR signal for three viral targets (N gene, ORF1ab, and S gene) when samples were stored in these media at room temperature for up to 18 hours. Results: using PBS as a transport medium has high intra-and inter-individual reliability, maintains viral stability, and is comparable to VTM in the detection of the three SARS-CoV-2 genes through 18 hours of storage. CI°: PBS as a clinically useful medium for transporting and short-term preservation of specimens containing SARS-CoV-2 has the potential to increase testing capacity for SARS-CoV-2

Journal and date	Title	Authors and link	Field of expertise	Key facts
Lancet 13MAY2020	**An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study**	Verdoni L et al Italy gotopaper	Clinic	29 children with Kawasaki disease Group1(n=19): before SARS-CoV-2 outbreak Group2(n=10): after SARS-CoV-2 outbreak Group1 versus group2: - Higher incidence in group2: 0,3 vs 10/month (p<0,05) - Older group2: 3,0 vs 7,5 y (p<0,05) - Abnormal echocardiogram: 60%(grp2) vs 10%(grp1), p<0,05 - More MAS group2: 50% vs 0% → 30-fold increased incidence of KD in the past month → **SARS-CoV-2 outbreak is associated with high incidence of severe form of KD**
Nature Medicine 13MAY2020	**Infection of bat and human intestinal organoids by SARS-CoV-2**	Zhou, Jie et al. Hong Kong gotopaper	Fundamental research	Establishment and characterization of intestinal organoids derived from horseshoe bats (*Rhinolophus sinicus*) can recapitulate bat intestinal epithelium: - bat enteroids are fully susceptible to SARS-CoV-2 infection and robust viral replication. - human intestinal organoids also sustain active replication of SARS-CoV-2 **-> First expandable organoid culture system of bat intestinal epithelium and evidence that SARS-CoV-2 can infect bat intestinal cells.** -> Robust SARS-CoV-2 replication in human intestinal organoids suggests that the human intestinal tract might be a transmission route of SARS-CoV-2.
JAMA 13MAY2020	**SARS-CoV-2 Rates in BCG-Vaccinated and Unvaccinated Young Adult**	Hamiel et al., Israel gotopaper	Vaccine	The BCG vaccine was routinely administered to all new-borns in Israel as part of the national immunization program between 1955 and 1982 Since 1982, the vaccine has been administered only to immigrants from countries with high prevalence of tuberculosis. This change allowed comparison of infection rates and propor- tions with severe COVID-19 disease in 2 similar populations with differing BCG status: individuals born during the 3 years before and 3 years after cessation of the universal BCG vaccine program. **-> This study does not support the idea that BCG vaccination in childhood has a protective effect against COVID-19 in adulthood.**
Annals of Internal Medicine 12MAY2020	**Pharmacokinetics of Lopinavir and Ritonavir in Patients Hospitalized With Coronavirus Disease 2019 (COVID-19)**	Schoergenhofer, Christian et al. Austria gotopaper	Therapeutic	**First pharmacokinetic data of lopinavir and ritonavir** in patients **hospitalized** with COVID-19. Series of 8 patients. - Lopinavir trough levels were approximately **2-fold higher** in this population **than in patients with HIV** receiving the same dose (7.1 µg/mL). - A correlation of drug concentrations with C-reactive protein, a downstream marker of IL-6, was observed. However, approximately **60- to 120-fold higher concentrations are required to reach the assumed EC50 at trough levels**, making effective treatment of COVID-19 with lopinavir and ritonavir at the currently used doses unlikely. **Limitations**: only trough levels were quantified, more detailed pharmacokinetics not available ; no data on the half-maximal effective dose of lopinavir for SARS-CoV-2 in vivo.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 12MAY2020	**Respiratory disease in rhesus macaques inoculated with SARS-CoV-2**	Munster, Vincent J. et al. USA gotopaper	Animal model	SARS-CoV-2 causes respiratory disease in infected rhesus macaques, with disease lasting 8-16 days: - 8 adult rhesus macaques (4 males, 4 females, age 4-6 yrs) inoculated with combination of intranasal (0.5ml per nostril), intratracheal, oral and ocular of a $4x10^5$ TCID50/ml ($3x10^8$ genome copies/ml). - Pulmonary infiltrates visible in lung radiographs - High viral load in nose and throat swabs and bronchoalveolar lavages of all animals. - prolonged rectal shedding detected in 1 animal **-> Rhesus macaque recapitulates moderate disease with regard to virus replication, shedding, presence of pulmonary infiltrates, histological lesions and seroconversion.**
Nat Med 12MAY2020	**A serological assay to detect SARS-CoV-2 seroconversion in humans**	Amanat et al., USA gotopaper	Diagnostic	**Describing a** a serological enzyme-linked immunosorbent assay for the screening and identification of human SARS-CoV-2 seroconverters. -> based on reactivity to the immunogenic S protein of the virus, is relatively simple and quick in its execution and can be performed at biosafety level 2 -> there is no or only negligible cross-reactivity from human coronaviruses to SARS-CoV-2 in the tested individuals -> strong seroconversion with ELISA AUC values in the 1:1,000 range after natural infection with SARS-CoV-2
Cancer discovery 12MAY2020	**Impact of PD-1 blockade on severity of COVID-19 in patients with lung cancers**	Luo, Jia et al. USA gotopaper	Therapeutic/ Clinic	Analyses on **69 consecutive patients with lung cancers** who were diagnosed with COVID-19. Severity based on no or prior receipt of PD-1 blockade was examined. - Overall, the **severity of COVID-19 in patients with lung cancer was high**, including need for hospitalization in more than half of patients and death in nearly a quarter. - Prior PD-1 blockade was, as expected, associated with smoking status. - After adjustment for smoking status, **PD-1 blockade exposure was not associated with increased risk of severity of COVID-19**. PD-1 blockade does not appear to impact the severity of COVID-19 in patients with lung cancers. These initial results in patients with lung cancers support the **safety of PD-1 blockade treatment to achieve optimal cancer outcomes**.
