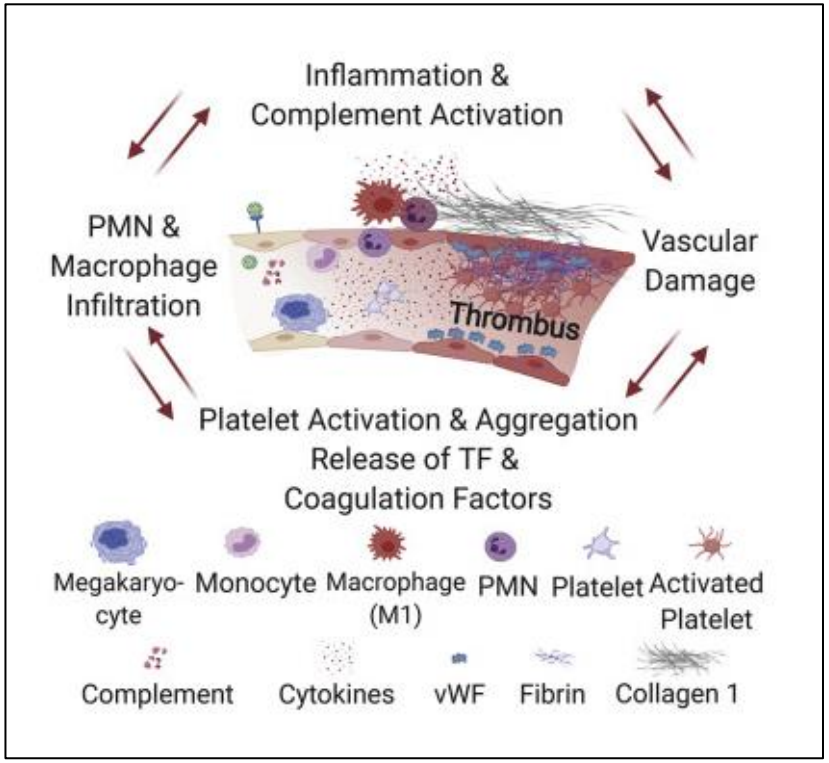
RICERCA BIBLIOGRAFICA COVID 19

SETTIMANA 30.11 – 6.12.2020

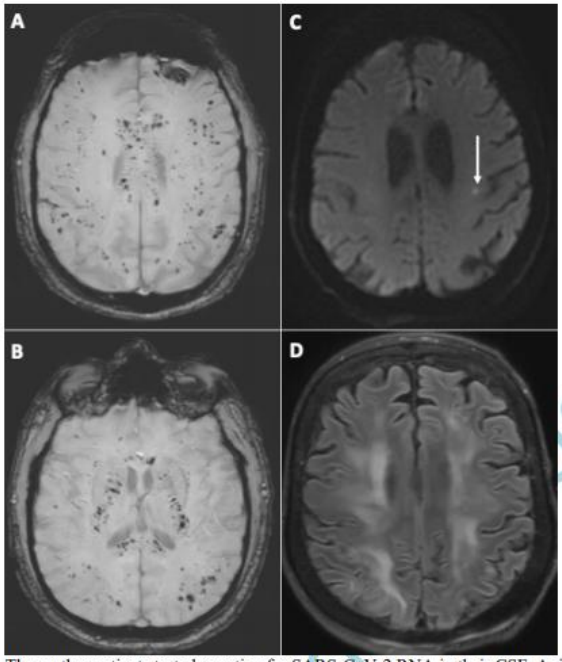
FONDAZIONE POLICLINICO UNIVERSITARIO A. GEMELLI IRCCS, UOC MALATTIE INFETTIVE

DOTT.SSA ELEONORA TADDEI

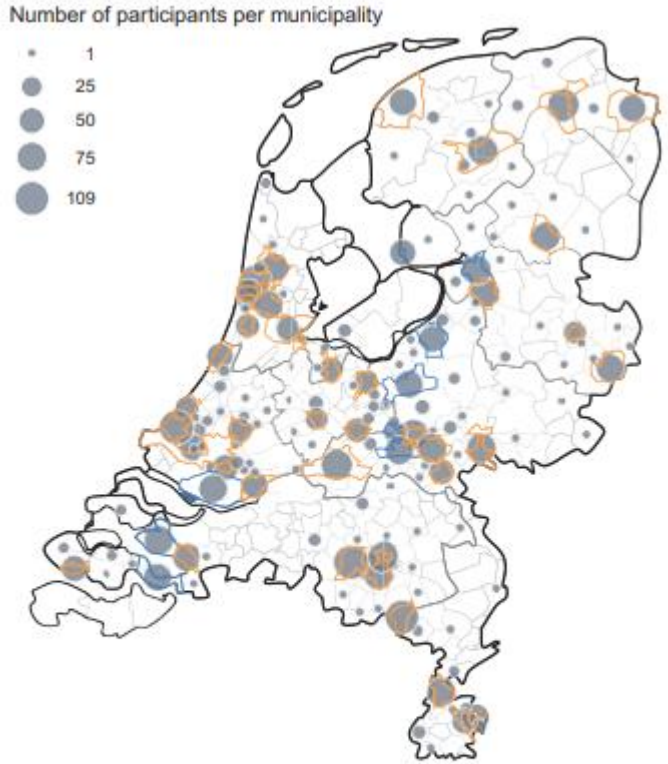
AUTORE/RIVISTA	TITOLO	OUTCOME PRINCIPALE	ABSTRACT
Aid M et al Cell https://www.cell.com/cell/fulltext/S0092-8674(20)31311-8	Vascular Disease and Thrombosis in SARS-CoV-2-Infected Rhesus Macaques	Interazione fra infiammazione e cascata coagulativa a livello dell'endotelio polmonare di macachi infettati da SARS-CoV-2.	The COVID-19 pandemic has led to extensive morbidity and mortality throughout the world. Clinical features that drive SARS-CoV-2 pathogenesis in humans include inflammation and thrombosis, but the mechanistic details underlying these processes remain to be determined. In this study, we demonstrate endothelial disruption and vascular thrombosis in histopathologic sections of lungs from both humans and rhesus macaques infected with SARS-CoV-2. To define key molecular pathways associated with SARS-CoV-2 pathogenesis in macaques, we performed transcriptomic analyses of bronchoalveolar lavage and peripheral blood and proteomic analyses of serum. We observed macrophage infiltrates in lung and upregulation of macrophage, complement, platelet activation, thrombosis, and proinflammatory markers, including C-reactive protein, MX1, IL-6, IL-1, IL-8, TNFα, and NF-κB. These results suggest a model in which critical interactions between inflammatory and thrombosis pathways lead to SARS-CoV-2-

			induced vascular disease. Our findings suggest potential therapeutic targets for COVID-19. 
Lersy F et al Journal of Infectious Diseases https://doi.org/10.1093/infdis/jiaa745	Cerebrospinal fluid features in COVID-19 patients with neurologic manifestations: correlation with brain MRI findings in 58 patients.	Studio monocentrico sulle caratteristiche cliniche, ematobiochimiche, liquorali e di neuroimaging di 58 pazienti con manifestazioni neurologiche in corso di infezione da SARS-CoV-2.	BACKGROUND: Neurological manifestations are common in patients with COVID-19, but little is known about pathophysiological mechanisms. In this single-center study, we describe neurological manifestations of 58 patients, regarding cerebrospinal fluid (CSF) analysis and neuroimaging findings. METHODS: 58 COVID-19 patients with neurologic manifestations and SARS-CoV-2 RT-PCR screening on CSF analysis were included. Clinical, laboratory, and brain MRI data were retrospectively collected and analyzed.

			RESULTS: Patients were mostly men (66%) with a median age of 62 years. Encephalopathy was frequent (81%), followed by a pyramidal dysfunction (16%), seizures (10%), and headaches (5%). Protein and albumin levels in CSF were increased in 38% and 23%, respectively. A total of 40% of patients displayed an elevated albumin quotient suggesting impaired blood-brain barrier integrity. CSF-specific IgG oligoclonal band was found in five (11%) cases, suggesting an intrathecal synthesis of IgG, and 26 (55%) patients presented identical oligoclonal bands in serum and CSF. Four (7%) patients harbored a positive SARS-CoV-2 RT-PCR in CSF. Regarding brain MRI, 20 (38%) patients presented leptomeningeal enhancement. CONCLUSIONS: Brain MRI abnormalities, especially leptomeningeal enhancement, and increased inflammatory markers in CSF are frequent in patients with neurological manifestations related to COVID-19, whereas SARS-CoV 2 detection in CSF remained scanty.

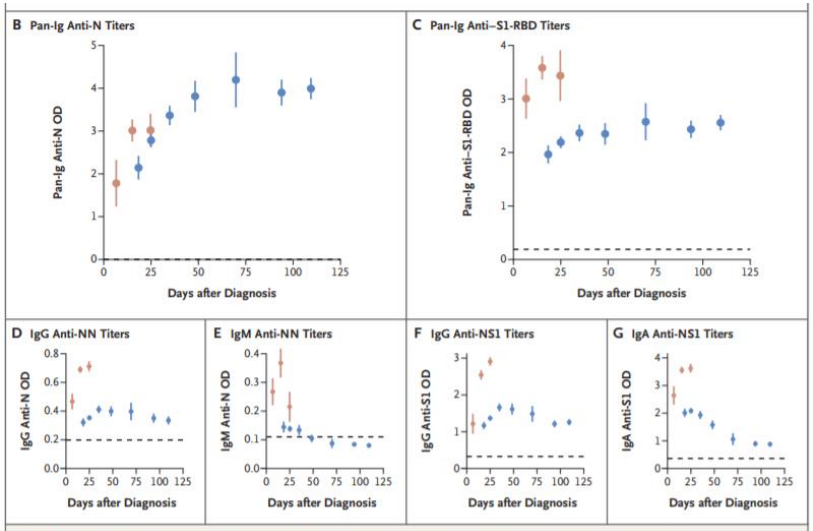
			Figure 2 :  Three other patients tested negative for SARS-CoV-2 RNA in their CSF. Axial susceptibility-weighted MR images (A, B), axial Diffusion (C), and axial FLAIR (D). A, B : 57-year old man with white matter diffuse microhemorrhages appearing as multiple small hypointense foci within the corpus callosum, the internal capsules, and the juxtacortical white matter. C: 81-year old woman with watershed cerebral infarction. D: 71-year old woman with extensive and confluent supratentorial white matter FLAIR hyperintensities.
Vos ERA et al Journall of Epidemiology and Community Health https://doi.org/10.1136/jech-2020-215678	Nationwide seroprevalence of SARS-CoV-2 and identification of risk factors in the general population of the Netherlands during the first epidemic wave.	Studio di sieroprevalenza su 3207 abitanti dei Paesi Bassi per infezione da SARS-CoV-2 : si stima una sieroprevalenza nazionale di 2.8%, con positività anticorpale associata a fascia d'età giovanile, immunosoppressione,	BACKGROUND: We aimed to detect SARS-CoV-2 serum antibodies in the general population of the Netherlands and identify risk factors for seropositivity amidst the first COVID-19 epidemic wave. METHODS: Participants (n=3207, aged 2-90 years), enrolled from a previously established nationwide serosurveillance study, provided a self-collected fingerstick blood sample and completed a questionnaire (median inclusion date 3 April 2020). IgG antibodies targeted against the spike S1-protein of SARS-CoV-2 were quantified using a validated multiplex-immunoassay. Seroprevalence was

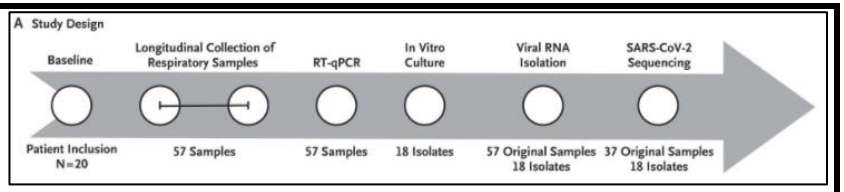
		appartenenza religiosa (protestanti ortodossi).	estimated controlling for survey design, individual pre-pandemic concentration, and test performance. Random-effects logistic regression identified risk factors for seropositivity. RESULTS: Overall seroprevalence in the Netherlands was 2.8% (95% CI 2.1 to 3.7), with no differences between sexes or ethnic background, and regionally ranging between 1.3 and 4.0%. Estimates were highest among 18-39 year-olds (4.9%), and lowest in children 2-17 years (1.7%). Multivariable analysis revealed that persons taking immunosuppressants and those from the Orthodox-Reformed Protestant community had over four times higher odds of being seropositive compared to others. Anosmia/ageusia was the most discriminative symptom between seropositive (53%) and seronegative persons (4%, p<0.0001). Antibody concentrations in seropositive persons were significantly higher in those with fever or dyspnoea in contrast to those without (p=0.01 and p=0.04, respectively). CONCLUSIONS: In the midst of the first epidemic wave, 2.8% of the Dutch population was estimated to be infected with SARS-CoV-2, that is, 30 times higher than reported. This study identified independent groups with increased odds for seropositivity that may require specific surveillance measures to guide future protective interventions internationally, including vaccination once available.

