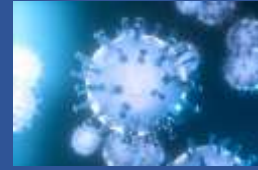


# COVID-19

Jun 25 – Jul 01, 2020



## RESEARCH PUBLICATIONS

**Publication Date: July 01, 2020**

### Subcutaneous tocilizumab treatment in patients with severe COVID-19–related cytokine release syndrome: An observational cohort study

#### **Abstract**

*Background:* Patients with severe coronavirus disease 2019 (COVID-19) have elevated levels of acute phase reactants and inflammatory cytokines, including interleukin-6, indicative of cytokine release syndrome (CRS). The interleukin-6 receptor inhibitor tocilizumab is used for the treatment of chimeric antigen receptor T-cell therapy–induced CRS.

*Methods:* Patients aged 18 years or older with laboratory-confirmed COVID-19 admitted to the Annunziata Hospital in Cosenza, Italy, through March 7, 2020, who received at least one dose of tocilizumab 162 mg subcutaneously for the treatment of COVID-19–related CRS in addition to standard care were included in this retrospective observational study. The primary observation was the incidence of grade 4 CRS after tocilizumab treatment. Chest computed tomography (CT) scans were evaluated to investigate lung manifestations.

*Findings:* Twelve patients were included; all had fever, cough, and fatigue at presentation, and all had at least one comorbidity (hypertension, six patients; diabetes, five patients; chronic obstructive lung disease, four patients). Seven patients received high-flow nasal cannula oxygen therapy and five received non-invasive mechanical ventilation for lung complications of COVID-19. No incidence of grade 4 CRS was observed within 1 week of tocilizumab administration in all 12 patients (100%) and within 2 days of tocilizumab

administration in 5 patients (42%). The predominant pattern on chest CT scans at presentation was ground-glass opacity, air bronchograms, smooth or irregular interlobular or septal thickening, and thickening of the adjacent pleura. Follow-up CT scans 7 to 10 days after tocilizumab treatment showed improvement of lung manifestations in all patients. No adverse events or new safety concerns attributable to tocilizumab were reported.

*Interpretation:* Tocilizumab administered subcutaneously to patients with COVID-19 and CRS is a promising treatment for reduction in disease activity and improvement in lung function. The effect of tocilizumab should be confirmed in a randomised controlled trial.

## **Reference**

[https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370\(20\)30154-1/fulltext](https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30154-1/fulltext)

## **Emergence of SARS-CoV-2 through recombination and strong purifying selection**

### **Abstract**

COVID-19 has become a global pandemic caused by the novel coronavirus SARS-CoV-2. Understanding the origins of SARS-CoV-2 is critical for deterring future zoonosis, discovering new drugs, and developing a vaccine. We show evidence of strong purifying selection around the receptor binding motif (RBM) in the spike and other genes among bat, pangolin, and human coronaviruses, suggesting similar evolutionary constraints in different host species. We also demonstrate that 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. Similar purifying selection in different host species, together with frequent recombination among coronaviruses, suggests a common evolutionary mechanism that could lead to new emerging human coronaviruses.

### **Reference**

Li, Xiaojun, Elena E. Giorgi, Manukumar Honnayakanahalli Marichannegowda, Brian Foley, Chuan Xiao, Xiang-Peng Kong, Yue Chen, S. Gnanakaran, Bette Korber, and

Feng Gao. "Emergence of SARS-CoV-2 through recombination and strong purifying selection." *Science Advances* (2020): eabb9153 (IF: 12.804).

## **Association between mobility patterns and COVID-19 transmission in the USA: A mathematical modelling study**

### **Abstract**

*Background:* Within 4 months of COVID-19 first being reported in the USA, it spread to every state and to more than 90% of all counties. During this period, the US COVID-19 response was highly decentralised, with stay-at-home directives issued by state and local officials, subject to varying levels of enforcement. The absence of a centralised policy and timeline combined with the complex dynamics of human mobility and the variable intensity of local outbreaks makes assessing the effect of large-scale social distancing on COVID-19 transmission in the USA a challenge.

*Methods:* We used daily mobility data derived from aggregated and anonymised cell (mobile) phone data, provided by Teralytics (Zürich, Switzerland) from Jan 1 to April 20, 2020, to capture real-time trends in movement patterns for each US county, and used these data to generate a social distancing metric. We used epidemiological data to compute the COVID-19 growth rate ratio for a given county on a given day. Using these metrics, we evaluated how social distancing, measured by the relative change in mobility, affected the rate of new infections in the 25 counties in the USA with the highest number of confirmed cases on April 16, 2020, by fitting a statistical model for each county.