JAMA Intern Med 12MAY2020	**Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19**	Liang W et al, China gotopaper	Clinic	Develop and validate a clinical score at admission for predicting critical illness Retrospective cohort (575 hospital in China) 1590 patients with data were include for variable selection: - Mean age: 48,9y – 57,3% were men – 25,1% had at least 1 comorbidity - 72 variables entered in selection process (LASSO and logistic regression) 10 variables were independently statistically significant predictors of critical illness: - CXR abnormality: OR: 3,39 - Age OR: 1,03 - Hemoptysis OR 4,53 - Dyspnea OR 1,88 - Unconsciousness OR 4,71 - Number of comorbidities OR 1,60 - Cancer history OR 4,07 - Neutrophil to lymphocyte ratio OR 1,06 - Lactate dehydrogenase OR: 1,002 - Direct bilirubin OR: 1,15 Validation: cohort of 710 patients AUC of COVID-GRAM 0,88 $IC_{95\%}$ [0,84 – 0,93] Limitations: data are entirely from China → **risk score at the admission for predicting critical illness**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 11MAY2020	**Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State**	Rosenberg, Eli S. et al. USA gotopaper	Therapeutic	**Retrospective multicenter cohort study** of **1438 hospitalized patients** who received both hydroxychloroquine and azithromycin, hydroxychloroquine alone, azithromycin alone, or neither. => Compared with patients receiving neither drug, there **were no significant differences in mortality** for patients receiving hydroxychloroquine + azithromycin (HR, 1.35 [95% CI, 0.76-2.40]), hydroxychloroquine alone (HR, 1.08 [95% CI, 0.63-1.85]), or azithromycin alone (HR, 0.56 [95% CI, 0.26-1.21]). => Compared with patients receiving neither drug, **cardiac arrest was significantly more likely in patients receiving hydroxychloroquine + azithromycin** (adjusted OR, 2.13 [95% CI, 1.12-4.05]), but not hydroxychloroquine alone (adjusted OR, 1.91 [95% CI, 0.96-3.81]) or azithromycin alone (adjusted OR, 0.64 [95% CI, 0.27-1.56]). => No significant differences in the relative likelihood of abnormal electrocardiogram findings. **Limitations**: mortality limited to in-hospital death ; potential confounders such as inflammatory markers were not frequently measured ; confidence intervals for some of the findings are wide, reflecting limits in study power for some analyses
Bio-design and manufacturing 11MAY2020	**Development of a rapid test kit for SARS-CoV-2: an example of product design**	Cui, Zhanfeng and al. China gotopaper	Diagnostic	The urgent need for large numbers of tests in field setting imposes constraints such as short test time and lack of access to specialist equipment, laboratories and skilled technicians to perform the test and interpret results. To meet these needs, an antigen test based on RT-LAMP with colorimetric readout was chosen. Direct use of swab sample with no RNA extraction was explored. After extensive experimental study, a rapid test kit has been fabricated to satisfy all design criteria
J. Clin. Microbiol. 11MAY2020	**Open Development and Clinical Validation Of Multiple 3D-Printed Nasopharyngeal Collection Swabs: Rapid Resolution of a Critical COVID-19 Testing Bottleneck**	Callahan, Cody J. and al. USA gotopaper	Diagnostic	To address the shortage of the nasopharyngeal swabs, we designed and executed a translational-research program to allow immediate mass production by 3D printing. We validated four prototypes through an institutional review board (IRB)-approved clinical trial that involved 276 outpatient volunteers. Each participant was swabbed with a reference swab (the control) and a prototype, and SARS-CoV-2 reverse-transcriptase polymerase chain reaction (RT-PCR) results were compared. All prototypes displayed excellent concordance with the control. Contact information for ordering can be found at http://printedswabs.org
Nature Medicine 11MAY2020	**Real-time tracking of self-reported symptoms to predict potential COVID-19**	Menni et al, UK gotopaper	Public Health/Epidemio	A total of 2,618,862 participants reported their potential symptoms of COVID-19 on a smartphone-based app. -> Of 18,401 who had undergone a SARS-CoV-2 test, participants reporting loss of smell and taste was 65.03% in those with a positive test result and 21.72% in those with a negative test result (odds ratio = 6.74; 95% CI = 6.31–7.21). ->A model combining symptoms to predict probable infection was applied to the data from all app users who reported symptoms (805,753) and predicted that 140,312 (17.42%) participants are likely to have COVID-19

Journal and date	Title	Authors and link	Field of expertise	Key facts
Journal of Allergy and Clinical Immunology 11MAY2020	**Safety and efficacy of early high-dose IV anakinra in severe COVID-19 lung disease**	Pontali, Emanuele et al. Italy gotopaper	Therapeutic	**Pilot study** of **early use of high IV doses of anti-IL-1 anakinra** in **5 patients** with severe/moderate COVID-19 with pulmonary involvement. ->All five patients experienced **rapid resolution of systemic inflammation**, and **remarkable improvement of respiratory parameters**, with reduction of oxygen support requirement and early amelioration of chest CT scan abnormalities before discharge in 3 patients. -> All patients were discharged 6 to 13 days after the start of anakinra. -> No secondary infections or other adverse events were observed. **Limitations**: non-controlled study ; small size ; short-term duration of the treatment ; variability of laboratory biomarkers.
Clin. Infect. Dis. 11MAY2020	**Hydroxychloroquine in COVID-19 patients: what still needs to be known about the kinetics**	Martin-Blondel, G. et al. France gotopaper	Therapeutic	Aim: to determine whether or not the pharmacokinetics in systemic lupus erythematosus (SLE) patients can be applied to COVID-19 patients. Different dosage regimens were applied based on data that emerged: regimen 1 (200 mg x 3/day), regimen 2 (400 mg x 2 on day 1 followed by 200 mg x 3/day), regimen 3 (400 mg x 2 on day 1 followed by 400 mg x 1/day) and regimen 4 (600 mg x 2 followed by 400 mg x 1 /day). Blood samples (n=101) were collected from 57 COVID-19 patients for 7 days and concentrations were compared with simulated kinetic profiles. ⇒ **Hydroxychloroquine exposure tends to be low** and in most instances lower than the values reported in SLE patients, in particular for the standard regimen of "200 mg x 3/day". => The **pharmacokinetic behavior in COVID-19 patients cannot be predicted by the SLE population or by rheumatoid arthritis patients**.
European heart journal 11MAY2020	**Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019**	Shi S and al, China gotopaper	Clinic	671 hospitalized patients COVID-19 Median age: 63 years Main cormorbidities: hypertension (29,7%) –diabetes (14,5%) – CHD(9%) Case fatality rate 9,2% <u>Death versus survivor group</u> - Older and more often male (p<0,001) - More comorbidities (p<0,001) - More myocardial injury: 75,8% vs 9,7% (p<0,001) <u>Cardiac troponin I predicting in-hospital mortality:</u> - AUC 0,92 - Se 86% and Spe 86% - Single cut-off concentrations 73 µg/L <u>Predictor of myocardial injury:</u> - Older age – comorbidities - High level of CRP Limitation: small sample size, cause of death or myocardial injury underestimated → **CtnI and CK-MB predict risk for in hospital mortality**

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA ped 11MAY2020	**Characteristics and Outcomes of Children with Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units**	Shekerdemian LS and al, USA gotopaper	Clinic	46 PICU (March 14 and April 3) → 48 children (40 in US & 6 in Canada) Median age: 13 years [4,2 – 16,6] Comorbidities (83%) Median PICU lenght of stay: 5 days Respiratory symptoms: 73 % → 39/48 required ventilatory support: 21 non-invasively and 19 IMV Specific therapies (28/46): Hydroxychloroquine or hydroxy+azythro or remdesivir or tocilizumab Case fatality rate: 4,2% (2/48) →**pre-hospital comorbidities = important factor**
Emerging Infectious Disease journal 08MAY2020	**Prolonged Persistence of SARS-CoV-2 RNA in Body Fluids**	Jiufeng Sun and al. gotopaper	Virology	To estimate the frequency and duration of detectable SARS-Cov-2 RNA in human body fluids. The prolonged persistence of virus RNA in various body fluids may guide the clinical diagnosis and prevention of onward virus transmission. 43 patients with mild cases of COVID-19 - 490 specimens collected. **Results:** through an AFT-based modeling study: persistent shedding of virus RNA in nasopharyngeal swab and feces samples. The estimated time until loss of virus RNA detection ranged from 45.6 days for nasopharyngeal swab samples to 46.3 days for feces samples in mild cases and from 48.9 days for nasopharyngeal swab samples to 49.4 days for feces samples in severe cases (longer than those fo SARS-Cov and MERS-Cov). **CI°:** results show prolonged persistence of SARS-CoV-2 RNA in hospitalized patients with COVID-19. Health professionals should consider these findings in diagnostic recommendations and prevention measures for COVID-19.