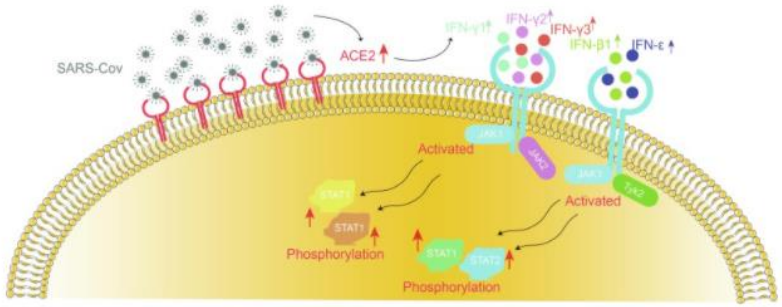
			 **Figure 1** Geographical representation of number of participants in the PICO-study, the Netherlands, first round of inclusion, per municipality. The size of the dots reflect the absolute number of participants. Thicker grey and smaller light grey boundaries represent provinces and municipalities, respectively, and orange and blue boundaries characterise municipalities from the national and low vaccination coverage sample, respectively.
Kuiper V et al Clinical Infectious Diseases	Assessment of risks associated with SARS-CoV-2 experimental human infection studies.	Un commento sulla prospettiva di condurre studi di « infezione umana	Controlled human infection (CHI) models for the novel coronavirus (SARS-CoV-2) have been proposed as a tool to accelerate the development of vaccines and drugs. Such models carry inherent risks. Participants may develop severe disease or complications after deliberate infection. Prolonged isolation may negatively

https://doi.org/10.1093/cid/ciaa1784		controllata » (CHI) da SARS-CoV-2 a scopo di ricerca.	impact their wellbeing. Through secondary infection of study personnel or participant household contacts, the experimental virus strain may cause a community outbreak. We identified risks associated with such a SARS-CoV-2 CHI model and assessed their likelihood and impact and propose strategies that mitigate these risks. In this report, we show that risks can be minimized with proper risk mitigation strategies; the residual risk however should be weighed carefully against the scientific and social values of such a CHI model.
Vogel G et al Science https://science.sciencemag.org/content/370/6520/1023	Grade: incomplete	Effetti della riapertura delle scuole nell'esperienza internazionale maturata finora e possibili misure per il futuro con il protrarsi della pandemia di COVID-19.	Schools around the world are again the site of a large, and largely uncontrolled, experiment. When schools from New Zealand to Norway to Japan reopened in April and May as the first wave of COVID-19 cases subsided, the virus stayed mostly at bay. Health and education officials cheered, having bet that the huge benefits of in-person schooling outweighed the risk of viral spread among children and teachers—and from schools to wider communities
Chiu T et al Journal of Formosan Medical Association https://doi.org/10.1016/j.jfma.2020.11.006	Changes in pediatric seizure-related emergency department attendances during COVID-19 - A territory-wide observational study.	Riduzione degli accessi in DEA per convulsioni nel bambino durante il periodo gennaio-aprile 2020 rispetto agli anni precedenti : minore ricorso alle cure o effettiva riduzione dell'incidenza di infezioni che provocano convulsioni febbrili ?	A territory-wide retrospective observational study was conducted in Hong Kong between January 23 to April 22, 2020 to demonstrate changes in pediatric seizure-related accident and emergency department (A&E) visits during the COVID-19 pandemic. Parallel periods from 2015 to 2019 were used as control. All-cause A&E attendances in all paediatric age groups decreased significantly during the study period. Seizure-related attendances decreased across all pediatric age-groups in 2020 (RR 0.379, 95% CI 0.245-0.588), with a disproportionately large decrease in the 0-6 years age group (RR 0.303, 95% CI 0.174-0.526) compared with the 7-18 years age group (RR 0.534, 95% CI 0.393-0.719). Decrease in RTI-related

			A&E attendances was also more drastic in the 0-6 age group. The two time trends are congruent in the 0-6 years but not the 7-18 years age group. Such a trend is suggestive of the usefulness of infection control measures in seizure prevention, especially amongst young children.
Gudbjartsson DF et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2026116?query=featured_coronavirus	Humoral Immune Response to SARS-CoV-2 in Iceland	Esiti dello studio della risposta anticorpale contro SARS-CoV-2 di più di 30.000 persone in Islanda, fra cui 1797 guariti da COVID-19 : in questi ultimi la risposta anticorpale mantiene livelli elevati fino a 4 mesi dopo l'infezione.	BACKGROUND Little is known about the nature and durability of the humoral immune response to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). METHODS We measured antibodies in serum samples from 30,576 persons in Iceland, using six assays (including two pan-immunoglobulin [pan-Ig] assays), and we determined that the appropriate measure of seropositivity was a positive result with both pan-Ig assays. We tested 2102 samples collected from 1237 persons up to 4 months after diagnosis by a quantitative polymerase-chain-reaction (qPCR) assay. We measured antibodies in 4222 quarantined persons who had been exposed to SARS-CoV-2 and in 23,452 persons not known to have been exposed. RESULTS Of the 1797 persons who had recovered from SARS-CoV-2 infection, 1107 of the 1215 who were tested (91.1%) were seropositive; antiviral antibody titers assayed by two pan-Ig assays increased during 2 months after diagnosis by qPCR and remained on a plateau for the remainder of the study. Of quarantined persons, 2.3% were seropositive; of those with unknown exposure, 0.3% were positive. We estimate that 0.9% of Icelanders were infected with SARS-CoV-2 and that the infection was fatal in 0.3%. We also estimate that 56% of all SARS-CoV-2 infections in Iceland had been diagnosed with qPCR, 14% had occurred in quarantined persons who had not been tested with qPCR (or who had not received a positive result, if tested), and 30% had occurred in persons outside quarantine and not tested with qPCR.

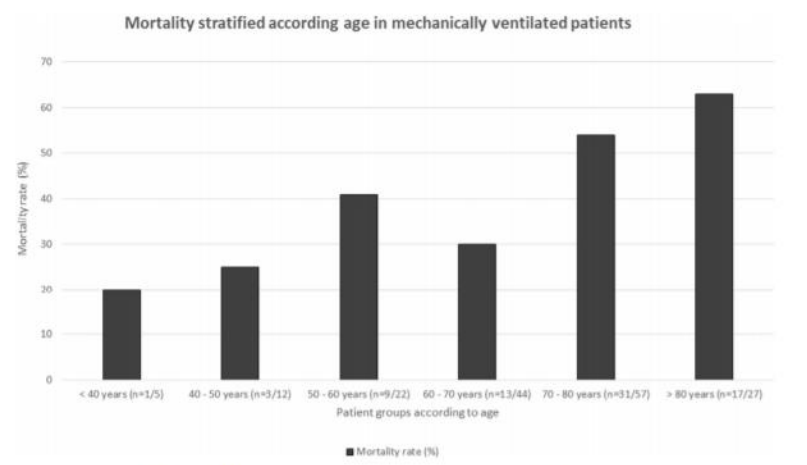
			CONCLUSIONS Our results indicate that antiviral antibodies against SARS-CoV-2 did not decline within 4 months after diagnosis. We estimate that the risk of death from infection was 0.3% and that 44% of persons infected with SARS-CoV-2 in Iceland were not diagnosed by qPCR.  **Figure 2. Antibody Prevalence and Titers among qPCR-Positive Cases as a Function of Time since Diagnosis by qPCR.** Shown are the percentages of samples positive for both pan-Ig antibody assays and the antibody titers. Red denotes the count or percentage of samples among persons during their hospitalization (249 samples from 48 persons), and blue denotes the count or percentage of samples among persons after they were declared recovered (1853 samples from 1215 persons). Vertical bars denote 95% confidence intervals. The dashed lines indicated the thresholds for a test to be declared positive. OD denotes optical density, and RBD receptor binding domain.
Aydillo t ET AL Nejm https://www.nejm.org/doi/full/10.1056/NEJMc2031670?query=featured_coronavirus	Shedding of Viable SARS-CoV-2 after Immunosuppressive Therapy for Cancer	Studio dello shedding virale da parte di 20 soggetti immunodepressi (ematologici) con infezione da SARS-CoV-2 : si dimostra eliminazione di virus infettante fino a 60 giorni dopo l'esordio dell'infezione.	Detection of replication-competent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the most reliable indicator of contagiousness.1 Although the duration of live-virus shedding is well-characterized in immunocompetent patients with coronavirus disease 19 (Covid-19), little is known about how long immunocompromised patients are contagious. Consequently, the Centers for Disease Control and Prevention (CDC) guidelines on transmission-based precautions for immunocompromised patients are based on limited data.

			
Luo J et al Gene https://doi.org/10.1016/j.gene.2020.145325	The potential involvement of JAK-STAT signaling pathway in the COVID-19 infection assisted by ACE2.	L'attivazione della via di JAK-STAT da parte di ACE2, recettore cellulare di SARS-CoV-2, offre un interessante bersaglio terapeutico.	COVID-19, a novel identified coronavirus disease due to Severe Acute Respiratory Syndrome coronaviruses 2 (SARS-Cov-2) infection, has posed a significant threat to public health worldwide. It has been reported COVID-19 keeps substantial nucleotide similarity and shares common receptor, Angiotensin-converting enzyme 2 (ACE2) with Severe Acute Respiratory Syndrome coronaviruses (SARS-Cov). Here, we investigated the gene expression of ACE2 and identified associated pathways of SARS-Cov as a useful reference for a deepening understanding of COVID-19. The results indicated the ACE2 was overexpressed in human airway epithelial cells (HAEs), especially at 72h after SARS-Cov infection. We found ACE2 might regulate immune response through immunological activation-associated pathways in the process of in both SARS-Cov and SARS-Cov-2 infection, where the activation of B cells, macrophages, helper T cells 1(Th1 cells) and the inhibition of Foxp3+ regulatory T (Treg) cells and CD8+T cells were found to be prominent. Finally, significant correlation between ACE2 and JAK-STAT signaling pathway was identified which indicate that JAK-STAT signaling pathway might involve in the downstream action of the overactivation of ACE2. These findings are expected to gain a further insight into the action mechanism of COVID-19 infection and provide a promising target for designing effective therapeutic strategies.