*Findings:* Our analysis revealed that mobility patterns are strongly correlated with decreased COVID-19 case growth rates for the most affected counties in the USA, with Pearson correlation coefficients above 0.7 for 20 of the 25 counties evaluated. Additionally, the effect of changes in mobility patterns, which dropped by 35–63% relative to the normal conditions, on COVID-19 transmission are not likely to be perceptible for 9–12 days, and potentially up to 3 weeks, which is consistent with the incubation time of severe acute respiratory syndrome coronavirus 2 plus additional time for reporting. We also show evidence that behavioural changes were already underway in many US counties days to weeks before state-level or local-level stay-at-home policies were

implemented, implying that individuals anticipated public health directives where social distancing was adopted, despite a mixed political message.

*Interpretation:* This study strongly supports a role of social distancing as an effective way to mitigate COVID-19 transmission in the USA. Until a COVID-19 vaccine is widely available, social distancing will remain one of the primary measures to combat disease spread, and these findings should serve to support more timely policy making around social distancing in the USA in the future.

## Reference

[https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30553-3/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30553-3/fulltext)

**Publication Date: June 30, 2020**

## Suppression of a SARS-CoV-2 outbreak in the Italian municipality of Vo'

### Abstract

On the 21<sup>st</sup> of February 2020 a resident of the municipality of Vo', a small town near Padua, died of pneumonia due to SARS-CoV-2 infection. This was the first COVID-19 death detected in Italy since the emergence of SARS-CoV-2 in the Chinese city of Wuhan, Hubei province. In response, the regional authorities imposed the lockdown of the whole municipality for 14 days. We collected information on the demography, clinical presentation, hospitalization, contact network and presence of SARS-CoV-2 infection in nasopharyngeal swabs for 85.9% and 71.5% of the population of Vo' at two consecutive time points. On the first survey, which was conducted around the time the town lockdown started, we found a prevalence of infection of 2.6% (95% confidence interval (CI) 2.1-3.3%). On the second survey, which was conducted at the end of the lockdown, we found a prevalence of 1.2% (95% Confidence Interval (CI) 0.8-1.8%). Notably, 42.5% (95% CI 31.5-54.6%) of the confirmed SARS-CoV-2 infections detected across the two surveys were asymptomatic (i.e. did not have symptoms at the time of swab testing and did not develop symptoms afterwards). The mean serial interval was 7.2 days (95% CI 5.9-9.6). We found no statistically significant difference in the viral load of symptomatic versus asymptomatic infections (p-values 0.62 and 0.74 for E and RdRp genes, respectively,

Exact Wilcoxon-Mann-Whitney test). This study sheds new light on the frequency of asymptomatic SARS-CoV-2 infection, their infectivity (as measured by the viral load) and provides new insights into its transmission dynamics and the efficacy of the implemented control measures.

## Reference

Lavezzo, Enrico, Elisa Franchin, Constanze Ciavarella, Gina Cuomo-Dannenburg, Luisa Barzon, Claudia Del Vecchio, Lucia Rossi *et al.* "Suppression of COVID-19 outbreak in the municipality of Vo, Italy." *medRxiv* (2020).

## Endotheliopathy in COVID-19-associated coagulopathy: Evidence from a single-centre, cross-sectional study

### Abstract

*Background:* An important feature of severe acute respiratory syndrome coronavirus 2 pathogenesis is COVID-19-associated coagulopathy, characterised by increased thrombotic and microvascular complications. Previous studies have suggested a role for endothelial cell injury in COVID-19-associated coagulopathy. To determine whether endotheliopathy is involved in COVID-19-associated coagulopathy pathogenesis, we assessed markers of endothelial cell and platelet activation in critically and non-critically ill patients admitted to the hospital with COVID-19.

*Methods:* In this single-centre cross-sectional study, hospitalised adult ( $\geq 18$  years) patients with laboratory-confirmed COVID-19 were identified in the medical intensive care unit (ICU) or a specialised non-ICU COVID-19 floor in our hospital. Asymptomatic, non-hospitalised controls were recruited as a comparator group for biomarkers that did not have a reference range. We assessed markers of endothelial cell and platelet activation, including von Willebrand Factor (VWF) antigen, soluble thrombomodulin, soluble P-selectin, and soluble CD40 ligand, as well as coagulation factors, endogenous anticoagulants, and fibrinolytic enzymes. We compared the level of each marker in ICU patients, non-ICU patients, and controls, where applicable. We assessed correlations between these laboratory results with clinical outcomes, including hospital discharge and

mortality. Kaplan–Meier analysis was used to further explore the association between biochemical markers and survival.