Pediatric Blood Cancer 08MAY2020	**COVID-19 infection in children and adolescents with cancer in Madrid**	De Roja T and al, Spain gotopaper	Clinic	15 pediatric oncology patients Median age: 10,6 years [0,6 – 18,6] Hematological malignancy (73%) and solid tumor (27%) 60% received chemotherapy in the 15 days before infection Symptoms: fever (67%) – cough (40%) – asymptomatic (13%) Radiological finding: 8/14 pathological findings 2 patients received oxygen therapy Median hospital stays: 8 days **All favorable outcome** → **prevalence among children with cancer in Madrid: 1,3%** → mild symptomatic and better prognosis than adults
American Journal of Obstetrics & Gynecology MFM 08MAY2020	**Clinical course of severe and critical COVID-19 in hospitalized pregnancies: a US cohort study**	**Rebecca Am, and al USA** gotopaper	Clinic	**64 pregnant women** hospitalized: 44 severe and 20 critical – no death Gestational age at admission: 30 ± 6 weeks Admission: 7 days after onset symptoms Majoration of dyspnea at day 8 and MV at day 9 Median duration of hospital stays: 6 day for severe and 12 for critical Delivery preterm: 75% of critical women - Severe: 37 ± 2 - Critical: 32 ± 4 Critical cases: 95% required MV - 70% ARDS - 20% prone position Neonate: - 64% need ICU - One tested positive at 48-h without any symptoms → clinical course not different from not pregnant women → **pregnancy should not be considered an independent risk of factor**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Cell 08MAY2020	**Host-viral infection maps reveal signatures of severe COVID-19 patients**	Bost, Pierre; et al. Israel-France-China gotopaper	Fundamental research	Viral-Track, a new computational method to analyze host-viral infection maps : **- enables transcriptional sorting of infected vs bystander cells and reveals virus-induced expression** (scans unmapped scRNA-seq data for presence of viral RNA). - Applicable to multiple models of infection (HBV, HIV, VSV, etc) Applied to Bronchoalveloar-Lavage samples from severe vs mild COVID-19 patients, reveals: - SARS-CoV-2 infects epithelial cells and alters immune landscape in severe patients. **- detected unexpected coinfection with hMPV** (human MetaPneumoVirus) mainly in monocytes, dampening interferon response. **-> robust technology for dissecting mechanisms of viral-infection and pathology.**
Lancet 08MAY2020	**Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial**	Hung, Ivan Fan-Ngai et al. China gotopaper	Therapeutic	**Multicentre, prospective, open-label, randomised, phase 2 trial** in **127 adults** with COVID-19 hospitalized in Hong Kong. Random assignement (2:1) to the **combination group (lopinavir-ritonavir + ribavirin+ interferon beta-1)** or to the **control group (lopinavir-ritonavir)**. => The **triple combination**, when **given within 7 days of symptom onset**, is **effective in suppressing the shedding of SARS-CoV-2**, not just in a nasopharyngeal swab, but in all clinical specimens, compared with lopinavir-ritonavir alone. => The **significant reductions in duration of RT-PCR positivity and viral load were associated with clinical improvement** as shown by the significant reduction in NEWS 2 and duration of hospital stay. => Subgroup comparison suggested interferon beta-1b to be a key component of the combination treatment. **Limitations**: open label, no placebo group, confounded by a subgroup omitting interferon beta-1b within the combination group, no critically ill patients.
Science 08MAY2020	**A highly conserved cryptic epitope in the receptor-binding domains of SARS-CoV-2 and SARS-CoV**	Yuan, Meng; et al. USA-China gotopaper	Fundamental research	Crystal **structure of CR3022 (neutralizing antibody from convalescent SARS-CoV infected patient) in complex with the receptor-binding domain of the SARS-CoV-2 spike** : - 3.1a resolution **-> CR3022 targets a highly conserved epitope (conserved in SARS-CoV-2 and SARS-CoV) that is distal from the receptor binding site, and enables cross-reactive binding between SARS-CoV-2 and SARS-CoV.** - CR3022 likely binds more tightly to SARS-CoV because its epitope contains a glycan absent in SARS-CoV-2. -> Modeling showed this epitope only accessible when at least 2 of the 3 spike proteins are in a conformation competent to bind the receptor.
Science 08MAY2020	**Harnessing multiple models for outbreak management**	Shea et al, USA gotopaper	Public Health/Epidemio	COVID-19 pandemic has triggered the development of several valuable models that can differ in various elements and provide disparate predictions, which could ultimately hinder intervention planning and response by policymakers. We advocate a more systematic approach, by merging two well-established research fields. 1. Formal expert elicitation methods applied to multiple models to deliberately generate, retain, and synthesize valuable individual model ideas and share important insights during group discussions, while minimizing various cognitive biases. 2. Using a decision-theoretic framework to capture and account for within- and between-model uncertainty as we evaluate actions in a timely manner to achieve management objectives.

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 08MAY2020	**Changes in SARS-CoV-2 Positivity Rate in Outpatients in Seattle and Washington State, March 1-April 16, 2020**	Randhawa et al, USA gotopaper	Public Health/Epidemio	Patient demographics: SARS-CoV-2 positivity rates were 8.2% in Washington State outpatient clinics, 8.4% in Seattle-area outpatient clinics, and 14.4% in Seattle EDs. The SARS-CoV-2 positivity rate was analysed by fitting penalized cubic regression splines to binomial testing data, and accounting for variation in the daily testing totals. SARS-CoV-2 positivity rate was 17.6% in the outpatient clinics and 14.3% in EDs at the peak period and 3.8% and 9.8%, respectively, at the end of the analysis period. SARS-CoV-2 infections in patients of Washington outpatient clinics and Seattle ED settings peaked in late March and have been declining. -> This trajectory is aligned with local physical distancing and the "Stay Home, Stay Healthy" order announced March 23, 2020.
Nature structural & molecular biology 07MAY2020	**Structural basis for the inhibition of SARS-CoV-2 main protease by antineoplastic drug carmofur**	Jin, Zhenming et al. China gotopaper	Therapeutic	The antineoplastic drug **carmofur is shown to inhibit the SARS-CoV-2 main protease (M^{pro})**.Tthe X-ray crystal structure of M^{pro} in complex with carmofur reveals that the carbonyl reactive group of carmofur is covalently bound to catalytic Cys145, whereas its fatty acid tail occupies the hydrophobic S2 subsite. **Carmofur inhibits viral replication in VeroE6 cells (EC50 = 24.30 μM)**. Carmofur has a favorable selectivity index (SI) of 5.36, but further optimization will be required to develop an effective drug. This study provides a basis for rational **design of carmofur analogs with enhanced inhibitory efficacy to treat COVID-19**.
The Lancet Rheumatology 07MAY2020	**Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study**	Cavalli, Giulio et al. Italy gotopaper	Therapeutic	**Retrospective cohort study** in adult patients with COVID-19, **moderate-to-severe ARDS, and hyperinflammation**, managed with non-invasive ventilation outside of the ICU and who received **standard treatment of hydroxychloroquine and lopinavir-ritonavir, with or without anakinra**. **29 patients** received high-dose intravenous anakinra, **16 patients** comprised the comparison group for this study, and 7 patients received low-dose subcutaneous anakinra but treatment was interrupted after 7 days. At 21 days, **treatment with high-dose anakinra was associated with clinical improvement in 21 (72%)** of 29 patients versus 8 (50%) in the standard treatment group. At 21 days, **survival was 90% in the high-dose anakinra group** and 56% in the standard treatment group (**p=0.009**). Discontinuation of anakinra was not followed by inflammatory relapses. **Limitations**: retrospective nature, relatively small size of the cohorts (particularly the historical comparator group), a more extended follow-up is also needed to assess long-term outcomes of treated patients.
Journal of Clinical Virology 07MAY2020	**SARS-CoV-2 detection by direct rRT-PCR without RNA extraction**	Merindol, Natacha, and al. gotopaper	Diagnostic	There are many challenges associated with ramping up testing capacity, including shortage in the chain of supplies for extraction reagents. This situation called for alternatives protocols with similar sensitivity to ensure the continuity of testing in laboratories. ->Comparison of sensitivity of 2 approved rRT-QPCR Assays with and without RNA extraction. **Conclusion :** the two tests provided the same sensitivity. Direct rRT-PCR without RNA extraction is possible if samples are in UTM or molecular water; specimens collected in water should be screened rapidly. RNA extraction is necessary if samples are in saline water or Hanks medium.

Journal and date	Title	Authors and link	Field of expertise	Key facts
JAMA 07MAY2020	**Necessity of a development and widespread distribution of COVID-19 medical treatments**	Bollyky, T. et al, US gotopaper	HSS/Politic	1- Equitable Distribution Plan for manufacturing capacity, financing, and distribution infrastructure necessary to produce sufficient quantities to meet global needs in a fair, public health–driven manner. 2- Framework for Distribution =>For flexible, trusted governance - take advantage of well-established international forums (e.g: G7) rather than build something new + central role of WHO in planning and coordinating the implementation of the framework - requires coordination of several institutions, donors, governments and pharmaceutical companies - COVID-19 access accelerator (ACT), recently launched and supported by the European Commission, should extend to other major contributors, members of the G20. - involve entities that develop vaccines, treatments and diagnostics and support group supply in LMICs (CEPI, Gavi, the Global Fund...) => Adequate, Predictable Financing Provide a funding mechanism to generate income for R&D + deployment of vaccines and therapeutic products (advance purchase commitments (APC) for COVID-19 products + profiles of target products) Funds => mixture of national and philanthropic contributions, mobilized to raise additional funds on the capital markets Contribution from world leaders + subscription depending on payment capacity of countries. = low-income countries highly subsidized /free. Transparent regulatory pathway for approval of COVID-19 products → instill global confidence, reduce development costs and accelerate access to less profitable markets.