			 Download : Download high-res image (518KB) Download : Download full-size image Fig. 7. The schematic model showing the hypothesis for COVID-19 infection.
Stefanelli P et al Clinical Microbiology and Infection	Prevalence of SARS-CoV-2 IgG antibodies in an area of North-eastern Italy with a high incidence of COVID-19 cases: a population-based study.	Studio di sieroprevalenza di infezione da SARS-CoV-2 su 6098 abitanti della Provincia di Trento, in Italia.	OBJECTIVES: A seroprevalence study of SARS-CoV-2 was conducted in a high-incidence area located in North-eastern Italy. METHODS: All citizens above ten years of age resident in 5 municipalities of the Autonomous Province of Trento, with the highest incidence of COVID-19 cases, were invited to participate in the study. Overall, among 6098 participants, 6075 sera and a standardized questionnaire administered face-to-face were collected between May 5 and 15, 2020 and examined. Symptomatic individuals and their family contacts were tested by RT-PCR. Anti-SARS-CoV-2 antibodies were detected using an Abbott SARS-CoV-2 IgG assay which was performed on the Abbott Architect i2000SR automated analyzer. Seroprevalence was calculated as the proportion of positive people on the total number of tested. A multivariable logistic regression model was performed to assess the relationship between seropositive versus seronegative individuals for a set of explanatory variables. RESULTS: A total of 1402 participants were positives for IgG antibodies against SARS-CoV-2, with a prevalence of 23.1% (1402/6075). The highest prevalence was found in the age

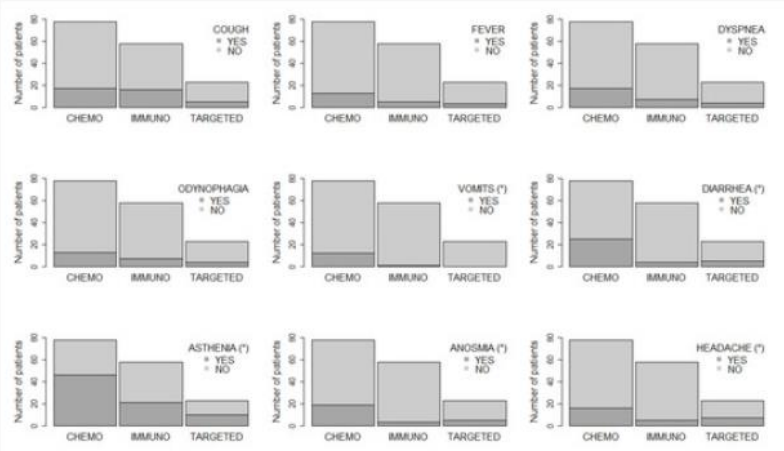
			class 40-49 years. Overall, 34.4% (2096/6098) of the participants reported at least 1 symptom. The ratio between reported cases identified by molecular test and those resulting seropositive was 1:3, with a maximum ratio of about 1:7 in the age group <20 years and a minimum around 1:1 in those >70 years old. The infection fatality rate was 2.5% (35/1402). Among the symptoms, anosmia and ageusia were strongly associated with seropositivity. CONCLUSIONS: The estimated seroprevalence of 23% was 3-fold higher than the number of cases reported in the COVID-19 Integrated Surveillance data in the study area. This may be explained in part by a relatively high number of individuals presenting mild or no illness, especially of younger age, and/or who did not seek medical care or testing, but who may contribute to virus transmission in the community.

Roedl K et al Austrian Critical Care https://doi.org/10.1016/j.aucc.2020.10.009	Mechanical ventilation and mortality among 223 critically ill patients with coronavirus disease 2019: A multicentric study in Germany.	Caratteristiche ed esito dell'infezione in 223 pazienti critici con COVID-19 ricoverati in rianimazione in Germania.	BACKGROUND: There are large uncertainties with regard to the outcome of patients with coronavirus disease 2019 (COVID-19) and mechanical ventilation (MV). High mortality (50-97%) was proposed by some groups, leading to considerable uncertainties with regard to outcomes of critically ill patients with COVID-19. OBJECTIVES: The aim was to investigate the characteristics and outcomes of critically ill patients with COVID-19 requiring intensive care unit (ICU) admission and MV. METHODS: A multicentre retrospective observational cohort study at 15 hospitals in Hamburg, Germany, was performed. Critically ill adult patients with COVID-19 who completed their ICU stay between February and June 2020 were included. Patient demographics, severity of illness, and ICU course were retrospectively evaluated. RESULTS: A total of 223 critically ill patients with COVID-19 were included. The majority, 73% (n = 163), were men; the median age was 69 (interquartile range = 58-77.5) years, with 68% (n = 151) patients having at least one chronic medical condition. Their Sequential Organ Failure Assessment score was a median of 5 (3-9) points on admission. Overall, 167 (75%) patients needed MV. Noninvasive ventilation and high-flow nasal cannula were used in 31 (14%) and 26 (12%) patients, respectively. Subsequent MV, due to noninvasive ventilation/high-flow nasal cannula therapy failure, was necessary in 46 (81%) patients. Renal replacement therapy was initiated in 33% (n = 72) of patients, and owing to severe respiratory failure, extracorporeal membrane oxygenation was necessary in 9% (n = 20) of patients. Experimental antiviral therapy was used in 9% (n = 21) of patients. Complications during the ICU stay were as follows: septic shock (40%, n = 90), heart failure (8%, n = 17), and pulmonary embolism (6%, n = 14). The length of ICU stay was a median of 13 days (5-24), and the duration of MV was 15 days (8-25). The ICU mortality was 35% (n =

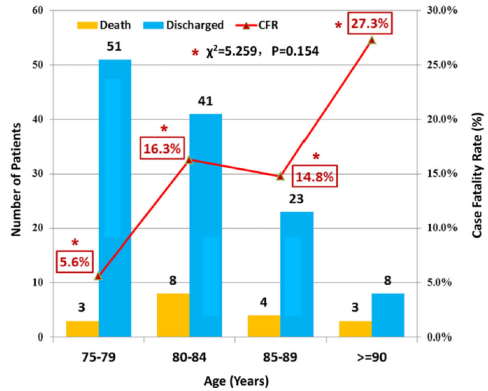
			78) and 44% (n = 74) among mechanically ventilated patients. CONCLUSION: In this multicentre observational study of 223 critically ill patients with COVID-19, the survival to ICU discharge was 65%, and it was 56% among patients requiring MV. Patients showed high rate of septic complications during their ICU stay.  **Figure 1.** Mortality stratified as per age in mechanically ventilated patients.
Thémans P et al European Journal of Drug Metabolism and Pharmacokinetics https://pubmed.ncbi.nlm.nih.gov/32968954/	Population Pharmacokinetics of Hydroxychloroquine in COVID-19 Patients: Implications for Dose Optimization	Modello farmacocinetico per idrossiclorochina nella popolazione dei malati di COVID-19.	Background and Objective In the absence of characterization on pharmacokinetics and reference concentrations for hydroxychloroquine in COVID-19 patients, the dose and treatment duration for hydrochloroquine are currently empirical, mainly based on in vitro data, and may vary across national guidelines and clinical study protocols. The aim of this paper is to describe the pharmacokinetics of hydroxychloroquine in COVID-19 patients, considered to be a key step toward its dosing optimization. Methods We have developed a population pharmacokinetic model for hydroxychloroquine in COVID-19 patients using prospectively

			collected pharmacokinetic data from patients either enrolled in a clinical trial or treated with hydroxychloroquine as part of standard of care in two tertiary Belgian hospitals. Results The final population pharmacokinetic model was a one-compartment model with first-order absorption and elimination. The estimated parameter values were 9.3/h, 860.8 L, and 15.7 L/h for the absorption rate constant, the central compartment volume, and the clearance, respectively. The bioavailability factor was fixed to 0.74 based on previously published models. Model validations by bootstraps, prediction corrected visual predictive checks, and normalized prediction distribution errors gave satisfactory results. Simulations were performed to compare the exposure obtained with alternative dosing regimens. Conclusion The developed models provide useful insight for the dosing optimization of hydroxychloroquine in COVID-19 patients. The present results should be used in conjunction with exposure-efficacy and exposure-safety data to inform optimal dosing of hydroxychloroquine in COVID-19.
Garde-Noguera J et al Cancers (Basel) https://doi.org/10.3390/cancers12123513	Impact of SARS-CoV-2 Infection on Patients with Cancer: Retrospective and Transversal Studies in Spanish Population.	Esito di uno studio retrospettivo condotto in Spagna sulla popolazione di pazienti affetti da neoplasia e infezione da SARS-CoV-2.	BACKGROUND: Studies of patients with cancer affected by coronavirus disease 2019 (COVID-19) are needed to assess the impact of the disease in this sensitive population, and the influence of different cancer treatments on the COVID-19 infection and seroconversion. MATERIAL AND METHODS: We performed a retrospective analysis of all patients hospitalized with RT-PCR positive for COVID-19 in our region to assess the prevalence of cancer patients and describe their characteristics and evolution (Cohort 1). Concurrently, a transversal study was carried out in patients on active systemic cancer treatment for symptomatology and seroprevalence (IgG/IgM by ELISA-method) against Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (Cohort 2).

			RESULTS: A total of 215 patients (Cohort 1) were admitted to hospital with a confirmed COVID-19 infection between February 28 and April 30, 2020, and 17 died (7.9%). A medical record of cancer was noted in 43 cases (20%), 6 of them required Intensive care unit ICU attention (14%), and 7 died (16%). There were thirty-six patients (83%) who tested IgG/IgM positive for SARS-CoV-2. Patients on immunosuppressive therapies presented a lower ratio of seroconversion (40% vs. 8%; $p = 0.02$). In Cohort 2, 166 patients were included in a symptoms-survey and tested for SARS-CoV-2. Any type of potential COVID-19-related symptom was referred up to 67.4% of patients (85.9% vs. 48.2% vs. 73.9%, for patients on chemotherapy, immunotherapy and targeted therapies respectively, $p < 0.05$). The seroprevalence ratio was 1.8% for the whole cohort with no significant differences by patient or treatment characteristics. CONCLUSION: Patients with cancer present higher risks for hospital needs for COVID-19 infection. The lack of SARS-CoV-2 seroconversion may be a concern for patients on immunosuppressive therapies. Patients receiving systematic therapies relayed a high rate of potentially COVID-19-related symptoms, particularly those receiving chemotherapy. However, the seroconversion rate remains low and in the range of general population.

			 Figure 1
Riou M et al Respiratory Medical Research https://doi.org/10.1016/j.resmer.2020.100801	Clinical characteristics of and outcomes for patients with COVID-19 and comorbid lung diseases primarily hospitalized in a conventional pulmonology unit: A retrospective study.	Caratteristiche cliniche ed esito dell'infezione da SARS-CoV-2 in 124 pazienti ricoverati in un reparto di Pneumologia in marzo-aprile 2020.	BACKGROUND: Scant data are currently available about a potential link between comorbid chronic lung diseases (CLD) and the risk and severity of the coronavirus disease 2019 (COVID-19) infection. METHODS: To describe the clinical characteristics of and outcomes for patients with COVID-19 infection, including patients with comorbid respiratory diseases, who have been primarily hospitalized in the pulmonology department of Strasbourg University Hospital, France. In this retrospective, single-center study, we included all confirmed cases of COVID-19 from March 3 to April 15, 2020. We then compared the symptoms, biological and radiological findings, and outcomes for patients with and without CLD. RESULTS: Of the 124 patients that were enrolled, the median age was 62 years, and 75 patients (60%) were male. Overall, 40% of patients (n=50) had preexisting CLD, including chronic obstructive pulmonary disease (COPD) (n=15, 12%) and asthma (n=19, 15%). Twenty-eight patients were transferred to the intensive care unit (ICU), and six patients died in our unit. CLD were not predictive of