*Findings:* 68 patients with COVID-19 were included in the study from April 13 to April 24, 2020, including 48 ICU and 20 non-ICU patients, as well as 13 non-hospitalised, asymptomatic controls. Markers of endothelial cell and platelet activation were significantly elevated in ICU patients compared with non-ICU patients, including VWF antigen (mean 565% [SD 199] in ICU patients vs 278% [133] in non-ICU patients;  $p < 0.0001$ ) and soluble P-selectin (15.9 ng/mL [4.8] vs 11.2 ng/mL [3.1];  $p = 0.0014$ ). VWF antigen concentrations were also elevated above the normal range in 16 (80%) of 20 non-ICU patients. We found mortality to be significantly correlated with VWF antigen ( $r = 0.38$ ;  $p = 0.0022$ ) and soluble thrombomodulin ( $r = 0.38$ ;  $p = 0.0078$ ) among all patients. In all patients, soluble thrombomodulin concentrations greater than 3.26 ng/mL were associated with lower rates of hospital discharge (22 [88%] of 25 patients with low concentrations vs 13 [52%] of 25 patients with high concentrations;  $p = 0.0050$ ) and lower likelihood of survival on Kaplan–Meier analysis (hazard ratio 5.9, 95% CI 1.9–18.4;  $p = 0.0087$ ).

*Interpretation:* Our findings show that endotheliopathy is present in COVID-19 and is likely to be associated with critical illness and death. Early identification of endotheliopathy and strategies to mitigate its progression might improve outcomes in COVID-19.

## Reference

[https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026\(20\)30216-7/fulltext](https://www.thelancet.com/journals/lanhae/article/PIIS2352-3026(20)30216-7/fulltext).

## **Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease: Retrospective long-term follow-up of the LIR!C trial**

### Abstract

*Background:* The LIR!C trial showed that laparoscopic ileocaecal resection is a cost-effective treatment that has similar quality-of-life outcomes to treatment with infliximab, an anti-tumour necrosis factor (TNF) drug. We aimed to compare long-term outcomes of

both interventions and identify baseline factors associated with the duration of treatment effect in each group.

*Methods:* In this retrospective follow-up study, we collected data from patients who participated in the LIR!C trial, a multicentre randomised controlled trial that compared quality of life after surgical resection versus infliximab in adult patients with non-stricturing and immunomodulator-refractory ileocaecal Crohn's disease. From Jan 1 to May 1, 2018, we collected follow-up data from the time from enrolment in the LIR!C trial until the last visit at either the gastrointestinal surgeon or gastroenterologist. In this study, outcomes of interest were need for surgery or repeat surgery or anti-TNF therapy, duration of treatment effect, and identification of factors associated with the duration of treatment effect. Duration of treatment effect was defined as the time without need for additional Crohn's disease-related treatment (corticosteroids, immunomodulators, biologics, or surgery).

*Findings:* We collected long-term follow-up data for 134 (94%) of 143 patients included in the LIR!C trial, of whom 69 were in the resection group and 65 were in the infliximab group. Median follow-up was 63.5 months (IQR 39.0–94.5). In the resection group, 18 (26%) of 69 patients started anti-TNF therapy and none required a second resection. 29 (42%) patients in the resection group did not require additional Crohn's disease-related medication, although 14 (48%) of these patients were given prophylactic immunomodulator therapy. In the infliximab group, 31 (48%) of 65 patients had a Crohn's disease-related resection, and the remaining 34 patients maintained, switched, or escalated their anti-TNF therapy. Duration of treatment effect was similar in both groups, with a median time without additional Crohn's disease-related treatment of 33.0 months (95% CI 15.1–50.9) in the resection group and 34.0 months (0.0–69.3) in the infliximab group (log-rank  $p=0.52$ ). In both groups, therapy with an immunomodulator, in addition to the allocated treatment, was associated with duration of treatment effect (hazard ratio for resection group 0.34 [95% CI 0.16–0.69] and for infliximab group 0.49 [0.26–0.93]).

*Interpretation:* These findings further support laparoscopic ileocaecal resection as a treatment option in patients with Crohn's disease with limited (affected segment  $\leq 40$  cm) and predominantly inflammatory terminal ileitis for whom conventional treatment is not successful.

## Reference

Ponsioen, Cyriel Y., E. Joline de Groof, Emma J. Eshuis, Tjibbe J. Gardenbroek, Patrick MM Bossuyt, Ailsa Hart, Janindra Warusavitarne et al. "Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn's disease: a randomised controlled, open-label, multicentre trial." *The Lancet Gastroenterology & Hepatology* 2, no. 11 (2017): 785-792 (IF: 14.789).