The Lancet. Respiratory medicine 07MAY2020	**Tropism, replication competence, and innate immune responses of the coronavirus SARS-CoV-2 in human respiratory tract and conjunctiva: an analysis in ex-vivo and in-vitro cultures**	Hui, Kenrie P. Y.; et al. China gotopaper	Fundamental research	SARS-CoV-2 tissue and cellular tropism in ex-vivo cultures of human bronchus, lung, conjunctiva, and innate immune responses vs other coronavirus and influenza virus (H1N1). SARS-CoV-2 isolated from COVID-19 patients: - infected ciliated, mucus-secreting, and club cells of bronchial epithelium, type 1 pneumocytes in the lung, and the conjunctival mucosa. - In bronchus : replication similar to MERS-CoV, and higher than SARS-CoV, but lower than H1N1. - In lung: replication similar to SARS-CoV and H1N1, but lower than MERS-CoV. - In conjunctiva: replication greater than SARS-CoV. **- SARS-CoV-2 was a less potent inducer of proinflammatory cytokines than H5N1, H1N1pdm, or MERS-CoV.** **-> Conjunctival epithelium and conducting airways are potential portals of infection for SARS-CoV-2. SARS-CoV-2 replicated similarly to SARS-CoV in alveolar epithelium; but more extensively in bronchus.**
Cell 07MAY2020	**Coast-to-Coast Spread of SARS-CoV-2 during the Early Epidemic in the United States**	Fauver et al, USA gotopaper	Public Health/Epidemiology	SARS-CoV-2 detected in all 50 states of USA. Data on sequencing of nine viral genomes from early reported COVID-19 patients, the majority of which from Washington State, combined with domestic and international travel patterns, showed: - SARS-CoV-2 transmission in Connecticut was likely driven by domestic introductions - the risk of domestic importation to Connecticut exceeded that of international importation by mid-March regardless of our estimated effects of federal travel restrictions → Widespread transmission of SARS-CoV-2 within USA, need for critical surveillance

Journal and date	Title	Authors and link	Field of expertise	Key facts
Infect. Control Hosp. Epidemiol. MAY2020	**Effect of ambient air pollutants and meteorological variables on COVID-19 incidence**	Jiang et al, China gotopaper	Public Health/Epidemiology	The multivariate Poisson regression used to analyse correlation between COVID-19 incidence, eight air pollutants and three meteorological variables in three China's worst COVID-19 hit provinces. Daily COVID-19 incidence was positively associated with PM2.5 and humidity in all cities. The relative risk (RR) of PM2.5 was 1.036 (95% CI, 1.032 -1.039), 1.059 (95% CI, 1.046 - 1.072) and 1.144 (95% CI, 1.12 - 1.169) for COVID-19 incidence per day in the three provinces. The RR of humidity was lower than that of PM2.5, difference ranging from 0.027 to 0.111. PM10 and temperature exhibited a negative correlation with daily COVID-19 incidence: the RR of PM10 raged from 0.915 (95% CL, 0.896 - 0.934) to 0.961 (95% CL, 0.95 - 0.972) while that of temperature was 0.738 (95% CL, 0.717 - 0.759) to 0.969 (95% CL, 0.966 - 0.973). Data suggest that PM2.5/humidity and PM10/temperature could substantially increase and decrease the risk of COVID-19 incidence, respectively.
Nature 07MAY2020	**The pathogenicity of SARS-CoV-2 in hACE2 transgenic mice**	Bao, Linlin; et al. China gotopaper	Animal model	**Human ACE2 transgenic mice infected with SARS-CoV-2** : - SARS-CoV-2 intranasal inoculation at 10^5 $TCID_{50}$/50 µL inoculum volume per mouse. (14 days observation) - 6-11 month-old, male and female WT (n=15) and hACE2 mice (n=19). - Typical histopathology: interstitial pneumonia with infiltration of significant macrophages and lymphocytes into the alveolar interstitium, and accumulation of macrophages in alveolar cavities. **- Weight loss observed in hACE2 mice (up to 8% at 5 dpi), not in WT mice.** - **viral load detectable** (qRT-PCR) at 1, 3, 5 and 7 dpi (peak at 3 dpi) **in lungs of hACE2 mice but not in WT mice.** - infectious virus isolated from lungs of hACE2 mice at 1, 3 dpi and 5 dpi (peak titers at 3 dpi), but not WT mice. - **Viral antigens detected** in bronchial epithelial cells, macrophages and alveolar epithelia. **-> Confirmed pathogenicity of SARS-CoV-2 in hACE2 expressing mice and suggests that hACE2 was essential for infection and replication in mice.**
The Journal of Infectious Diseases 07MAY2020	**T cell subset counts in peripheral blood can be used as discriminatory biomarkers for diagnosis and severity prediction of COVID-19**	Jiang, Mei and al. China gotopaper	Diagnostic	Assessment of the significance of lymphocyte subsets detection in peripheral blood in the diagnosis and prognosis of Covid-19 disease. The counts of CD8+T and CD4+T cells can be used as diagnostic markers of COVID-19 and predictors of disease severity.
The Lancet Psychatry 07MAY2020	**COVID-19, unemployment, and suicide**	*Kawohl* And Nordt., Switzerland gotopaper	Psy	**High scenario:** the worldwide unemployment rate would increase from 4·936% to 5·644%, which would be associated with an increase in suicides of about 9570 per year. **Low scenario:** the unemployment would increase to 5·088%, associated with an increase of about 2135 suicides.
New England Journal of Medicine 07MAY2020	**Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19**	Geleris, Joshua et al. USA gotopaper	Therapeutic	**Observational study** involving consecutive patients with Covid-19 admitted to a hospital, and **comparaing outcomes in patients who received hydroxychloroquine with those in patients who did not**. The primary end point was a composite of intubation or death in a time-to-event analysis. Of the **1376 patients**, 811 (58.9%) received hydroxychloroquine and 565 (41.1%) did not. Hydroxychloroquine-treated patients were more severely ill at baseline than those who did not receive hydroxychloroquine. Overall, 346 patients (25.1%) had a primary end-point of respiratory failure. In the main analysis, there was **no significant association between hydroxychloroquine use and intubation or death** (hazard ratio, 1.04, 95% confidence interval, 0.82 to 1.32). Results were similar in multiple sensitivity analyses.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nat Rev Immunology 06MAY2020	**Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages**	Merad et al., USA gotopaper	Immuno	The delay in production of type I interferon promotes the enhanced release of monocyte chemoattractants by alveolar epithelial cells leading to sustained recruitment of blood monocytes into the lungs. · Monocytes differentiate into pro-inflammatory macrophages · Activated natural killer (NK) cells and T cells further promote the recruitment and activation of monocyte-derived macrophages through the production of granulocyte–macrophage colony-stimulating factor (GM-CSF), tumour necrosis factor (TNF) and interferon-γ (IFNγ). · Oxidized phospholipids (OxPLs) are accumulated in infected lungs and activate monocyte-derived macrophages through the Toll-like receptor 4 (TLR4)–TRAF6–NF-κB pathway. · It is possible that type I interferons induce the expression of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) entry receptors, enabling the virus to gain access to the cytoplasm of macrophages and to activate the NLRP3 inflammasome, leading to the secretion of mature IL-1βand/or IL-18. · IL-1β can amplify activation of monocyte-derived macrophages in an autocrine or paracrine way, but it can also reduce type I interferon production in infected lungs. · The engagement of Fcγ receptors (FcγRs) by anti-spike protein IgG immune complexes can contribute to increased inflammatory activation of monocyte-derived macrophages. **Conclusion:** Identifying the mechanisms that contribute to reduced type I interferon activity will be critical for the development of targeted immunomodulatory strategies in patients with COVID-19
Antimicrobial agents and chemotherapy 06MAY2020	**Inhibition of SARS-CoV-2 infection by the cyclophilin inhibitor Alisporivir (Debio 025)**	Softic, Lauren et al. France, gotopaper	Therapeutic	Cyclophilins play a key role in the lifecycle of coronaviruses. **Alisporivir (Debio 025) is a non-immunosuppressive analogue of cyclosporin A with potent cyclophilin inhibition properties**. It has been administered to more than 1,800 patients with chronic hepatitis C virus infection in Phase 2 and 3 clinical trials, alone or in combination with pegylated interferon alpha and/or ribavirin. => Alisporivir reduced SARS-CoV-2 RNA production in a dose-dependent manner in VeroE6 cell line, with an **EC50 of 0.46±0.04 µM**. => Anti-SARS-CoV-2 effectiveness of alisporivir was confirmed by immunofluorescence. => Alisporivir did not inhibit SARS-CoV-2 entry into VeroE6 cells. Effect of alisporivir was preserved when the compound was added 3 h post-infection. These results suggest that **alisporivir inhibits a post-entry step of the SARS-CoV-2 life cycle**.