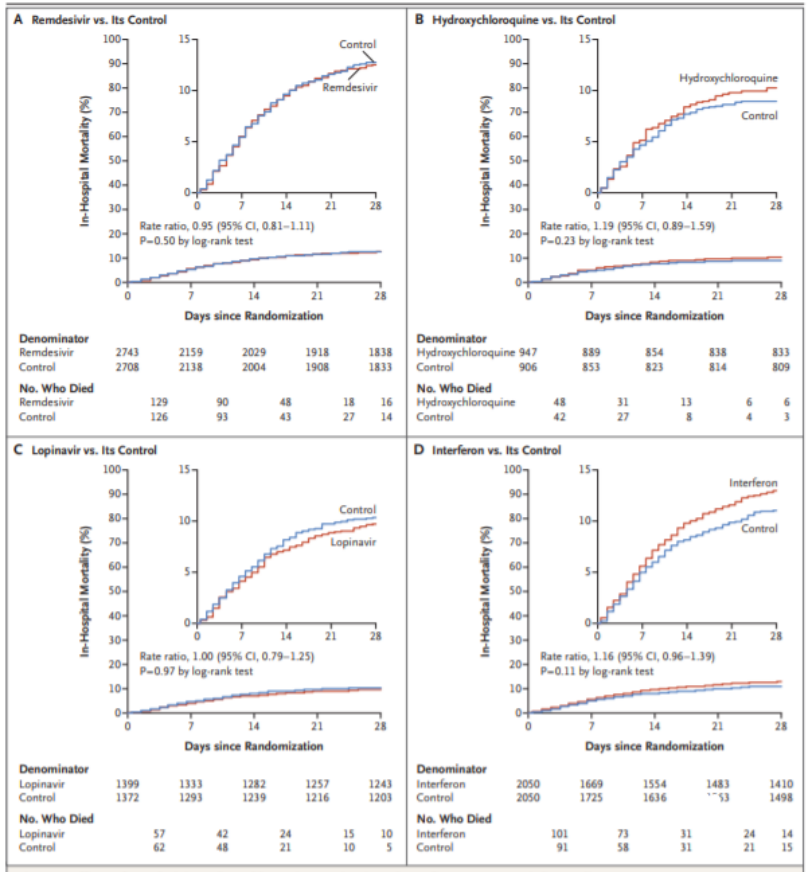
			ICU hospitalization, but a significantly higher total mortality was observed (17.6% vs. 5.5%, P<0.05) in these patients. CONCLUSIONS: Our results suggest the lack of an over-representation of CLD in COVID-19, representing 40% of patients in this cohort and even within a pulmonology department. CLD were not a risk factor for ICU management. However, a tendency to higher global mortality was observed in COVID-19 patients with CLD. Further studies are warranted to determine the risk of COVID-19 for patients with comorbid CLD.
Yu Z et al BMC Geriatrics https://doi.org/10.1186/s12877-020-01921-0	Clinical characteristics on admission predict in-hospital fatal outcome in patients aged >/=75 years with novel coronavirus disease (COVID-19): a retrospective cohort study.	Studio di coorte retrospettivo su 141 pazienti di età superiore a 75 anni ricoverati per COVID-19 in febbraio 2020.	BACKGROUND: Novel coronavirus disease 2019 (COVID-19) has become a worldwide pandemic and precise fatality data by age group is needed urgently. This study to delineate the clinical characteristics and outcome of COVID-19 patients aged >/=75 years and identify the risk factors of in-hospital death. METHODS: A total of 141 consecutive patients aged >/=75 years who were admitted to the hospital between 12th and 19th February 2020. In-hospital death, clinical characteristics and laboratory findings on admission were obtained from medical records. The final follow-up observation was on the 31st March 2020. RESULTS: The median age was 81 years (84 female, 59.6%). Thirty-eight (27%) patients were classified as severe or critical cases. 18 (12.8%) patients had died in hospital and the remaining 123 were discharged. Patients who died were more likely to present with fever (38.9% vs. 7.3%); low percutaneous oxygen saturation (SpO2) (55.6% vs. 7.3%); reduced lymphocytes (72.2% vs. 35.8%) and platelets (27.8% vs. 4.1%); and increased D-dimer (94.4% vs. 42.3%), creatinine (50.0% vs. 22.0%), lactic dehydrogenase (LDH) (77.8% vs. 30.1%), high sensitivity troponin I (hs-TnI) (72.2% vs. 14.6%), and N-terminal pro-brain natriuretic peptide (NT-proBNP) (72.2% vs. 6.5%; all P < 0.05) than patients who recovered. Male sex (odds ratio [OR] = 13.1, 95%

			confidence interval [CI] 1.1 to 160.1, P = 0.044), body temperature > 37.3 degrees C (OR = 80.5, 95% CI 4.6 to 1407.6, P = 0.003), SpO2 </= 90% (OR = 70.1, 95% CI 4.6 to 1060.4, P = 0.002), and NT-proBNP> 1800 ng/L (OR = 273.5, 95% CI 14.7 to 5104.8, P < 0.0001) were independent risk factors of in-hospital death. CONCLUSIONS: In-hospital fatality among elderly COVID-19 patients can be estimated by sex and on-admission measurements of body temperature, SpO2, and NT-proBNP.  **Fig. 1** Number of patient dead or discharged and corresponding case fatality rate across age subgroups. Patients were stratified to 4 age subgroups by every 5-year increment. Bars and numerals on the top showed number of patients who were dead or discharged in each sub-group. Numeral in red frame indicated corresponding case fatality rate (CFR) in each sub-group. There was no significant different in CFR across 4 age subgroups ($\chi^2 = 5.259$, P = 0.154)
Bulfone TC et al Journal of Infectious Diseases https://academic.oup.com/jid/advance-	Outdoor Transmission of SARS-CoV-2 and Other Respiratory Viruses, a Systematic Review	Il fatto che le infezioni virali si trasmettano difficilmente all'aperto è comunemente accettato, tuttavia la letteratura al riguardo è scarsa.	Background : While risk of outdoor transmission of respiratory viral infections is hypothesized to be low, there is limited data of SARS-CoV-2 transmission in outdoor compared to indoor settings. Methods :We conducted a systematic review of peer-reviewed papers indexed in PubMed, EMBASE and Web of Science and pre-prints in Europe PMC through August 12 th, 2020 that described cases of human transmission of SARS-CoV-2. Reports of other respiratory virus transmission were included for reference.

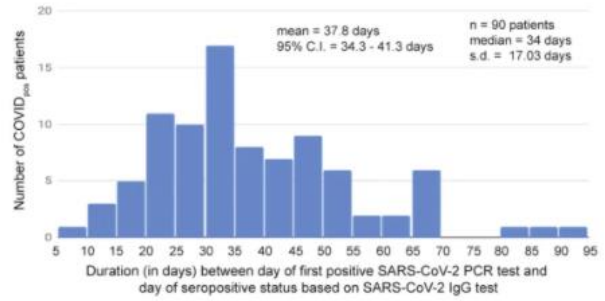
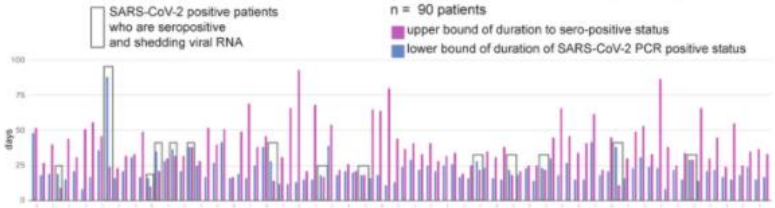
article/doi/10.1093/infdis/jiaa742/6009483			Results : Five identified studies found that a low proportion of reported global SARS-CoV-2 infections have occurred outdoors (<10%) and the odds of indoor transmission was very high compared to outdoors (18.7 times; 95% CI 6.0, 57.9). Five studies described influenza transmission outdoors and two described adenovirus transmission outdoors. There was high heterogeneity in study quality and individual definitions of outdoor settings which limited our ability to draw conclusions about outdoor transmission risks. In general, factors such as duration and frequency of personal contact, lack of personal protective equipment and occasional indoor gathering during a largely outdoor experience were associated with outdoor reports of infection. Conclusion : Existing evidence supports the wide-held belief that the the risk of SARS-CoV-2 transmission is lower outdoors but there are significant gaps in our understanding of specific pathways.
Young B et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30911-7/fulltext	The place for remdesivir in COVID-19 treatment	Quale ruolo per remdesivir contro COVID-19, alla luce delle ultime raccomandazioni OMS ?	Finding antivirals that reduce mortality from severe respiratory viral infections has proven challenging. Phase 3 trials of baloxavir and pimodivir for severe influenza were unsuccessful (NCT03684044 and NCT03376321). Lopinavir–ritonavir and hydroxychloroquine are not efficacious in treating COVID-19. Interim results from the WHO-led, open-label, randomised SOLIDARITY trial3 of patients with COVID-19 report that 301 (11·0%) of 2743 patients analysed who received remdesivir and 303 (11·2%) of 2708 patients analysed who received standard care died by day 28 (Kaplan-Meier rate ratio [RR] 0·95, 95% CI 0·81–1·11; p=0·50). Final results from the ACTT-1 study sponsored by the National Institute of Allergy and Infectious Diseases are broadly similar: this randomised, placebo-controlled trial of patients with COVID-19 reported a 29-day mortality of 11·4% in 541 individuals assigned remdesivir and 15·2% in 521 assigned placebo (hazard ratio [HR] 0·73, 95% CI 0·52–1·03).

WHO Solidarity Trial Consortium NEJM https://www.nejm.org/doi/10.1056/NEJMoa2023184	Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results	Risultati preliminari del trial open-label SOLIDARITY, promosso da WHO su 4 farmaci per il trattamento di COVID-19 : remdesivir, idrossiclorochina, lopinavir e interferone. Nessun farmaco ha dimostrato un beneficio su mortalità, ventilazione meccanica e durata di degenza, incluso il remdesivir (2743 pazienti trattati).	BACKGROUND : World Health Organization expert groups recommended mortality trials of four repurposed antiviral drugs — remdesivir, hydroxychloroquine, lopinavir, and interferon beta-1a — in patients hospitalized with coronavirus disease 2019 (Covid-19). METHODS : We randomly assigned inpatients with Covid-19 equally between one of the trial drug regimens that was locally available and open control (up to five options, four active and the local standard of care). The intention-to-treat primary analyses examined in-hospital mortality in the four pairwise comparisons of each trial drug and its control (drug available but patient assigned to the same care without that drug). Rate ratios for death were calculated with stratification according to age and status regarding mechanical ventilation at trial entry. RESULTS At 405 hospitals in 30 countries, 11,330 adults underwent randomization; 2750 were assigned to receive remdesivir, 954 to hydroxychloroquine, 1411 to lopinavir (without interferon), 2063 to interferon (including 651 to interferon plus lopinavir), and 4088 to no trial drug. Adherence was 94 to 96% midway through treatment, with 2 to 6% crossover. In total, 1253 deaths were reported (median day of death, day 8; interquartile range, 4 to 14). The Kaplan–Meier 28-day mortality was 11.8% (39.0% if the patient was already receiving ventilation at randomization and 9.5% otherwise). Death occurred in 301 of 2743 patients receiving remdesivir and in 303 of 2708 receiving its control (rate ratio, 0.95; 95% confidence interval [CI], 0.81 to 1.11; P=0.50), in 104 of 947 patients receiving hydroxychloroquine and in 84 of 906 receiving its control (rate ratio, 1.19; 95% CI, 0.89 to 1.59; P=0.23), in 148 of 1399 patients receiving lopinavir and in 146 of 1372 receiving its control (rate ratio, 1.00; 95% CI, 0.79 to 1.25; P=0.97), and in 243 of 2050 patients receiving

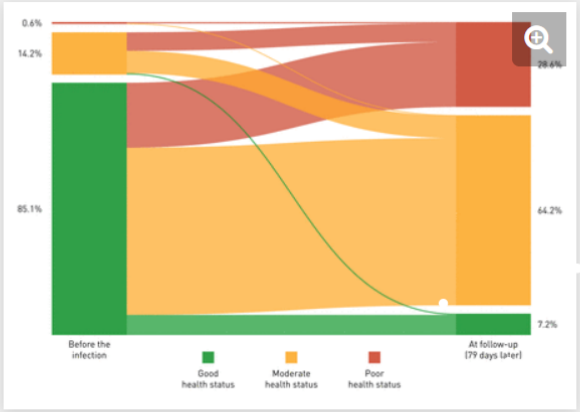
			interferon and in 216 of 2050 receiving its control (rate ratio, 1.16; 95% CI, 0.96 to 1.39; P=0.11). No drug definitely reduced mortality, overall or in any subgroup, or reduced initiation of ventilation or hospitalization duration. CONCLUSIONS These remdesivir, hydroxychloroquine, lopinavir, and interferon regimens had little or no effect on hospitalized patients with Covid-19, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay.