**Publication Date: June 29, 2020**

## Digital tools against COVID-19: taxonomy, ethical challenges, and navigation aid

### Abstract

Data collection and processing via digital public health technologies are being promoted worldwide by governments and private companies as strategic remedies for mitigating the COVID-19 pandemic and loosening lockdown measures. However, the ethical and legal boundaries of deploying digital tools for disease surveillance and control purposes are unclear, and a rapidly evolving debate has emerged globally around the promises and risks of mobilising digital tools for public health. To help scientists and policy makers to navigate technological and ethical uncertainty, we present a typology of the primary digital public health applications that are in use. These include proximity and contact tracing, symptom monitoring, quarantine control, and flow modelling. For each, we discuss context-specific risks, cross-sectional issues, and ethical concerns. Finally, recognising the need for practical guidance, we propose a navigation aid for policy makers and other decision makers for the ethical development and use of digital public health tools.

### Reference

[https://www.thelancet.com/journals/landig/article/PIIS2589-7500\(20\)30137-0/fulltext](https://www.thelancet.com/journals/landig/article/PIIS2589-7500(20)30137-0/fulltext)

**Publication Date: June 25, 2020**

## Revealing the molecular mechanisms of proteolysis of SARS-CoV-2 M<sup>Pro</sup> from QM/MM computational methods



## **Abstract**

SARS-CoV-2 Mpro is one of the enzymes essential for the replication process of the virus responsible of the COVID19 pandemic. This work is focused on exploring its proteolysis reaction by means of QM/MM methods. The resulting free energy landscape of the process provides valuable information on the species appearing along the reaction path and suggests that the mechanism of action of this enzyme, taking place in four steps, slightly differs from other cysteine proteases. Our predictions, supported by the agreement with some recently published experimental data, can be used to guide the design of COVID-19 antiviral compounds with clinical potential.

## **Reference**

Świderek, Katarzyna, and Vicent Moliner. "Revealing the Molecular Mechanisms of Proteolysis of SARS-CoV-2 M pro from QM/MM Computational Methods." *Chemical Science* (2020) (IF: 9.556).

# NEWSLETTER

**Publication Date: June 29, 2020**

## **New White House rules restrict use of grant funding to deal with COVID-19 impacts**

New rules on how U.S. universities manage federal research grants leave them with less flexibility to cope with the pandemic. The changes, which rescind many temporary measures adopted this spring as COVID-19 shuttered campuses and froze the economy, come despite continued uncertainty over the fall semester and the status of research on U.S. campuses. For more details, view the link given below.

### **Reference**

<https://www.sciencemag.org/news/2020/06/new-white-house-rules-restrict-use-grant-funding-deal-covid-19-impacts>

## **The line is forming for a COVID-19 vaccine. Who should be at the front?**

When and if the world has a COVID-19 vaccine, who should get it first? That question came into sharp relief last week. A committee that makes vaccine use recommendations to the U.S. Centers for Disease Control and Prevention (CDC) wrestled with the issue in a virtual meeting, and new data suggested how fraught any prioritization is likely to be: Pregnant women—normally the last to receive a new vaccine, given the possibility of harm to a fetus—may have an increased risk of severe illness from COVID-19, suggesting they should be high on the list. Sonja Rasmussen, a pediatrician at the University of Florida, who has collaborated with Jamieson on studies of different infections during pregnancy, said it may turn out that having COVID-19 harms not only mothers, but fetuses in the first trimester.

In addition, WHO on June 18, 2020 laid out its own rough “*strategic allocation*.” It would give priority to nearly 2 billion people, lumping together “healthcare system workers,” adults older than 65 or as young as 30 if they are at higher COVID-19 risk. Because they have comorbidities, such as cardiovascular disease, cancer, diabetes, obesity, or chronic respiratory disease.



GRAPHIC: N. DESAI/SCIENCE; DATA: WORLD HEALTH ORGANIZATION

For more details, view the link given below.

## Reference

<https://www.sciencemag.org/news/2020/06/line-forming-covid-19-vaccine-who-should-be-front>

**Publication Date: June 26, 2020**

## It's safe to go back to the gym—if there's little COVID-19 around, study suggests

A study on the risk of coronavirus transmission in Oslo found that people, who went to a gym were no more likely to get infected, or sick, than people who didn't. Norway has reopened its gyms based on the tentative results, which were published as a preprint yesterday and still need to go through peer review. But Emily Smith, an epidemiologist at George Washington University, highlighted that zero COVID cases were covered in this study as well as also pointed brief time period covered by the study.