Journal of the American College of Cardiology 06MAY2020	**Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19**	Paranjpe, Ishan et al. USA gotopaper	Therapeutic	Association between administration of in-hospital anticoagulation (AC) and survival in a large cohort of 2,773 hospitalized patients with COVID-19, among which 786 (28%) received systemic AC during their hospital course. => **Systemic AC may be associated with improved outcomes** among patients hospitalized with COVID-19. Potential benefits of systemic AC need to be weighed against the risk of bleeding and therefore should be individualized. The association of in-hospital AC and mechanical ventilation likely reflects reservation of AC for more severe clinical presentations. => **Association with AC and improved survival after adjusting for mechanical ventilation**. **Limitations**: observational study, unobserved confounding, unknown indication for AC, lack of metrics to further classify illness severity in the mechanically ventilated subgroup, and indication bias.

Journal and date	Title	Authors and link	Field of expertise	Key facts
BMC 06MAY2020	**A single-center, retrospective study of COVID-19 features in children: a descriptive investigation**	Ma H, and al China gotopaper	Clinic	50 children COVID19+ and 26 with PCR- and CT+ with history of exposure Symptoms: - More frequent: fever (64%) – cought (44%) - Less frequent: diarrhea (6%) – abdominal pain (4%) – rhinorrhea (16%) - Asymptomatic 12% Laboratory: - Lymphopenia (16%) – thrombocytopenia (14%) - Elevated CRP (20%) – anemia (12%) 43/50 had abnormalities on CT: - Ground glass opacity (64%) 29/50 >1 CT which 65% had improved CT and 28% had more lesions **At discharge: no association between changes in CT lesions** →CT allow to detect COVID19 but do not evaluated the resolution of illness for children
Cell host & microbe PREPRINT	**Identification of human single-domain antibodies against SARS-CoV-2**	Yanling Wu et al, China gotopaper	Therapeutic	SARS-CoV-2 spike protein, containing the receptor-binding domain (RBD) and S1 subunit involved in receptor engagement, is a potential therapeutic target. - **Development of a phage-displayed single-domain antibody library** by grafting naïve complementarity-determining regions (CDRs) into framework regions of a human germline immunoglobulin heavy chain variable region (IGHV) allele. - Panning this library against SARS-CoV-2 RBD and S1 subunit **identified fully human single-domain antibodies targeting five distinct epitopes on SARS-CoV-2 RBD with subnanomolar to low nanomolar affinities**. Some of these antibodies neutralize SARS-CoV-2 by targeting a cryptic epitope located in the spike trimeric interface.
SCIENCE 06MAY2020	**Development of an inactivated vaccine candidate for SARS-CoV-2**	Qiandg Gao et al, China gotopaper	Vaccine	**Development of PiCoVacc Vaccine based on the inactivated SARS-CoV-2 virus (Sinovac vaccine currently in ph1)** -> Isolation of 11 SARS-CoV-2 strains COVID19 patients BALF (China, Italy, Switzerland, UK, and Spain) to developed preclinical in vitro neutralization and challenge models. A strain from a Chinese patient inactivated with b-propiolactione was used for vaccine development (not causing severe disease). **Immunogenicity in BAL/C mice:** -> Inactivated Chinese patient virus+adjuvant (PiCoVacc) was injected at day 0 and 7 at different doses (0ug, 1,5ug, 3ug, 6ug) -> SARS-CoV-2 S and RBD specific IgGs were developed very quickly in mice sera ->The dominant immunogen was shown to be the RBD (no response to N protein) ->Neutralizing antibodies against all the SARS-CoV-2strains were also produced **Immunogenicity and protection in macaques** **->** 3 immunizations at d 0, 7 and 14 with at different doses of PiCoVacc (3 or 6ug) -> Specific S IgG and neutralizing antibodies were induced from two weeks after vaccination -> macaques at day 22 after fist immunization: viral loads were shown to decrease. -> No detectable viral load in pharynx, crissum and lung in high dose vaccinated monkeys from 7 d after challenge. no changes on serological markers (CD3+, CD4+ CD88+, TNF-a, IFN-g, IL2, IL4…) nor pathologies in heart, spleen kidney or lung were observed suggesting that PiCoVacc do not induce exacerbated T cell response nor organ pathology.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Pediatr Infect Dis J 6MAY2020	**The risk of children Hospitalized with severe COVID-19 in Wuhan**	Wang Y and al China https://doi.org/10.1097/INF.0000000000002739	Clinic	Retrospective case-control study – 8 severe children matched with 35 - Median age of severe cases: 5,06 years 2/8 had comorbidities Symptoms in both groups: fever – cough – dyspnea – diarrhea/vomiting Laboratory: -WBC higher in severe group -No difference for lymphocytes counts *p>0,05* -IL6 – IL10, D-dimer higher in severe group Hospital stay: 13,5 (severe) versus 11 days (non severe) Time for PCR turning negative: 10,5 (severe) versus 7,1 (p<0,05) **More lung segment involves in severe children** → unique risk factor for severe → mild symptomatic (8 severe cases on 260 COVID-19) – rare mortality → **some factors associated with severity**: CT scan lesions – immune response (IL-6) – intravascular coragulation (D-dimer)
Science 05MAY2020	**Rapid implementation of mobile technology for real-time epidemiology of COVID-19**	Drew et al, USA https://doi.org/10.1126/science.abc0473	Public Health/Epidemiology	The Coronavirus Pandemic Epidemiology (COPE) consortium developed a Symptom Tracker mobile application, launched in the UK on March 24, 2020 and the US on March 29, 2020 garnering more than 2.8 million users as of May 2, 2020. This mobile application offers data on risk factors, herald symptoms, clinical outcomes, and geographical hot spots. This initiative offers critical proof-of-concept for the repurposing of existing approaches to enable rapidly scalable epidemiologic data collection and analysis which is critical for a data-driven response to this public health challenge.
Autoimmunity reviews 05MAY2020	**Continuous hydroxychloroquine or colchicine therapy does not prevent infection with SARS-CoV-2: Insights from a large healthcare database analysis**	Gendelman, Omer et al, Israel https://doi.org/10.1016/j.autrev.2020.102566	Therapeutic	**Retrospective study based on a large healthcare computerized database** including all patients that were screened for the SARS-CoV-2 in the study period from February 23rd 2020 to March 31st 2020. Comparison between subjects tested positive for SARS-CoV-2 and those found negative in terms of rate of **administration of hydroxychloroquine/ colchicine therapy**. - An overall sample of **14,520 subjects** were screened for SARS-CoV-2 infection and **1317 resulted positive**. - **No significant difference was found in terms of rates of usage of hydroxychloroquine or colchicine** between those who were found positive for SARS-CoV-2 and those who were found negative (0.23% versus 0.25% for hydroxychloroquine, and 0.53% versus 0.48% for colchicine, respectively).