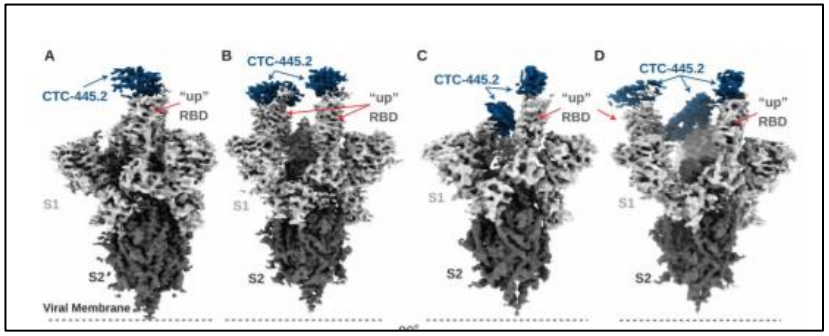
			 **Figure 2. Effects of Remdesivir, Hydroxychloroquine, Lopinavir, and Interferon on In-Hospital Mortality.** Shown are Kaplan–Meier graphs of in-hospital mortality at any time (the primary outcome), comparing each treatment with its control without standardization for any initial patient characteristics. Insets show the same data on an expanded y axis. The rate ratios for death were standardized for age and for ventilation status at entry. Denominators for the few events on day 0, but not thereafter, include patients with no follow-up. Numbers of deaths are by week, and then deaths after day 28. CI denotes confidence interval.
Rubin D et al NEJM https://www.nejm.org/doi/full/10.1056/NEJMp203	FDA Approval of Remdesivir — A Step in the Right Direction	Editoriale del NEJM che commenta come i risultati di SOLIDARITY su remdesivir non siano in contrasto con quanto dimostrato nel trial ACTT-1 (non beneficio sulla	On January 31, 2020, the U.S. secretary of health and human services declared a public health emergency in response to Covid-19. This disease, caused by the SARS-CoV-2 virus, can have severe manifestations, including pneumonia, respiratory failure, multiorgan failure, and death. Although there is now an extensive

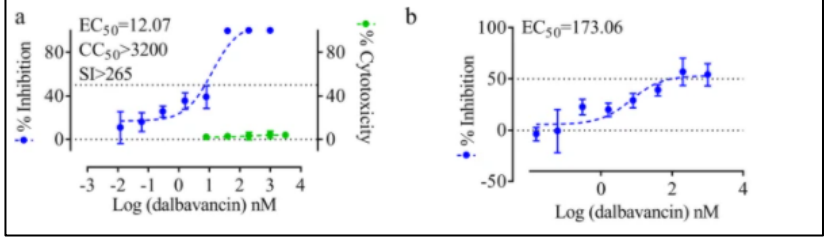
2369?query-featured_coronavirus=		mortalità ma sulla durata di degenza, quest'ultima non studiata da SOLIDARITY). Viene sostenuta la decisione della FDA americana di approvare remdesivir per l'utilizzo contro SARS-CoV-2.	global search for therapies, there remains an unmet need for safe and effective treatment options for patients.
Agarwal V et al Cell Death Discovery – Nature https://www.nature.com/articles/s41420-020-00375-y	Long-term SARS-CoV-2 RNA shedding and its temporal association to IgG seropositivity	Analisi retrospettiva su lla durata dello shedding virale e la risposta anticorpiale in 851 pazienti con infezione da SARS-CoV-2 : vengono quantificati i tempi medi tra primo e ultimo tampone positivo (17.3 giorni) e tra primo tampone positivo e secondo tampone negativo (22.7 giorni) ; 99 persone hanno ancora tampone positivo dopo 4 settimane dalla diagnosi ; il tempo medio di sviluppo di IgG è 37.8 giorni dalla diagnosi, alcuni pazienti hanno ancora tampone positivo pur con IgG positive. Non si possono tuttavia trarre conclusioni sulla infettività di tali soggetti.	Longitudinal characterization of SARS-CoV-2 PCR testing from COVID-19 patient's nasopharynx and its juxtaposition with blood-based IgG-seroconversion diagnostic assays is critical to understanding SARS-CoV-2 infection durations. Here, we retrospectively analyze 851 SARS-CoV-2-positive patients with at least two positive PCR tests and find that 99 of these patients remain SARS-CoV-2-positive after 4 weeks from their initial diagnosis date. For the 851-patient cohort, the mean lower bound of viral RNA shedding was 17.3 days (SD: 7.8), and the mean upper bound of viral RNA shedding from 668 patients transitioning to confirmed PCR-negative status was 22.7 days (SD: 11.8). Among 104 patients with an IgG test result, 90 patients were seropositive to date, with mean upper bound of time to seropositivity from initial diagnosis being 37.8 days (95% CI: 34.3–41.3). Our findings from juxtaposing IgG and PCR tests thus reveal that some SARS-CoV-2-positive patients are non-hospitalized and seropositive, yet actively shed viral RNA (14 of 90 patients). This study emphasizes the need for monitoring viral loads and neutralizing antibody titers in long-term non-hospitalized shedders as a means of characterizing the SARS-CoV-2 infection lifecycle.

			Fig. 3: Distribution of upper bound of the duration to seropositive status based on SARS-CoV-2 IgG test and comparison to SARS-CoV-2-positive status based on PCR test. a Distribution of upper-bound of sero-positive transition duration based on SARS-CoV-2 IgG test  b Comparison of sero-positive status (based on antibody test) and SARS-CoV-2 PCR positive status  c Comparison of sero-positive status (based on antibody test) and SARS-CoV-2 PCR positive status
Olusola-Makinde O et al Environmental Pollution https://doi.org/10.1016/j.envpol.2020.115485	Ticking bomb: Prolonged faecal shedding of novel coronavirus (2019-nCoV) and environmental implications.	Riflessione sulla rilevanza dell'eliminazione fecale di SARS-CoV-2 ai fini della prevenzione della sua trasmissione, in particolare nei Paesi a basso reddito.	The current global coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been a tremendous public health challenge globally. While the respiratory transmission of SARS-CoV-2 has been established, evolving reports on the impact of the gastrointestinal system and the prolonged faecal shedding of SARS-CoV-2 show the likelihood of faecally mediated transmission. The increasing evidential presence of SARS-CoV-2 in wastewater and faecal material poses a significant public health threat which may potentiate global vulnerability to high risk of human exposure through environmental drivers especially in less developed

			countries. While extensively exploring the likelihood of faecally mediated SARS-CoV-2 transmission, infection control and prevention measures aimed at mitigating this pandemic should holistically include environmental drivers.
Goertz YMJ et al ERJ Open Research https://openres.ersjournals.com/content/6/4/00542-2020	Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome?	Dati raccolti nell'estate 2020 contattando due comunità online di pazienti con storia di COVID-19 in Belgio e Paesi Bassi: 2113 pazienti di cui 112 ospedalizzati riferiscono persistenza di astenia e dispnea a lungo termine. Si tratta di dati autoriportati ma pur sempre interessanti per comprendere la percezione soggettiva della malattia.	Background Many patients with COVID-19 did not require hospitalisation, nor underwent COVID-19 testing. There is anecdotal evidence that patients with "mild" COVID-19 may complain about persistent symptoms, even weeks after the infection. This suggests that symptoms during the infection may not resolve spontaneously. The objective of this study was to assess whether multiple relevant symptoms recover following the onset of symptoms in hospitalised and nonhospitalised patients with COVID-19. Methods A total of 2113 members of two Facebook groups for coronavirus patients with persistent complaints in the Netherlands and Belgium, and from a panel of people who registered on a website of the Lung Foundation Netherlands, were assessed for demographics, pre-existing comorbidities, health status, date of symptoms onset, COVID-19 diagnosis, healthcare utilisation, and the presence of 29 symptoms at the time of the onset of symptoms (retrospectively) and at follow-up (mean±sd 79±17 days after symptoms onset). Results Overall, 112 hospitalised patients and 2001 nonhospitalised patients (confirmed COVID-19, n=345; symptom-based COVID-19, n=882; and suspected COVID-19, n=774) were analysed. The median number of symptoms during the infection reduced significantly over time (median (interquartile range) 14 (11–17) versus 6 (4–9); p<0.001). Fatigue and dyspnoea were the most prevalent symptoms during the infection and at follow-up (fatigue: 95% versus 87%; dyspnoea: 90% versus 71%).

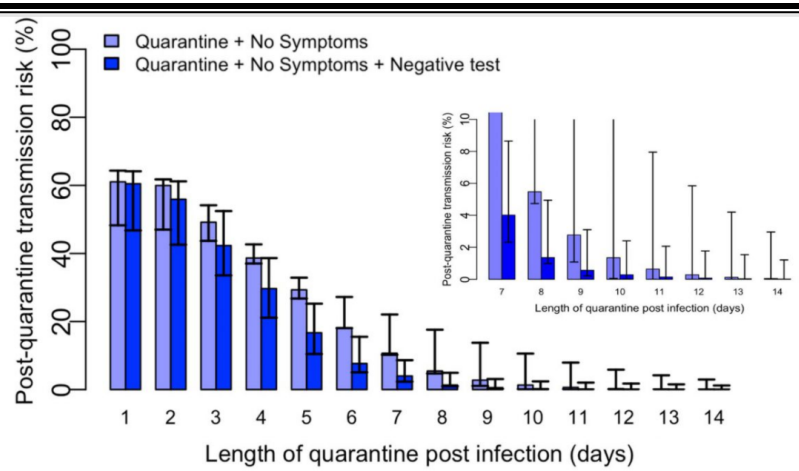
			Conclusion In previously hospitalised and nonhospitalised patients with confirmed or suspected COVID-19, multiple symptoms are present about 3 months after symptoms onset. This suggests the presence of a “post-COVID-19 syndrome” and highlights the unmet healthcare needs in a subgroup of patients with “mild” or “severe” COVID-19.  FIGURE 3 Download figure | Open in new tab | Download powerpoint Prevalence and change in self-reported health status during and 3 months after the infection. The width of lines in the figure are proportional to the flow rate.
Armitage R et al The Lancet https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30917-8/fulltext	Antibiotic prescribing in general practice during COVID-19	La prescrizione di antibiotici da parte di Medici di Medicina Générale nel Regno Unito si è ridotta nel periodo aprile-agosto 2020, rispecchiando tuttavia un ridotto ricorso alle cure mediche nel periodo pandemico. In proporzione, la prescrizione è aumentata, possibilmente per aumento	National Health Service (NHS) England publishes monthly data on national appointment activity in general practice.1 The number of face-to-face appointments in this setting from April 1, to Aug 31, 2020 (46 550 551), decreased by 51·50% compared with the corresponding period in 2019 (95 975 048), whereas the number of telephone appointments increased by 270·45% (from 16 333 705 to 44 174 700) and the absolute number of appointments decreased by 20·80% (from 120 693 985 to 95 594 911). This 5 month period in 2020 comprises all data available to date following the first UK

		delle consultazioni « a distanza ».	COVID-19 lockdown, which began on March 23, 2020, and progressed into the summer.
Linsky T et al Science https://science.sciencemag.org/content/370/6521/1208.full	De novo design of potent and resilient hACE2 decoys to neutralize SARS-CoV-2	Versione definitiva di un lavoro già presentato, che illustra la “pipeline” di sintesi di trappole molecolari per il recettore ACE2 di SARS-CoV-2, in grado di prevenire l’infezione nel criceto dopo somministrazione intranasale.	We developed a de novo protein design strategy to swiftly engineer decoys for neutralizing pathogens that exploit extracellular host proteins to infect the cell. Our pipeline allowed the design, validation, and optimization of de novo human angiotensin-converting enzyme 2 (hACE2) decoys to neutralize severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The best monovalent decoy, CTC-445.2, bound with low nanomolar affinity and high specificity to the receptor-binding domain (RBD) of the spike protein. Cryo–electron microscopy (cryo-EM) showed that the design is accurate and can simultaneously bind to all three RBDs of a single spike protein. Because the decoy replicates the spike protein target interface in hACE2, it is intrinsically resilient to viral mutational escape. A bivalent decoy, CTC-445.2d, showed ~10-fold improvement in binding. CTC-445.2d potently neutralized SARS-CoV-2 infection of cells in vitro, and a single intranasal prophylactic dose of decoy protected Syrian hamsters from a subsequent lethal SARS-CoV-2 challenge. 