Additionally, according to Hilda Bastian, a former consumer health care advocate, who studied evidence-based medicine: Widespread publicity of the results without noting the caveats could be harmful. She applauded the use of a clinical trial to study the safety of reopening. Hence, newly reopened gyms will be studied for the infection risk at Oslo that have more or less stringent hygiene and social distancing measures. For more details, view the link given below.

## Reference

<https://www.sciencemag.org/news/2020/06/it-s-safe-go-back-gym-if-there-s-little-covid-19-around-study-suggests>

# PERSPECTIVE

**Publication Date: June 26, 2020**

## Evolution after genome duplication

Genome duplication generates an extra copy of nearly all genes carried by an organism, providing a potential substrate for evolution. Although many duplicate genes will be eliminated after a genome duplication, those that are retained may evolve distinct functions over time. This process can be studied by characterizing the shared and divergent functions of duplicate genes in present-day organisms whose ancestors experienced genome duplication in the past. However, such work requires examining the functional relationships between each copy of a duplicated gene and the other genes in the genome. This is inherently difficult for duplicate genes because of their redundancy. However, on page 1445 of this issue, Kuzmin *et al.* show that systematic analysis of di- and trigenic genetic interactions in budding yeast can overcome this challenge. With this approach, they discover general constraints that influence the retention and divergence of duplicate genes.

## **Reference**

<https://science.sciencemag.org/content/368/6498/1424>

## Reducing transmission of SARS-CoV-2

Respiratory infections occur through the transmission of virus-containing droplets (>5 to 10  $\mu\text{m}$ ) and aerosols ( $\leq 5 \mu\text{m}$ ) exhaled from infected individuals during breathing, speaking, coughing, and sneezing. Traditional respiratory disease control measures are designed to reduce transmission by droplets produced in the sneezes and coughs of infected individuals. However, a large proportion of the spread of coronavirus disease 2019 (COVID-19) appears to be occurring 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. For society to resume, measures designed to reduce aerosol transmission must

be implemented, including universal masking and regular, widespread testing to identify and isolate infected asymptomatic individuals.

In addition, a multidisciplinary approach is needed to address a wide range of factors that lead to the production and airborne transmission of respiratory viruses, including the minimum virus titer required to cause COVID-19; viral load emitted as a function of droplet size before, during, and after infection; viability of the virus indoors and outdoors; mechanisms of transmission; airborne concentrations; and spatial patterns. More studies of the filtering efficiency of different types of masks are also needed. COVID-19 has inspired research that is already leading to a better understanding of the importance of airborne transmission of respiratory disease. For more details, read the link given below.

### **Reference**

<https://science.sciencemag.org/content/368/6498/1422>

# BLOG

**Publication Date: June 30, 2020**

## The tricky math of herd immunity for COVID-19

While much about the COVID-19 pandemic remains uncertain, we know how it will likely end: when the spread of the virus starts to slow (and eventually ceases altogether) because enough people have developed immunity to it. At that point, whether it's brought on by a vaccine or by people catching the disease, the population has developed "herd immunity." While determining that threshold for COVID-19 is critical, a lot of nuance is involved in calculating exactly how much of the population needs to be immune for herd immunity to take effect and protect the people who aren't immune.

For more details, view the link given below.

### **Reference**

<https://www.quantamagazine.org/the-tricky-math-of-covid-19-herd-immunity-20200630/>

# SPOTLIGHT

**Publication Date: June 29, 2020**

## Child poverty, food insecurity, and respiratory health during the COVID-19 pandemic

### **Abstract**

The eradication of poverty and hunger are the top sustainable development goals, adopted by UN Member States in 2015. Yet the World Food Programme estimates that, in the wake of the COVID-19 pandemic, acute food insecurity could double from 135 to 265 million people worldwide. In the absence of mitigating policies, poverty leading to food insecurity will damage the respiratory health of a generation of children.

Inequalities in lifelong respiratory health originate in childhood, when adequate nutrition is essential. The respiratory system starts to develop 3 weeks after conception, and grows until adolescence, with the lungs maturing most rapidly in size and intricacy in the first three years of life. Disruption to this development in childhood contributes considerably to the early onset of adult illnesses, such as chronic obstructive pulmonary disease (COPD). This disruption can be driven by many of the consequences of living in poverty, including malnutrition. Even in cystic fibrosis, an inherited genetic disease, health inequalities can be seen: social disadvantages can disrupt respiratory development, influencing survival in people with the condition. On moral, ethical, and medical grounds, we must ensure that children have enough food to eat, and national programmes to reduce inequalities in respiratory health will not succeed unless they were addressed. For more details, read the link below.

### **Reference**

[https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30280-0/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30280-0/fulltext)