Cell 05MAY2020	**Structural Basis for Potent Neutralization of Betacoronaviruses by Single-domain Camelid Antibodies**	DanielWrapp and al, https://doi.org/10.1016/j.cell.2020.04.031	Therapeutic	Isolation of single-domain antibodies (VHHs) from a llama immunized with prefusion-stabilized coronavirus spikes. These VHHs neutralize MERS-CoV or SARS-CoV-1 S pseudotyped viruses, respectively. Crystal structures of these VHHs bound to their respective viral targets reveal two distinct epitopes, but both VHHs interfere with receptor binding. Cross-reactivity between the SARS-CoV-1 S-directed VHH and SARS-CoV-2 S. Cross-reactive VHH neutralizes SARS-CoV-2 S pseudotyped viruses as a bivalent human IgG Fc-fusion. => These data provide a **molecular basis for the neutralization of pathogenic betacoronaviruses by VHHs** and suggest that these molecules may serve as useful therapeutics during coronavirus outbreaks.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature Communications 04MAY2020	**A human monoclonal antibody blocking SARS-CoV-2 infection**	Wang, Chunyan et al, https://www.nature.com/articles/s41467-020-16256-y	Therapeutic	First report of a (human) monoclonal antibody that neutralizes SARS-CoV-2 (and SARS-CoV) in cell culture. 47D11 binds a conserved epitope on the spike RBD explaining its ability to cross-neutralize SARS-CoV and SARS-CoV-2, using a mechanism that is independent of receptor-binding inhibition.
Intensive Care Med 04MAY2020	**High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study**	Helms J, and al France https://doi.org/10.1007/s00134-020-06062-x	Clinic	Multicentric study – 4 ICU in France – 150 patients with ARDS Historical prospective cohort → comparison of COVID to non-COVID by propensity score matching At baseline: >95% patients elevated had D-dimer and fibrinogen Median age = 63 years 64/150 thrombotic complications and **16,7% pulmonary embolisms** COVID19 (=77) vs non-COVID19 (=145): - More thrombotic complication in COVID19 (11,7 vs 2,1%, *p*<0,008) Thrombotic complications despite prophylactic or therapeutic anticoagulation → large number of patients still intubated → under-estimated → monitoring anticoagulant treatment/ higher targets than usual?
Nature 04MAY2020	**Effect of non-pharmaceutical interventions to contain COVID-19 in China**	Lai, Shengjie et al, https://www.nature.com/articles/s41586-020-2293-x	Public Health/Epidemio	**Modelling framework that uses daily travel networks to simulate different outbreak and intervention scenarios across China**, using epidemiological and anonymised human movement data. -> Total of 114,325 COVID-19 cases (interquartile range 76,776 - 164,576) estimated in mainland China as of February 29, 2020. -> Without non-pharmaceutical interventions (NPIs), the COVID-19 cases would likely have shown a 67-fold increase (interquartile range 44 - 94) by February 29, 2020, with the effectiveness of different interventions varying. -> The early detection and isolation of cases was estimated to have prevented more infections than travel restrictions and contact reductions, but combined NPIs achieved the strongest and most rapid effect. -> The lifting of travel restrictions since February 17, 2020 does not appear to lead to an increase in cases across China if the social distancing interventions can be maintained, even at a limited level of 25% reduction on average through late April.
Cell host & microbe 04MAY2020	**Heightened innate immune responses in the respiratory tract of COVID-19 patients**	Zhou, Zhuo; et al. China https://doi.org/10.1016/j.chom.2020.04.017	Immunology	Metatranscriptomic seq. to profile immune signatures in bronchoalveolar lavage fluid of 8 COVID-19, 146 community-acquired pneumonia patients, and 20 healthy controls : - Proinflammatory gene expression, especially chemokines, markedly elevated in COVID-19 vs community-acquired pneumonia patients and healthy controls, **suggesting SARS-CoV-2 causes hypercytokinemia.** - SARS-CoV-2 triggered **robust expression of IFN-inducible genes (ISGs) with immunopathogenic potential** (overrepresentation of genes involved in inflammation), unlike SARS-CoV which is thought to induce inadequate IFN. **- Estimations of immune cell populations, show increased activated dendritic cells and neutrophils.**
Science 04MAY2020	**Site-specific glycan analysis of the SARS-CoV-2 spike**	Watanabe, Yasunori, et al. UK - USA https://doi.org/10.1126/science.abb9983	Structural biology	**Revealing the glycan structures on a recombinant SARS-CoV-2 spike (S) glycoprotein immunogen by site-specific mass spectrometry.** -SARS-CoV-2 S gene encodes 22 N-linked glycan sequons per protomer, which likely play a role in protein folding and immune evasion. **-> Glycosylation analysis enables detailed mapping of the glycan-processing states and signatures across the trimeric viral spike**. **Glycan profiling have implications in viral pathobiology as well as vaccine design for comparing immunogen integrity and monitoring manufacturing processes .**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Nature 04MAY2020	**Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform**	Thao, Tran Thi Nhu, et al. Switzerland - Germany - Russia https://www.nature.com/articles/s41586-020-2294-9	Fundamental research	Accelerated yeast-based reverse genetics pipeline can genetically reconstruct diverse long RNA viruses, including Coronaviridae, Flaviviridae and Paramyxoviridae families : - Viral subgenomic fragments (from viral isolates, cloned viral DNA, clinical samples, or synthetic DNA) are reassembled in one step in S. cerevisiae using transformation associated recombination (TAR) cloning to maintain the genome as a yeast artificial chromosome (YAC). T7-RNA polymerase then used to generate infectious RNA and viable virus. **-> Approach to generate SARS-CoV-2 is rapid** (1 week after receipt of synthetic DNA fragments) **and applicable to other emerging RNA viruses, and can provide infectious virus to health authorities and diagnostic labs without the need of access to clinical samples.** **- Also possible to rapidly introduce sequence variations to functionally characterize phenotypic consequences of SARS-CoV-2 evolution in real-time.**
Autoimmunity reviews 03MAY2020	**Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy**	Toniati, Paola et al, Italy https://doi.org/10.1016/j.autrev.2020.102568	Therapeutic	A **prospective series of 100 consecutive patients** admitted to a Hospital in Brescia (Italy) between March 9th and March 20th with confirmed COVID-19 pneumonia and ARDS requiring ventilatory support **were administred Tocilizumab** (TCZ, monoclonal antibody that targets the interleukin 6 receptor). The outcome measure was an improvement in ARDS assessed by means of the Brescia COVID Respiratory Severity Score. Out of 100 treated patients (88 M, 12 F; median age: 62 years), the **respiratory condition was improved or stabilized in 77 (77%) patients**, of whom 61 showed a significant clearing of diffuse bilateral opacities on chest x-ray and 15 were discharged from the hospital. Respiratory condition worsened in 23 (23%) patients, of whom 20 (20%) died. All the patients presented with lymphopenia and high levels of C-reactive protein (CRP), fibrinogen, ferritin and interleukin 6 (IL-6) indicating a HIS. During the 10-day follow-up, three cases of severe adverse events were recorded.
Immunity 03MAY2020	**Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals**	Ling et al., China https://www.sciencedirect.com/science/article/pii/S1074761320301813	Diagnostic	1. SARS-CoV-2-specific antibodies are detected in COVID-19 convalescent subjects. 2. Most COVID-19 convalescent individuals have detectable neutralizing antibodies. 3. Cellular immune responses to SARS-CoV-2 are found in COVID-19 convalescent subjects 4. Neutralization antibody titers correlate with the numbers of virus-specific T cells.
American journal of obstetrics and gynecology 03MAY2020	**Evidence for and against vertical transmission for SARS-CoV-2 (COVID-19)**	A, Amouroux; et al. France http://www.sciencedirect.com/science/article/pii/S0002937820305240X	Clinic	Observations from 12 articles published from 10 February to 4 April 2020 reporting on 68 deliveries and 71 neonates with maternal infection in the third trimester of pregnancy: **- SARS-CoV-2 recovered (RT-PCR) from** nasal and throat swabs, sputum and feces of symptomatic patients including **neonates but not from vaginal swabs, amniotic fluid, placenta, cord blood, neonatal blood or breast milk.** **- Neonatal infection was diagnosed within 48 hours of life in 4 cases.** **-> More complete evidence and reliable serological studies needed** before counselling pregnant women on the risk of congenital infection with SARS-CoV-2.