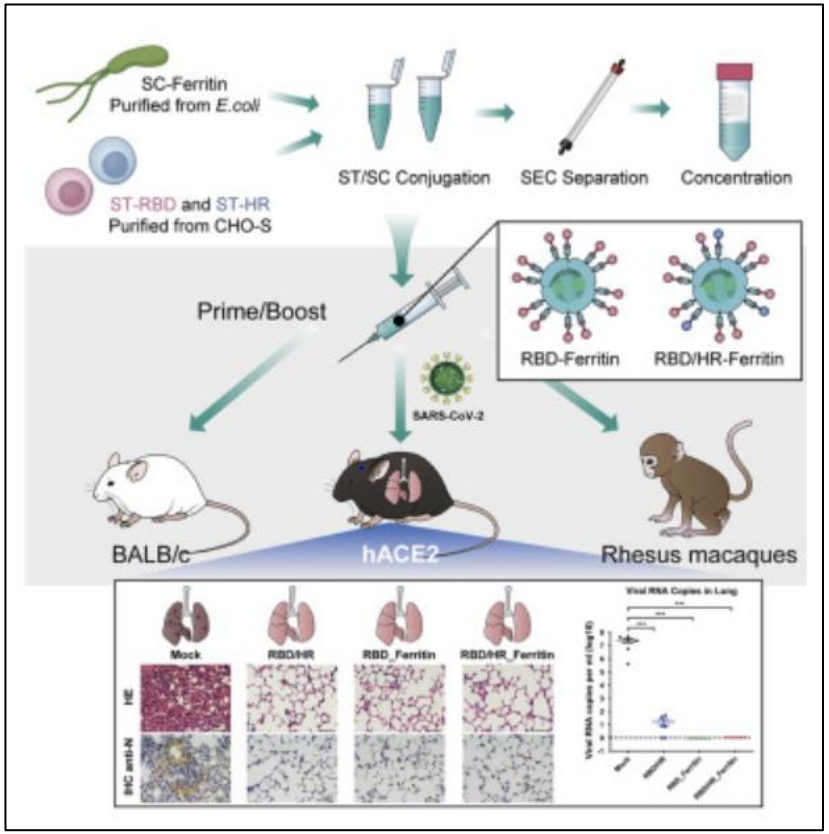
Gan W et al Cell Research – Nature https://www.nature.com/articles/s41422-020-00450-0	Dalbavancin binds ACE2 to block its interaction with SARS-CoV-2 spike protein and is effective in inhibiting SARS-CoV-2 infection in animal models	Il lipoglicopeptide dalbancina, attivo contro i Gram-positivi multiresistenti, ha affinità per il recettore ACE2 e impedisce la replicazione di SARS-CoV-2 in coltura cellulare e sembra ridurre i danni causati dal virus nel topo e nel macaco: un "repurposing" inaspettato.	Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a pandemic worldwide. Currently, however, no effective drug or vaccine is available to treat or prevent the resulting coronavirus disease 2019 (COVID-19). Here, we report our discovery of a promising anti-COVID-19 drug candidate, the lipoglycopeptide antibiotic dalbavancin, based on virtual screening of the FDA-approved peptide drug library combined with in vitro and in vivo functional antiviral assays. Our results showed that dalbavancin directly binds to human angiotensin-converting enzyme 2 (ACE2) with high affinity, thereby blocking its interaction with the SARS-CoV-2 spike protein. Furthermore, dalbavancin effectively prevents SARS-CoV-2 replication in Vero E6 cells with an EC50 of ~12 nM. In both mouse and rhesus macaque models, viral replication and histopathological injuries caused by SARS-CoV-2 infection are significantly inhibited by dalbavancin administration. Given its high safety and long plasma half-life (8–10 days) shown in previous clinical trials, our data indicate that dalbavancin is a promising anti-COVID-19 drug candidate. **Fig. 3: Antiviral activity of dalbavancin against SARS-CoV-2 in vitro.** 

Dugdale CM et al Open Forum Infectious Diseases https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofaa559/5999190	Clinical, laboratory, and radiologic characteristics of patients with initial false-negative SARS-CoV-2 nucleic acid amplification test results	Caratteristiche di 60 pazienti con test positivo per SARS-CoV-2 dopo un iniziale risultato negativo entro 14 giorni prima: per lo più sintomatici, con radiologia toracica positiva e testati molto precocemente dall'inizio dei sintomi.	Background: Concerns about false-negative (FN) SARS-CoV-2 nucleic acid amplification tests (NAATs) have prompted recommendations for repeat testing if suspicion for COVID-19 infection is moderate to high. However, the frequency of FNs and patient characteristics associated with FNs are poorly understood. Methods: We retrospectively reviewed test results from 15,011 adults who underwent ≥1 SARS-CoV-2 NAATs; 2,699 had an initial negative NAAT and repeat testing. We defined FNs as ≥1 negative NAATs followed by a positive NAAT within 14 days during the same episode of illness. We stratified subjects with FNs by duration of symptoms prior to the initial FN test (≤5 days versus >5 days) and examined their clinical, radiologic, and laboratory characteristics. Results: Sixty of 2,699 subjects (2.2%) had a FN result during the study period. The weekly frequency of FNs among subjects with repeat testing peaked at 4.4%, coinciding with peak NAAT positivity (38%). Most subjects with FNs had symptoms (52/60; 87%) and chest radiography (19/32; 59%) consistent with COVID-19. Of the FN NAATs, 18/60 (30%) were performed early (i.e., ≤1 day of symptom onset), and 18/60 (30%) were performed late (i.e., >7 days after symptom onset) in disease. Among 17 subjects with two consecutive FNs on NP NAATs, 9 (53%) provided lower respiratory tract (LRT) specimens for testing, all of which were positive. Conclusions: Our findings support repeated NAATs among symptomatic patients, particularly during periods of higher COVID-19 incidence. LRT testing should be prioritized to increase yield among patients with high clinical suspicion for COVID-19.
The CDC https://www.cdc.gov/coronavirus/2019-ncov/more/scientific-	Options to Reduce Quarantine for Contacts of Persons with SARS-CoV-2 Infection Using Symptom	I CDC americani indicano la possibilità di ridurre il periodo di quarantena nei contatti di persone con infezione da SARS-CoV-2:	Local public health authorities determine and establish the quarantine options for their jurisdictions. CDC currently recommends a quarantine period of 14 days. However, based on

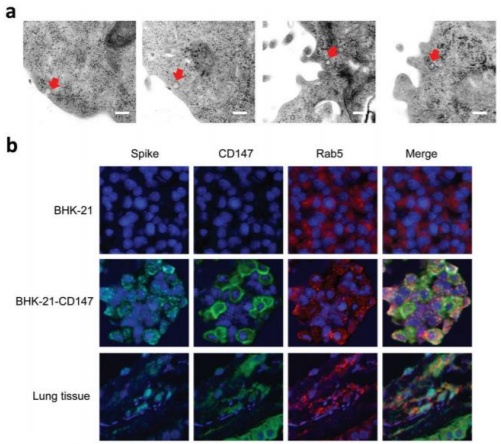
brief-options-to-reduce-quarantine.html	Monitoring and Diagnostic Testing	per chi rimane del tutto asintomatico, termine a 10 giorni dal test positivo senza test di controllo, oppure a 7 giorni con test di controllo al quinto-settimo giorno (ma sospensione dell'isolamento non prima del settimo giorno). Ridurre la durata della quarantena sarebbe proficuo per garantire maggiore adesione da parte della popolazione.	local circumstances and resources, the following options to shorten quarantine are acceptable alternatives. Quarantine can end after Day 10 without testing and if no symptoms have been reported during daily monitoring. With this strategy, residual post-quarantine transmission risk is estimated to be about 1% with an upper limit of about 10%. When diagnostic testing resources are sufficient and available (see bullet 3, below), then quarantine can end after Day 7 if a diagnostic specimen tests negative and if no symptoms were reported during daily monitoring. The specimen may be collected and tested within 48 hours before the time of planned quarantine discontinuation (e.g., in anticipation of testing delays), but quarantine cannot be discontinued earlier than after Day 7. With this strategy, the residual post-quarantine transmission risk is estimated to be about 5% with an upper limit of about 12%. In both cases, additional criteria (e.g., continued symptom monitoring and masking through Day 14) must be met and are outlined in the full text.

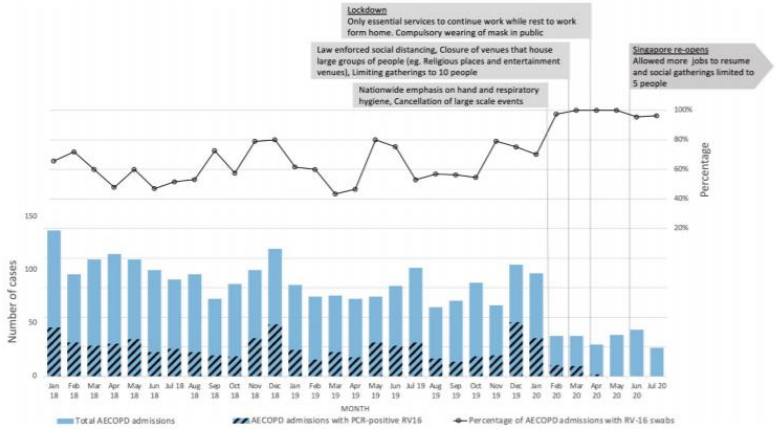
			 Figure. Modeled estimates of post-quarantine transmission risk quarantine duration. The light blue bars indicate the daily post-quarantine transmission risk if there is no clinical evidence of COVID-19 elicited during daily symptom monitoring. The dark blue bars indicate the post-quarantine transmission risk with the addition of a negative RT-PCR result from a specimen collected 24-48 hours prior.
The CDC https://www.cdc.gov/coronavirus/2019-ncov/travelers/travel-during-covid19.html	Domestic Travel During the COVID-19 Pandemic	Se intenzionati a viaggiare durante il periodo pandemico, il CDC consiglia di eseguire un test per SARS-CoV-2 da 1 a 3 giorni prima di partire e di nuovo 3-5 giorni dopo il ritorno, osservando una riduzione delle attività non essenziali per 7 giorni dopo il viaggio anche con test negativo.	If you are traveling, consider getting tested with a viral test 1-3 days before your trip. Also consider getting tested with a viral test 3-5 days after your trip and reduce non-essential activities for a full 7 days after travel, even if your test is negative. If you don't get tested, consider reducing non-essential activities for 10 days after travel. Keep a copy of your test results with you during travel; you may be asked for them. Do not travel if you test positive; immediately isolate yourself, and follow public health recommendations.

WHO Ad Hoc Expert Group on the Next Steps for Covid-19 Vaccine Evaluation NEJM https://www.nejm.org/doi/10.1056/NEJMp2033538	Placebo-Controlled Trials of Covid-19 Vaccines — Why We Still Need Them	La dimostrazione preliminare dell'efficacia dei vaccini contro SARS-CoV-2, pur giustificandone l'introduzione in uso, non rende meno importante l'ottenimento di altre informazioni (sicurezza, durata dell'immunità, conseguenze di un'eventuale infezione). Per questo motivo i trial clinici saranno ancora necessari anche dopo l'approvazione dei primi vaccini.	Recent announcements that some Covid-19 vaccines are estimated to have high short-term efficacy provide new hope that vaccination will soon contribute to controlling the pandemic. The initial roll-out of limited quantities of vaccines that are still investigational will provide the opportunity to ethically obtain pivotal data to improve regulatory and public health decision making, thereby increasing public and professional confidence in these and other vaccines.
Ma X et al Immunity https://www.cell.com/immunity/fulltext/S1074-7613(20)30502-1?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS1074761320305021%3Fshowall%3Dtrue	Nanoparticle Vaccines Based on the Receptor Binding Domain (RBD) and Heptad Repeat (HR) of SARS-CoV-2 Elicit Robust Protective Immune Responses	Messa a punto di un vaccino a nanoparticelle basato sul receptor-binding domain (RBD) e la heptad repeat della proteina S di SARS-CoV-2: effetto sul topo e sul macaco.	Various vaccine strategies have been proposed in response to the global COVID-19 pandemic, each with unique strategies for eliciting immune responses. Here, we developed nanoparticle vaccines by covalently conjugating the self-assembled 24-mer ferritin to the receptor binding domain (RBD) and/or heptad repeat (HR) subunits of the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) spike (S) protein. Compared to monomer vaccines, nanoparticle vaccines elicited more robust neutralizing antibodies and cellular immune responses. RBD and RBD-HR nanoparticle vaccinated hACE2 transgenic mice vaccinated with RBD and/or RBD-HR nanoparticles exhibited reduced viral load in the lungs after SARS-CoV-2 challenge. RBD-HR nanoparticle vaccines also promoted neutralizing antibodies and cellular immune responses against other coronaviruses. The nanoparticle vaccination of rhesus macaques induced neutralizing antibodies, and T and B cell responses prior to

			boost immunization; these responses persisted for more than three months. RBD- and HR-based nanoparticles thus present a promising vaccination approach against SARS-CoV-2 and other coronaviruses. 
Wabg K et al Signal Tranasduction Targeted Therapy	CD147-spike protein is a novel route for SARS-CoV-2 infection to host cells.	Il recettore CD147 potrebbe conferire una diversa via di ingresso nelle cellule per SARS-CoV-2 rispetto ad ACE2.	In face of the everlasting battle toward COVID-19 and the rapid evolution of SARS-CoV-2, no specific and effective drugs for treating this disease have been reported until today. Angiotensin-converting enzyme 2 (ACE2), a receptor of SARS-CoV-2, mediates the virus infection by binding to spike protein. Although ACE2 is expressed in the lung, kidney, and intestine, its expressing levels are rather low,

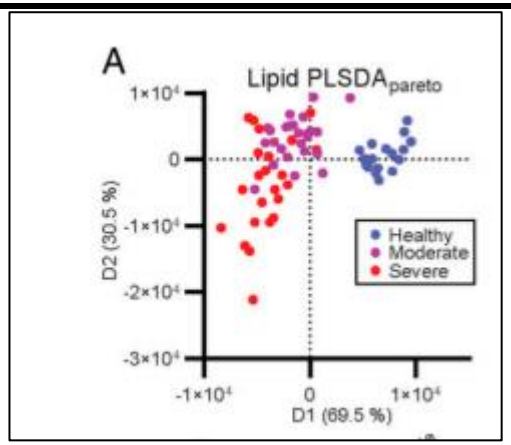
https://doi.org/10.1038/s41392-020-00426-x			especially in the lung. Considering the great infectivity of COVID-19, we speculate that SARS-CoV-2 may depend on other routes to facilitate its infection. Here, we first discover an interaction between host cell receptor CD147 and SARS-CoV-2 spike protein. The loss of CD147 or blocking CD147 in Vero E6 and BEAS-2B cell lines by anti-CD147 antibody, Meplazumab, inhibits SARS-CoV-2 amplification. Expression of human CD147 allows virus entry into non-susceptible BHK-21 cells, which can be neutralized by CD147 extracellular fragment. Viral loads are detectable in the lungs of human CD147 (hCD147) mice infected with SARS-CoV-2, but not in those of virus-infected wild type mice. Interestingly, virions are observed in lymphocytes of lung tissue from a COVID-19 patient. Human T cells with a property of ACE2 natural deficiency can be infected with SARS-CoV-2 pseudovirus in a dose-dependent manner, which is specifically inhibited by Meplazumab. Furthermore, CD147 mediates virus entering host cells by endocytosis. Together, our study reveals a novel virus entry route, CD147-spike protein, which provides an important target for developing specific and effective drug against COVID-19.

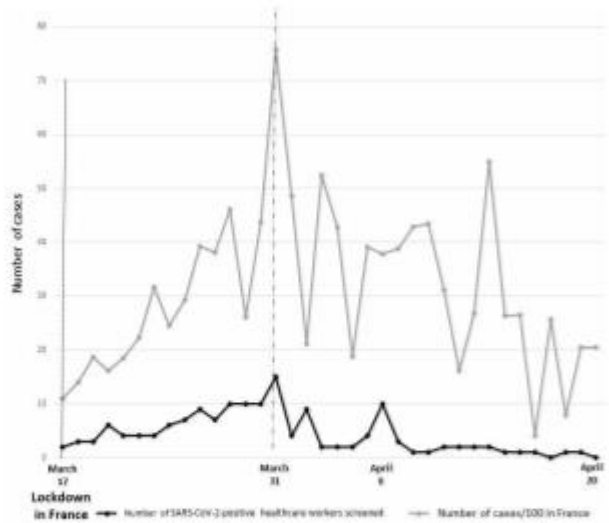
			 **Fig. 6** SARS-CoV-2 enters the host cells through CD147-mediated endocytosis. **a** The sequential endocytosis of SARS-CoV-2 was observed in Vero E6 cells by electron microscope. Scale bars: 200 nm. **b** The co-localization of spike protein, CD147, and Rab5 were analyzed in BHK-21-CD147 cells and lung tissues from COVID-19 patient by multicolor immunofluorescence staining. Magnification: ×200.
Tan JY et al Thorax https://thorax.bmj.com/content/early/2020/12/02/thoraxjnl-2020-216083	COVID-19 public health measures: a reduction in hospital admissions for COPD exacerbations	Uno studio retrospettivo condotto nel Regno Unito mostra una riduzione degli accessi ospedalieri per riacutizzazione di BPCO nel periodo pandemico iniziale di COVID-19: probabile effetto delle misure di distanziamento sociale.	Hospitalisations for acute exacerbations of COPD (AECOPD) carry significant morbidity and mortality. Respiratory viral infections (RVIs) are the most common cause of AECOPD and are associated with worse clinical outcomes. During the COVID-19 pandemic, public health measures, such as social distancing and universal masking, were originally implemented to reduce transmission of SARS-CoV-2; these public health measures were subsequently also observed to reduce transmission of other common circulating RVIs. In this study, we report a significant and sustained decrease in hospital admissions for all AECOPD as well as RVI-associated AECOPD, which coincided with the introduction of public health measures during the COVID-19 pandemic.

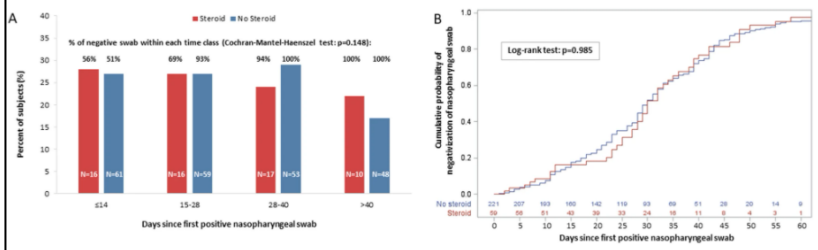
			 **Figure 1** Trend of AECOPD admissions and proportion with PCR-positive RV-16. Line graph depicts the percentage of AECOPD admissions tested for respiratory viruses.The standard respiratory virus multiplex panel (RV-16) at our institution included: respiratory syncytial virus A/B, influenza A/B, parainfluenza viruses 1–4, metapneumovirus, rhinovirus A/B/C, human coronovirus OC43/229E/NL63, adenovirus, human enterovirus, human bocavirus 1–4.
Waissberg D et al BMC https://aricjournal.biomedcentral.com/articles/10.1186/s13756-020-00861-z	Does respiratory co-infection facilitate dispersal of SARS-CoV-2? investigation of a super-spreading event in an open-space office	Descrizione di un evento di superspreading di SARS-CoV-2 in un ufficio: il caso indice era coinfetto con un Adenovirus, il che potrebbe aver incrementato la sua contagiosità.	Background: Super-spreaders are individuals infecting disproportionately large numbers of contacts. They probably play a crucial role in the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). We describe a super-spreading event within a team working in an open-space office and investigate factors potentially having facilitated SARS-CoV-2 transmission. Methods: In this retrospective cohort study, semi-structured telephone interviews with all team members were carried out to identify symptoms, contacts, and adherence to basic hygiene measures. During site visits, we gathered information about workplace and seating arrangements. The secondary attack rate in office and households was calculated. Potential respiratory viral co-infections were assessed by multiplex PCR. SARS-CoV-2 whole-genome sequencing was performed using a tiled-amplicon sequencing approach.

			Results: Of 13 team members, 11 fell ill with Coronavirus disease 2019 (COVID-19). Due to the sequence of events and full genome sequence data, one person was considered the index case for this outbreak, directly infecting 67 to 83% of the teammates. All team members reported repetitive close contacts among themselves during joint computer work, team meetings and a "Happy Birthday" serenade. Two individuals shared nuts and dates. The arrangement of the office and meeting rooms precluded sufficient adherence to physical distancing. The index case and a further individual were diagnosed with an adenovirus serotype 4 co-infection. Conclusion: We identified several environmental and behavioral factors that probably have facilitated the transmission of SARS-CoV-2. The relevance of the adenovirus co-infection remains unclear and merits further investigation.
Toubiana J et al Eurosurveillance https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.48.2001813	Association between SARS-CoV-2 infection and Kawasaki-like multisystem inflammatory syndrome: a retrospective matched case–control study, Paris, France, April to May 2020	Studio caso-controllo condotto a Parigi che dimostra una associazione fra infezioni da SARS-CoV-2 e casi di sindrome infiammatoria multisistemica nel bambino.	Multisystem inflammatory syndrome in children and adolescents (MIS-C) emerged during the coronavirus disease (COVID-19) pandemic, leading to a first alert by the United Kingdom National Health Service on 25 April 2020. Since then, several case studies in regions with high rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) community transmission have reported MIS-C cases, with a substantial proportion of patients meeting the American Heart Association criteria for Kawasaki disease (KD). We investigated this potential association in the Paris metropolitan area (Île-de-France), France, using a matched case–control design.
Paul Offitt JAMA Network – Youtube	Coronavirus Vaccine Update with Paul Offitt	Una discussione dei temi più rilevanti legati alla prossima disponibilità di vaccini contro SARS-CoV-2 con il pediatra e vaccinologo Paul	With the Pfizer and Moderna coronavirus vaccines reportedly under review at the US FDA for emergency use authorization (EUA), Paul A. Offit, MD of the Children's Hospital of Philadelphia, returns to JAMA's Q&A series to provide an update on what to expect,