Journal and date	Title	Authors and link	Field of expertise	Key facts
Int. J. Infect. Dis. 03MAY2020	**Viral kinetics of SARS-CoV-2 in asymptomatic carriers and presymptomatic patients**	Kim, Seong Eun; et al. South Korea https://doi.org/10.1016/j.ijid.2020.04.083	Virology	71 laboratory-confirmed SARS-CoV-2 cases, identified 3 presymptomatic patients and 10 entirely asymptomatic infections: **- 2 out of 3 incubation period patients (presymptomatic) had very high viral titer (Ct value <20).** **- In entirely asymptomatic carriers : median days to first negative RT-PCR was 4.5 (2.5–9) days and all reached a first Ct>35 RT-PCR within 14 days after diagnosis.** **-> COVID-19 patients may already be infectious before symptoms manifestation, and 14 days isolation after diagnosis may be sufficient in entirely asymptomatic cases.**
Gastroentero logy 01MAY2020	**Gastrointestinal and Hepatic Manifestations of 2019 Novel Coronavirus Disease ina Large Cohort of Infected Patients From New York: Clinical Implications**	Kaveh H and al USA https://doi.org/10.1053/j.gastro.2020.05.010	Clinic	1059 patients COVID-19 - 33% at least one gastrointestinal symptom **GI symptom**: diarrhea (22%) – abdominal pain (7%) – nausea (16%) 62% had biochemical liver injury GI manifestation and liver injury were associated with higher admission rate Multivariate analysis→ independent predictor of death or ICU admission - Liver injury at presentation OR:2,53 - Older age OR:1,03 - Tachypnea OR:1,73 - Severe hypoxemia OR:1,47 GI manifestation → no effect on the outcome **→ COVID-19 patients had commonly GI manifestation**
JAMA Cardiology 01MAY2020	**Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19)**	Mercuro, Nicholas J. Et al, USA https://jamanetwork.com/journals/jamacardiology/fullarticle/2765631	Therapeutic	**Cohort study of hospitalized patients** with coronavirus disease 2019. Among **90 patients given hydroxychloroquine, 53 received concomitant azithromycin**. Those receiving concomitant azithromycin had a greater median change in QT interval compared with those receiving hydroxychloroquine. Seven patients (19%) who received hydroxychloroquine monotherapy developed prolonged QTc of 500 milliseconds or more, and 3 patients (3%) had a change in QTc of 60 milliseconds or more. Of those who received concomitant azithromycin, 11 of 53 (21%) had prolonged QTc of 500 milliseconds or more and 7 of 53 (13 %) had a change in QTc of 60 milliseconds or more. Ten patients had hydroxychloroquine discontinued early because of potential adverse drug events, including intractable nausea, hypoglycemia, and **1 case of torsades de pointes**.
Molecular Cell 01MAY2020	**A Multibasic Cleavage Site in the Spike Protein of SARS-CoV-2 Is Essential for Infection of Human Lung Cells**	Hoffmann, Markus; et al. Germany https://doi.org/10.1016/j.molcel.2020.04.022	Fundamental research	The spike protein of SARS-CoV-2 harbors a multiple arginine residues (multibasic) S1/S2 site. - The host cell protease furin cleaves the SARS-CoV-2 spike protein at the S1/S2 site. **- Cleavage at the S1/S2 site is essential for spike-driven cell-cell fusion and viral entry entry into lung cells.** **-> Suggests that acquisition of a S1/S2 multibasic cleavage site was essential for SARS-CoV-2 infection of humans and identify furin as a potential target for therapeutic intervention.**
New England Journal of Medicine 01MAY2020	**Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19**	Mehra M, and al USA https://doi.org/10.1056/NEJMoa2007621	Clinic	169 hospitals in Asia, Europe, North America 8910 patients → 5,8 % died Use of ACE inhibitors or ARBDs → no associated to death Independently associated with increase of in hospital death: - **Age > 65 y** [OR:1,93 (1,6 – 2,4)] - **Coronary artery disease** [OR:2,7 (2,08 – 3,51)] - **Heart failure** [OR:2,48 (1,62 – 3,79)] - **Cardiac arrythmia** [OR:1,95 (1,33 – 2,86)] - **Chronic obstructive pulmonary disease** [OR:2,96 (2,0 – 4,4)] - **Current smoking** [OR:1,79 (1,29 – 2,47)] → underlying cardiovascular disease is associated with an increased risk of in hospital death

Journal and date	Title	Authors and link	Field of expertise	Key facts
New England Journal of Medicine 01MAY2020	**Early Detection of Covid-19 through a Citywide Pandemic Surveillance Platform**	Chu, Helen Y. and al. USA https://www.nejm.org/doi/full/10.1056/NEJMc2008646	Public Health/Epidemio	The Seattle Flu Study is a multi-institutional, community-wide pandemic surveillance platform that was established in November 2018. -> Persons enrolled online and were sent kits, by rapid-delivery services, for home collection of a midnasal swab; samples were returned by mail. ->Persons reporting symptoms of respiratory illness provided informed consent for testing to identify influenza and other respiratory pathogens. ->The first Covid-19 case detected through the Seattle Flu Study, in a specimen collected on February 24, 2020, was the first documented U.S. case of community transmission at the time. **Conclusion:** widespread implementation of simple methods that are scalable and require minimal interaction for collection of samples from persons who may not seek clinical care is critical for early detection of community cases. An ubiquitous, community-based sampling for respiratory illnesses appears as an essential infrastructure for early detection and mitigation of future pandemics
Clin. Infect. Dis 01MAY2020	**Early detection of SARS-CoV-2 antibodies in COVID-19 patients as a serologic marker of infection**	Zhao, Rongqing and al. https://doi.org/10.1093/cid/ciaa523	Diagnostic	**A COVID-19/SARS-CoV-2 S1 serology ELISA kit was developed.** The overall accuracy rate reached 97.3%. The assay was able to detect SARS-CoV-2 antibody on day one after the onset of COVID-19 disease. SARS-CoV-2 antibodies were detected in 28 out of 276 asymptomatic medical staff and one out of five nucleic acid test-negative “Close contacts” of COVID-19 patient. **Conclusion:** the assays developed here can screen medical staff, in-coming patients, passengers and people who are in close contact with the confirmed patients to identify the “innocent viral spreaders”, protect the medical staff and stop the further spreading of the virus.
J. Clin. Virol. 01MAY2020	**A RT-PCR Assay for the Detection of Coronaviruses from Four Genera**	Xiu, Leshan and al. China https://www.sciencedirect.com/science/article/pii/S1386653220301335	Diagnostic	A better understanding of the natural hosts and genetic diversity of CoVs are needed to help mitigate these threats. Objective: to design and evaluate a molecular diagnostic tool for detection and identification of all currently recognized and potentially future emergent CoVs from the Orthocoronavirinae subfamily. **Conclusion:** a semi-nested, reverse transcription RT-PCR assay capable of detecting and identifying all previously recognized CoVs, including SARS-CoV-2, and potentially any emergent CoVs in this subfamily.