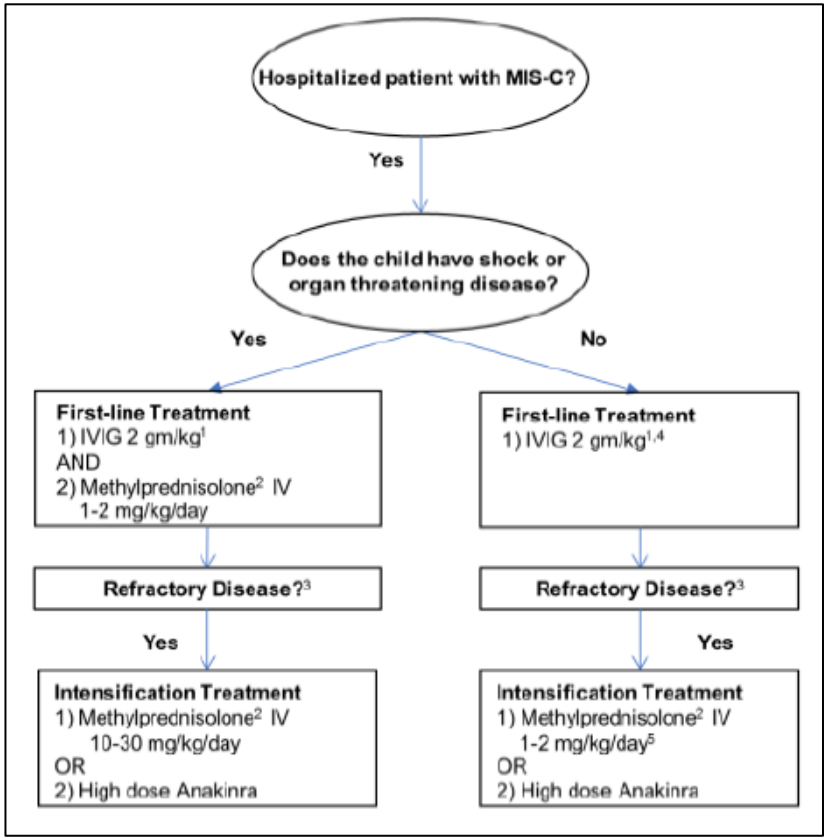
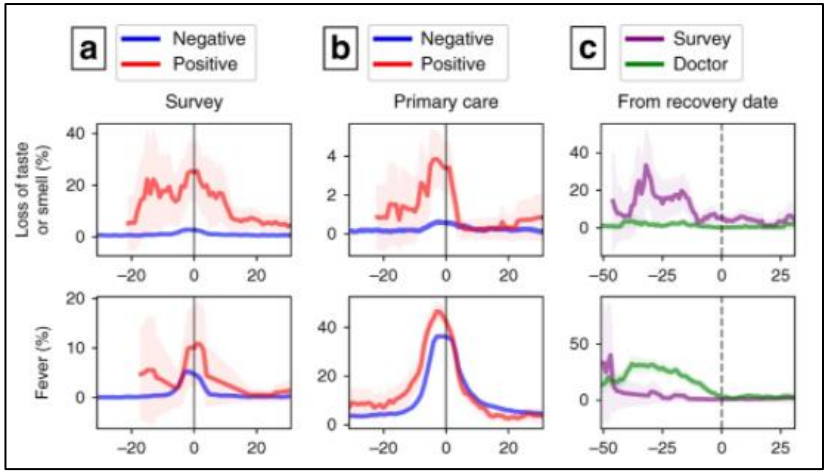
https://www.youtube.com/watch?v=V4xClOYM3iE&utm_source=silverchair&utm_campaign=jama_network&utm_content=covid_weekly_highlights&cmp=1&utm_medium=email		Offitt della University of Pennsylvania.	prospects for vaccine rollout and distribution in the coming months, and ongoing safety surveillance. Recorded December 2, 2020.
Schwartz B et al Journal of Immunology https://doi.org/10.4049/jimmunol.2001025	Cutting Edge: Severe SARS-CoV-2 Infection in Humans Is Defined by a Shift in the Serum Lipidome, Resulting in Dysregulation of Eicosanoid Immune Mediators.	Studio del "lipidoma" sierico di 18 pazienti con COVID-19 ricoverati in degenza ordinaria, 20 ricoverati in terapia intensiva e 19 controlli sani, con riscontro di differenze significative nella produzione di lipidi con funzione immunoregolatoria (in figura gli acidi grassi polinsaturi- PUFA) in base alla diversa gravità delle condizioni cliniche.	The COVID-19 pandemic has affected more than 20 million people worldwide, with mortality exceeding 800,000 patients. Risk factors associated with severe disease and mortality include advanced age, hypertension, diabetes, and obesity. Each of these risk factors pathologically disrupts the lipidome, including immunomodulatory eicosanoid and docosanoid lipid mediators (LMs). We hypothesized that dysregulation of LMs may be a defining feature of the severity of COVID-19. By examining LMs and polyunsaturated fatty acid precursor lipids in serum from hospitalized COVID-19 patients, we demonstrate that moderate and severe disease are separated by specific differences in abundance of immune-regulatory and proinflammatory LMs. This difference in LM balance corresponded with decreased LM products of ALOX12 and COX2 and an increase LMs products of ALOX5 and cytochrome p450. Given the important immune-regulatory role of LMs, these data provide mechanistic insight into an immuno-lipidomic imbalance in severe COVID-19.

			
Krasinova E et al Occupational Environmental Medicine https://doi.org/10.1136/oemed-2020-106866	Household transmission and incidence of positive SARS-CoV-2 RT-PCR in symptomatic healthcare workers, clinical course and outcome: a French hospital experience.	Esito di uno screening per infezione da SARS-CoV-2 condotto su 2188 operatori sanitari in Francia nel periodo 17 marzo – 20 aprile 2020: incidenza di sintomatici 5%, di questi 35% positivi per SARS-CoV-2 e 9 ospedalizzati. Risultano, come è prevedibile, maggiormente a rischio gli operatori a contatto diretto con i pazienti positivi.	OBJECTIVES: Although healthcare workers (HCWs) have been particularly affected by SARS-CoV-2, detailed data remain scarce. In this study, we investigated infection rates, clinical characteristics, occupational exposure and household transmission among all symptomatic HCWs screened by SARS-CoV-2 RT-PCR between 17 March (French lockdown) and 20 April. METHODS: SARS-CoV-2 RT-PCR was proposed to symptomatic (new cough or dyspnoea) HCWs at Creteil Hospital in one of the Parisian suburbs most severely affected by COVID-19. Data on occupational profile, living situation and household, together with self-isolation and mask use at home were collected, as well as the number of cases in the household. RESULTS: The incidence rate of symptomatic SARS-CoV-2 was estimated to be 5% (110/2188). A total of 110 (35%) of the 314 HCWs tested positive and 9 (8%) were hospitalised. On multivariate analysis, factors independently associated with positive RT-PCR were occupational profile with direct patient facing (OR 3.1, 95% CI 1.1 to 8.8), p<0.03), and presence of anosmia (OR 5.7, 95% CI 3.1 to 10.6), p<0.0001). Being a current smoker was associated with negative RT-PCR (OR 0.3, 95% CI 0.1 to 0.7), p=0.005). Transmission

			from HCWs to household members was reported in 9 (14%) cases, and 2 deaths occurred. Overall, self-isolation was possible in 52% of cases, but only 31% of HCWs were able to wear a mask at home. CONCLUSION: This is the first study to report infection rates among HCWs during the peak of the SARS-CoV-2 epidemic in France and the lockdown period, highlighting the risk related to occupational profile and household transmission.  **Figure 1** Number of positive SARS-CoV-2 RT-PCR tests per day in the general population in France (divided by 100) and among screened healthcare workers at Creteil Hospital between 17 March and 20 April.
Spagnuolo V et al Scientific Reports	Viral clearance after early corticosteroid treatment in patients with moderate or severe covid-19.	Analisi retrospettiva di 280 pazienti ricoverati presso l'Ospedale San Raffaele di Milano per COVID-19, di cui 59 trattati con steroidi: non si rileva una differenza	The aim of this study was to evaluate the impact of early treatment with corticosteroids on SARS-CoV-2 clearance in hospitalized COVID-19 patients. Retrospective analysis on patients admitted to the San Raffaele Hospital (Milan, Italy) with moderate/severe COVID-19 and availability of at least two nasopharyngeal swabs. The primary

https://doi.org/10.1038/s41598-020-78039-1		significativa nel tempo di negativizzazione del tampone nasofaringeo.	outcome was the time to nasopharyngeal swab negativization. A multivariable Cox model was fitted to determine factors associated with nasopharyngeal swab negativization. Of 280 patients included, 59 (21.1%) patients were treated with steroids. Differences observed between steroid users and non-users included the proportion of patients with a baseline PaO2/FiO2 </= 200 mmHg (45.8% vs 34.4% in steroids and non-steroids users, respectively; p = 0.023) or </= 100 mmHg (16.9% vs 12.7%; p = 0.027), and length of hospitalization (20 vs 14 days; p < 0.001). Time to negativization of nasopharyngeal swabs was similar in steroid and non-steroid users (p = 0.985). According to multivariate analysis, SARS-CoV-2 clearance was associated with age </= 70 years, a shorter duration of symptoms at admission, a baseline PaO2/FiO2 > 200 mmHg, and a lymphocyte count at admission > 1.0 x 10(9)/L. SARS-CoV-2 clearance was not associated with corticosteroid use. Our study shows that delayed SARS-CoV-2 clearance in moderate/severe COVID-19 is associated with older age and a more severe disease, but not with an early use of corticosteroids. **Figure 1** From: Viral clearance after early corticosteroid treatment in patients with moderate or severe covid-19  Distribution of follow-up nasopharyngeal swabs according to days since first positive swab and use of steroid (**A**); time to negativization of nasopharyngeal swab according to the use of steroid (**B**).

Henderson L et al Arthritis and Rheumatology https://doi.org/10.1002/art.41616	American College of Rheumatology Clinical Guidance for Pediatric Patients with Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 and Hyperinflammation in COVID-19. Version 2.	Linee guida per il trattamento della sindrome infiammatoria multisistemica (MIS-C) nel bambino legata a COVID-19.	OBJECTIVE: To provide guidance on the management of Multisystem Inflammatory Syndrome in Children (MIS-C), a condition characterized by fever, inflammation, and multiorgan dysfunction that manifests late in the course of SARS-CoV-2 infection. The Task Force also provided recommendations for children with hyperinflammation during COVID-19, the acute, infectious phase of SARS-CoV-2 infection. METHODS: The Task Force was composed of 9 pediatric rheumatologists, 2 adult rheumatologists, 2 pediatric cardiologists, 2 pediatric infectious disease specialists, and 1 pediatric critical care physician. Preliminary statements addressing clinical questions related to MIS-C and hyperinflammation in COVID-19 were developed based on evidence reports. Consensus was built through a modified Delphi process that involved anonymous voting and discussion through webinars. A 9-point scale was used to determine the appropriateness of each statement (1-3, inappropriate; 4-6, uncertain; 7-9, appropriate), and consensus was rated as low (L), moderate (M), or high (H) based on dispersion of the votes along the numeric scale. Approved guidance statements had to be classified as appropriate with moderate or high levels of consensus, which were pre-specified prior to voting. RESULTS: The first version of the guidance was approved by the Task Force in June 2020 and consisted of 40 final guidance statements accompanied by a flow diagram depicting the diagnostic pathway for MIS-C. The document was revised in November 2020, and a new flow diagram with recommendations for initial immunomodulatory treatment of MIS-C was added. CONCLUSION: Our understanding of SARS-CoV-2-related syndromes in the pediatric population continues to evolve. This guidance document reflects currently available evidence coupled

			with expert opinion but is meant to be modified as additional data become available. 
Mizrahi B et al Nature communications https://doi.org/10.1038/s41467-020-20053-y	Longitudinal symptom dynamics of COVID-19 infection.	Studio retrospettivo sull'andamento dei sintomi di 2471 pazienti con storia di COVID-19 a confronto con persone negative: perdita di gusto e olfatto sono i più tipici ed è comune la	As the COVID-19 pandemic progresses, obtaining information on symptoms dynamics is of essence. Here, we extracted data from primary-care electronic health records and nationwide distributed surveys to assess the longitudinal dynamics of symptoms prior to and throughout SARS-CoV-2 infection. Information was available for 206,377 individuals, including 2471 positive cases. The two datasources were discordant, with survey data capturing most of

		persistenza di sintomi a settimane dalla guarigione.	the symptoms more sensitively. The most prevalent symptoms included fever, cough and fatigue. Loss of taste and smell 3 weeks prior to testing, either self-reported or recorded by physicians, were the most discriminative symptoms for COVID-19. Additional discriminative symptoms included self-reported headache and fatigue and a documentation of syncope, rhinorrhea and fever. Children had a significantly shorter disease duration. Several symptoms were reported weeks after recovery. By a unique integration of two datasources, our study shed light on the longitudinal course of symptoms experienced by cases in primary care.