Science 01MAY2020	**SARS-CoV-2 productively infects human gut enterocytes**	Lamers, Mart M.; et al. Netherlands https://doi.org/10.1126/science.abc1669	Fundamental research	Infection of human small intestinal organoids (hSIOs) grown from primary gut epithelial stem cells to investigate intestine as another viral target organ : - hSIOs enterocytes were readily infected by SARS-CoV and SARS-CoV-2 (confocal- and electron-microscopy) and significant titers of infectious viral particles detected. - SARS-CoV-2 infected airway and gut organoids. - mRNA expression analysis revealed **strong induction of a generic viral response program. SARS-CoV-2 induced a stronger interferon response than SARS-CoV in HIOs.** **-> intestinal epithelium supports SARS-CoV-2 replication, and data imply that human organoids represent faithful experimental models to study of coronavirus infection and biology.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
Emerging Microbes & Infections 01MAY2020	**Kinetics of SARS-CoV-2 specific IgM and IgG responses in COVID-19 patients**	Sun et al., China https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1762515#	Immuno	· **Kinetic steps:** - A total of 130 blood samples from 38 COVID-19 patients were analyzed. - Study showed that the seropositive rates of N-IgM, N-IgG, S-IgM and S-IgG antibody responses in non-ICU (intensive care unit) patients gradually increased within 1-3 weeks after the onset. - N-IgM and S-IgM reached a peak in the second week, while N-IgG and S-IgG antibodies continued to increase in the third week. - The joint detection of N-IgM, N-IgG, S-IgM, and S-IgG antibodies, could detect up to 75% of infections in the first week and the joint detection of N-IgM+N- IgG, or N-IgG+S-IgG could detect up to 94.7% of infections in the second week. Finally, in the third weeks after symptom onset, seropositive rates for N-IgG and S-IgG reached 100%. · **Comparison between ICU and non-ICU patients** - Most ICU patients had higher N-IgG than S-IgG after the symptom onset - ICU patients had SARS-CoV-2 nucleic acid positive days of 31.0, whereas non-ICU patients had SARS-CoV-2 nucleic acid positive days of 13. Therefore, a continuous increase of N-IgG may indicate disease progression towards more severe illness. - S-IgG in ICU patients was significantly lower than non-ICU patients by 2 weeks after the onset **Conclusion:** Intensive care unit monitoring the kinetics of S- IgG should help to predict prognosis.
Science 01MAY2020	**Structural basis for inhibition of the RNA-dependent RNA polymerase from SARS-CoV-2 by remdesivir**	Yin, Wanchao; et al. China https://doi.org/10.1126/science.abc1560	Structural biology	Cryo-EM structure of the SARS-CoV-2 RNA-dependent RNA polymerase (RdRp) in the apo form (unbound) (2.8 Å) or in complex with a 50-base template-primer RNA and the active form of Remdesivir (2.5 Å). - Structure comparison and sequence alignment suggest that mode of substrate RNA recognition and Remdesivir inhibition of RdRp is highly conserved in diverse RNA viruses **-> providing a basis for designing broad spectrum antiviral drugs based on nucleotide analogs and a template struture for modeling/modifying existing nucleotide drugs (ex. EIDD-2801).** **-> Complex structure reveals the partial double-stranded RNA template is inserted into the central channel of the RdRp where Remdesivir is covalently incorporated into the primer strand at the first replicated base pair and terminates chain elongation.**
Gastroenterology 01MAY2020	Taste Changes (Dysgeusia) in COVID-19: A systematic review and metaanalysis	Aziz, Muhammad; et al. USA https://doi.org/10.1053/j.gastro.2020.05.003	Clinic	Systematic review (case series/case-control/ cohort studies) (January 1st - April 21st, 2020) reporting on ageusia/dysgeusia: - 4 single-nation studies, 1 multinational study from Europe = total of 817 patients included. **-> Prevalence : almost half of patients (49.8%) with COVID-19 have altered taste sensation across the five studies.** **Limitations :** lack of data comparing ageusia/dysgeusia in COVID-19 +ve vs -ve patients, or severe COVID-19. In contexts of lack of diagnostic tests (ex. developing world), **distinctive clinical features like ageusia/dysgeusia can be useful in identifying suspected COVID-19 patients.**
New England Journal of Medicine 01MAY2020	**Renin–Angiotensin–Aldosterone System Inhibitors and Risk of Covid-19**	Reynolds H, and al USA https://doi.org/10.1056/NEJMoa2008975	Clinic	Relation between previous treatment that act on the RAAS and the likelihood of a positive test or the likelihood of severe illness? Five class of antihypertensive medication examined. Estimated a propensity score for the likelihood of treatment with each medication class -> 12594 patients were tested -> 5894 patients positive COVID19 which 17% had severe illness -> 2573(/5894) had HTA which 24,6% had severe illness **No association between medication examined and increased likelihood of a positive test or in the risk of severe Covid19.**

Journal and date	Title	Authors and link	Field of expertise	Key facts
NEJM 01MAY2020	**Inhibitors of the Renin–Angiotensin–Aldosterone System and Covid-19**	Jarcho, John A.; et al. USA https://doi.org/10.1056/NEJMe2012924 Mehra MR, et al. USA https://doi.org/10.1056/NEJMoa2007621 Mancia, Giuseppe; et al. Italy https://doi.org/10.1056/NEJMoa2006923 Reynolds HR, et al. USA https://doi.org/10.1056/NEJMoa2008975	Clinic	Analysis of 3 *N Engl J Med*articles, as clincians weigh alleged harm of continuing RAAS inhibitor medications (like ACE inhibitors and angiotensin-receptor blockers (ARBs)) often prescribed to patient with hypertension, diabetes, and coronary artery disease (high risk groups for severe COVID-19): - Mehra et al. database study, 8910 hospitalised Covid-19 patients, 11 countries : **ACE inhibitors nor ARBs associated with increased risk in-hospital death. Secondary analysis restricted to hypertension patients (for whom ACE inhibitor or ARB would be indicated) also did not show harm.** - Mancia et al. case–control study, 6272 confirmed SARS-CoV-2 patients in Lombardy (Italy) vs 30,759 matched controls : **ACE inhibitors nor ARBs associated with likelihood of SARS-CoV-2 infection. In severe/fatal infections vs matched controls, no association between these drugs and severe Covid-19.** - Reynolds et al. electronic health records, 12,594 people in New York University -> 5894 tested +ve, of which 1002 had severe illness (admission to ICU/mechanical ventilation/death): **no +ve association for drug classes, ACE inhibitors and ARBs, for a +ve test result or severe illness.** **-> none of the 3 studies showed evidence of harm with continued use of ACE inhibitors and ARBs.**
JAMA Cardiology 30APR2020	**Assessment of QT Intervals in a Case Series of Patients With Coronavirus Disease 2019 (COVID-19) Infection Treated With Hydroxychloroquine Alone or in Combination With Azithromycin in an Intensive Care Unit**	Bessiere, Francis et al, France https://jamanetwork.com/journals/jamacardiology/fullarticle/2765633	Therapeutic	40 consecutive patients with COVID-19 confirmed by positive RT-PCR results on respiratory samples admitted to the ICU who received hydroxychloroquine with or without were included. -> 30 patients (75%) required invasive mechanical ventilation and 25 (63%) received vasoactive drugs. -> Hydroxychloroquine with or without azithromycin was given to 18 (45%) and 22 patients (55%), respectively. 20 patients (50%) also received other treatments favoring QT prolongation in the ICU. ⇒ Most patients (37 [93%]): increase in QTc. Prolonged QTc was observed in 14 patients (36%) after a duration of antiviral treatment of 2 to 5 days. No ventricular arrhythmia, including torsades de pointes. ⇒ Among patients treated with hydroxychloroquine and azithromycin, 6 of 18 (33%) developed an increase in QTc of 500 milliseconds or greater vs 1 of 22 (5%) of those treated with hydroxychloroquine alone (P = .03). ⇒ The antiviral treatment ceased before completion for 7 patients (17.5%) following ECG abnormalities and in 10 (25%) for acute renal failure.
Nature 30APR2020	**A SARS-CoV-2 protein interaction map reveals targets for drug repurposing**	Gordon, David E et al, https://www.nature.com/articles/s41586-020-2286-9#Abs1	Therapeutic	**26 of the 29 SARS-CoV-2 proteins in human cells were cloned, tagged and expressed, and the human proteins physically associated with each were identified** using affinity-purification mass spectrometry (AP-MS) -> Identification of 332 high-confidence SARS-CoV-2-human protein-protein interactions (PPIs). -> Among these, 66 druggable human proteins or host factors targeted by 69 compounds (29 FDA-approved drugs, 12 drugs in clinical trials, and 28 preclinical compounds). -> Screening a subset of these in multiple viral assays identified **two sets of pharmacological agents that displayed antiviral activity**: inhibitors of mRNA translation and predicted regulators of the Sigma1 and Sigma2 receptors. Further studies of these host factor targeting agents, including their combination with drugs that directly target viral enzymes, could lead to a therapeutic regimen to treat COVID-19.